EQUINE VETERINARY EDUCATION/AMERICAN EDITION VOLUME 33 NUMBER 9 SEPTEMBER 2021

EQUINE VETERINARY EDUCATION

American Edition | September 2021

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

IN THIS ISSUE:

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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.
[2] Couetil LL, Cardwell J.M, Gerber V, Lavoie J.-P, Leguillette R, Richard E.A. Inflammatory Airway Disease of Horses. ACVIM Consensus Statement J of Vet Intern Med 2016; 30:503-515 p. 508-510.

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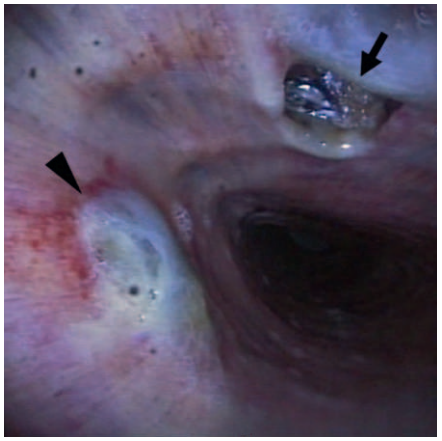

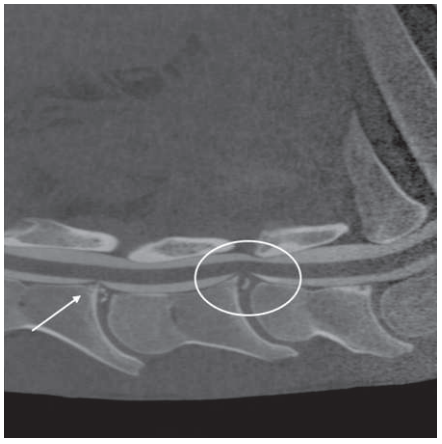

AAEP NEWS In this issue

Cover photo by Dr. Nat White.

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AAEP Mission Statement: To improve the health and welfare of the horse, to further the professional development of its members, and to provide resources and leadership for the benefit of the equine industry.

Equine Veterinary Education is a refereed educational journal designed to keep the practicing veterinarian up to date with developments in equine medicine and surgery. Submitted case reports are accompanied by invited reviews of the subject (satellite articles) and clinical quizzes. Tutorial articles, both invited and submitted, provide in-depth coverage of issues in equine practice.

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From the president: Turning exodus to influx

By Scott Hay, DVM

Dr. Scott Hay

Perhaps the most important issue facing our profession in a number of years is the retention of veterinarians in equine practice. While not a new concern, the last year has brought us to what may be a tipping point created by practitioners leaving the profession and fewer veterinary students choosing to pursue a career as a horse doctor.

We've heard from private practice owners who are urgently seeking job applicants for open positions—my own practice included. We've talked to young practitioners about the current equine practice model and how, for many, it simply does not meet their needs for professional and personal satisfaction. And many in academia have shared the unfortunate reality of a dwindling interest in equine among veterinary students.

Our profession has reached a critical juncture.

The AAEP board of directors in 2019 identified the retention of veterinarians in the profession as priority No. 1 in our current Strategic Plan, and this issue is the board's primary focus. The AAEP Retention Task Force, chaired by Dr. Carol Clark, is working with consultant Dr. Rob Trimble to uncover the multitude of factors for the exodus from equine practice and, most importantly, strategies to right the ship.

Currently, in-depth interviews are being conducted with veterinary students, new practitioners and practice owners to understand their career expectations and pain points. By early fall, we will move to phase 2, which will be the validation of our early learnings through a membership survey. The data from this research will be shared during the 2021 Annual Convention this December in Nashville.

Our Task Force will then determine the actions necessary—based on the research—to truly evolve the current equine practice model into one which nurtures career satisfaction and longevity.

If you are contacted by the AAEP in the next few months to share your viewpoints about retention, please add your voice to this project. We need you.

We as equine veterinarians are not strangers to change. The solutions which will solve this dilemma likely will require many of us to change how we do things. But I'm confident that our love for this profession and love for the horse will help us embrace the transformation of equine practice.

Switching gears, the AAEP Foundation since its inception in 1994 has served as the charitable arm of the AAEP, providing an avenue for benevolence from our members for the horse and those who care for them. In the last several years, our volunteers on the Foundation Advisory Council, led by Chair Dr. Rick Mitchell and Vice Chair Dr. Anthony Blikslager, have worked hard to escalate The Foundation's impact. A 2018 strategic planning session led the AAEP into rebranding our charitable arm as The Foundation for the Horse for increased emphasis on "the horse." The planning also created a more focused approach for The Foundation's benevolence. This focus is basically a three-pronged approach to address horses at risk, educational support and research. Your Foundation is working to address all these issues, and your support is important.

Our Task Force will then determine the actions necessary—based on the research—to truly evolve the current equine practice model into one which nurtures career satisfaction and longevity.

To learn more about your Foundation, please go to foundationforthehorse.org for information on its activities and how to help. There are many ways we can help our Foundation, not least of which is spreading the word to those who may want to join in on the cause.

You will hear more about the efforts and changes taking place within The Foundation for the Horse soon. Stay tuned!

Finally, plans continue for our in-person convention in Nashville in December. Registration and housing are open at convention.aaep.org, and there is much anticipation to get back together again. We are committed to implementing all necessary safety protocols at the time of the event. A 100% refund guarantee is in place should you change your plans after registering, and a virtual registration option is available. I look forward to seeing everyone and safely celebrating our Horse Doctor community.

5 things to know about AAEP this month

1. Space is limited at convention dry labs—don't get shut out. Register for one or more labs when registering for the convention at convention.aaep.org.
2. If you can't join us for the in-person annual convention, register for the virtual option at convention.aaep.org to receive on-demand access to 24 educational sessions and 12 live Table Topics.
3. Want to serve as a Virtual Round Table moderator next year? Simply complete or update your preferences on the Volunteer Interest Form at aaep.org/dashboard.
4. Access a joint virtual issue of *EVE* and *EVJ* highlighting recent advances in donkey medicine and welfare at https://tinyurl.com/5dms6pc2. The issue is free access until Oct. 29.
5. Register to watch on-demand recordings of the recently concluded AAEP Summer Series and earn CE credit through Nov. 30. Register at aaep.org/meetings/2nd-annual-virtual-ce-summer-series.

Retention, other strategic priorities in focus at summer board meeting

By David Foley, AAEP Executive Director

David Foley

The AAEP board of directors convened July 20 in Lexington, Ky., for its first in-person board meeting in 18 months. (The board had met several times by videoconference in the interim.)

The meeting began with a report from Nominating Committee Chair Dr. Jeff Berk and approval of his committee's recommendations to (1) accept Dr. Katherine Garrett as the next AAEP vice president, and (2) approve the annual award recipients for 2021. Those recipients will be announced at the Dec. 7 President's Luncheon during the annual convention.

Following updates from representatives of The Foundation for the Horse, discussion turned to the Strategic Plan tactics established in January 2021, including the work, early findings and proposed timelines for the Retention Task Force. An association priority, the task force has conducted interviews with over 60 veterinary students, early-career practitioners and practice owners. Their responses will help shape a broader member survey in fall 2021. Ultimately, this data collection and analysis will lead to the development of actionable recommendations. Some of the initial data will be highlighted during an educational session at the upcoming annual convention, with action items to roll out in early 2022.

Review of progress on other aspects of the Strategic Plan included discussion of educational goals, particularly those involving online learning and hands-on opportunities; and Horse Owner education, with a primary focus on the work of the Scope of Practice Subcommittee of the Welfare & Public Policy Advisory Council. Formed earlier this year, the subcommittee is in the process of developing recommendations related to unregulated individuals engaging in the practice of veterinary medicine. The subcommittee plans to create educational resources to (1) help members impact scope of practice concerns in their states, and (2) clearly define the role of AAEP concerning scope of practice issues.

During discussion of the Diversity, Equity and Inclusion Task Force led by board liaison Dr. Mitchell Rode, the board approved a revised motion "to approve the creation of an AAEP DEI Advisory Group." The role of the advisory group will be to provide feedback to the task force on recommendations. Any AAEP member interested in participating should update their profile on the Volunteer Interest Form by checking the DEI box.

Following the Strategic Plan discussions, the meeting's focus shifted to general and informational items:

- AAEP staff is actively planning for an in-person annual convention, and registration opened in early August. A virtual component containing the scientific programming will be available a week after the live convention for those members unable to attend in person. Those attending in Nashville will receive the on-demand sessions as part of their registration fees.
- Applications for the reinstated Leadership Program planned for mid-October in Lexington were being accepted through August. Approximately 15 members will be selected to participate.
- CareCredit has signed on as an Educational Partner and American Regent Animal Health has renewed as an Educational Partner.

The next board meeting will be held in December in conjunction with the annual convention.

Diagnostic imaging expert from Kentucky appointed 2022 vice president

Dr. Katherine Garrett

Dr. Katherine Garrett, shareholder and director of diagnostic imaging at Rood & Riddle Equine Hospital in Lexington, Ky., has been named the AAEP's 2022 vice president. She will be installed during the Dec. 7 President's Luncheon at the 67th Annual Convention and will assume the role of AAEP president in 2024.

A 2003 graduate of the Cornell University College of Veterinary Medicine, Dr. Garrett completed two internships and an equine surgery residency at Rood & Riddle before achieving board certification in the American College of Veterinary Surgeons in 2012. She remained on staff as an associate focused on Thoroughbred sales work before her emphasis shifted to diagnostic imaging, with particular interests in musculoskeletal MRI and upper airway imaging. She became a shareholder in 2018.

"I am fortunate to have been involved in volunteer service with the AAEP since early in my veterinary career," said Dr. Garrett. "The organization has provided opportunities for me to work with colleagues from a wide variety of backgrounds for the benefit of the horse and the equine veterinary profession, which has been a very rewarding experience. I look forward to continuing to serve the AAEP in this new role."

Dr. Garrett served on the board of directors from 2015–2017, chaired both the Educational Programs Committee and Member Engagement Committee, and served as program chair of the AAEP's 2011 Resort Symposium. She has co-anchored the popular Kester News Hour session at the annual convention since 2019. Dr. Garrett has authored multiple textbook chapters and peer-reviewed journal articles, and she frequently speaks at national and international veterinary conferences.

AAEP welcomes Synchrony, provider of CareCredit financing solution, as Educational Partner

Synchrony, provider of the CareCredit financing solution for health, veterinary and personal care, has been approved as AAEP's ninth Educational Partner. Synchrony's CareCredit joins a distinguished group of organizations and brands dedicated to providing resources and education through the AAEP to equine veterinarians and horse owners to improve the health and welfare of the horse.

Synchrony is expanding within the equine market with new, contactless payment solutions from CareCredit that are customized for veterinary practices and their clients, making it easier for veterinarians to collect payment for services at the point of care or any location. The company's commitment to the AAEP represents the first such investment in the equine space by a healthcare financing company.

"We understand the passion of equine veterinarians and are committed to supporting their financial health," said Boo Larsen, General Manager and VP, Veterinary, Synchrony Health and Wellness. "We are thrilled to be selected as an AAEP Educational Partner so we can help provide resources that build equine veterinarians' businesses and enhance their relationship with their equally passionate clients."

CareCredit's suite of digital tools empowers veterinarians and their clients to provide a lifetime of care for horses.

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Making care possible...today.

From planned visits to unexpected treatments to specialty care, horse owners and equine veterinarians can benefit from a dedicated solution to pay for the care horses need through every stage of life.

"Promoting the importance of lifelong equine health care is a mission of the AAEP, and it is rewarding to welcome a company who shares this core value," said AAEP Executive Director David Foley. "We look forward to working with the CareCredit team on educational initiatives designed to support the business side of providing equine care."

In addition to Synchrony, the AAEP's other Educational Partners are American Regent Animal Health, Boehringer Ingelheim, Cargill, Dechra Veterinary Products, Merck Animal Health, Platinum Performance, Purina and Zoetis. The AAEP also has three Media Partners—*EquiManagement*, *EQUUS* and *The Horse: Your Guide to Equine Health Care*—that support the AAEP through education and dissemination to members and their clients of leading-edge horse health and practice management news.

ASSOCIATION

New Practice Life podcast provides marketing tips for your practice

Does your practice's marketing strategy reflect your brand? What are some key considerations that go into development of a successful strategy? Do you understand the demographics of your audience and using this information to best reach them on the different social media platforms? Do you even have a marketing strategy?

In the latest episode of the AAEP Practice Life podcast, entitled "Marketing the Equine Veterinary Practice," host Dr. Mike Pownall discusses the intricacies of effectively marketing your equine practice with marketing specialists Dr. Karen Bolten, a former practice owner who now runs a veterinary business consulting firm in Myrtle Beach, S.C.; Heather McPherson, marketing manager for McKee Pownall Equine Services in Newmarket, Ontario; and Kelly Graber, associate director of equine marketing for Boehringer Ingelheim in Duluth, Ga.

Among the topics addressed during the 40-minute episode are the importance of marketing and who in the practice should be responsible, the social media platforms best suited for an equine practice, what tends to work well and not so well, how to tell if your marketing is working and more.

Download or listen to the episode at podcast.aaep.org or on iTunes.

The AAEP Practice Life podcast is sponsored by Boehringer Ingelheim.

FOUNDATION

Foundation scholarships make an impact

Catching up with scholarship recipient Dr. Anne Hutton

"The Coyote Rock Ranch Scholarship not only recognized and validated my efforts put forth in veterinary school, but it also continues to encourage me to put my best foot forward and become the best equine practitioner that I can be."
—Anne Hutton, DVM, 2018 Coyote Rock Ranch Scholarship recipient

After receiving her veterinary degree in 2018 from Washington State University, Dr. Anne Hutton used the financial flexibility afforded by her scholarship to complete a pair of year-long internships—first at Pioneer Equine Hospital in Oakdale, Calif., followed by a rotating medicine and surgery internship at Virginia Tech's Marion duPont Scott Equine Medical Center in Leesburg, Va.

Dr. Hutton acquired valuable experience with wide and varied caseloads—from diagnosis and treatment of routine cases to management of more complex and critical cases. These experiences, together with the strong guidance and mentorship from veteran colleagues at both practices, have advanced her skills and knowledge while reaffirming her passion for equine medicine.

Equipped with substantive training in sports medicine, surgery, and emergency and critical care, Dr. Hutton returned to her native Montana in November 2020 as an associate at Tammany Veterinary Hospital in Corvallis. It has been very rewarding for her to bring back a specialized skill set to her local community and continue to treat a wide variety of equine cases. Her pursuance of internships for advanced learning would have been very difficult without the Coyote Rock Ranch Scholarship, and the benefit has been great—not only for her, but also for her clients and patients.

Penelope Knight created the Coyote Rock Ranch Veterinary Scholarship program through The Foundation for the Horse in 2015. Since award of the first scholarships five years ago, 16 AAEP student members have benefited from a cumulative $1.275 million in assistance. The Foundation, AAEP's charitable arm, awards over $700,000 annually in scholarships and grants to impact equine health and well-being throughout the U.S. and developing countries.

To learn more, visit foundationforthehorse.org.

COYOTE ROCK RANCH

Reunite with colleagues old and new at convention social events

Celebrate a long-awaited homecoming in the heart of downtown Nashville when the AAEP's 67th Annual Convention convenes in-person at the Music City Center, Dec. 4–8. While making a little time after educational sessions to experience one of the world's top travel destinations according to *Conde Nast Traveler,* don't miss the opportunity to gather and engage with colleagues at the slate of social events.

Catch up and share a laugh

Nothing exemplifies the community and camaraderie of horse doctors quite like the Welcome Reception, the traditional kick off to the convention's social calendar. If you're like many, this year's Welcome Reception on Saturday, Dec. 4 from 5:30–7:00 p.m. will be your first time connecting with former classmates and colleagues in person since before the pandemic. Complimentary drinks and hors d'oeuvres will be available. *Sponsored by Rood & Riddle Equine Hospital and Nutrena®.*

Build your network

Recent graduates will expand not only their clinical knowledge and skills at the convention but also their professional circle during the New Practitioners' Reception on Sunday, Dec. 5 from 6:30–8:00 p.m. Meet and chat with fellow colleagues in their first five years of practice while enjoying complimentary food and beverages. In addition, obtain a professional headshot photo at no charge for your practice website and social media. *Sponsored by IDEXX.*

Celebrate in song

Nashville is known as the Songwriting Capital of the World, and several of the best hit-writers in country music will share the stage with ultra-talented veterinarian storytellers from 8:00–10:30 p.m. on Sunday, Dec. 5 for Storytelling Nashville Style. This unforgettable night will feature performances by Grammy Award winner Rory Feek and a couple of his hit-writing friends, Wynn Varble and Brice Long. Reserve your seat for $75, which includes a complimentary beverage and gift to The Foundation for the Horse. *Sponsored by Merck Animal Health, Boehringer Ingelheim, National Veterinary Associates and Zoetis.*

Connect across borders

If you're making the trip to Nashville from outside the U.S. and Canada, meet and network with fellow AAEP members from around the world at the International Members' Breakfast and the International Members' Reception on Monday, Dec. 7 from 6:30–8:00 a.m. and 6:30–8:00 p.m., respectively. Enjoy complimentary food and refreshments. *Sponsored by Antech, SOUND.*

Join the party

Cap the convention social scene with a night to remember at the world-famous Wildhorse Saloon from 6:30–10:30 p.m. on Tuesday, Dec. 7. Enjoy music, dancing, food and more inside a historic, three-story line dancing and live music mecca. The After Party is free for registered attendees and exhibitors, although a ticket is required. When registering for the convention, just check the After Party box and a ticket will be included in your attendee packet. *Sponsored by Zoetis.*

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

Mother was always right

Maternal words of wisdom help shape professional ethics

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

Dr. Peter Morresey

Most of us have come to realize the truth in the above headline, especially when it comes to the ongoing formation of our professional ethics.

As new graduates, we all have gotten in over our heads. One of mine was a bovine dystocia during my days in mixed practice. Exhaustion and a desire for expediency led me to call in a senior member of the practice. He arrived, barked at me, unceremoniously completed the dystocia, berated me at length for the situation in full view of the client, and left with hardly a word to said client (now pale with mouth agape wondering why anyone would work within that culture).

I made up my mind on a few things that day: I would never ask that person for help again; I would willingly give my help to anyone when able; and I would never criticize another veterinarian in front of a client, preferring, if necessary, a quiet, frank and beneficial conversation afterwards. Before our mouths are engaged, we should always remember that enshrined within veterinary practice acts are non-disparagement clauses.

Mother would say, "Treat others like you want to be treated."

I was still the young vet in town and worked for a successful horse trainer who was a longstanding client of the practice. Another veterinarian had extended their practice into the area and coveted this client. Out of the blue, I was asked to administer an anabolic to a horse in competition. The justification was, "your predecessor didn't get caught." My reply was when inevitably caught, my right to practice and his right to train were revoked, so not happening. Within 10 days, I no longer worked for that trainer, a chronic case was in the care of the other practitioner with no warning, and the owner of that horse went from grateful to livid. Particularly stinging was the instigator was someone I had looked up to as an extern veterinary student, and they were a regular on the family farm. In practice, I had let them borrow equipment and supplies when they were caught short.

This breach of professionalism and collegiality cut deeply. To this day, I wonder if the anabolic was administered. My competence was called needlessly into doubt for financial gain. The ethics of supersession were breached.

Fast forward 18 months, and I was offered a job by this veterinarian. They couldn't understand why I didn't accept. Our values were completely misaligned.

Mother would say, "Love many, trust few, always paddle your own canoe."

Years later, and with a change in hemisphere, I am in referral equine practice. A valuable yearling had flipped over backwards and was unable to stand. Blood poured from both nostrils. The farm manager was crying outside the stall repeating, "Pete you have to save this horse." Time and sheer force of will from the amazing technician team around me got the horse standing. A slight head tilt remained, gait deficits were on the improve and, while a prolonged recovery was ahead, the horse no longer met requirements for euthanasia. This had been relayed to the insurance company. The story takes a dark turn: the long shadow of the dollar altered the farm's desired outcome. It was first requested, then demanded, I immediately euthanize as the horse would never race. The referring veterinarian, fearful of blowback, refused to support me.

Before our mouths are engaged, we should always remember that enshrined within veterinary practice acts are non-disparagement clauses.

A second opinion agreed with my assessment. The client became belligerent and removed the horse from my care, vowing never to send me another patient. The insurance adjustor during our farm visit agreed their policy requirements for euthanasia were not met. We left a hostile manager. Talks led to a financial, not clinical, decision (partial payout and the farm kept the horse).

Outcome? The insurance company never questions my opinion of a horse in my care. The farm sent me cases again. The horse raced and ended up in the money. The farm went out of business.

Mother would say, "In the end all you have is your name."

Our dedicated nursing staff saved a maladjusted neonate. Discharge was scheduled to a happy client. Colic occurred and surgery was needed. The client's tone soured, "…you need to say the foal never got on the mare so it's not worth doing surgery…" As problematic as the underwriter knew it was, the client demanded I say otherwise so they could collect. They were told firmly I would not

continued on next page

AAEP ETHICAL PRACTICE Every Day-Every Time

Dr. Morresey is a shareholder at Rood & Riddle Equine Hospital in Lexington, Ky., and a member of the AAEP's Professional Conduct & Ethics Committee and Scientific Review & Editorial Committee.

Ethics, continued

revise my daily updates, nor would I falsify the hospital record clearly stating the foal was on the mare. The room temperature dropped 30 degrees in 30 seconds.

The foal went to surgery, swiftly recovered and enjoyed a successful athletic career. I had serviced this client over many years. I chalked it up to "temporary loss of reason" as the impossibility of their request was obvious. Had I buckled, future courtesies would likely have been sought.

Mother would say, "Be sure your sins will find you out."

Anecdotes maybe; learning experiences, most definitely. Ethics are common sense. Showing respect to each other makes us all look good. People will disillusion you over a dollar, so be approachable but trust sparingly. You are long remembered for your deeds. If it stinks, you can never bury it deeply enough.

If you recognize yourself above, that is purely intentional. You know who you are, or when you have been that person.

MEMBERSHIP

AAEP mourns the loss of three members

Dr. Timothy O'Brien

Dr. Timothy O'Brien

Dr. Timothy O'Brien, who served on faculty at the University of California, Davis School of Veterinary Medicine for 39 years until his retirement in 2008, died July 26 at age 81.

A veterinary graduate of the University of Illinois and diplomate of the American College of Veterinary Radiologists, Dr. O'Brien was a longtime professor of radiology who also served as chair of the Department of Radiological Services and chair of Surgical and Radiological Sciences. His leadership was crucial to development of the school's veterinary diagnostic imaging training program, and many of his mentees in clinical research became faculty at UC Davis and other veterinary schools.

Dr. O'Brien developed special projections to evaluate disorders of the carpal, navicular and pedal bones, as well as the fetlock, stifle and tarsal joints of horses. In 1979, with his wife Janet, he founded and directed for more than four decades the annual Lake Tahoe Equine Disease Conference; and in 2005, he published a monograph *O'Brien's Radiology for the Ambulatory Equine Practitioner* to guide acquisition of high-quality radiographic images of equine limbs.

Passionate about continuing education and improving the quality of equine radiographs, Dr. O'Brien for many years delivered the highly regarded Radiology/Equine Lameness Panel at the AAEP Annual Convention. AAEP recognized his many contributions to the profession by awarding Dr. O'Brien its Distinguished Educator Award in 2008. He also served AAEP on the Educational Programs, Purchase Exam, and Research committees.

Dr. R. Jay Bickers

Dr. R. Jay Bickers

Dr. R. Jay Bickers, owner of Bickers Equine Surgery and Consulting in Weatherford, Texas, died June 20. He was 59.

A board-certified surgeon, Dr. Bickers started his practice in 2017 after nearly 11 years as an equine surgeon at Brazos Valley Equine Hospital – Stephenville in Texas. His practice focused on mobile equine surgery, acupuncture and chiropractic as well as lameness, X-ray and ultrasound consultation.

Dr. Bickers received his veterinary degree from Texas A&M University and completed his surgical residency at the University of Tennessee, where he helped develop the Emergency and Critical Care Department as the first emergency clinician.

Dr. Gary Shelton

Dr. Gary Shelton

Dr. Gary Shelton, animal welfare advocate and founder of the Shelton Veterinary Clinics in northeast Florida, died June 20 at age 63.

Dr. Shelton opened his first clinic in Interlachen in 1985 soon after receiving his veterinary degree from the University of Florida. He opened additional practices in Elkton and Bunnell. He also gathered with several other veterinarians to open the St. Augustine Regional Veterinary Emergency Center. From 2012-2017, Dr. Shelton served as medical director of the Flagler Humane Society in Palm Coast, ensuring shelter animals received appropriate medical care to facilitate adoption.

Members in the News

Dr. Martin Nielsen

Dr. Martin Nielsen elected president of AAVP

Dr. Martin Nielsen, Schlaikjer Professor of Equine Infectious Disease at the University of Kentucky's Gluck Equine Research Center, was installed as president of the American Association of Veterinary Parasitologists on June 21 during the AAVP's annual meeting in Lexington, Ky.

Dr. Nielsen received his veterinary degree from The Royal Veterinary and Agricultural University in Denmark.

Dr. Michael Harrison

Dr. Michael Harrison re-elected to MHBA board

Dr. Michel Harrison, who served as president of the Maryland Horse Breeders Association from 2018–2020, has been re-elected to a 3-year term on the association's board of directors.

Dr. Harrison, who received his veterinary degree from the University of Florida, also chairs the MHBA's Legislative Committee. He owns and operates his family's Willowdale Farm in Butler, Md.

Dr. Doug Daniels

Dr. Doug Daniels elected National HBPA president

Dr. Doug Daniels, owner of Virginia Equine PLLC in Manakin-Sabot, Va., has been elected president of the National Horsemen's Benevolent and Protective Association.

Dr. Daniels has served as vice president of the Virginia HBPA and a member of the National HBPA's executive committee since 2019. He also works for the Virginia Racing Commission when needed as a regulatory veterinarian. Dr. Daniels received his veterinary degree from Auburn University.

Dr. Stuart Brown

Dr. Stuart Brown receives AVMA Meritorious Service Award

Dr. Stuart Brown, equine safety director at Keeneland Association Inc., in Lexington, Ky., accepted the AVMA Meritorious Service Award on July 29.

Dr. Brown, who received his veterinary degree from Tuskegee University, is AAEP's delegate to the AVMA House of Delegates and a former AAEP board member. He's also served on the Welfare and Public Policy Advisory Council and Racing Committee, among others. Dr. Brown currently serves as chair of the Gluck Equine Research Foundation, trustee for the AVMA Trust and board chair for the University of Kentucky Equine Analytical Chemistry Laboratory.

Dr. Rick Mitchell

Dr. Glenn Blodgett

Drs. Rick Mitchell, Glenn Blodgett elected AHC officers

AAEP Honor Roll members and former board members Dr. Rick Mitchell and Dr. Glenn Blodgett have been elected chair and secretary, respectively, of the American Horse Council board of trustees.

Dr. Mitchell, who has served on the AHC board since 2012, is president of Fairfield Equine Associates in Newtown, Conn. A veterinary graduate of Oklahoma State University, Dr. Mitchell is chair of The Foundation for the Horse and serves on the Performance Horse Committee.

Dr. Blodgett, who received his veterinary degree from Texas A&M University, is resident veterinarian and horse division manager of the Four Sixes Ranch in Guthrie, Texas. He has served on the AHC board since 2015 and received the AAEP's Distinguished Life Member Award in 2016.

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INDUSTRY

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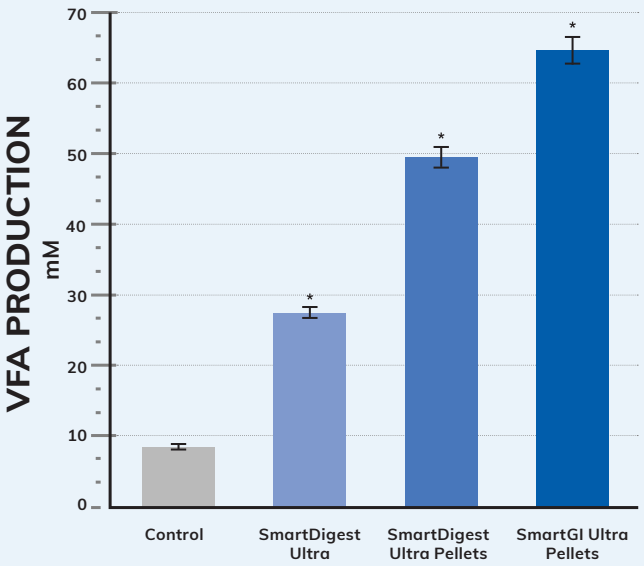

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Highlights of recent clinically relevant papers

DDFT lesions in the pastern and tendinopathy

In this retrospective study, Elizabeth Acutt and co-workers in the USA assessed pathological changes within the deep digital flexor tendon (DDFT) in the pastern with concurrent tendon injury to determine whether tendon lesions in the pastern are associated with tendinopathy within the hoof capsule.

Cases with DDFT lesions in the pastern diagnosed by magnetic resonance imaging (MRI) or ultrasonography of the foot were evaluated. Lesion location and type were recorded. Odds ratios were calculated to determine the associations between more distal tendinopathy and the presence of different DDFT lesion types in the pastern.

Thirty-four MRI scans of 33 horses and 64 ultrasonographic examinations of 58 horses were analysed. Distal DDFT lesions were found in 75% of cases of pastern DDF tendinopathy and in 97% of cases with core lesions of the DDFT in the pastern. A core lesion in the pastern was significantly more likely to be associated with injury in the foot than other types of pastern lesion. DDFT pathological change in the pastern, particularly core lesions, is associated with additional tendinopathy within the hoof capsule. When a DDFT lesion is found in the pastern, further imaging of the tendon within the foot is indicated to direct appropriate treatment and improve prognostication.

Training related risk factors for EIPH

This prospective study by Tegan McGilvray and Jacqueline Cardwell performed at the Royal Veterinary College, UK, followed 177 healthy National Hunt racehorses in training on five training yards over two seasons. The objectives were to estimate the prevalence of exercise induced pulmonary haemorrhage (EIPH) and to identify training-related risk factors for these outcome measures.

Post-exercise tracheobronchoscopy and tracheal wash were performed monthly while in training and 1184 observations were gathered. The prevalence of tracheal blood was 7.2% and the prevalence of significant (>25%) haemosiderophages in tracheal wash fluid was 36%. Increased time in training was significantly associated with increased odds of EIPH. For each additional year spent in training the odds of tracheal blood and presence of significant proportions haemosiderophages increased approximately 1.5-fold. The odds of tracheal blood and significant of haemosiderophages were increased in both spring and winter, compared to autumn. Increased neutrophil percentage was associated with previous haemorrhage, but not current haemorrhage, suggesting that haemorrhage leads to inflammation but not that inflammation leads to haemorrhage.

Laparoscopic suture techniques

This study by Rodolfo Gialletti and co-workers in Italy compared mesh and barbed suture for laparoscopic nephrosplenic space ablation in horses.

Nephrosplenic space (NSS) ablation has been demonstrated to be an effective technique for prevention of left dorsal displacement of the large colon. Multiple laparoscopic techniques, including ablation with mesh or with a barbed suture, have been proposed. In this study two laparoscopic techniques for closure of the NSS in 28 horses diagnosed with nephrosplenic entrapment were compared. Medical records of horses that had laparoscopic NSS ablation in two referral centres were retrieved. Duration of surgery, complications, short- and long-term follow-up information and costs were collected and compared. All horses met the inclusion criteria: 9 had NSS ablation with a mesh implant (group M), 19 with barbed suture material (group B). One horse in group B had recurrent colic after discharge. At control laparoscopy after 5 months, the NSS resulted in still not being ablated because of a failure of the suture. In group M, three horses had recurrent colic. One was successfully treated medically, one died of unknown causes and the third required a second laparoscopic suturing at 3-6 months because of failure of the mesh implant. The mean time of surgery and costs were lower in group B compared to group M. The barbed suture technique was faster, more cost-effective and had a lower complication rate than the mesh implant.

Cervical vertebral interbody fusion

This retrospective case series by Lynn Pezzanite and co-workers in the USA and New Zealand examined the use of an interbody fusion device for cervical vertebral fusion in horses with cervical vertebral compressive myelopathy (CVCM). This method requires less bone removal leaving a thicker vertebral canal floor, and the screw design allows for consistent application to the ventral aspect of the vertebral body.

Data from 10 horses (median age 24 months, mixed breeds) that underwent placement of an interbody fusion device and polyaxial pedicle screw and rod construct under general anaesthesia were analysed. Fusion was performed at one (n = 3) or two (n = 7) sites. Two horses were euthanised within the first year, one due to upper respiratory tract obstruction post-operatively and one due to persistent recumbency. In 6/8 horses with >1 year follow-up, ataxia improved by 1–3 grades, with an average improvement of 1.25 grades. In four horses, ataxia improved to grade 0–1. In the remaining two horses, the gait was unaffected, but neck comfort improved.

The most common post-operative complications were seroma formation (n = 9), pain (n = 5) and fever (n = 4). Implant infection and nondisplaced fracture occurred in one horse. All eight owners reported that they were positive about the procedure and would recommend this surgery. Fatal complications related to implant placement did not occur.

This method may represent an alternative to current techniques of ventral interbody fusion with similar outcomes and no fatal complications associated with implant placement in CVCM; however, larger studies are needed.

Probiotic bacteria for equine use

This review article by Giselle Cooke and co-workers in Australia summarised the current evidence reporting on the

safety, tolerability and efficacy of probiotic bacteria use in horses.

The authors conducted an online search of five databases for studies reporting on the use of probiotic bacteria use in horses which were either healthy or had a gastrointestinal or extraintestinal disease, which identified 18 eligible articles. No clear benefits were identified to support supplementation of equids with probiotic bacteria to improve starch and fibre digestion, nor for the treatment of colic or prevention of salmonellosis. Conflicting results were seen with the management of scouring in neonatal foals. Exacerbation of diarrhoea and additional adverse events were reported in response to the administration of high doses of novel probiotic bacterial species. Improved aerobic fitness and stamina was reported in exercising horses given probiotic bacteria.

The majority of probiotic bacteria used in equine studies are species commonly used for human consumption and indigenous to the human gastrointestinal microbiota. There is little evidence to support the use of probiotic bacteria to maintain health and manage disease in horses. While results associated with probiotic bacteria use for gastrointestinal conditions in both horses and foals are unclear and conflicting, the administration of multistrain bacterial formulations to increase stamina in exercising horses shows promise.

Positron emission tomography

This study by Sabrina Wilson and co-workers in the USA assessed the ability of ^{18}fluorine-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) to detect deep digital flexor tendon (DDFT) lesions and compared the PET findings with computed tomography (CT) and magentic resonance imaging (MRI) findings.

Eight horses with lameness due to pain localised to the front feet were included. Both front limbs of all horses were imaged with ^{18}F-FDG PET, noncontrast CT, and arterial contrast-enhanced CT; 11 limbs were also assessed using MRI. Two observers graded independently ^{18}F-FDG PET, noncontrast CT, arterial contrast CT, T1-weighted (T1-w) MRI, and T2-weighted (T2-w)/STIR MRI. Maximal standardised uptake values were measured. Lesions were found in 7/16 DDFT on PET, 12/16 DDFT on noncontrast CT, 6/15 DDFT on arterial contrast CT, 8/11 DDFT on T1-w MRI, and 6/11 DDFT on T2-w/STIR MRI. Positron emission tomography was in better agreement with arterial contrast CT and T2-w/STIR MRI than with noncontrast CT and T1-w MRI. Chronic lesions with scar tissues identified on noncontrast CT or T1-w MRI did not have increased ^{18}F-FDG uptake. These results demonstrated that ^{18}F-FDG PET agreed more closely with modalities previously used to detect active tendon lesions, i.e., arterial contrast CT and T2-w/STIR MRI. ^{18}F-FDG PET can be used to identify metabolically active DDFT lesions in horses.

Ultrasound-guided cervical perineural injection

In this prospective study Jonuel Cruz-Sanabria and co-workers in the USA developed an ultrasound-guided cervical perineural injection technique for horses and evaluated the distribution of contrast agent among perineural, intra-articular and periarticular injections.

A bilateral ultrasound-guided perineural injection technique for the caudal cervical spinal nerve roots (CSNRs 5-7) was developed. Paramagnetic or iodinated contrast was injected into 14 equine cadaveric necks and the distribution of contrast was evaluated using magnetic resonance (MR) or computed tomography (CT) imaging, respectively. The presence of contrast in the CSNR region was determined by an observer unaware of the injection technique used. The distribution of contrast agent to the CSNR region using the perineural injection technique was compared with intra- articular and periarticular injection techniques.

Perineural injection delivered contrast agent to the CSNR region 100% of the time and was significantly different when compared with intra-articular injection. The ability to deliver contrast agent to the CSNR region between the perineural and periarticular injection techniques or between the intra-articular and periarticular injection techniques did not differ.

The ultrasound-guided perineural injection technique accurately delivered contrast agent to the CSNR region in equine cadavers. This technique could potentially be used for the diagnosis and treatment of cervical pain in horses, particularly in cases where intra-articular cervical articular process joint injections have not been beneficial. Further studies are necessary to assess the effectiveness of the technique in live horses.

S. WRIGHT
EVE Editorial Office

References

Acutt, E.V., Contino, E.K., Frisbie, D.D. and Barrett, M.F. (2021) Deep digital flexor tendon lesions in the pastern are associated with the presence of distal tendinopathy. *Equine Veterinary Journal*. Epub ahead of print: https://beva.onlinelibrary.wiley.com/doi/https://doi.org/10.1111/evj.13470

Cooke, C.G., Gibb, Z. and Harnett, J.E. (2021) The safety, tolerability and efficacy of probiotic bacteria for equine use. *Journal of Equine Veterinary Science*, **99**, 103407.

Cruz-Sanabria, J.A., Gaschen, L., Bragulla, H.H., Mitchell, M. and Leise, B.S. (2021) A study of ultrasound-guided perineural injection of the caudal cervical spinal nerve roots in equine cadavers. *Veterinary Anaesthesia and Analgesia* **8**, 603-611.

Gialletti, G., Nannarone, S., Gandini, M., Cerullo, A., Bertoletti, A., Scilimati, N., et al. (2021) Comparison of mesh and barbed suture for laparoscopic nephrosplenic space ablation in horses. *Animals* **11**(**4**), 1096.

McGilvray, T.A. and Cardwell, J.M. (2021) Training related risk factors for exercise induced pulmonary haemorrhage in British National Hunt racehorses. *Equine Veterinary Journal*. https://beva.onlinelibrary.wiley.com/doi/https://doi.org/10.1111/evj.13448. Epub ahead of print.

Pezzanite, L.M., Easley, J.T., Bayless, R., Aldrich, E., Nelson, B.B., Seim, H.B. III, et al. (2021) Outcomes after cervical vertebral interbody fusion using an interbody fusion device and polyaxial pedicle screw and rod construct in 10 horses (2015-2019). *Equine Veterinary Journal*. https://beva.onlinelibrary.wiley.com/doi/https://doi.org/10.1111/evj.13449. Epub ahead of print.

Wilson, S., Spriet, M., Espinosa Mur, P., Anishchenko, S., Beylin, D., Katzman, S., et al. (2021) ^{18}Fluorine-fluorodeoxyglucose positron emission tomography for assessment of deep digital flexor tendinopathy: An exploratory study in eight horses with comparison to CT and MRI. *Veterinary Radiology & Ultrasound*. https://doi.org/10.1111/vru.13001. Epub ahead of print.

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Case Report

Equine focal mucopurulent placentitis associated with *Stenotrophomonas maltophilia*

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Keywords: horse; abortion; premature delivery; nocardioform; allantochorionitis

Summary

Reported herein are two cases of focal mucopurulent placentitis (FMP) associated with *Stenotrophomonas maltophilia,* a ubiquitous multidrug-resistant Gram-negative bacterium with emerging significance as a human nosocomial pathogen. The first patient, a 12-year-old multiparous Quarter Horse mare, aborted at 287 days of gestation, and the fetus and placenta were submitted for post-mortem examination. The second patient, a 10-year-old Thoroughbred mare, had unexplained pregnancy losses prior to 7 months of gestation for three consecutive years and prematurely delivered a live foal at 293 days of gestation. The foal was severely compromised and was subjected to euthanasia. The patients were current on vaccination programmes, and no abnormalities were noted on transrectal and transabdominal ultrasonography during repeated reproductive examinations throughout pregnancy, including fetal cardiac activity and combined thickness of the uterus and placenta. Mild premature mammary gland development for at least 7 days before pregnancy loss occurred in both cases. On post-mortem examination, the foals from both patients presented lesions indicative of sepsis. The stillborn foal from the first patient had mild multifocal suppurative hepatitis and the foal from the second patient had pneumonia, myocardial and hepatic necrosis, and mild splenitis with lymphoid depletion. The fetal membranes of both mares had a thick yellow adherent mass of exudate overlaying the chorionic surface. The lesions were well-delineated, and the underlining chorion was avillous, pale and thickened (**Fig 1**). Histopathological findings included chronic, fibrosing, necrotising allantochorionitis, with squamous metaplasia of the chorionic surface (**Fig 2**) and adenomatous hyperplasia of the allantois. In the second case, there was also chronic perifunisitis, with neutrophilic, necrotic exudate. *S. maltophilia* was isolated from the exudate of both mares and from the lungs and stomach of the stillborn fetus. To the authors' knowledge, this is the first clinical description of FMP associated with *S. maltophilia* in the USA. The aetiopathogenesis of placentitis induced by this micro-organism and its relevance as an emerging pathogen in equine reproduction remains to be further elucidated. The mares recovered uneventfully: the first patient was able to carry pregnancies to term for two consecutive years; the second patient's owner decided to no longer use the mare for reproduction.

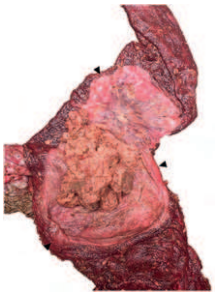

Fig 1: Gross appearance of the chorionic surface of the placenta in a case of equine focal mucopurulent placentitis associated with* Stenotrophomonas maltophilia *(Case 2). There is an approximately 40 × 30 cm thick, friable mass of exudate at the base of the pregnant uterine horn. The periphery of the mass was firm and green to grey, and the inner portion was yellow and soft. The chorion in this region was avillous and yellow/pale with well-delineated borders (arrow heads).

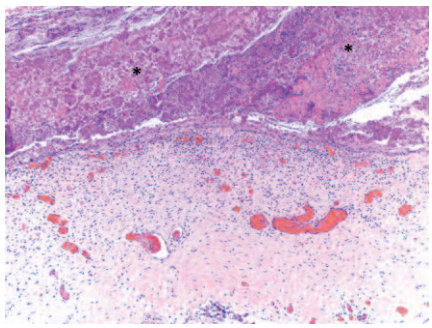

Fig 2: Photomicrograph of the allantochorion from Case 2. Severe chorionitis. The chorionic epithelium was overlaid by abundant necrotic exudate (asterisks). Fibrosis and inflammatory infiltrate of lymphocytes, plasma cells and neutrophils were also seen. Haematoxylin and eosin stain, 100× magnification.

Key points

- Micro-organisms other than Gram-positive nocardioform branching actinomycetes may cause FMP, including the multidrug-resistant *S. maltophilia*.
- The cases associated with these bacteria differed from the classical presentation of FMP because of concurrent fetal infection.
- Clinical diagnosis prior to abortion or premature parturition is challenging, especially under field conditions. Prodromal signs are often rare or nonexistent, and lesions may not be detected on transrectal or transabdominal ultrasonography. Mild premature mammary gland development may be the sole clinical sign.

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Case Report

Asystole associated with cerebrospinal fluid collection in a 3-month-old foal under general anaesthesia

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Keywords: horse; anaesthesia; bradycardia; asystole; CSF collection; intracranial pressure

Summary

A 3-month-old colt foal presented for investigation of progressive neurological signs after a 3-week history of neck pain following microchip implantation. Clinical signs consisted of pyrexia, behavioural changes, gait abnormalities, proprioceptive and sensory deficits of the hindlimbs and increasing periods of recumbency.

Diagnostic investigation included cerebrospinal fluid (CSF) collection, which was performed under general anaesthesia. During atlanto-occipital CSF collection, severe bradycardia (21 beats/min) with unconducted P-waves was evident. Treatment with intravenous glycopyrrolate showed no response, and atropine was then administered intravenously. The heart rate increased to 30 beats/min, although unconducted P-waves and S-T segment depression remained present (see **Fig 1**). Atropine administration was repeated, and the foal progressed to 3rd degree AV block, initially with occasional ventricular escape complexes (14/min) then complete systole. External cardiac compressions were initiated at 60/min and after intravenous adrenaline administration, ventricular tachycardia (170 beats/min) developed. Cardiac compressions were stopped, and the ventricular tachycardia resolved spontaneously into sinus tachycardia (153 beats/min). The heart rate continued to fall and when it reached 60 beats/min, further atropine was administered intravenously. It was elected to recover the foal from general anaesthesia, and the foal was extubated when signs of returning consciousness were noted. Arterial hypoxaemia was noted post-recovery, and the foal had clinical signs consistent with cerebral hypoxia post-resuscitation. The foal was managed overnight with symptomatic therapy and was sedated by propofol constant rate infusion. The signs of forebrain disease progressed, and the foal was subjected to euthanasia the following day due to deterioration of neurological function. Post-mortem examination showed severe suppurative osteomyelitis within T1 and osteonecrosis of S1.

The cardiovascular events and asystole were presumed due to a Cushing-type reflex as a result of changes in intracranial pressure during the sampling procedure.

Key points

- CSF sampling from the atlanto-occipital space is not benign, and although complications are uncommon, these can be fatal
- CSF sampling during general anaesthesia should be accompanied, where possible, by cardiovascular monitoring including placement of an ECG and continuous invasive arterial blood pressure monitoring
- Attention should be paid to rate and volume of CSF collection in smaller patients and the patient closely monitored throughout the procedure

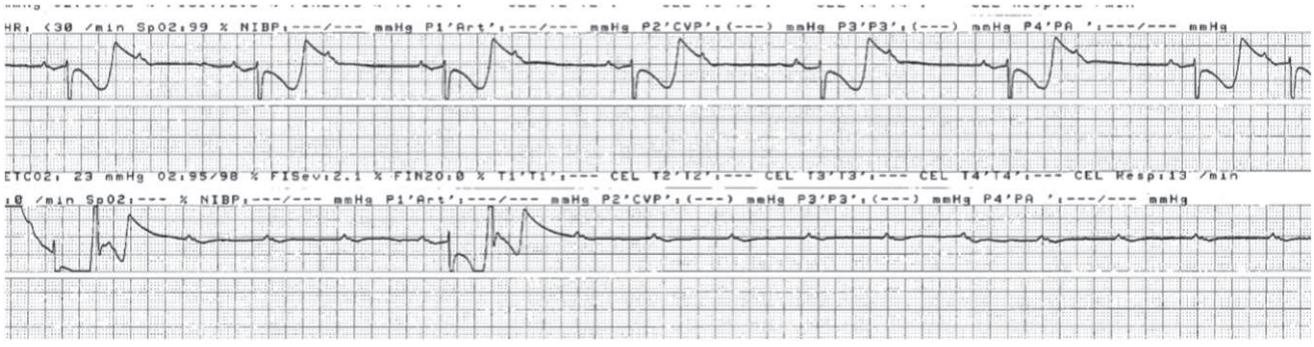

***Fig 1:** ECG trace observed during CSF sampling, after initial treatment with intravenous glycopyrrolate then atropine. Bradycardia with unconducted P-waves and S-T segment depression which progressed to asystole. Paper speed 25 mm/sec.*

EQUINE VETERINARY EDUCATION
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Case Report

Clinical pathology and ultrasonographic findings from a Warmblood gelding with primary, severe, acute pancreatitis

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Keywords: horse; pancreatitis; colic; ultrasonography

Summary

A 24-year-old Warmblood gelding presented with a 6-hour history of recurrent colic signs of increasing severity. Upon presentation, he was mildly painful, tachycardic, tachypnoeic and had decreased borborygmi. Nasogastric intubation resulted in no net reflux and rectal palpation revealed an ascending colon impaction. Percutaneous abdominal ultrasonography revealed dilated (6–8 cm diameter, rr < 5 cm), thickened (3.7–10.0 mm, rr < 3 mm) and hypomotile loops of small intestine. Complete blood count revealed leucopenia (3.00×10^9/L; rr 5.0–11.9) with neutropenia (1.4×10^9/L; rr 2.5–6.0) and an increased packed cell volume (0.51; rr 0.26–0.42). Serum biochemistry revealed hyperproteinaemia (94 g/L; rr 61–84), hyperglycaemia (24.36 mmol/L; rr 3.33–6.77), hypocalcaemia (1.98 mmol/L; rr 2.80–3.40), hyperbilirubinaemia (107.76 μmol/L; rr 3.42–59.86), hypercholesterolaemia (10.54 mmol/L; rr 2.02–3.11), elevated aspartate transaminase (20.21 μkat/L; rr 2.24–6.78), elevated alkaline phosphatase (6.10 μkat/L; rr 1.02–2.56) and elevated gamma glutamine transferase (2.20 μkat/L; rr 0–0.67). Despite sedation and fluid resuscitation, the gelding became severely colicky. A repeat ultrasound was performed, revealing a moderate amount of free fluid and a mass effect between the liver and right dorsal colon. A hyperechoic structure containing hypoechoic regions was seen between right dorsal colon, a segment of small intestine, liver and surrounded by anechoic free fluid (**Figs 1** and **2**). Abdominocentesis yielded a yellow, turbid fluid containing free-floating white debris with an increased total protein and lactate concentration. Cytology of the fluid revealed necrotic mesothelial cells. The gelding was humanely euthanised due to poor prognosis. Necropsy revealed acute, severe pancreatitis and duodenitis. The mass effect on ultrasonography was retrospectively identified as the pancreas. Given the difficulty in reaching an ante-mortem diagnosis of pancreatitis in horses, these ultrasonographic findings may improve the diagnosis of acute pancreatitis and provide justification for its consideration in unusual cases of colic.

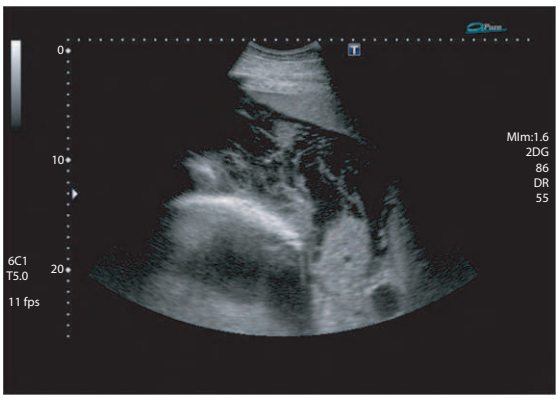

Fig 1: The liver and right dorsal colon are surrounded by increased peritoneal fluid. To the right of the right dorsal colon in the image is a hyperechoic structure.

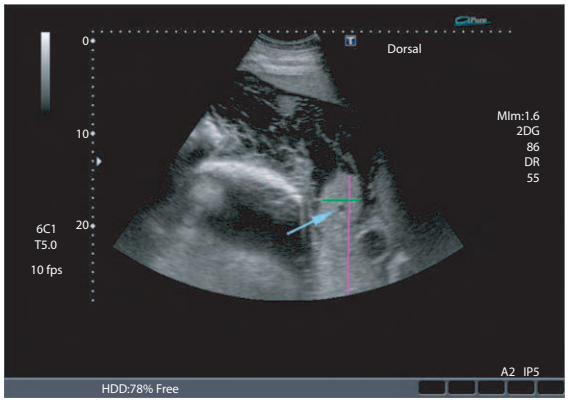

Fig 2: Arrow: Tubular anechoic structure within hyperechoic structure adjacent to right dorsal colon. Hyperechoic structure measuring 4.5 cm (green line) by 12.6 cm (purple line).

Key points

- Abdominal ultrasonography may be helpful in diagnosis of acute pancreatitis in horses presenting with acute onset, severe colic signs.
- Identification of a mixed echogenicity oblong structure containing a duct between the liver and right dorsal colon is consistent with the right limb of the pancreas. Increased peritoneal fluid with or without fibrin is frequently present.
- Pancreatitis should be considered a differential diagnosis in horses with colic signs, small intestinal dilation, peritoneal effusion, severe bloodwork derangements and abnormal peritoneal fluid.

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Case Report

Acquired peri-articular ganglion cyst in the lateral femorotibial joint in an 18-year-old Percheron cross mare

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Keywords: horse; ganglion cyst; lameness; stifle joint

Summary

An 18-year-old Percheron cross mare presented for evaluation of an acute lameness in the left hindlimb after presumably being kicked by another horse. Three days following the trauma, the mare developed an acute swelling over the stifle area and was persistently lame. On presentation, physical examination identified a smooth, firm, non-movable, 11.75 × 3.93 cm soft tissue mass on the left hindlimb attached to the lateral aspect of the lateral femorotibial joint. Palpation of the mass was painful and resented by the mare. No external wound or abrasions were identified. Flexion of the stifle joint displaced the mass and exacerbated the lameness. The rest of the physical examination was unremarkable. Lameness examination revealed a grade 3/5 left hindlimb lameness, based on the AAEP grading system. Radiographic examination of the left stifle joint revealed no abnormalities and the mass was not detectable. Ultrasonographic examination of the left lateral aspect of the femorotibial joint showed a well-circumscribed, cyst-like structure filled with anechoic fluid with no apparent direct communication with the lateral femorotibial joint. The margins of the mass were well demarcated (**Fig 1**). The mare was prepared for a standing surgery and excision of the cyst-like structure was performed. Histopathological examination of the excised mass revealed loose and dense immature connective tissue containing a collapsed cyst lined by inner myxomatous and outer immature connective tissue. No synovial lining cells were detected in the wall, and the tissue was diagnosed as a ganglion cyst. Lameness re-evaluation 2 weeks post-operatively found the mare to be sound. Four weeks post-operatively, the mare resumed her previous athletic performance.

Key points

- A ganglion cyst is a fluid-filled structure consisting of inner myxomatous and an outer fibromatous wall that lacks synovial lining cells and is usually associated with a tendon sheath or a joint.
- A ganglion cyst should be considered as a cause for a significant lameness in horses.
- Physical examination, radiographic and ultrasound evaluations, regional analgesia and histopathological confirmation are essential to confirm the diagnosis of a ganglion cyst.

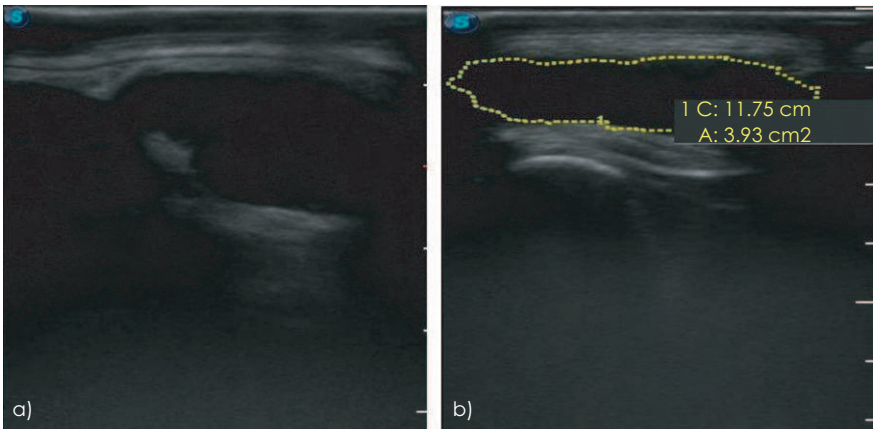

Fig 1: Transverse ultrasound images 'a' and 'b' of the lateral femorotibial joint showing an encapsulated cyst-like structure with no evident connection to the joint.

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Case Report

Ultrasonography and surgical management of a perineal hernia in a donkey

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Keywords: horse; bowel; herniorrhaphy; hernia ring; hernia sac; pelvic diaphragm

Summary

This case report describes a unilateral perineal hernia in a 7-year-old female donkey. The donkey had a 2-month history of being fed on poor quality hay, constipation and severe straining during defaecation. During this time, the donkey had normal urination, attitude and appetite, but experienced weight loss. Three days prior to presentation, the donkey developed a large perineal swelling and a loss of appetite. The constipation and straining increased. Urination was not affected by the perineal swelling. There were no indications of severe dehydration or infection.

Upon evaluation of the perineal region, a 15 cm swelling was noted lateral to the left vulvar lip (**Fig 1**). The swelling was soft and painless on palpation. The perineal swelling was easily reduced in size by direct manual pressure and increased by manual pressure on the left flank region. A 5-cm-length hernia opening was palpated 3 cm lateral to the left vulvar lip.

Ultrasonography revealed a hyperechoic hernia sac containing dilated nonmotile bowel with homogenous hypoechoic contents (**Fig 2**).

Based on the clinical signs, palpation and ultrasonography, the swelling was diagnosed as a left unilateral perineal hernia.

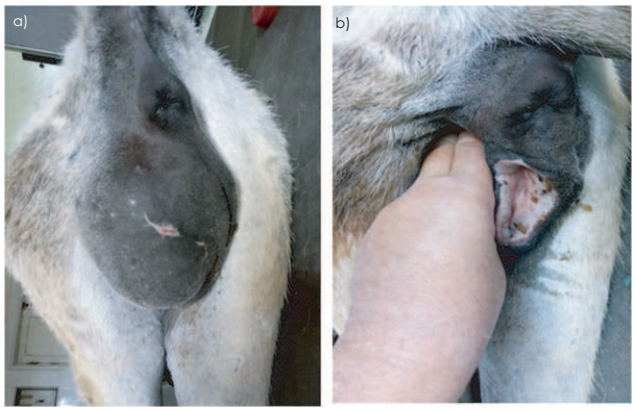


Fig 1: a) A 7-year-old female donkey with a unilateral left perineal hernia. b) The same animal showing reducibility of the perineal hernia.

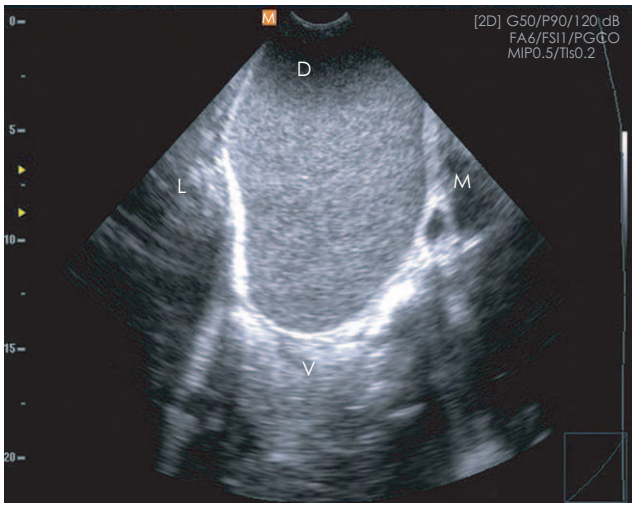
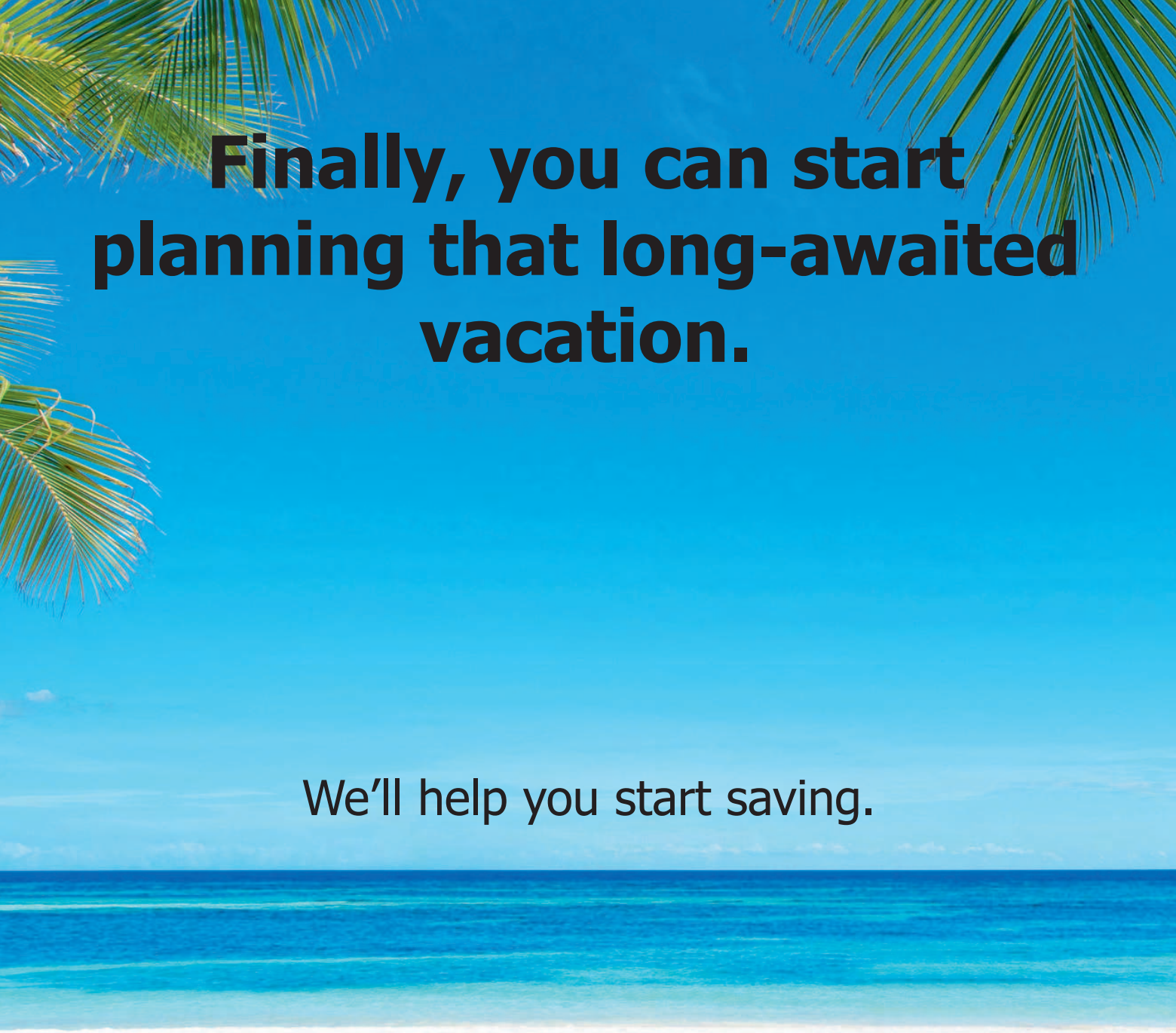


Fig 2: Ultrasonogram of the perineal hernia using a 5 MHz convex abdominal ultrasound transducer placed longitudinally over the swelling showing a hyperechoic hernia sac and a hypoechoic homogenous hernia content. D, dorsal; V, ventral; L, lateral; M, medial.

Primary herniorrhaphy was performed after repositioning of the herniated bowel. The owner was advised to stop feeding the donkey hay and give the donkey cereal and grass fodders for 30 days. The case was followed up for 6 months, and uneventful recovery with neither recurrence nor complications was seen. The constipation and straining disappeared a few days after surgery, and the donkey's weight increased 2 months after surgery.

Key points

- Perineal hernia should be considered in the differential diagnosis of perineal swellings in donkeys.
- Ultrasonography is a valuable tool for the diagnosis of perineal hernia in donkeys.
- Surgical herniorrhaphy was successful in correcting the problem in this case.



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3 Burba DJ, Collier MA, DeBault LE, Hanson-Painton O, Thompson HC, Holder CL: In vivo kinetic study on uptake and distribution of intramuscular tritium-labeled polysulfated glycosaminoglycan in equine body fluid compartments and articular cartilage in an osteochondral defect model. *J Equine Vet Sci* 1993; 13: 696-703.

4 Kim DY, Taylor HW, Moore RM, Paulsen DB, Cho DY. Articular chondrocyte apoptosis in equine osteoarthritis. The Veterinary Journal 2003; 166: 52-57.

5 McIlwraith CW, Frisbie DD, Kawcak CE, van Weeren PR. Joint Disease in the Horse.St. Louis, MO: Elsevier, 2016; 33-48.

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Clinical Commentary

Perineal hernia in large animals: A brief introduction and a comparative view

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The preceding report by Torad *et al*. (2021) describes the diagnosis and surgical correction of a perineal hernia in a donkey, a previously unreported hernia in equids. The authors of that report also review the prevalence of perineal herniation in other species and discuss the regional anatomy and techniques of perineal herniorrhaphy in these species. In this accompanying commentary, I will briefly review the types of hernias encountered in equids and provide some information about perineal herniation in other species, potential aetiologies and an update on surgical techniques used to correct this condition.

The types of hernias reported in horses include the following: umbilical, inguinal (or scrotal), incisional, traumatic body wall and diaphragmatic (Toth and Schumacher 2019). A true hernia, such as an umbilical hernia, is a protrusion of an organ through a normal or congenitally enlarged aperture (i.e. the hernial ring) and contains a hernial sac. A false hernia, such as some diaphragmatic hernias, is a protrusion of an organ through a tear or rupture in a structure adjacent to the herniated organ and has no hernia sac (Kelmer *et al*. 2008). Some types of hernia may have several different aetiologies. Diaphragmatic and inguinal hernias, for example, can result from trauma or from a congenitally enlarged aperture. Umbilical hernias, on the other hand, are consistently congenital in nature (Toth and Schumacher 2019).

The content of the hernia and the ability of the clinician to manually reduce it are clinically important characteristics. Incisional hernias of horses may occur after a celiotomy, usually performed because the horse displayed signs of colic, and are often associated with infection of the sutured celiotomy incision (Kelmer and Schumacher 2008). Some methods of surgical correction (i.e. herniorrhaphy) involve closing the hernia ring with sutures only, whereas others entail the use of a mesh to provide additional strength to the sutured hernia ring (Kelmer and Schumacher) or to span a hernial ring too large to be closed with sutures alone, such as a large rent in the diaphragm (Shnaiderman-Turban *et al*. 2015).

A perineal hernia is a true hernia, because the pelvic diaphragm serves as the hernial sac (Gill and Barstad 2018). Organs commonly entrapped within a perineal hernia of any species, including those within the perineal hernia of the donkey reported by Torad *et al*. (2021), are the urinary bladder, retroperitoneal fat and colon. The uterus is occasionally entrapped within perineal hernias of ruminants, and the prostate is occasionally entrapped within perineal hernias of dogs (Singh *et al*. 2017; Gill and Barstad 2018). The clinical signs displayed by the affected animal are often related to the organs entrapped, but the only abnormality observed may be perineal swelling (Singh *et al*. 2017). Entrapment of the bladder may cause the animal to develop stranguria and tenesmus (Singh *et al*. 2017; Gill and Barstad 2018).

Perineal herniation in dogs and ruminants can usually be diagnosed by using physical examination alone (Singh *et al*. 2017; Gill and Barstad 2018). In the accompanying report by Torad *et al*. (2021), the perineal herniation of a donkey was diagnosed by examining a perineal swelling ultrasonographically. This examination provided detailed identification of the contents of the hernia (Torad *et al*. 2021).

Perineal herniation in an equid has not been reported previous to the report by Torad *et al*. (2021), found in this issue, but it has been reported to occur uncommonly in ruminants, especially water buffalo and cattle (Singh *et al*. 2017; Vadalial *et al*. 2017). Dogs, particularly intact, old males, frequently suffer from perineal herniation (Neibauer *et al*. 2005), whereas ruminants that develop perineal herniation are nearly exclusively female (Singh *et al*. 2017; Vadalial *et al*. 2017). Neibauer *et al*. (2005) reported that relaxin, a hormone abundant in the prostate and especially abundant in prostatic cysts, is likely responsible for weakening of the muscles of the pelvic diaphragm, thereby predisposing male dogs with prostatic cysts to perineal herniation. According to some authors (Prasad *et al*. 2015; Singh *et al*. 2017), trauma or tenesmus caused by diarrhoea may be a predisposing factor in the development of perineal herniation in ruminants. Nevertheless, because the preponderance of ruminants that develop perineal herniation is female, hormones likely contribute to the development of perineal herniation in these animals and may even be a necessary prerequisite.

Dogs frequently experience recurrence of perineal herniation after traditional techniques of appositional herniorrhaphy (AH). In a recent review of perineal herniation in dogs, Gill and Barstad (2018) reported that nearly 50% of AHs failed. In view of this high incidence of failure, techniques of perineal herniorrhaphy using transposition of the semitendinosus or internal obturator muscles were developed. A biomechanical study, however, revealed that neither of these techniques of muscle transposition was superior to AH (Igna *et al*. 2015).

An innovative and promising technique for repair of ventral perineal hernias, using a bilateral flap of superficial gluteus muscle, was recently reported (Milgram *et al*. 2019). Other techniques of perineal herniorrhaphy include using synthetic mesh and a technique of immobilising the bladder, prostate and colon to the body wall with sutures (Gill and Barstad 2018). Perineal herniorrhaphy using biomaterials, such as free grafts of the fascia lata, the common vaginal tunic or canine small intestinal submucosa, has also been described in dogs (Lee *et al*. 2012; Pratummintra *et al*. 2013; Bongarts *et al*. 2015).

Though the anatomy of the pelvic diaphragm is similar among quadrupedal mammals (Dyce *et al*. 2009), perineal herniation of ruminants has usually been resolved by using AH alone (Singh *et al*. 2017; Vadalial *et al*. 2017). Thus, the more elaborate surgical techniques used to treat dogs for perineal herniation may not be necessary when treating ruminants for perineal herniation. Nevertheless, large perineal hernias in buffalos and cattle were successfully repaired by hernioplasty using a synthetic mesh (Sobti *et al*. 1994; Dabas *et al*. 1996; Malik *et al*. 2012).

It is interesting that perineal herniation is frequently encountered in old, intact male dogs (Gill and Barstad 2018), uncommonly encountered in ruminants (Singh *et al*. 2017; Vadalial *et al*. 2017) and reported only once in equids (Torad *et al*. 2021). The donkey affected with perineal herniation reported by Torad *et al*. (2021) was a female, as are most ruminants affected with perineal herniation (Sobti *et al*. 1994; Dabas *et al*. 1996; Singh *et al*. 2017; Vadalial *et al*. 2017). Torad *et al*. (2021) assumed constipation to be a contributing factor to the development of perineal herniation in the donkey of their report, though I can find no reports indicating constipation to be a cause of perineal herniation in other species. Constipation may have been the result, rather than the cause, of perineal herniation in the donkey. Tenesmus caused by diarrhoea, however, is reported to be a predisposing cause of perineal herniation in ruminants (Prasad *et al*. 2015). Perineal herniation in ruminants has also been associated with pregnancy (Sobti *et al*. 1994; Singh *et al*. 2017). In one report, nearly all bovines suffering from perineal herniation were either in an advanced stage of pregnancy or recently calved (Singh *et al*. 2017).

Perineal hernia of dogs is a common condition, and perineal herniorrhaphy performed on dogs has a high tendency to fail. Perineal herniation of ruminants, on the other hand, is uncommon, and perineal herniorrhaphy performed on ruminants seldom fails. The pelvic diaphragm of ruminants and equids may be inherently stronger than that of dogs and that may explain why the perineal herniation occurs less commonly in ruminants and why, when it does occur, AH is usually successful.

The report by Torad *et al*. (2021) is important, because perineal hernia of an equid has not been reported previously, and it should be considered a possible cause of perineal swelling in an equid.

Author's declaration of interests

No conflicts of interest have been declared.

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References

Bongartz, A., Carofiglio, F., Balligand, M., Heimann, M. and Hamaide, A. (2015) Use of autogenous fascia lata graft for perineal herniorrhaphy in dogs. *Vet. Surg.* **34**, 405–413.

Dabas, V.S., Ashwar, B.K. and Tadkod, D.M. (1996) Repair of Perineal Hernia in three Kankrej Cows. *Indian J. Vet. Surg.* **17**, 48–49.

Dyce, K.M., Sack, W.O. and Wensing, C.J.G. Eds. (2009) The locomotor apparatus. In: *Textbook of Veterinary Anatomy*, 4th edn., Saunders, Canada, ON. pp 51–56.

Gill, S.S. and Barstad, R.D. (2018) A review of surgical management of perineal hernia in dogs. *J. Am. Anim. Hosp. Assoc.* **54**, 179–187.

Igna, C., Bumb, D., Proteasa, A., Dascalu, R. and Schuszler, L. (2015) Biomechanical testing to failure of the pelvic diaphragm in dogs after three techniques of herniorrhaphy. *Lucrari Sci Vet Med* **4**, 70–76.

Kelmer, G. and Schumacher, J. (2008) Repair of Abdominal Wall Hernias in Horses using Primary Closure and Subcutaneous Implantation of Mesh. *Vet. Rec.* **163**, 677–679.

Kelmer, G., Kramer, J. and Wilson, D.A. (2008) Diaphragmatic hernia: etiology, clinical presentation and diagnosis. *Compendium Equine* **3**, 28–36.

Lee, A.J., Chung, W.H., Kim, D.H., Lee, K.P., Suh, H.J., Do, S.H., Eom, K.D. and Kim, H.Y. (2012) Use of canine small intestinal submucosa allograft for treating perineal hernias in two dogs. *J. Vet. Sc.* **13**, 327–330.

Malik, V., Purohit, S., Panday, R.P. and Singh, B. (2012) Surgical management of perineal hernia using nylon mesh in a buffalo. *Indian J. Vet. Surg.* **33**, 71.

Milgram, J., Keinan, Y., Bitton, E. and Shipov, A. (2019) Use of the superficial gluteal muscle for the repair of ventral perineal hernia in dogs: a cadaveric study and case report. *Vet. Surg.* **48**, 1091–1170.

Neibauer, G.W., Shibly, S., Seltenhammer, M., Pirker, A. and Brandt, S. (2005) Relaxin of prostatic origin might be linked to perineal hernia formation in dogs. *Ann. N.Y. Acad. Sci*. **1041**, 415–422.

Prasad, V.D., Prasad, B.C., Kamalakar, G. and Mahesh, R. (2015) Perineal hernia in a buffalo heifer: a case report. *J. Vet. Sc. Tech.* **4**, 5–8.

Pratummintra, K., Chuthatep, S., Banlunara, W. and Kalpravidh, M. (2013) Perineal hernia repair using an autologous tunica vaginalis communis in nine intact male dogs. *J. Vet. Med. Sc.* **75**, 337–341.

Shnaiderman-Torban, A., Epstein, A. and Kelmer, G. (2015) Thoracotomy for repair of a large dorsal diaphragmatic hernia in an 18-year-old mare. *Equine. Vet. Educ.* **27**, 391–395.

Singh, S., Bishoi, P., Palecha, S., Jhirwal, S.K. and Gahlet, T.K. (2017) Surgical management of perineal hernia- a clinical study of 10 bovines. *Intas. Polivet.* **18**, 362–364.

Sobti, V.K., Singh, K.L., Saini, N.S. and Bansal, P.S. (1994) Surgical management of perineal hernia in buffaloes–A review of five cases. *Indian. J. Vet. Surg.* **15**, 43.

Torad, F.A., Abu-Seida, A.M., Shamaa, A.A., Hassan, E.A. and Abdelgalil, A.I. (2021) Ultrasonography and surgical management of a perineal hernia in a donkey. *Equine. Vet. Educ*. **33**, 456, e313–e316.

Toth, F. and Schumacher, J. (2019) Body wall hernias. In: *Equine Surgery*,5th edn., Eds: J.A. Auer, J.A. Stick, J.M. Kummerle and T. Prange. Elsevier, St. Louis, Missouri. pp 552–554.

Vadalial, J.V., Kumar, V., Dodia, V.D., Padaliya, N.R. and Gameti, K.S. (2017) Surgical management of perineal hernia - a study in four jafarabadi buffaloes. *Intas Polivet* **18**, 365–366.

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Case Report

Open approach to correct traumatic closed tracheal lacerations: A case series

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Keywords: horse; trachea; trauma; surgery; repair

Summary

Reports of tracheal injuries in horses are rare compared with those in small animals and humans. Although uncommon tracheal injuries can be life threatening, if they progress or are not treated. Different treatments have been described depending on the severity of the problem. This report describes the successful surgical treatment of three cases of closed tracheal lacerations through an intraluminal surgical approach.

Abnormalities observed on the initial clinical examination were as follows: subcutaneous emphysema in all cases combined with a moderate increase in respiratory rate (about 36 breaths/min). Respiratory distress was evident in all three horses in more stressful situations. Upper-airway endoscopy was performed in all cases and a defect in the dorsal aspect of the trachea was observed (**Fig 1**).

Surgical repair of the tracheal laceration was performed in all three cases. Prior to the anaesthesia, the respiratory distress was obvious but it was not deemed necessary to perform a tracheostomy prior to surgery. The distance to the tracheal laceration was measured with the endoscope to determine the location of the surgical approach. The skin of the ventral aspect of the neck at the distance from the nostrils previously measured was incised and dissection was continued to gain access to the tracheal lumen. The laceration defect was evaluated, debrided with a scalpel blade if necessary and closed with the placement of two interrupted sutures using polyglyconate USP 3-0. In one case, the surgical glue n-Butyl-2 cyanoacrylate was applied over the sutures (**Fig 2**). The subcutaneous emphysema and the respiratory distress were completely resolved at the time of discharge.

Several treatment options have been described, depending on the degree of perforation and the severity of the clinical signs, mainly respiratory distress and associated risk of asphyxia. In conclusion, surgical primary closure with open approach should be considered as a treatment option when large defects of the tracheal mucosa are present due to blunt trauma.

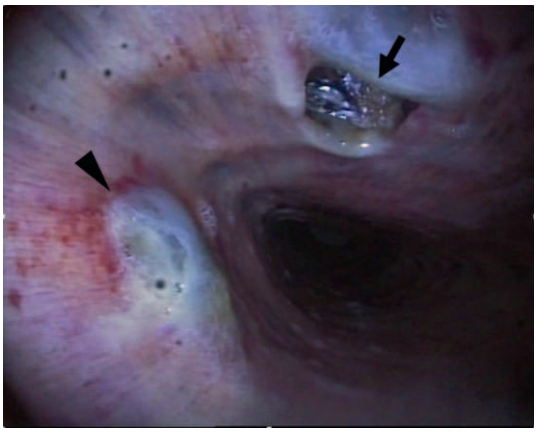

Fig 1: Endoscopic view of the defect in the dorsal aspect of the trachea (black arrow). There is also another site of superficial mucosal erosion compatible with damage to the mucosa without disruption of the mucosal wall (arrowhead).

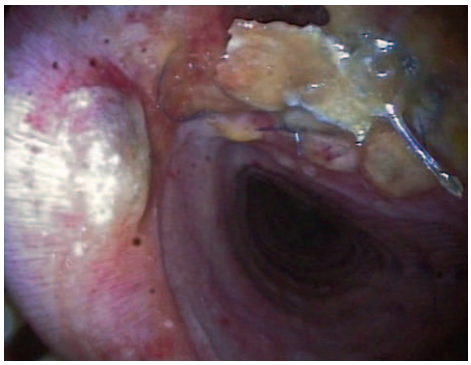

Fig 2: Endoscopic image on the second examination at Days 11 post-operatively: fibrin is covering the sutures and the surgical glue. Minimal inflammatory reaction around the sutures is noted. A small defect can still be observed in the trachea near to the sutures.

Key points

- Closed lacerations of the trachea should be considered in the differential diagnosis of emphysema in the head and neck region in horses.
- Several treatment options are available depending on the severity of the disease and the clinical presentation.
- The open surgical technique described in the Case Report allows direct closure of the laceration with either sutures or a combination of sutures and medical glue.

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Clinical Commentary

Tracheal perforations: Finding the ideal treatment option

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The article in this issue by Iglesias-García *et al*. (2021) describes a case series of three horses that presented with subcutaneous emphysema due to dorsal tracheal perforations. All horses underwent surgical repair under general anaesthesia and trans-tracheal endoscopic guidance. Repair was performed via a window created by removal of the ventral third of the opposing tracheal ring. All three horses progressed well post-operatively. This case series adds another treatment option to the management strategies for tracheal perforation. The merits and potential drawbacks of these treatment options will be discussed.

Tracheal perforations in horses are most frequently due to trauma (Trostle *et al*. 1995; Saulez *et al*. 2005, 2009). Perforations can result in air efflux into the subcutaneous tissues, resulting in subcutaneous emphysema (Trostle *et al*. 1995; Prange 2018). This can then progress to pneumomediastimum and pneumothorax (Caron and Townsend 1984; Hance and Robertson 1992; Trostle *et al*. 1995). Another potential complication is the development of retropharyngeal emphysema (Marble *et al*. 1996). Although tracheal perforations frequently occur in the absence of tracheal ring disruption, it is also important to assess the tracheal rings, where possible, for evidence of fracture (Gillen *et al*. 2015). Furthermore, the presence of more than one tracheal perforation is not uncommon (Gillen *et al*. 2015) and time should be spent thoroughly evaluating the trachea endoscopically to ensure that all perforations have been visualised. In addition, the structures surrounding the trachea are also vulnerable to injury and the occurrence of concurrent oesophageal and tracheal perforations has been documented (Findley and Rubio-Martinez 2013).

Given the range and potential severity of complications discussed above, early intervention is crucial to ascertain the number and location of tracheal perforations, as well as stopping additional air dissecting through muscle and fascial planes. In more severe cases, for example, where a pneumothorax has already occurred, treatment must also focus on stabilisation as well as re-establishing negative pleural pressure (Sprayberry and Barrett 2015). In addition, the majority of cases require anti-inflammatory as well as antimicrobial therapy. Many treatment options for tracheal perforations exist and the clinician's choice of treatment method will depend on the extent and location of the perforation.

Small tracheal perforations can be treated conservatively via a pressure bandage over the affected area (Prange 2018). Unfortunately, it is hard to determine what size of tracheal perforation can be considered 'small' and, therefore, likely to respond favourably to conservative therapy. Caron and Townsend (1984) and Gronvold *et al*. (2005) treated perforations of 1 cm^2 and 1 × 2 cm, respectively, with conservative management, with good results. However, it does not follow that every defect of this size should be managed conservatively. Other factors, including the horse's presenting signs and the location of the perforation, also play a role. The literature suggests particular caution with dorsally located defects (Coco *et al*. 2020). Although conservative therapy has the benefit of low costs and negates the possibility of surgery-related morbidity, it cannot be considered suitable for larger defects. In addition, it is also less likely to be successful when multiple defects are present, particularly if one is located dorsally. Having said this Gronvold *et al*. (2005) reported a case with two tracheal perforations which resolved successfully following conservative management. One of the most crucial aspects of treatment when managing tracheal perforations conservatively is that the horse requires close monitoring to ensure subcutaneous emphysema is not worsening and to ensure that the horse is showing no evidence of respiratory difficulties. If this occurs, the conservative approach should be abandoned and another method used to reduce airflow from the tracheal defect.

Placing a tracheostomy tube either distal to the defect (Saulez *et al*. 2005), or through the perforation, when opposing dorsal and ventral perforations are present distally (Gillen *et al*. 2015), can result in positive outcomes. The approach appears to be particularly beneficial when either the primary defect (Saulez *et al*. 2005), or a secondary defect (Gillen *et al*. 2015), is located dorsally. Documented lesion sizes that have been managed in this way are less than 2 cm^2, as secondary intention healing of the perforation site is still required. The logic of the temporary tracheostomy tube is that it will divert airflow from the site of injury, reducing intraluminal pressure at the location of the lesion, and reducing airflow through the defect. The correct tube to place and its management schedule has not been proven; however, the author has had success with 16–18 mm short cuffed J-shaped endotracheal tubes in horses of approximately 450 kg. These tubes were filled with 15 mL of air to further divert airflow from the perforations. However, there are clear risks to inflating the cuff which should not be ignored. The pressure of the cuff should not be greater than the capillary perfusion pressure (20–30 mmHg) to avoid potential ischaemic necrosis of the trachea (Nordin 1997). This is difficult to assess and the author recommends close monitoring and regular endoscopy to ensure any subcutaneous emphysema is not increasing and also to monitor the integrity of the primary injury and the tracheostomy tube site.

Coco *et al*. (2020) describes the use of a fibrin sealant (Tisseel®[1]) to resolve a 1 × 1.5 cm dorsally located tracheal laceration, in which conservative management had been unsuccessful. Coco *et al*. (2020) found the fibrin sealant easier to apply than using a medicinal gelatin sponge. The strategy used by the authors involved placing an endoscope through a tracheostomy incision and placing a needle, followed by a catheter at a slightly more proximal location, opposite the laceration. Four millilitres of fibrin sealant was

applied to the defect, and Coco *et al*. (2020) reported that the glue hardened quickly. Twenty-four hours following the procedure, endoscopy revealed the sealant to no longer be visible; however, strands of fibrin were visible in the defect. Seven days following the procedure, the defect had filled with granulation tissue and had completely resolved after 24 days. Use of this product in horses is still in its infancy, and the author assumes that the application technique takes some practice; however, this method is an exciting alternative to more traditional techniques.

Perforations of the cervical trachea, where there is minimal loss of tissue and where there is little or no damage to the tracheal rings, can be debrided and sutured with 0 USP (3.5 M) absorbable suture in a simple interrupted pattern (Fubini *et al*. 1985). The location of the defect can present some difficulties, and Prange (2018) describes the necessity of having to rotate the trachea in some cases so achieve sufficient exposure of the lateral or dorsal aspect. In addition, drains may be required for 48–72 h (Prange 2018). Fubini *et al*. (1985) describe using 0USP (3.5 M) polyglactin 910 to close a 15 cm defect in the dorsal aspect of the trachea. In certain cases, when concurrent dorsal and ventral tracheal perforations exist, the ventral perforation can be used as a window through which to suture the dorsal perforation (Gillen *et al*. 2015). In this case, 2-0USP (3 metric) polydioxanone suture was placed in a simple interrupted pattern. In order to gain access to the dorsal aspect of the trachea when a ventral perforation is not present, Iglesias-García *et al*. (2021) removed the ventral aspect of the overlying tracheal ring in order to gain access to, and close, the dorsal perforation. Iglesias-García *et al.* (2021) used 3-0 USP (2M) copolymer of glycolide, ε-caprolactone and trimethylene carbonate in a simple interrupted pattern to close the defects. The ventral surgical site was closed at the end of the procedure. All the patients recovered well. The author suggests this would be a suitable approach when a fracture or marked injury to the ventral aspect of the tracheal ring is present, together with a dorsal perforation. Iglesias-García *et al*. (2021) performed this procedure under general anaesthesia as the patients exhibited respiratory difficulties. The author hypothesises that this procedure may be performed standing in more stable patients.

Larger perforations, particularly those that involve complete rupture between tracheal rings, may require resection and anastomosis (Scott 1978; Kirker-Head and Jakob 1990). This technique, while having positive results in the above reports, should not be undertaken lightly due to the potential morbidities, including difficulty in recovery due to application of a martingale apparatus (Kirker-Head and Jakob 1990), infection, peritracheal abscessation and the formation of intraluminal granulation tissue or mucosal webs (Prange 2018). Kirker-Head and Jakob (1990) describe anastomosis of a lacerated trachea, the free ends of which were separated by 15 cm. A potential complication of tracheal perforations themselves is tracheal stenosis. Barnett *et al*. (2014) describe removal of one tracheal ring to perform a resection and anastomosis to resolve this complication. The duration of convalescence and the degree of management required depend largely on the number of tracheal rings removed but wearing a harness for 3-4 weeks and box rest for a period of at least 4 weeks should be anticipated (Kirker-Head and Jakob 1990; Barnett *et al*. 2014; Prange 2018). Endoscopy, and potentially radiography, should be performed, and the external surgical sites should be completely healed prior to a return to activity.

Differences in healing times when different methods are utilised are hard to ascertain, due to the sparsity of cases and the differences in lesion size; however, I have attempted to briefly review this. The cases treated purely by conservative management had perforations between 1 cm^2 and 1×2 cm. Complete healing times were approximately 28 days; however, one defect had formed a fibrin seal after 8 days. One horse was declared normal after 2 months (Caron and Townsend 1984), and the other had returned to exercise after 3 months (Gronvold *et al*. 2005). The range of healing times achieved when a tracheostomy tube was placed is hugely variable, ranging from 7 (Saulez *et al*. 2005) to 20 days (Gillen *et al*. 2015). The cases with longer durations had concurrent dorsal and ventral perforations. Whether application of a fibrin sealant (Tisseel®[1]) results in a more rapid resolution of a defect is unknown; however, Coco *et al*. (2020) reported the defect to have sealed in 7 days and to have resolved after 24 days. The technique used by Iglesias *et al*. (2020) resulted in a fibrin seal in evidence 2 days following surgical intervention, and by 10–13 days, the dorsal perforations had sealed. The 15 cm perforation discussed by Fubini *et al.* (1985) was discharged from hospital after 9 days, and 12 months later was reported to be exercising as normal. As expected, the perforations which cause sufficient injury to warrant a resection and anastomosis required a longer convalescence period. The case described by Kirker-Head remained in hospital for 35 days and exhibited a 70% reduction in tracheal lumen diameter at this time. Repeat endoscopy 5 months post-operatively revealed minimal cicatrisation at the anastomosis site. The patient described by Barnett *et al*. (2014) received repeat endoscopy at 6 weeks post-operatively, where the anastomosis site exhibited a mucosa web. This was subsequently transected and endoscopy at 24 weeks post-operatively confirmed a well-healed tracheal anastomosis. Unfortunately, the number of cases managed with different surgical techniques are too small to draw firm conclusions as to the optimum treatment method; however, the more recent technique described by Iglesias-García *et al*. (2021) shows promise.

As shown by Iglesias-García *et al*. (2021), cases of tracheal perforation typically have a good prognosis when treated promptly and appropriately. It is also important to be aware of potential injury to surrounding structures, and the possibility of subcutaneous emphysema resulting in pneumomediastinum and pneumothorax. Close monitoring, anti-inflammatory and anti-microbial therapy, as well as closing, or diverting the airflow from, the perforation are the mainstays of therapy. Iglesias-García *et al*. (2021) introduce an excellent technique to manage dorsal tracheal perforations, or concurrent, opposing dorsal and ventral tracheal perforations.

Author's declaration of interests

No competing interests have been declared.

Ethical animal research

Not applicable.

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Manufacturer's address

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References

Barnett, T.P., Hawkes, C.S. and Dixon, P.M. (2014) Tracheal resection and anastomosis after traumatic tracheal stenosis in a horse. *Vet. Surg.* **44**, 265-269.

Caron, J.P. and Townsend, H.G.G. (1984) Tracheal perforation and widespread subcutaneous emphysema in a horse. *Can. Vet. J.* **25**, 339-341.

Coco, L., Dahmen, K., Bach, N., Fischer, H., Albanese, V., Dylewski, L. and Munoz, E. (2020) Use of fibrin sealant in a horse with an intratracheal dorsal laceration. *Equine Vet. Educ.* **32**(**6**), O50-O55. https://doi.org/10.1111/eve.13006

Findley, J.A. and Rubio-Martinez, L.M. (2013) Diagnosis of concurrent oesophageal and tracheal rupture in a horse. *Vet. Rec. Case Reports* **1**, e000007.

Fubini, S.L., Todhunter, R.J., Vivrette, S.L. and Hackett, R.P. (1985) Tracheal rupture in two horses. *J. Am. Vet. Med. Assoc.* **187**, 69-70.

Gillen, A., Munsterman, A., Pinto, N., Caldwell, F., Wooldridge, A., Cumming, R. and Hanson, R. (2015) Management of opposing full-thickness tracheal perforations in two horses. *Equine Vet. Educ.* **27**, 561-565.

Gronvold, A.M.R., Kohler, C.F. and Hanche-Olsen, S. (2005) Conservative treatment of tracheal perforation in a 13-year-old hunter stallion. *Equine Vet. Educ.* **17**, 142-145.

Hance, S.R. and Robertson, J.T. (1992) Subcutaneous emphysema from an axillary wound that resulted in pneumomediastinum and bilateral pneumothorax in a horse. *J. Am. Vet. Med. Assoc.* **200**, 1107-1110.

Iglesias-García, M., Lepage, O.M., Ezquerra Calvo, L.J. and Munoz Morán, J.A. (2021) Open approach to correct traumatic closed tracheal lacerations: a case series. *Equine Vet. Educ*. **33**, 459, e317–e320.

Kirker-Head, C.A. and Jakob, T.P. (1990) Surgical repair of rupture trachea in a horse. *J. Am. Vet. Med. Assoc.* **196**, 1635-1638.

Marble, S.L., Edens, L.M., Shiroma, J.T. and Savage, C.J. (1996) Subcutaneous emphysema in a neonatal foal. *J. Am. Vet. Med. Assoc.* **208**, 97-99.

Nordin, U. (1997) The trachea and cuff-induced tracheal injury. An experimental study on causative factors and prevention. *Acta Otolaryngol. Suppl.* **345**, 1-71.

Prange, T. (2018) Trachea. In: *Equine Surgery*, 5th edn., Eds: J.A. Auer, J.A. Stick, J.M. Kummerle and T. Prange, Elsevier, St. Louis, Missouri. pp 798-835.

Saulez, M.N., Slovis, N.M. and Louden, A.T. (2005) Tracheal perforation managed by temporary tracheotomy in a horse. *J. S. Afr. Vet. Assoc.* **76**, 113-115.

Saulez, M.N., Dzikiti, B. and Vogt, A. (2009) Traumatic perforation of the trachea in two horses caused by orotracheal intubation. *Vet. Rec.* **164**, 719-722.

Scott, E. (1978) Ruptured trachea in the horse: a method of surgical reconstruction. *Vet. Med. Small Animal Clin.* **73**, 485-489.

Sprayberry, K.A. and Barrett, E.J. (2015) Thoracic trauma in horses. *Resp. Med. Surg.* **31**, 199-219.

Trostle, S., Semrad, S. and Hendrickson, D. (1995) Tracheal perforation in horses. *Comp. Cont. Educ. Pract. Vet.* **17**, 952-958.

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Case Report

Surgical treatment of a mammary gland comedocarcinoma in an Arabian mare: Post-operative management, and histopathological and immunohistochemical features

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Keywords: horse; comedocarcinoma; histopathology; mare; surgery

Summary

A lactating 20-year-old, brown, Arabian mare, weighing about 300 kg, presented for bleeding from one teat and massive swelling of the mammary gland. The mare had untreated mastitis 10 months previously. Subsequently, a gangrenous teat developed following chronic discharge of bloody and purulent material. The teat was removed surgically by the field veterinarian. At that time, the mammary gland increased in size. Bloody and purulent discharges restarted 10 days prior to examination. Under general anaesthesia, the entire mammary gland was removed (**Fig 1**). Comedocarcinoma was diagnosed after histopathological assessment (**Fig 2**).

Immunohistochemical staining was performed for pan-cytokeratin and vimentin. Microscopic examination of immunohistochemical stained slides revealed expression of pan-cytokeratin.

In conclusion, this report described the clinical, macroscopic, histopathological and immunohistochemical characteristics of comedocarcinoma that did not metastasise to regional lymph nodes.

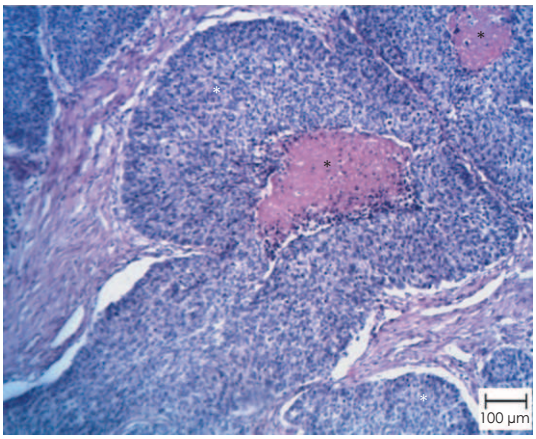

Fig 2: Comedocarcinoma of the mammary gland of a mare. Proliferative cells (white asterisks) are present in sheets and nests of cells. Note the existence of necrotic areas in the centre of neoplastic cells (black asterisks)

Fig 1: Cross section of comedocarcinoma of the mammary gland of a mare. Cut surface of the mass shows firm, yellow and solid lobules with different sizes which are surrounded by a thick capsule (E). Also in some parts, cavitation (C) is present and they are filled with purulent (P) or serosanguinous fluids. A deep ulcer (U) is seen in the ventral part of mass

Key points

- Mammary tumours in mares are rare (0.11%).
- Comedocarcinoma is one of the mammary malignant epithelial tumours. It is characterised by the presence of necrotic areas within the centre of the neoplastic cell aggregates. The necrotic foci consist of amorphous eosinophilic material admixed with cell debris.
- The comedocarcinoma reported in this paper showed an epithelial and mesenchymal origin.

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Clinical Commentary

The known unknowns of equine mammary neoplasia

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Keywords: horse; carcinoma; mammary gland; mastitis; tumour

Introduction

Primary equine mammary tumours are rare entities that are considered to have a poor prognosis (Shank 2009). In the case report associated with this clinical commentary, the authors describe the clinical presentation, management and histopathological assessment of a comedocarcinoma arising in the mammary gland of a 20-year-old Arabian mare (Sabiza *et al*. 2021). In their article, the authors allude to some of the challenges of diagnosis and prognostication in cases of equine mammary neoplasia. In spite of a number of detailed descriptions of individual cases or case series of equine mammary tumours, there are numerous unanswered questions regarding carcinomas arising in the equine mammary gland, and the concept of 'known unknowns' springs to mind. This clinical commentary will consider a selection of interesting and challenging 'known unknowns' relating to the pathogenesis, diagnosis and prognosis of equine mammary tumours.

The relationship between mammary tumourigenesis and mare reproductive history is currently undetermined

At the time of presentation for investigation of mammary enlargement and bleeding from the teat, the mare in the associated case report was lactating (Sabiza *et al*. 2021). This highlights an interesting question regarding the role, if any, of parity as a risk factor for equine mammary tumour development. In dogs and cats, the currently available data suggest that parity is not a risk factor for mammary tumourigenesis (Taylor *et al*. 1976; Overley *et al*. 2005). By contrast, in humans, there is an elevated breast cancer risk associated with lifetime nulliparity, and for women who have had their first childbirth at a more advanced age. Thus, for younger women having a full-term pregnancy has a relative 'protective' effect against breast cancer, quantified as a 50% reduced risk for women who had their first full-term pregnancy whilst under 20 years old (Subramani and Lakshmanaswamy 2017). Childbirth at any age is associated with a transiently increased breast cancer risk and, in essence, this phase of elevated risk extends for women who are older at the time of their first full-term pregnancy (Borges *et al*. 2020).

Identification of such patterns requires large and sophisticated epidemiological studies (Lambe *et al*. 1994), and execution of similar veterinary investigations is often challenging. The associated difficulties are compounded and elevated in the case of rare veterinary tumour types where limited numbers of cases are recorded. Furthermore, in many cases, equine patients will have multiple owners over the course of a lifetime, and a complete reproductive history may be unavailable to the attending veterinarian and cannot be accurately documented for research purposes. At present, there is therefore insufficient evidence available to interrogate any potential relationship between mammary tumourigenesis and parity in the mare.

Initial clinical distinction between mastitis and mammary neoplasia may be challenging

In the mare, clinical distinction between mastitis and mammary neoplasia may be difficult (Reppas *et al*. 1996; Kato *et al*. 1998; Hirayama *et al*. 2003; Shank 2009; Hughes *et al*. 2015; Sabiza *et al*. 2021). Indeed, it has been suggested that horse owners and those caring for horses may associate any form of mammary gland enlargement with mastitis (Canisso *et al*. 2021). The presence of discharge from mammary tumours, potentially associated with draining sinus tracts, necrosis and/or secondary infection, may complicate the clinical picture. Whilst non-specific clinical signs such as ventral or hindlimb oedema are unhelpful and may be associated with a diagnosis of a mammary tumour (Munson 1987) or mastitis (Mccue and Wilson 1989), some authors have postulated that ulceration of the overlying skin may be more indicative of a mammary tumour than of mastitis (Prendergast *et al*. 1999). The two conditions may also occur in tandem, with mastitis arising as a consequence of the presence of mammary neoplasia.

An erroneous diagnosis of primary mastitis may lengthen the time to correct diagnosis of a mammary tumour and may consequently delay surgical removal of the mass, if this treatment is selected as appropriate (Shank 2009). In this regard, cytology can be a valuable tool in distinguishing some cases of mastitis from cases of mammary neoplasia. Although the secretions from a mastitic mamma have an inconsistent composition and may therefore appear cytologically normal in some cases, in other instances mastitic secretions are characterised by the presence of viable and degenerate neutrophils, necrosis and/or other degenerate debris. By contrast, cytology from neoplastic masses may reveal an abnormal population of cells exhibiting criteria of malignancy although, again, in some cases it is not helpful (Freeman 2002; Shank 2009). The distinction is not absolute and, in general, chronic inflammatory processes may also result in some degree of cytological cellular atypia. Nonetheless, cytology may be a valuable tool in assessment of mammary enlargement and discharge.

A specific framework for phenotyping equine mammary tumours is yet to be established

Surgical excision of mammary masses in mares has been suggested to be the most viable therapeutic modality in

appropriately selected surgical candidates (Sysel *et al*. 1993; Shank 2009). In the associated clinical report, a radical mastectomy was undertaken and subsequently histological sections from the mass were examined (Sabiza *et al*. 2021). Currently, there is no classification system for the morphological diagnosis of equine mammary tumours, although veterinary pathologists tend to employ morphological diagnoses similar to those used in canine and feline systems (Goldschmidt *et al*. 2017).

Most primary mammary tumours are carcinomas and adenocarcinomas of epithelial origin, and therefore express pan-cytokeratin, as in the case described in the associated report (Sabiza *et al*. 2021). In the non-neoplastic mammary gland, the epithelial component comprises a bilayer (**Figs 1** and **2)** and the luminal and basal epithelia are distinguished by differing expression patterns of specific cytokeratins. Consequently, expression patterns of specific cytokeratins can potentially be employed to identify carcinomas of luminal and basal origin.

Cytokeratins 8 and 18 are two exclusively luminal markers in the human breast (Dontu and Ince 2015), and cytokeratin 8 has previously been demonstrated to be similarly expressed in non-neoplastic equine mammary luminal epithelia (Hirayama *et al*. 2003). Cytokeratin 18 expression has been reported to be negative in frozen sections of normal equine mammary gland (Bussche *et al*. 2017). We have detected weak cytokeratin 8/18 expression in luminal epithelial cells using sections from formalin-fixed, paraffin-embedded tissue (**Fig 1**). An equine mammary carcinoma expressing cytokeratin 18 has been described (Bussche *et al*. 2017).

Cytokeratin 14 is frequently used as a marker of basal, or myoepithelial, cells in the adult mouse (Gusterson and Eaves 2018). In humans, cytokeratin 14 is not exclusively expressed by basal epithelia, being expressed in basal epithelia in large ducts but in the luminal layer in lobules (Dontu and Ince 2015). In the horse, cytokeratin 14 appears to be expressed predominantly in the basal compartment (**Fig 2**) (Hirayama *et al*. 2003; Hughes *et al*. 2015) and mammary carcinomas expressing cytokeratin 14 have been described (Hughes *et al*. 2015). Alpha-smooth muscle actin is also expressed by most mammary basal epithelial cells, and it confers the contractile properties required for the expulsion of milk (Gusterson *et al*. 2005; Stewart *et al*. 2019; Hitchcock *et al*. 2020). Alpha-smooth muscle actin expression has previously been demonstrated in normal equine mammary gland (Kato *et al*. 1998; Hirayama *et al*. 2003) (**Fig 1**).

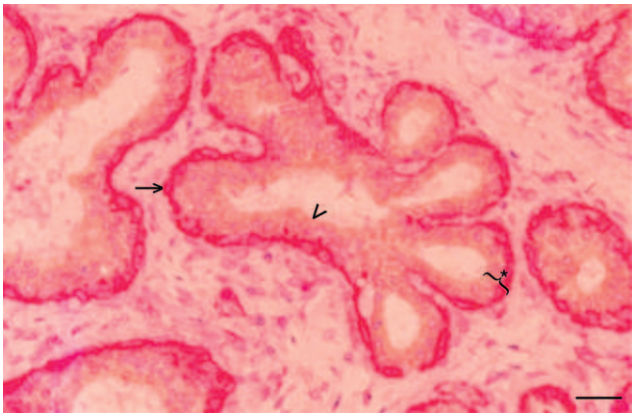

Fig 1: Luminal equine mammary epithelial cells weakly express cytokeratin 8/18, and basal mammary epithelial cells express alpha-smooth muscle actin. Dual immunohistochemical staining for cytokeratin 8/18 (brown; arrowhead) and alpha-smooth muscle actin (pink; arrow) in non-neoplastic equine mammary tissue. The mammary epithelial bilayer is indicated by a bracket and an asterisk. Haematoxylin counterstain. Scale bar indicates 50 μm.

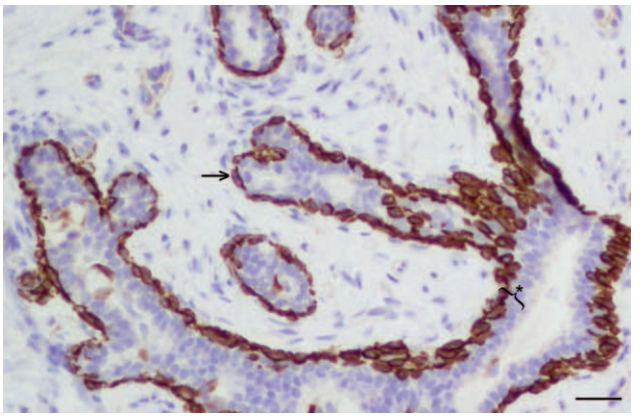

Fig 2: Basal equine mammary epithelial cells express cytokeratin 14. Immunohistochemical staining for cytokeratin 14 (brown) (Hughes et al. 2015) to delineate the basal epithelial cells (arrow) in non-neoplastic equine mammary tissue. The mammary epithelial bilayer is indicated by a bracket and an asterisk. Haematoxylin counterstain. Scale bar indicates 50 μm.

Taken together, these data suggest that assessment of expression of specific cytokeratins and contractile proteins such as alpha-smooth muscle actin would be a fruitful focus for further investigations delineating the histological phenotype, and cell type of origin, of equine mammary tumours. Given that commercial antibodies are most usually developed for use in human or murine tissues, it is vital that any such studies follow rigorous protocols and that antibodies are tested and standardised on equine tissues representing appropriate positive and negative controls (Ramos-Vara 2017).

Prognostic factors for mammary tumours are currently lacking

In their report, Sabiza *et al*. (2021) evaluated tubule formation, nuclear pleomorphism and mitotic count in histological sections from the mammary mass. These morphological features reflect degree of differentiation and form the basis of the Elston and Ellis system for grading breast cancer (Elston and Ellis 1991). However, although the Elston and Ellis system has been applied to veterinary mammary cancers, such as feline mammary neoplasia, authors studying mammary tumours in that species have recently proposed that adaptions to the grading system may provide more accurate prognostic value (Mills *et al*. 2015; Dagher *et al*. 2019). This illustrates the difficulties associated with applying a grading scheme designed for one species to the same tumour type occurring in a different species. Whilst the broad framework may be helpful, parameters, and cut-off points for numerical values such as mitotic count, are likely to require modification in order to offer optimum prognostic value. As noted, currently no such grading framework exists for mammary tumours arising in mares (Sabiza *et al*. 2021).

In addition to morphological assessment, expression of molecular markers may be evaluated in tissue sections to guide prognostication. Currently, robust data regarding such prognostic markers are lacking for equine mammary tumours. We have previously demonstrated that a subset of equine mammary carcinomas exhibit nuclear expression of STAT3 (Hughes *et al*. 2015), suggesting that this transcription factor, frequently constitutively active in invasive breast cancer in women (Watson and Miller 1995) might also be activated in some equine mammary tumours. However, we have yet to evaluate the use of STAT3 immunohistochemical staining as a prognostic marker for equine mammary tumours.

Other authors have utilised quantitative reverse transcription-polymerase chain reaction to demonstrate reduction in p53 expression in a single equine mammary tumour compared with adjacent non-neoplastic tissue. This observation indicates that evaluation of p53 expression in a larger set of tumours may be warranted (Bussche *et al*. 2017).

Conclusions

It has been previously noted that challenges surrounding the diagnosis and management of equine mammary tumours, particularly in remote areas, may constitute a significant psychological burden to the veterinary clinician as well as having deleterious effects on the patient's owner and/or groom (Boyce and Goodwin 2017). Some of the 'known unknowns' discussed here, particularly those associated with diagnosis and prognostication, contribute to this burden. This consideration, together with the veterinary community's strong desire to further scientific knowledge and to provide the best outcome for our patients, constitute strong drivers for continued research in this field.

Materials and methods for unpublished experiments

Dual immunohistochemical staining for alpha-smooth muscle actin (rabbit monoclonal antibody catalogue number ab124964; 1:2000)[1] and keratin 8/18 (mouse monoclonal antibody catalogue number #4546; 1:50)[2] was conducted using a standard protocol and an ImmPRESS Duet Double Staining Polymer Kit[3]. Negative control slides were prepared using species-matched immunoglobulins.

Authors' declarations of interests

No conflicts of interest have been declared.

Ethical animal research

Sections used for immunohistochemistry were obtained from tissues that were surplus to diagnostic requirements collected from cases examined post-mortem by the anatomic pathology service of the Department of Veterinary Medicine, University of Cambridge.

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Owner informed consent

Consent for retention of tissues for teaching and research purposes was granted at the time of submission for post-mortem examination.

Manufacturers' addresses

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[2]Cell Signaling Technology, Danvers, Massachusetts, USA.
[3]Vector Laboratories, Peterborough, Cambridgeshire, UK.

References

Borges, V.F., Lyons, T.R., Germain, D. and Schedin, P. (2020) Postpartum involution and cancer: an opportunity for targeted breast cancer prevention and treatments? *Cancer Res.* **80**, 1790-1798.

Boyce, S.D. and Goodwin, S.L. (2017) Mammary gland neoplasia in a Canadian mare: challenges of diagnosis and treatment in a rural setting. *Can. Vet. J.* **58**, 628-630.

Bussche, L., Harms, C., Buckles, E.L., Whelchel, D., Brosnahan, M. and Van De Walle, G.R. (2017) Carcinoma of the mammary gland in a mare. *Equine Vet. Educ.* **29**, 370-375.

Canisso, I.F., Podico, G. and Ellerbrock, R.E. (2021) Diagnosis and treatment of mastitis in mares. *Equine Vet. Educ.* **33**, 320-326.

Dagher, E., Abadie, J., Loussouarn, D., Campone, M. and Nguyen, F. (2019) Feline invasive mammary carcinomas: prognostic value of histological grading. *Vet. Pathol.* **56**, 660-670.

Dontu, G. and Ince, T.A. (2015) Of mice and women: a comparative tissue biology perspective of breast stem cells and differentiation. *J. Mammary Gland Biol. Neoplasia.* **20**, 51-62.

Elston, C.W. and Ellis, I.O. (1991) Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology* **19**, 403-10.

Freeman, K.P. (2002) Cytological evaluation of the equine mammary gland. *Equine Vet. Educ.* **14**, 97-98.

Goldschmidt, M.H., Pena, L. and Zappulli, V. (2017) Tumors of the mammary gland. In: *Tumors in Domestic Animals*, 5th edn., Ed: D.J. Meuten, John Wiley & Sons Inc., Ames, Iowa. pp 723-765.

Gusterson, B. and Eaves, C.J. (2018) Basal-like breast cancers: from pathology to biology and back again. *Stem Cell Rep.* **10**, 1676-1686.

Gusterson, B.A., Ross, D.T., Heath, V.J. and Stein, T. (2005) Basal cytokeratins and their relationship to the cellular origin and functional classification of breast cancer. *Breast Cancer Res.* **7**, 143-148.

Hirayama, K., Honda, Y., Sako, T., Okamoto, M., Tsunoda, N., Tagami, M. and Taniyama, H. (2003) Invasive ductal carcinoma of the mammary gland in a mare. *Vet. Pathol.* **40**, 86-91.

Hitchcock, J.R., Hughes, K., Harris, O.B. and Watson, C.J. (2020) Dynamic architectural interplay between leucocytes and mammary epithelial cells. *FEBS J.* **287**, 250-266.

Hughes, K., Scase, T.J. and Foote, A.K. (2015) Estrogen receptor and signal transducer and activator of transcription 3 expression in equine mammary tumors. *Vet. Pathol.* **52**, 631-634.

Kato, M., Higuchi, T., Hata, H., Ishikawa, Y. and Kadota, K. (1998) Lactalbumin-positive mammary carcinoma in a mare. *Equine Vet. J.* **30**, 358-360.

Lambe, M., Hsieh, C., Trichopoulos, D., Ekbom, A., Pavia, M. and Adami, H.O. (1994) Transient increase in the risk of breast cancer after giving birth. *N. Engl. J. Med.* **331**, 5-9.

Mccue, P.M. and Wilson, W.D. (1989) Equine mastitis–a review of 28 cases. *Equine Vet. J.* **21**, 351-353.

Mills, S.W., Musil, K.M., Davies, J.L., Hendrick, S., Duncan, C., Jackson, M.L., Kidney, B., Philibert, H., Wobeser, B.K. and Simko, E. (2015) Prognostic value of histologic grading for feline mammary carcinoma: a retrospective survival analysis. *Vet. Pathol.* **52**, 238-249.

Munson, L. (1987) Carcinoma of the mammary gland in a mare. *J. Am. Vet. Med. Assoc.* **191**, 71-2.

Overley, B., Shofer, F.S., Goldschmidt, M.H., Sherer, D. and Sorenmo, K.U. (2005) Association between ovarihysterectomy and feline mammary carcinoma. *J. Vet. Intern. Med.* **19**, 560-563.

Prendergast, M., Bassett, H. and Larkin, H.A. (1999) Mammary carcinoma in three mares. *Vet. Rec.* **144**, 731-732.

Ramos-Vara, J.A. (2017) Principles and methods of immunohistochemistry. *Methods Mol. Biol.* **1641**, 115-128.

Reppas, G.P., Mcclintock, S.A., Canfield, P.J. and Watson, G.F. (1996) Papillary ductal adenocarcinoma in the mammary glands of two horses. *Vet. Rec.* **138**, 518-519.

Sabiza, S., Rezaie, A., Naddaf, H., Sajjadi Dezfouli, M. and Kaamyab Niya, M. (2021) Surgical removal of a mammary gland comedocarcinoma in an Arabian mare: Post-operative management, histopathological and immunohistochemical features. *Equine Vet. Educ.* **33**, 463, e321–e325.

Shank, A.M. (2009) Mare mammary neoplasia: difficulties in diagnosis and treatment. *Equine Vet. Educ.* **21**, 475-477.

Stewart, T.A., Hughes, K., Hume, D.A. and Davis, F.M. (2019) Developmental stage-specific distribution of macrophages in mouse mammary gland. *Front. Cell. Dev. Biol.* **7**, 250.

Subramani, R. and Lakshmanaswamy, R. (2017) Pregnancy and breast cancer. *Prog. Mol. Biol. Transl. Sci.* **151**, 81-111.

Sysel, A.M., Moll, H.D., Livesey, M.A., Pringle, J. and Sloane, D.E. (1993) Mastectomy in three of six cases of equine mammary neoplasia. In: Scientific Presentation Abstracts ACVS 1993. *Vet. Surg.* **22**, 370-405.

Taylor, G.N., Shabestari, L., Williams, J., Mays, C.W., Angus, W. and Mcfarland, S. (1976) Mammary neoplasia in a closed beagle colony. *Cancer Res.* **36**, 2740-2743.

Watson, C.J. and Miller, W.R. (1995) Elevated levels of members of the STAT family of transcription factors in breast carcinoma nuclear extracts. *Br. J. Cancer* **71**, 840-844.

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Case Report

Hiatal hernia with focal megaoesophagus in a Friesian stallion

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Keywords: horse; hiatal hernia; megaoesophagus; oesophageal obstruction; Friesian

Summary

A 10-year-old Friesian stallion presented for further diagnosis of chronic recurrent oesophageal obstruction. Oesophageal endoscopy revealed dilation of the distal oesophagus with the mucosa appearing as gastric mucosa in the distal oesophagus. In addition, a moderate amount of feed material was identified in the distal oesophagus. Positive contrast upper gastrointestinal radiography revealed that approximately half of the stomach was herniated cranially through the diaphragm, supporting a diagnosis of hiatal herniation with focal megaoesophagus (**Fig 1**). Conservative management of the disease was recommended including elevating the patient's torso during feeding and provision of mash-only feeds. In addition, it was recommended to wait at least one hour following feedings before any activity such as riding or breeding. Provided that successful control of the megaoesophagus could be achieved with conservative management, surgical repair of the hiatal hernia may be an option for the future. At 5-month follow-up, the stallion was reported to be coping successfully with only intermittent mild oesophageal obstruction episodes and was able to maintain body condition on the mash diet. This is the first report of hiatal herniation in horses. We report the successful conservative management of a stallion with both megaoesophagus and hiatal herniation through elevated feeding and selective exercise management.

Key points

- Although rarely reported in horses, hiatal herniation should be considered as a differential diagnosis in cases of chronic recurrent oesophageal obstruction.
- Both endoscopy and positive contrast upper gastrointestinal radiography may be useful in the diagnosis of hiatal herniation and megaoesophagus in horses.
- Conservative management including elevated feeding, a mash-only diet and modified exercise routines may be successful in managing hiatal hernia and megaoesophagus in the horse.

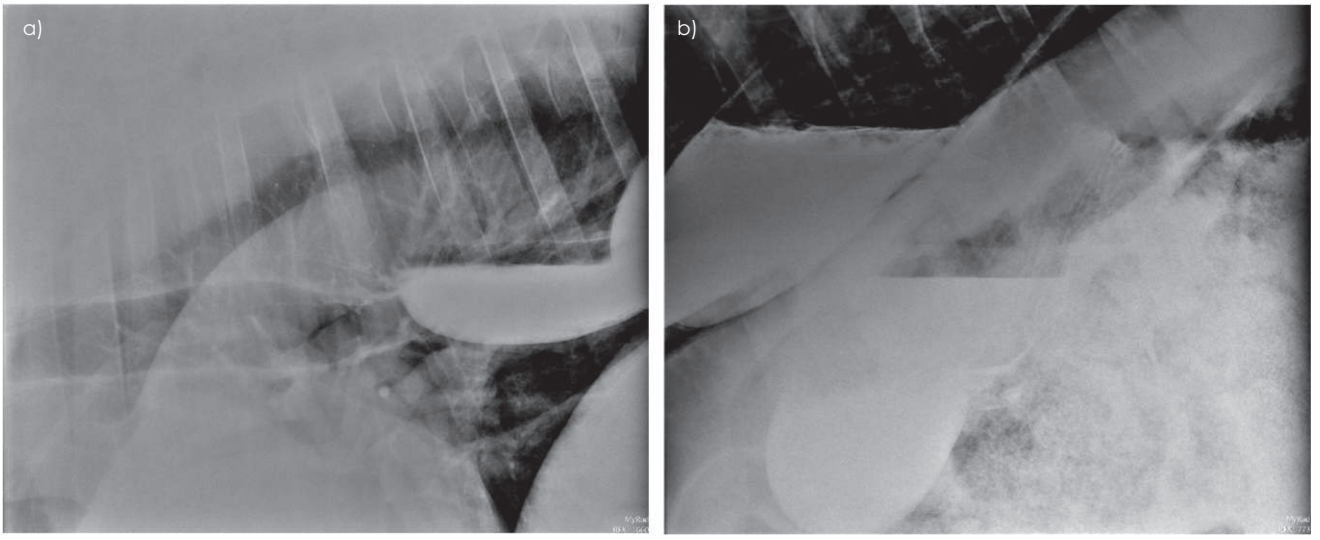

Fig 1: Barium was administered via nasoesophageal tube, and sequential radiographs were taken of the middle and distal oesophagus. Left lateral caudal thoracic radiographs are demonstrated, and cranial is to the left. Persistent oesophageal gas distention is noted, and there is a moderate amount of barium pooling in an ovoid structure cranial to the oesophageal hiatus. The caudal aspect of the structure tapered at the hiatus. Barium and gas are within the stomach caudal to the diaphragm.

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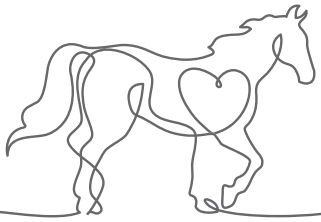

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Clinical Commentary

Diaphragmatic hernia with focal megaoesophagus: An extremely rare combination

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Diaphragmatic defects leading to (diaphragmatic) herniation (DH) of an abdominal organ or bowel is an extremely rare condition in horses. Causes may be either congenital or acquired. Most commonly small intestine herniates into the thorax resulting in incarceration with acute signs of colic. Hiatal herniation (HH), which entails bulging of the upper part of the stomach through the diaphragm, is even more rare in horses, unlike in humans, where it is a well-recognised problem, with a reported prevalence as high as 60% in people >50 years of age. Whether or not human patients develop clinical symptoms such as gastro-oesophageal reflux disease (GERD), depends on the integrity and functionality of the lower oesophageal sphincter (Hai-Xiang *et al*. 2018). Hiatal herniation is rare in horses, and in that respect, the current case report by Lehman *et al*. (2021) is unique in its manifestation. The report describes a 10-year-old Friesian stallion, where apparently parts of the dorsal squamous fundus of the stomach herniated through the diaphragm at the level where typically the oesophagus pass through the diaphragm into the stomach. Cranial (and orad) to the hiatus endoscopy showed a megaoesophagus-like dilation that tapered towards the hiatus with its caudal (aborad) portion showing an inner lining pattern of multidirectional mucosal folding, described as similar in appearance to the gastric mucosa. This, of course, raised the question as to whether HH could be a co-manifestation of megaoesophagus, which is a well-recognised and overrepresented disease in the Friesian horse.

Every intensely selected breed has to deal with breed specific disorders that unwillingly arise together with the selection for the desired genes. The Friesian horse breed originally started its reason for existence as a working horse in agriculture. The breed went through several genetic bottlenecks throughout its history. Ever since 1879, the founding year of the Friesian Stud Book, only a small selection of a few horses were used as bloodstock, probably due to the strict definition of the breed's standards. In 1913, only three stallions were registered. After WWII, a further decline in the Friesian horse population gradually occurred. In 1965, only 500 registered mares were left (Ducro *et al*. 2006). Ever since its foundation, The Royal Dutch Society 'the Dutch Royal Friesian horse-studbook' (KFPS), located in Drachten, Friesland, the Netherlands, records all Friesian horses worldwide. The Friesian breed is quite popular nowadays: there are more than 70,000 Friesian horses registered worldwide. Half of the approximately 4000 foals born annually in the Netherlands are exported to North America. However one should be aware of the fact that the entire population was created and expanded out of a very small post-WWII genetic pool.

Friesian horses are now registered in 72 countries across the world, and the breed is present on all continents. However, the fact that KFPS is a closed stud book causes some problems. The increase in inbreeding has been on average 1.5% per generation since 1920 which is well above the recommended threshold of 1%, leading to a current inbreeding percentage of 16% (Ducro 2014). As a result, the Friesian breed struggles with the manifestation of a number of hereditary disorders of which aortic rupture and megaoesophagus are currently most represented. Both diseases have a prevalence of ±2%, which entails a minimum of 1400 cases for each hereditary trait, and 80 additional cases per trait, on a yearly basis (Ploeg *et al*. 2015a, 2017b).

The current situation represents a serious problem from an animal welfare point of view, since both aortic rupture and megaoesophagus are often fatal; however, it will not be manifest at birth, leaving ample opportunity for either horses that are directly affected or are carriers to have an active breeding career. On top of that, diagnosis of aortic rupture is often missed due to vague, nonspecific clinical signs shown by these horses and by the fact that these pathologies are not well known among equine clinicians who are not that often confronted with Friesian horses. This has already led to many devastating and dangerous situations, such as horses that suddenly collapse and die during exercise (Ploeg *et al*. 2013).

Recently, a nonsense mutation in B3GALNT2 was identified as a specific cause for hydrocephalus in Friesian horses localised on chromosome 1: 68.5–69.7 Mb (Sipma *et al*. 2013; Ducro *et al*. 2015). Mutations in the exact same gene cause muscular dystrophy with hydrocephalus in humans (Stevens *et al*. 2013). Likewise, the responsible mutation for dwarfism has recently been identified. It is located on chromosome 14: 3.5–5.7 Mb in the B4GALT7. The mutated gene affects normal collagen and bone development (Leegwater *et al*. 2016). Both dwarfism and hydrocephalus occur with a much lower prevalence (±0.2%) when compared to aortic rupture and megaoesophagus.

At this point, subsidised DNA testing is available to horse-owners, to stimulate identification of carrier horses for either of these two diseases. Based upon the test results, horse-owners receive (sire and dam combination) breeding advice; however, at this point this breeding advice does not count in prevention of occurrence of aortic rupture and

megaoesophagus. On the contrary, we do not know whether the currently provided breeding advice could actually catalyse occurrence of aortic rupture and megaoesophagus or other less well known, most probably hereditary conditions and diseases in Friesian horses. Examples of these are cryptorchidism (Schurink *et al*. 2016), primary gastric overload (Scheidemann and Huthmann, 2011), umbilical hernia, corneal dystrophy and distichiasis (Lassaline-Utter *et al*. 2014). With that respect, hiatal hernia is extremely rare in the horse, and in the very rare event that it occurs, it usually involves a traumatic rent/enlargement of the diaphragmatic hiatus (Goehring *et al*. 1999). To our knowledge, there is only one other case reported concerning a nontraumatic diaphragmatic hernia in a 3-year-old Friesian mare that had been ridden under the saddle for one month and presented with acute colic to one of the authors. During autopsy, herniation of the large colon through the diaphragm was found. Herniation in this case was not localised at the level of the transdiaphragmatic oesophageal passage (**Fig 1**).

From a physiological point of view, it is important to realise that more and more evidence surfaces that problematic mutations on top of an aberrant connective tissue metabolism seem to be the most probable scenario that causes all these problems in the Friesian breed. Perfectly healthy Friesian horses show an increased connective tissue turn over (Saey *et al*. 2018). It would be understandable that mutations that, for example in other equine breeds do not cause problems, will cause pronounced problems in Friesian horses because they manifest themselves on top of an aberrant connective tissue metabolism. It is also important to realise from a breeding point of view that in an attempt to 'select away' from a certain hereditary disease, one can unwillingly promote occurrence of another or new hereditary problem, especially when the genetic diversity is very limited within a breed.

When taking a closer look at aortic rupture and megaoesophagus, it becomes clear that both of them share features of dysregulated connective tissue metabolism. This should also be kept in mind when looking at this hiatal herniation case report. For aortic rupture, several possible causes have been suggested in the past, such as thrombosis of the vasa vasorum (small blood vessels that feed the aortic wall), or an embryological defect developing during the fusion of the dorsal aorta wall with the developing heart base in cases of aortic rupture (Ploeg *et al*. 2015b, 2017a). For megaoesophagus in the Friesian, a loss of neurogenic input at the level of the interstitial cells of Cajal has been suggested. Another suggestion has been progressive distal muscular hypertrophy at the level of the thoracic part of the oesophagus (Benders *et al*. 2004). However, none of the aforementioned suggestions could be confirmed during large-scale studies that our research group has performed within the Friesian breed (Ploeg *et al*. 2015a,b). In none of these megaoesophagus cases was a hiatal hernia encountered. What is striking though, are the similar findings with respect to histopathology and biochemistry when it comes to extracellular matrix and connective tissue quality in both aortic rupture and megaoesophagus cases (Saey *et al*. 2015, 2016; Ploeg *et al*. 2015a,b; 2017a). Histological features at the site of aortic rupture in Friesian horses are cystic medial necrosis (CMN), disorganisation and fragmentation of elastic laminae, aortic medial smooth muscle hypertrophy and accumulation of mucoid material. In humans, CMN is often associated with connective tissue disorders (Yuan and Jing, 2011). The histological features of CMN were present in aortas of all affected Friesians, which are seemingly suggestive of a primary connective tissue disorder. To further elucidate this, our research group has performed biochemical analysis on both aortic tissue and (lower limb) tendon tissue of affected and healthy Friesian horses, respectively, as well as same tissues in Warmblood horses. This study revealed significant increases in metalloproteinase (MMP) activity and increased lysylpyridinoline (LP) and hydroxylysylpyridinoline (HP) cross-linking, as well as increased lysine hydroxylation and elastin cross-linking at the site of aortic rupture in affected Friesians

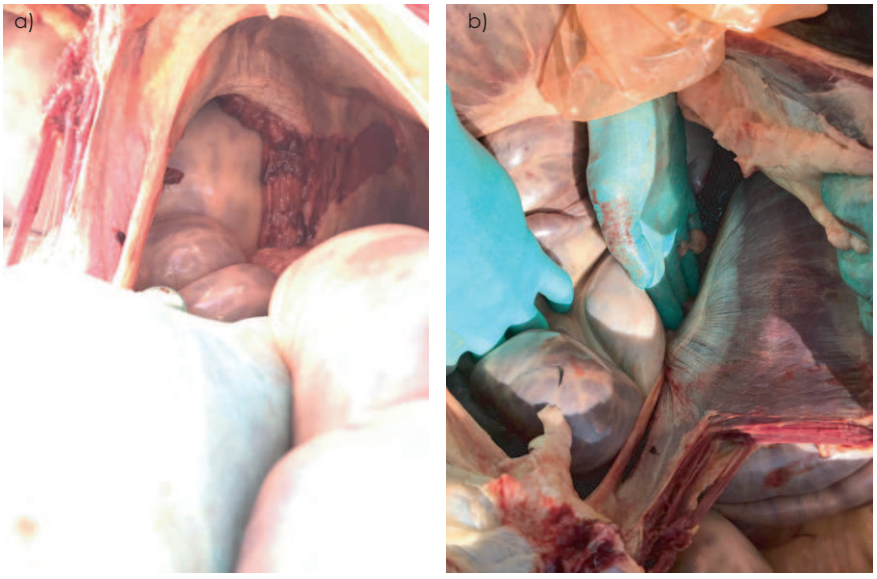

Fig. 1: Diaphragmatic hernia in a 3-year-old Friesian mare. The ascending colon was herniated through the diaphragmatic rent, causing signs of colic.

compared with matched sites in unaffected Friesians. Furthermore, unaffected Friesians showed significantly less lysine hydroxylation and pyrrole cross-linking within the tendons when compared to Warmblood horses, supporting the hypothesis that significant differences in connective tissue metabolism exist between both breeds.

Histopathological examination of megaoesophagus cases revealed features quite similar to those found in aortic rupture cases, for example: increased deposition of disorganised collagen and a decrease in elastin content. Strikingly, these changes were present in not only the dilated but also in the nondilated parts of the oesophagus (Ploeg *et al*. 2015b). These findings provide additional indirect evidence for an underlying systemic connective tissue disorder most probably expressed on top of a connective tissue metabolism that differs from that seen in Warmblood horses. With that respect, for instance, tendons of the Friesian horse are more elastic than their Warmblood counterparts, resulting in a different tendon injury healing and tendon ageing (Gussekloo *et al*. 2011). A recent training trial that our research group executed with Friesian horses has shown a significant upregulation of glycine and proline metabolism in response to training (unpublished data). These increases were not seen in other horse breeds. Chronic progressive lymphoedema (CPL) and corneal dystrophy are two other hereditary traits encountered within the Friesian breed, and both deemed to be based on a connective tissue disorder (Affolter 2013; Lassaline-Utter *et al*. 2014).

As for megaoesophagus, our research group has collected and analysed over 100 cases and we are currently performing genetic screening. The clinical picture of megaoesophagus is quite diverse, manifesting itself at different ages of detection and in degrees of severity. Typically, we encounter three groups of patients.

Starting with the youngest group, the disorder may manifest itself in a two-day-old foal with a completely normal birth process and first day of life but is now slightly febrile, dyspnoeic and on endoscopic examination one will notice milk in the trachea. Evaluating the oesophagus endoscopically is difficult since no real reference frame exists until now to endoscopically assess functional integrity of the oesophagus in the equine neonate. A second commonly encountered patient is the weanling or young Friesian horse which presents with recurrent oesophageal obstruction (choke). Although choke is a common disorder in many horse populations worldwide, this one occurs with roughage or even simply at pasture. Endoscopic examination in the nonsedated horse reveals presence of an asymmetric dilated and less motile oesophagus (**Fig 2**). This megaoesophagus misses the typical longitudinal folding and, in the more severe cases, food and saliva remain in the dilated part, which is typically more pronounced in the distal third of the oesophagus. Finally, there is a third group encountered of middle-aged or elderly horses which may have been thriving quite well until they take an increased amount of time to eat their food, especially concentrate. In doing so, they show extensive salivation and may pause now and then during their meal with their head and neck in an upright position. In contrast to hydrocephalus and dwarfism, two hereditary diseases for which DNA screening exists, aortic rupture and megaoesophagus may represent a far bigger problem since these conditions are rarely visible at birth, allowing for unidentified 'carriers' to potentially have a successful breeding and sports career. Quite often, in these cases a lot of money has been invested in breeding, training and showing. Therefore, the deception and economic losses are enormous and solving this disorder by developing genetic testing early in life should have the utmost priority.

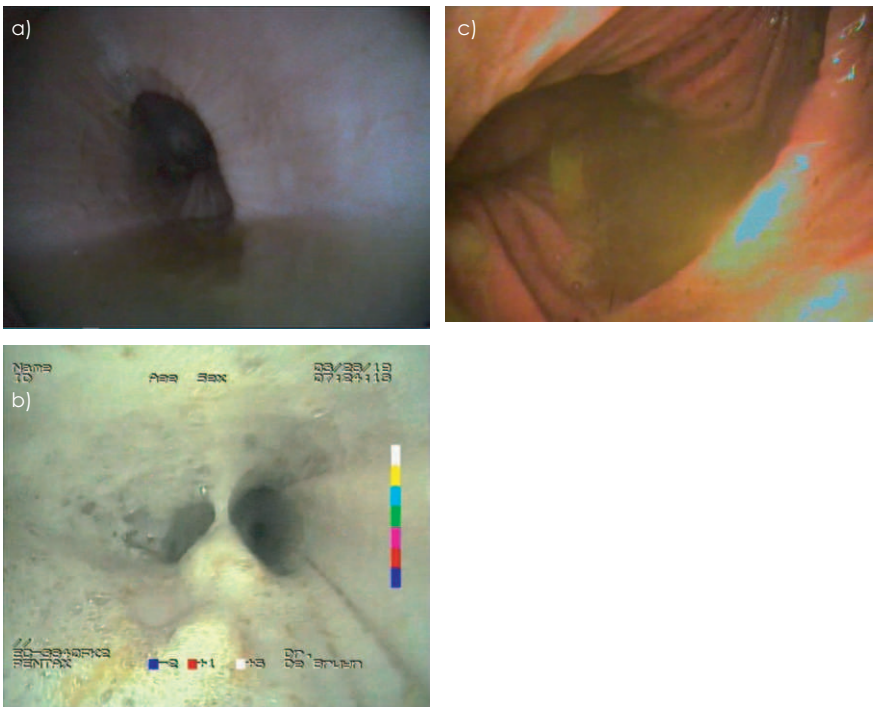

***Fig. 2:** Typical endoscopic images of classical megaoesophagus in the Friesian horse.*

Coming back to the hiatal hernia, the authors mentioned the endoscopic presence of gastric mucosa in the dilated part orad to the hernia port, stressing the idea that a piece of the squamous part of the stomach had herniated through the diaphragmatic defect into the thorax. The authors correctly refer to this as 'focal megaoesophagus', since this is not a typical megaoesophagus. Based upon our research in the past, hiatal hernia is not a co-morbidity with 'classical megaoesophagus' in the Friesian horse. Also, the fact that in none of the megaoesophagus cases that we have been studying in large-scale projects, hiatal hernia was never encountered, supports this vision. In human patients, hiatal herniation is not believed to have a hereditary background and, in the number of cases in which it does, most often there is an association with Ehlers–Danlos syndrome, a well-known genetic connective tissue disorder in people (Nelson *et al*. 2015). So, the case described in the current case report could represent yet another sign of dysregulation of connective tissue metabolism in this specific horse.

Authors' declaration of interests

No conflicts of interest have been declared.

Ethical animal research

Not applicable to this clinical commentary.

Authorship

All authors have contributed to this clinical vision on the case report.

References

Affolter, V.K. (2013) Chronic progressive lymphedema in draft horses. *Vet. Clin. North Am. Equine Pract.* **29**(**3**), 589-605.

Benders, N.A., Veldhuis Kroeze, E.J.B. and van der Kolk, J.H. (2004) Idiopathic muscular hypertrophy of the oesophagus in the horse: a retrospective study of 31 cases. *Equine Vet. J.* **36**(**1**), 46-50.

Ducro, B. (2014) Genetic diversity and measures to reduce inbreeding in Friesian Horses. In *Proc. 10th World Congress of Genetics Applied to Livestock Production*, Vancouver, Canada. pp 797.

Ducro, B.J., Bovenhuis, H., Neuteboom, J.H. and Hellinga, I. (2006) *Genetic diversity in the Dutch Friesian horse*. WUR Staff Publications. https://library.wur.nl/WebQuery/wurpubs/353309.

Ducro, B.J., Schurink, A., Bastiaansen, J.W., Boegheim, I.J., van Steenbeek, F.G., Vos-Loohuis, M., Nijman, I.J., Monroe, G.R., Hellinga, I., Dibbits, B.W., Back, W. and Leegwater, P.A. (2015) A nonsense mutation in B3GALNT2 is concordant with hydrocephalus in Friesian horses. *BMC Genom.* **16**, 761.

Goehring, L.S., Goodrich, L.R. and Murray, M.J. (1999) Tachypnoea associated with a diaphragmatic tear in a horse. *Equine Vet. J.* **34**, 443-445.

Gussekloo, S.W.S., Lankester, J., Kersten, W. and Back, W. (2011) Effect of differences in tendon properties on functionality of the passive stay apparatus in horses. *Am. J. Vet. Res.* **72**(**4**), 474-483.

Hai-Xiang, Yu, Han, Chun-Shan, Xue, Jin-Ru, Han, Zhi-Feng and Xin, Hua (2018) Esophageal hiatal hernia: risk, diagnosis and management. *Expert Rev. Gastroenterol. Hepatol.* **12**, 319-323.

Lassaline-Utter, M., Gemensky-Metzler, A.J., Scherrer, N.M., Stoppini, R., Latimer, C.A., MacLaren, N.E. and Myrna, K.E. (2014) Corneal dystrophy in Friesian Horses may represent a variant of pellucid marginal degeneration. *Vet. Ophthalmol.* **17**, *Suppl*. **1**, 186-194.

Leegwater, P.A., Vos-Loohuis, M., Ducro, B.J., Boegheim, I.J., van Steenbeek, F.G., Nijman, I.J., Monroe, G.R., Bastiaansen, J.W., Dibbits, B.W., van de Goor, L.H., Hellinga, I., Back, W. and Schurink, A. (2016) Dwarfism with joint laxity in Friesian horses is associated with a splice site mutation in B4GALT7. *BMC Genom.* **17**(**1**), 839.

Lehman, M., Hendrickson, D. and Selberg, K. (2021) Hiatal hernia with focal megaoesophagus in a Friesian stallion. *Equine Vet. Educ*. **33**, 468, e326–e330.

Nelson, A.D., Mouchli, M.A., Valentin, N., Deyle, D., Pichurin, P., Acosta, A. and Camilleri, M. (2015) Ehlers Danlos Syndrome and gastrointestinal manifestations: a 20-year experience at Mayo Clinic. *Neurogastroenterol. Motil.* **27**(**11**), 1657-1666.

Ploeg, M., Saey, V., de Bruijn, C.M., Gröne, A., Chiers, K., van Loon, G., Ducatelle, R., van Weeren, P.R., Back, W. and Delesalle, C. (2013) Aortic rupture and aorto-pulmonary fistulation in the Friesian horse: characterisation of the clinical and gross post-mortem findings in 24 cases. *Equine Vet. J.* **45**, 101-106.

Ploeg, M., Gröne, A., Saey, V., de Bruijn, C.M., Back, W., van Weeren, P.R., Scheideman, W., Picavet, T., Ducro, B.J., Wijnberg, I. and Delesalle, C. (2015a) Esophageal dysfunction in Friesian Horses: morphological features. *Vet. Pathol.* **52**(**6**), 1142-1147.

Ploeg, M., Saey, V., Delesalle, C., Gröne, A., Ducatelle, R., de Bruijn, C.M., Back, W., van Weeren, P.R., van Loon, G. and Chiers, K. (2015b) Thoracic aortic rupture and aortopulmonary fistulation in the Friesian horse: histomorphologic characterization. *Vet. Pathol.* **52**(**1**), 152-159.

Ploeg, M., Gröne, A., van de Lest, C.H.A., Saey, V., Duchateau, L., Wolsein, P., Chiers, K., Ducatelle, R., van Weeren, P.R., de Bruijn, C.M. and Delesalle, C. (2017a) Differences in extracellular matrix proteins between Friesian horses with aortic rupture, unaffected Friesians and Warmblood horses. *Equine Vet. J.* **49**, 609-613.

Ploeg, M., Saey, V., van Loon, G. and Delesalle, C. (2017b) Review: Thoracic aortic rupture in horses. *Equine Vet. J.* **49**(**3**), 269-274.

Saey, V., Famaey, N., Smoljkic, M., Claeys, E., van Loon, G., Ducatelle, R., Ploeg, M., Delesalle, C., Gröne, A., Duchateau, L. and Chiers, K. (2015) Biomechanical and biochemical properties of the thoracic aorta in warmblood horses, Friesian horses, and Friesians with aortic rupture. *BMC Vet. Res.* **18**(**11**), 285.

Saey, V., Ploeg, M., Delesalle, C., van Loon, G., Gröne, A., Ducatelle, R., Duchateau, L. and Chiers, K. (2016) Morphometric properties of the thoracic aorta of warmblood and Friesian horses with and without aortic rupture. *J. Comp. Pathol.* **154**(**2–3**), 225-230.

Saey, V., Tang, J., Ducatelle, R., Croubels, S., De Baere, S., Schauvliege, S., van Loon, G. and Chiers, K. (2018) Elevated urinary excretion of free pyridinoline in Friesian horses suggests a breed-specific increase in collagen degradation. *BMC Vet. Res.* **14**, 139.

Scheidemann, W. and Huthmann, S. (2011) A contribution to diseases of the equine stomach: chronic gastric impaction and dilation. *J Vet Int Med* **25**: 617–631. https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1939-1676.2011.0725.x.

Schurink, A., de Jong, A., de Nooij, H.R., Hellinga, I. and Ducro, B.J. (2016) Genetic parameters of cryptorchidism and testis size in Friesian colts. *Livestock Sci.* **190**, 136-140.

Sipma, K.D., Cornillie, P., Saulez, M.N., Stout, T.A., Voorhout, G. and Back, W. (2013) Phenotypic characteristics of hydrocephalus in stillborn Friesian foals. *Vet. Pathol.* **50**(**6**), 1037-1042.

Stevens, E., Carss, K.J., Cirak, S., Foley, A.R., Torelli, S., Willer, T. et al (2013) Mutations in B3GALNT2 cause congenital muscular dystrophy and hypoglycosylation of α-dystroglycan. *Am. J. Hum. Genet.* **92**, 354-365.

Yuan, S.M. and Jing, H. (2011) Cystic medial necrosis: pathological findings and clinical implications. *Braz. J. Cardiovasc. Surg.* **26**, 107-115.

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Case Report

Coronoidectomy as a treatment for mandibular immobility caused by fracture of the coronoid process in three horses

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Keywords: horse; coronoidectomy; coronoid process; fracture; mandible

Summary

Three horses were presented for mandibular deviation and inability or difficulty opening the mouth. The mandible of each horse could be moved neither to the left nor to the right, and the mouth of all horses opened less than 3 cm, prohibiting examination of the cheek teeth. Fracture of the coronoid process was identified by using radiography, ultrasonography, computed tomography, or a combination of two or more of these imaging modalities. Deviation and immobility resulted from impingement of a callus between the temporal bone and zygomatic arch (**Fig 1**). Osteoarthritis of the ipsilateral temporomandibular joint of two horses was identified. All horses were treated by excising the fractured coronoid process, and two were also treated by excising the diseased ipsilateral mandibular condyle (**Fig 2**). To remove the fractured coronoid process of all three horses, the palpable, proximal border of the coronoid process, lying between the zygomatic arch and the skull, was exposed through a longitudinal, cutaneous incision in the supraorbital fossa. The bony bridge between the coronoid process of two horses and surrounding bone was transected by using an osteotome or bone gouge and a mallet. The coronoid process was transected at its base through a longitudinal incision in all three horses but required removal of a portion of the zygomatic arch through a third incision in one horse.

All horses were able to open their mouth more widely immediately after surgery. One horse experienced moderate post-operative haemorrhage, and all had severe shear mouth. Shear mouth was ameliorated gradually over many months by rasping dental overgrowths. Mandibular movement of all horses improved, allowing efficient mastication of feed. One horse was able to be used as a showjumper, one horse was sold at Thoroughbred yearling sales and was lost to follow-up, and one horse died from an unrelated gastrointestinal disease 10 months after mandibular coronoidectomy and condylectomy.

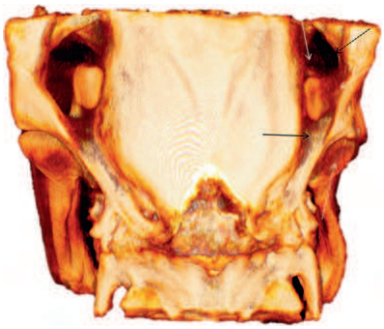

Fig 1: Reconstructed cone-beam computed tomographic image of the dorsal aspect of the caudal part of the skull of horse 2, showing reduction in the size of the right temporal fossa (dotted black arrow) and bony bridging (white arrows), healed fracture of the right zygomatic arch (black arrow), and deformation of the right mandibular condyle (dotted white arrow).

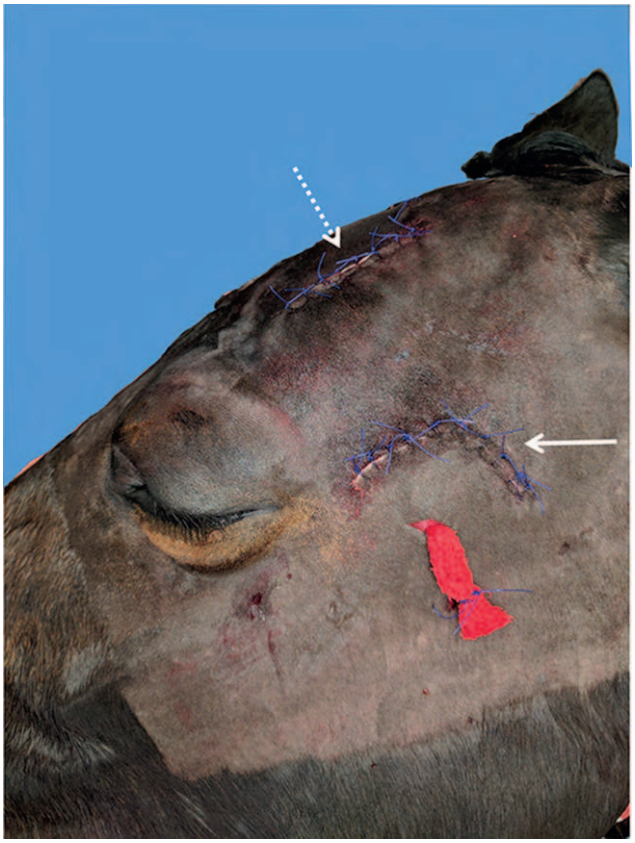

Fig 2: Post-operative view of the surgical approach to the left temporomandibular joint (white arrow) and coronoid process (dotted arrow) of Horse 1.

Key points

- Deviation and immobility of the mandible can be the result of fracture of the coronoid process.
- Fracture of the coronoid process can be associated with osteoarthritis of the ipsilateral temporomandibular joint.
- Coronoidectomy can restore mandibular mobility.

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Case Report

Acute suprarenal occlusion in an American Miniature Horse

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Keywords: horse; thrombus; kidney; azotaemia; pyelonephritis

Summary

A 7-month-old American Miniature filly was examined because of a 4-day history of abnormal posture, lethargy and weakness. On initial evaluation, the filly was quiet and dull but responsive. She presented with an abnormal stiff gait in her hindlimbs associated with grade 3/5 lower motor neuron hindlimb ataxia and lumbar kyphosis. The filly showed hindlimb discomfort by weight shifting from one hindlimb to the other but was not painful on palpation of the musculoskeletal system. She was moderately pyrexic (39.3°C), tachycardic (72 beats/min) and mildly dehydrated (3%). A complete blood count revealed an acute inflammatory leukogram associated with hyperfibrinogenaemia (8 g/L, RR 2–4 g/L). The measurement of the serum amyloid A concentration indicated an active inflammatory process (4895 mg/L, RR 0–8 mg/L). Biochemistry and urinalysis results revealed severe azotaemia (creatinine: 299 μmol/L, RR 75–126 μmol/L; urea: 49.6 mmol/L, RR 5–9.7 mmol/L) associated with diluted urine (USG = 1.013) despite clinical dehydration, consistent with acute renal failure.

Medical treatment was initiated with fluid therapy and antimicrobials. The pain was managed with morphine sulphate only, to avoid further kidney damage. Measurement of urea and creatinine were repeated during hospitalisation and were back to normal after 5 days of fluid therapy; however, SAA and fibrinogen values remained increased (SAA: 2201 mg/L; fibrinogen: 6.8 g/L). During hospitalisation, the filly maintained an abnormal gait, became progressively more ataxic and uncomfortable, and developed colic episodes. Because the horse was unresponsive to pain management, euthanasia was elected by the client.

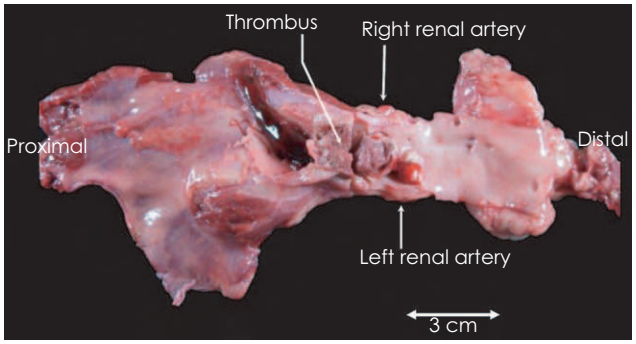

Fig 1: Post-mortem photograph of the abdominal aorta at the level of the aortic thrombus, dorsal view with dorsal wall removed.

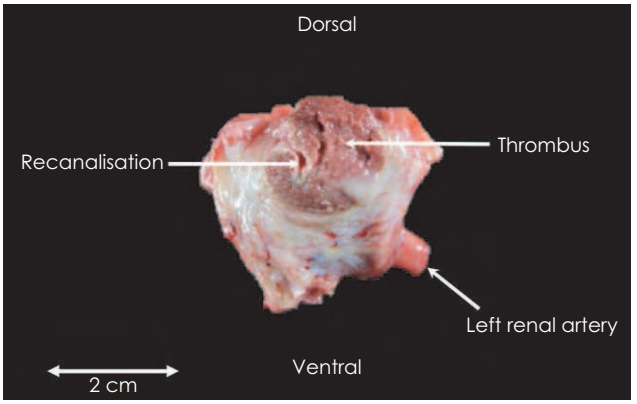

Fig 2: Post-mortem photograph of the abdominal aorta, transverse section through the aortic thrombus showing recanalisation and purulent material.

Post-mortem examination revealed an occlusive pink thrombus (18 mm diameter × 30 mm long) within the abdominal aorta, firmly attached to the intima, partially recanalised and extending from the aorta 1 cm along the right renal artery (**Figs 1** and **2**). In the left and right kidneys severe subacute neutrophilic pyelonephritis, with lymphoplasmacytic interstitial nephritis was noted. In the hindlimb muscles, multifocal myocyte necrosis and evidence of regeneration were present. To the authors' knowledge, this is the first case of acute suprarenal occlusion to be described in a horse.

Key points

- Acute renal failure can result from a suprarenal occlusion caused by a cranial abdominal aortic thrombus.
- Clinical manifestation and signs can include typical signs of aortic thrombus (hindlimb weakness and ataxia especially after effort) in addition to acute renal failure signs.
- Imaging modalities such as Doppler studies, CT angiography or scintigraphy could be helpful to aid premortem diagnosis.

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Original Article

Computed tomography and myelography of the equine cervical spine: 180 cases (2013–2018)

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Keywords: horse; computed tomography; myelography; cervical spine; articular process joint

Summary

Computed tomography (CT) with CT myelography is a novel imaging modality for detailed anatomical imaging and precise diagnosis of equine cervical spine pathology. Computed tomography of the complete cervical vertebral column in live horses has not been reported previously. The objectives of this study were to describe the diagnostic utility of CT and CT myelography in horses, the technique, the type and distribution of lesions and procedure-related complications. Medical records of horses subjected to cervical CT and CT myelography between 2013 and 2018 were reviewed for this retrospective descriptive study. The examinations were performed with horses in lateral recumbency using a large-bore CT scanner. In total, 180 horses were included. The study population consisted of 79.4% Warmblood breed horses, 68.3% were male, the mean age was 7.1 years (range 21 days–21 years), and the bodyweight ranged from 61 to 717 kg (mean 530 kg). Pathology of the cervical vertebral column was identified in 176/180 horses (97.8%) and included osteoarthritis of the articular process joints in 83%. Impingement and compression of the spinal cord were detected using CT myelography in 125/147 horses (85%). Pathology was localised caudal to C5 in 90%. The mean ± s.d. anaesthesia time was 34 ± 19 min and 52 ± 13 min for CT examinations, excluding and including myelography, respectively. Adverse events occurred in 7.2% of the examined horses. The caudal location of the majority of lesions emphasises the importance of good-quality imaging of the most caudal cervical vertebrae in horses with suspected cervical spinal pathology and/or spinal cord compression. Computed tomography imaging enables identification of bony and soft tissue lesions of the entire cervical vertebral column in live, large-breed adult horses.

Introduction

Cervical vertebral column pathology is the main cause of spinal ataxia of noninfectious origin in horses. The cervical vertebral articular processes joints (APJs) are of particular clinical interest, based on the high prevalence of APJ pathology (Powers *et al*. 1986; Hahn *et al*. 2008; Down and Henson, 2009). Articular processes joint enlargement has been associated with vertebral canal stenosis and spinal cord compression in ataxic horses diagnosed with cervical vertebral stenotic myelopathy (CVSM) (cervical vertebral malformation, wobbler syndrome) (Powers *et al*. 1986; Moore *et al*. 1992; Levine *et al*. 2007, 2008, 2010) and with nerve root compression at the intervertebral foramen, leading to local cervical pain, muscle atrophy and thoracic limb lameness (Moore *et al*. 1992; Ricardi and Dyson, 1993). Developmental defects, including osteochondrosis (OC) and vertebral malformation/malarticulation, and degenerative joint disease (Powers *et al*. 1986; Rombach *et al*. 2014), are implicated in APJ pathology.

Ante-mortem diagnosis of CVSM is based on a thorough clinical and neurological examination and diagnostic imaging findings. However, cervical survey radiography and myelography are limited to the detection of dorsal and ventral spinal cord compression in the sagittal plane, and the sensitivity and specificity may be site-dependent (Moore *et al*. 1992; van Biervliet *et al*. 2004; Levine *et al*. 2007; Hahn *et al*. 2008; Levine *et al*. 2010; Mitchell *et al*. 2012; Nelson *et al*. 2017), thus precluding a precise identification of vertebral pathology. Adequate visualisation of the type of lesion and site of compression is a prerequisite for successful surgical decompression, arthroscopic debridement or intra-articular medication (Fürst 2019).

Computed tomography and CT myelography are commonly used in dogs to diagnose spinal cord injuries and compression (Dennison *et al*. 2010). Computed tomography imaging of the equine neck has been described in post-mortem specimens, and CT myelography accurately identified histologically verified lateral compressive spinal cord lesions and nerve root compression (Moore *et al*. 1992; Claridge *et al*. 2010; Sleutjens *et al*. 2014). Recently, preliminary results from CT imaging of the entire cervical column in 16 live large-breed adult horses using a large-bore CT scanner were reported, demonstrating specific lesion identification and localisation of compression sites (Kristoffersen *et al*. 2014). To date, CT and CT myelography examination findings in a large number of clinical cases have not been reported. The objectives of this study were to describe the diagnostic utility of CT and CT myelography in horses with suspected cervical vertebral pathology, the technique, the type and distribution of lesions and procedure-related complications.

Materials and methods

Study subjects

All horses subjected to CT examination of the cervical vertebral column, with or without CT myelography, at Evidensia Equine Specialist Hospital Helsingborg, Sweden, between June 2013 and February 2018, were included. Data retrieved from the medical records included horse signalment, history and presenting signs, anaesthesia time, adverse events during the CT procedure, anaesthetic recovery or immediate postanaesthetic period.

Computed tomography examination

Anaesthesia

All horses were admitted to the hospital on the day preceding the CT examination and remained hospitalised for approximately 24 h post-anaesthesia for observation of potential adverse reactions. Flunixin meglumine (Flunixin N-vet 1.1 mg/kg bwt i.v.)[1] and dexamethasone (Dexadreson 20 mg/horse bwt i.m.)[2] were administered prior to induction of anaesthesia. Anaesthesia was maintained with an intravenous continuous rate infusion (CRI) of triple drip (in 553 mL; guaifenesin 50 g (Myorelax)[3], xylazine HCL 660 mg (Rompun)[4] and ketamine 2 g (Ketaminol)[2]) at an infusion rate of 1 mL/kg/h and a CRI of acetated Ringer's solution (Ringer-acetat Fresenius Kabi)[5] at 2 mL/kg/h.

Scanning procedure

A 16-slice Philips Brilliance Big Bore CT scanner[6] with a gantry opening of 85 cm and a scanning field of 70 cm in diameter was used in combination with a custom-made air-cushion table for horses[7] (**Supplementary Item 1**). The entire procedure including the CT examinations was supervised by board-certified surgeons. Horses were placed in left lateral recumbency with the head and neck in a neutral-extended position. To achieve maximum caudal examination, careful positioning was required; the neck and shoulder region were centred, and both front limbs tied caudally with approximately 90° flexion of the carpi. The CT examination proceeded from cranial to caudal until the antebrachium touched the gantry (**Fig 1**).

The examination protocol was developed over the first 10 cases. Based on the localiser images, the CT examination was subdivided into a caudal and cranial scan. The field of view and image acquisition parameters was adjusted to fit to the shape and thickness variations between cranial and caudal parts of the equine neck. The caudal examination included C5 to C7 and the cranial thoracic vertebrae if feasible, and the cranial examination proceeded from the occipital bone to include C5. The following parameters were used for the CT image acquisition: slice thickness 1 mm, rotation time 1.5 s, pitch 0.438, exposure settings 400 mA and 140 kV, for the caudal examination, and scan slice thickness 1 mm, rotation time 1.0 s, pitch 0.442, 300 mA and 120 kV for the cranial examination. Bone and soft tissue reconstructions were performed (**Fig 2**). Transverse plane reconstruction parameters for volume data are listed in **Table 1**.

Computed tomography myelography

Following the native CT examination, CT myelography was performed. The head and neck were positioned in 90° dorsoventral flexion. Under aseptic conditions, a spinal needle was inserted into the atlanto-occipital space and cerebrospinal fluid (CSF), 0.1 mL/kg, was withdrawn prior to injection of the same volume of positive contrast fluid, iohexol (Omnipaque 300 mg/mL)[8]. Cerebrospinal fluid aspiration and contrast injection, respectively, were performed over 3–5 min (**Supplementary Item 2**). The head and neck were fixed in a fully right latero-flexed position for 5 min (Grant and Paterson 2006) and then repositioned, and the CT examination repeated as described for the native scan.

Computed tomography imaging evaluation

The CT examination images were interpreted by a board-certified radiologist. Diagnostic imaging was part of the clinical work-up of the patient; thus, the radiologist had knowledge of the patient details. The reports were reviewed retrospectively to record the most caudal vertebra included in the examination, and the number and location of the following lesions: OA of the APJs, fracture or fragmentation, malformation/malarticulation, stenosis of the vertebral canal, impingement of the myelographic contrast column and spinal cord compression (**Fig 3**). Lesion location was assessed for each vertebral articulation level and only recorded once if both left and right sides were affected. A CT myelography study was considered to be of diagnostic quality if there was adequate filling/mixing of contrast media throughout the cranial to caudal length of the cervical spine. Areas where a lesser concentration of contrast media was present, defined as less radio-opaque subarachnoid space, were considered to be diagnostic if the spinal cord, subarachnoid space and intra- versus extradural could be defined. Compression for purposes of this study included complete attenuation of the contrast media due to extradural mass effect with or without shape change of spinal cord. Impingement was defined as incomplete attenuation of the subarachnoid contrast media due to change in shape of the dura mater.

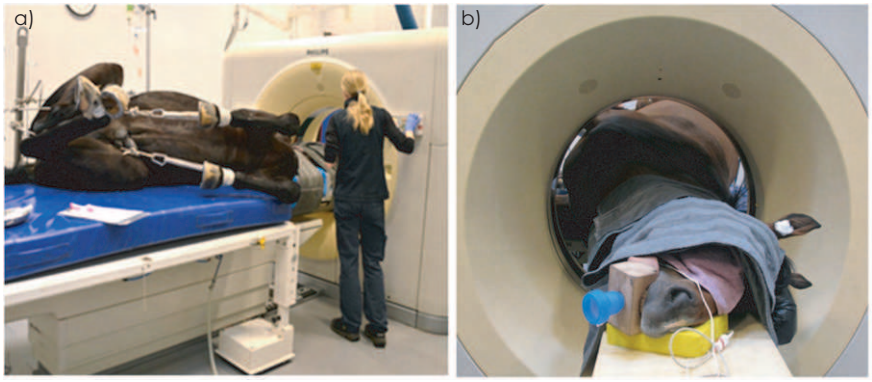

Fig 1: a) Warmblood horse (approximately 580 kg) positioned for a CT examination in left lateral recumbency, the front limbs tied tightly caudally. b) With the horse positioned correctly, the scan will be limited caudally by the antebrachium colliding with the front of the 85 cm gantry. If the horse is not centred correctly, the sternum, withers or point of the shoulder may collide with the gantry and limit the examination of the caudal vertebrae.

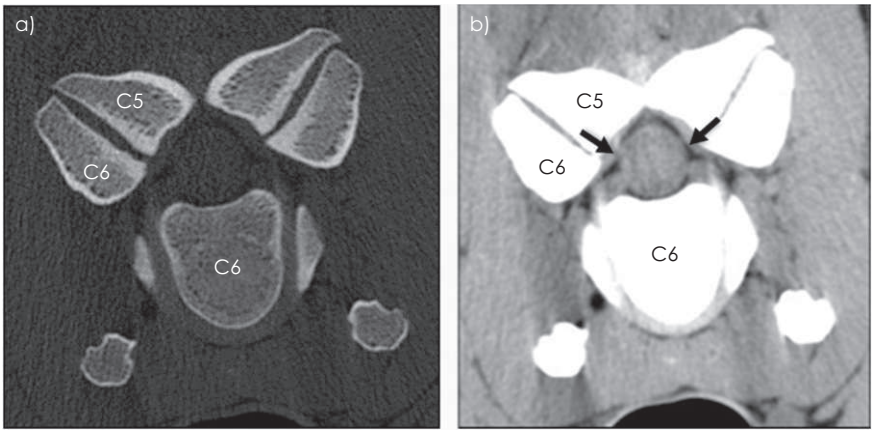

Fig 2: Transverse plane computed tomography images of the normal articulation of C5–C6. a) Bone reconstruction, 1 mm slice. b) Soft tissue reconstruction, 3 mm slice. The medial articular process joint pouch is distinctly outlined (black arrows).

TABLE 1: Overview of parameters for the transverse plane reconstruction of cervical spine computed tomography volume data

	Reconstruction	
	Bone	Soft tissue
Slice thickness (mm)	1	3
Matrix	768 × 768	512 × 512
Window level (HU)	1000	40
Window width (HU)	3000	400
Filter	Philips B and YD	Philips smooth (A)

HU, hounsfield units.

Results

Study subjects

In total, 180 horses were included in the study. Most horses were Warmbloods (n = 143, 79.4%). Other breeds included were pony breed (n = 16, 8.9%), Icelandic horse (n = 9, 5%) Standardbred trotter (n = 5, 2.8%), Thoroughbred (n = 5, 2.8%) and Quarter Horse/Paint (n = 2, 1.1%). Male horses (n = 123, 68.3%), including geldings (n = 97, 53.9%), and stallions/colts (n = 26, 14.4%) were >2 times more prevalent than female horses (n = 57, 31.7%). The age range was 20 days–21 years (mean 7.1 years), with a distribution of horses aged <1 year (n = 8, 4.4%), 1–2 years (n = 13, 7.2%), >2 to ≤ 4 years (n = 18, 10%),>4 to <7 years (n = 47, 26.1%) and ≥7 years (n = 94, 52.2%). The bodyweight ranged from 61 kg to 717 kg (mean 530 kg).

The history in all horses included, solely or in combination, the following signs: neurological deficits (n = 95, 52.8%), abnormal neck posture (n = 59, 32.8%), poor performance (n = 57, 31.7%), pain/swelling of the neck (n = 48, 26.7%) and thoracic limb lameness (n = 31, 17.2%).

Technique and diagnostic use

Computed tomography myelography was performed in 147/180 horses (81.6%). Areas with a less radio-opaque subarachnoid space were an occasional finding caudal to a compressive lesion; however, the spinal cord, subarachnoid, intra- and extradural space could be defined. Thus, all studies were considered to be of diagnostic quality. The entire

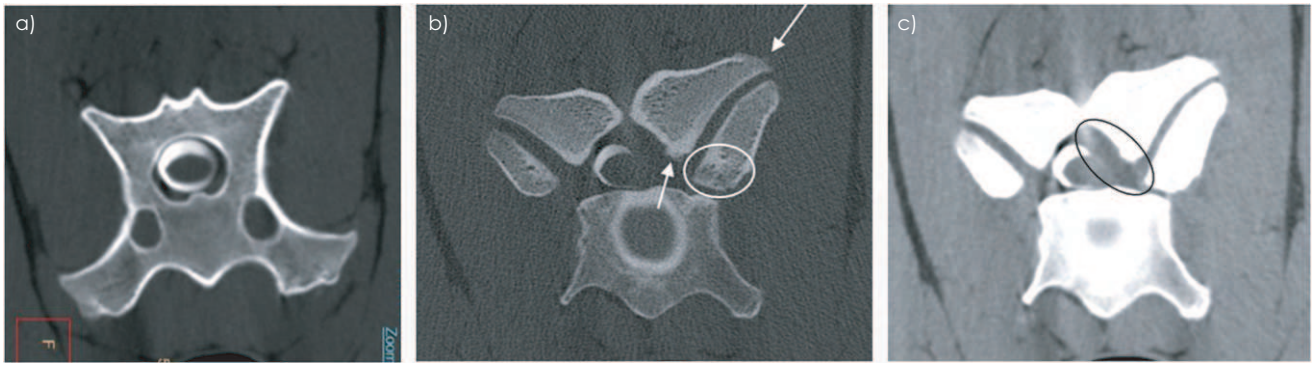

Fig 3: Transverse plane computed tomography myelogram in a 6-year-old Warmblood mare with sudden onset of grade 3/5 ataxia behind and caudal neck stiffness of 7-weeks duration. Right is to the right. a) Normal myelogram at mid-C6. b) Bone reconstruction. Osteoarthritis and enlargement of the right articular process joint (APJ) at C6–C7, lysis of the C7 process at the level of the intervertebral foramen (encircled) ventromedial and dorsal periarticular osteophyte formation (arrows). The ventral tubercles are asymmetric, left smaller than right. c) Soft tissue reconstruction. Increased soft tissue swelling on the medial margin of the right APJ (encircled), complete attenuation of the contrast column and marked leftward deviation of the spinal cord.

cervical vertebral column was included in the CT examination in 174/180 horses (96.7%), and vertebrae caudal to C7 was included in 159/180 horses (88.3%; **Fig 4**). At the level of T1–T2, bone detail is lost due to the use of 3 mm slices and the occurrence of artefacts; however, vertebrae can be imaged, and pathology, for example fractures, malformations and more marked OA can be identified (**Fig 5**).

Type and distribution of lesions

Pathology of the cervical vertebral column was identified in 176/180 horses (97.8%), 1588 lesions in total (**Fig 4**). In addition to bone abnormalities, soft tissue swelling, including effusion of the APJs and atlanto-occipital joint and soft tissue masses within the vertebral canal, comprised 26/1588 (1.6%) of the identified lesions. OA of the APJs was diagnosed in 150/180 horses (83.3%). The majority of lesions occurred at C5–C6 (n = 108), C6–C7 (n = 106), C4–C5 (n = 100) and C3–C4 (n = 98). The majority of OA lesions, fractures, malformations/malarticulations and swelling of the soft tissues was recorded at the C5–C6 articulation. OA was more commonly detected in Warmblood horses (83%) and horses older than 4 years (90%). Pathology caudal to C5 was present in 162/180 horses (90%).

Incomplete and complete attenuation of subarachnoid contrast media with or without shape change of the spinal cord consistent with extradural spinal cord impingement and compression was identified in 125/147 horses (85%). These findings were most prevalent in Warmblood breeds (86%) and horses older than 4 years (79%). The C6–C7 articulation was the most common site. Contrast attenuation was identified at 261 locations; in 63%, attenuation was caused by APJ OA. APJ OA-associated attenuation of the contrast column was dorsolateral in 82%, lateral in 10% and dorsal in 4%. Other causes of attenuation included malformation/malarticulation (15%), fracture/fragmentation (6.5%), space occupying soft tissue mass (3.5%) and attenuation dorsal to the intervertebral disc/disc space (12%).

Anaesthesia

Anaesthetic records were available for 175/180 horses (97.2%), for 145/147 of horses with myelography and for 30/33 horses without myelography. Mean (± s.d.) anaesthesia time for 145 CT examinations including CT myelography was 52 min (±13 min). For CT examinations without myelography (n = 30), mean anaesthesia time was 34 min (±19 min). Horses with adverse events had a mean anaesthesia time of 48 min (±17 min).

Adverse events

Adverse events occurred in 13 horses (7.2%). The majority were recorded after the examination, either in the anaesthetic recovery or after the horse had returned to its stable. The complication recorded during myelography was bleeding during puncture of the atlanto-occipital cistern in one horse. Equipment malfunction resulted in failure to perform a myelogram in one horse. Three horses made several unsuccessful attempts to stand; one had a prolonged recovery period before finally standing; in one, general anaesthesia was again induced and the horse transferred to a rope-assisted recovery. Both these horses recovered well. The third horse was subjected to euthanasia in the recovery stall as it was unable to stand. This horse was severely ataxic before the CT examination and had fallen during the neurologic examination; this was explained by a vertebral canal stenosis of T1 to T3 causing spinal cord compression. Five horses experienced a neurological episode following CT

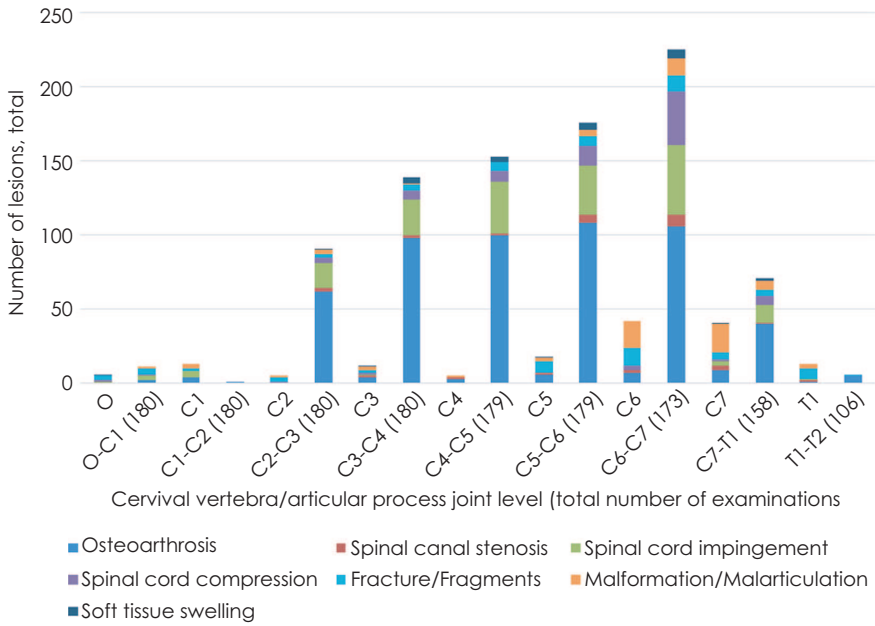

Fig 4: Distribution of lesions per cervical vertebral/articular process joint level in 180 horses identified with computed tomography (CT)/CT myelography. The number of horses included at each level is detailed in brackets. Compression was defined as complete attenuation of the contrast media due to extradural mass effect with or without shape change of spinal cord. Impingement was defined as incomplete attenuation of the subarachnoid contrast media due to change in shape of the dura mater.

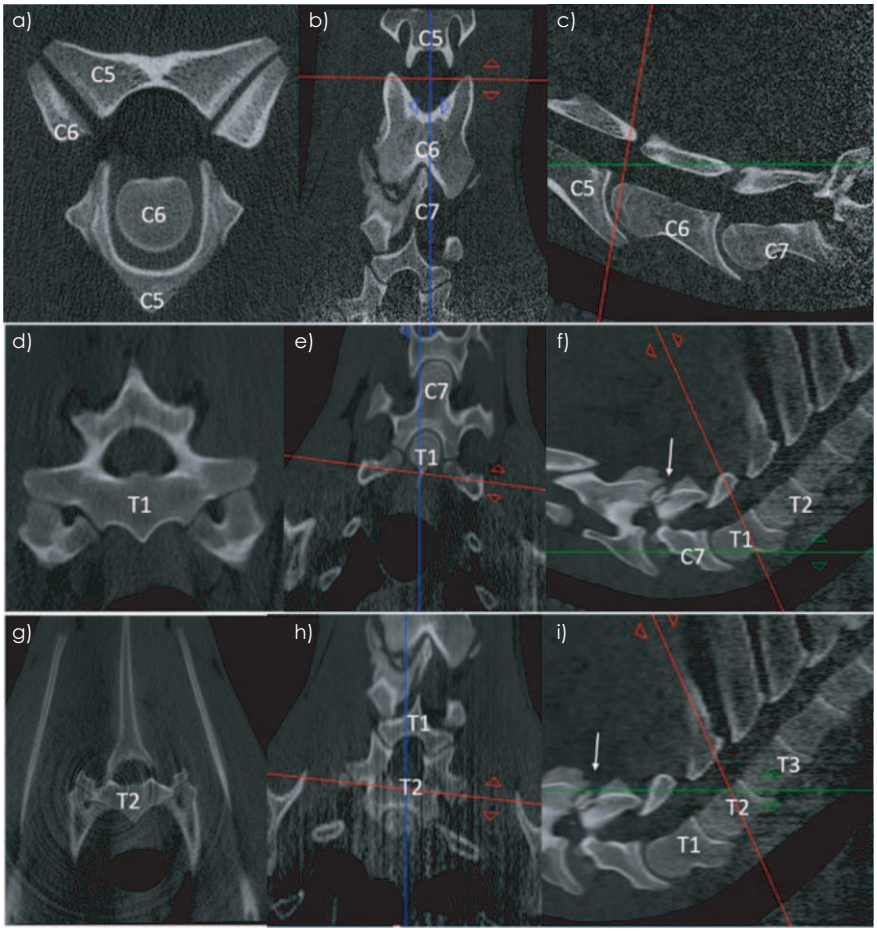

Fig 5: Changes in computed tomography image quality from the caudal cervical to T1 and T2 vertebrae in transverse (a, d, g), frontal (b, e, h) and sagittal (c, f, i) planes in a 2-year-old 500 kg Thoroughbred filly with a chronic fracture and osteoproliferation of C7 (arrows). In the cervical vertebrae, 1 mm slices with detailed bone imaging were obtained. At the level of T1, 3 mm slices were produced, resulting in loss of bone detail. The articulations with the first ribs were visualised. At T3, the scapulae and shoulder joints were within the scanning field, and in larger horses, this creates low signal to noise ratio, resulting in beam hardening and ring artefacts.

myelography, either immediately after recovery or later the same day. The episodes included progression of ataxia with or without seizures that could not be explained by the CT examination findings. Two horses suffered a mild colic episode after the CT examination, and one horse had a dull mentation the day after the examination.

Discussion

The present study demonstrates that CT imaging of the entire equine cervical vertebral column is feasible in live, large-breed adult horses. Using a large-bore human bariatric CT scanner, diagnostic images were acquired. This study is the first to report the incidence and distribution of bony and soft tissue lesions of the equine cervical vertebral column and spinal cord compression as detected on CT and CT myelography in clinical cases.

Cervical vertebral lesions were detected in the vast majority, 98%, of 180 examined horses with suspected neck pathology. OA of the APJs was the most common pathology, identified in 83% of horses, and occurred most commonly, with nearly equal frequency, at the articulations of C5–C6, C6–C7, C4–C5 and C3–C4. This finding is in agreement with previous studies reporting morphological changes and enlargement of the caudal APJs occurring primarily at C5–C6 and C6–C7 (Levine *et al*. 2007; Down and Henson, 2009; Janes *et al*. 2014).

The caudal cervical spine is critically important for the identification of cervical vertebral abnormalities as pathology and myelographic contrast attenuation caudal to C5 were present in 90% and 87% of horses, respectively. Good-quality imaging of the most caudal cervical vertebrae is of paramount importance. Detection of medial APJ lesions and dorsolateral spinal canal stenosis and spinal cord compression is limited with utilisation of standard radiographic and myelographic imaging angles (Moore *et al*. 1992; van Biervliet *et al*. 2004; Levine *et al*. 2007; Hahn *et al*. 2008; Levine *et al*. 2010; Mitchell *et al*. 2012). Medial lesions may be better visualised using oblique projections on radiographs and myelography (Withers *et al*. 2009). Multiplanar reformatting (MPR) of CT images, however, enables precise localisation of pathology, impingement and compression (**Fig 2**), even when it occurs in locations whose inspection is typically hindered by superimposition on radiographs.

Multiplanar reformatting aids in the decision to pursue treatment and may serve to specifically guide arthroscopic intervention or surgical spinal cord decompression (Fürst 2019). In combination, myelography and the CT image reconstruction techniques applied in the present study provided good soft tissue detail, enabling delineation of soft tissue masses within the spinal canal (**Fig 6**), intervertebral disc pathology and protrusion (**Fig 7**) and synovial joint outline (**Fig 2**).

In the present study, 78% of horses were older than 4 years; of these, 52% were 7 years or older, supporting previous reports of CVSM presenting clinically in older horses, an increased frequency of APJ OA and a higher occurrence of static stenosis at C5–C7 with increasing age (Powers *et al*. 1986; Levine *et al*. 2008; Reed *et al*. 2008; Down and Henson, 2009). The initiating cause may be chronic microtrauma or congenital, for example cervical vertebral subclinical malformation/malarticulation, progressing with age to become clinically significant (Levine *et al*. 2007) (**Fig 8**). Our study population consisted of 68% stallions and geldings and 79% Warmbloods, higher than the overall hospital admissions during the time period (52% male horses and 49% Warmblood breeds). This is in agreement with previous studies indicating that CVSM is more prevalent in male horses and Warmbloods (Levine *et al*. 2007, 2008, 2010). Breed predispositions are not fully understood; thus, the high proportion of Warmblood horses is interesting since a genetic inheritance of certain forms of developmental orthopaedic disease, for example OC, has been proposed (Levine *et al*. 2007, 2010).

Procedure-related adverse reactions occurred in 7%, a lower incidence than the previously reported 34% complication rate associated with standard radiographic myelography under general anaesthesia (Mullen *et al*. 2015). Mullen *et al*. (2015) concluded that longer anaesthesia times were significantly associated with adverse reactions. Horses that experienced any type of adverse reaction had a mean ± s.d. anaesthesia time of 101 ± 30 min. Mean anaesthesia duration for all horses in the present study was approximately half this time, which may account for the lower complication rate. In addition, neck manipulations during myelography could potentially cause or aggravate impingement. In the present study, the only manipulation performed was right lateroflexion to promote caudal flow of contrast material.

This study is limited by its retrospective nature. Referred cases were not subjected to a standardised clinical and neurological examination or cervical radiography at our hospital. Based on the variations in examinations performed and information provided, we did not aim to relate CT

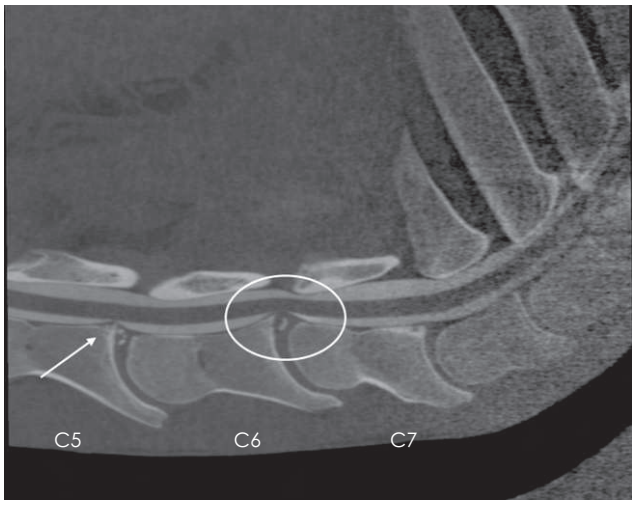

Fig 7: Sagittal plane computed tomography myelogram from a 6-year-old Warmblood gelding presented with neck stiffness, ataxia and unilateral front limb lameness. Epiphyseal flaring of the caudal aspect of C6 and dorsal protrusion of the C6–C7 intervertebral disc caused near-complete attenuation of the C6–C7 ventral subarachnoid space (encircled). The dorsal aspect of the intervertebral disc contained mineral material. Narrowing of the C5–C6 ventral subarachnoid space secondary to epiphyseal new bone of C5 and intervertebral disc disease was less marked (arrow).

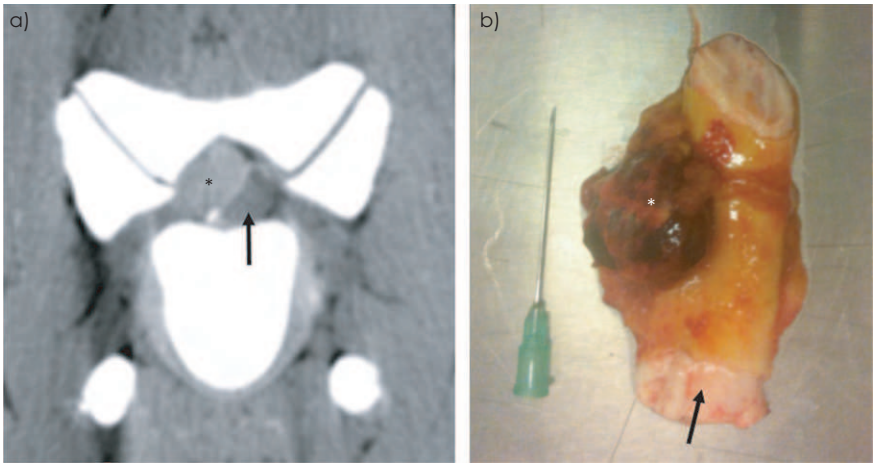

Fig 6: Extradural haematoma in a 2-year-old Warmblood stallion with ataxia grade 4/4. The horse was subjected to euthanasia based on the findings. a) The transverse plane computed tomography myelogram and soft tissue reconstruction revealed a left dorsolateral extradural mass (asterisk) causing marked compression and right ventral deviation of the spinal cord (arrow) from mid-C5 to mid-C6. b) Macroscopic appearance of the extradural haematoma (asterisk) causing the compression of the spinal cord (arrow).

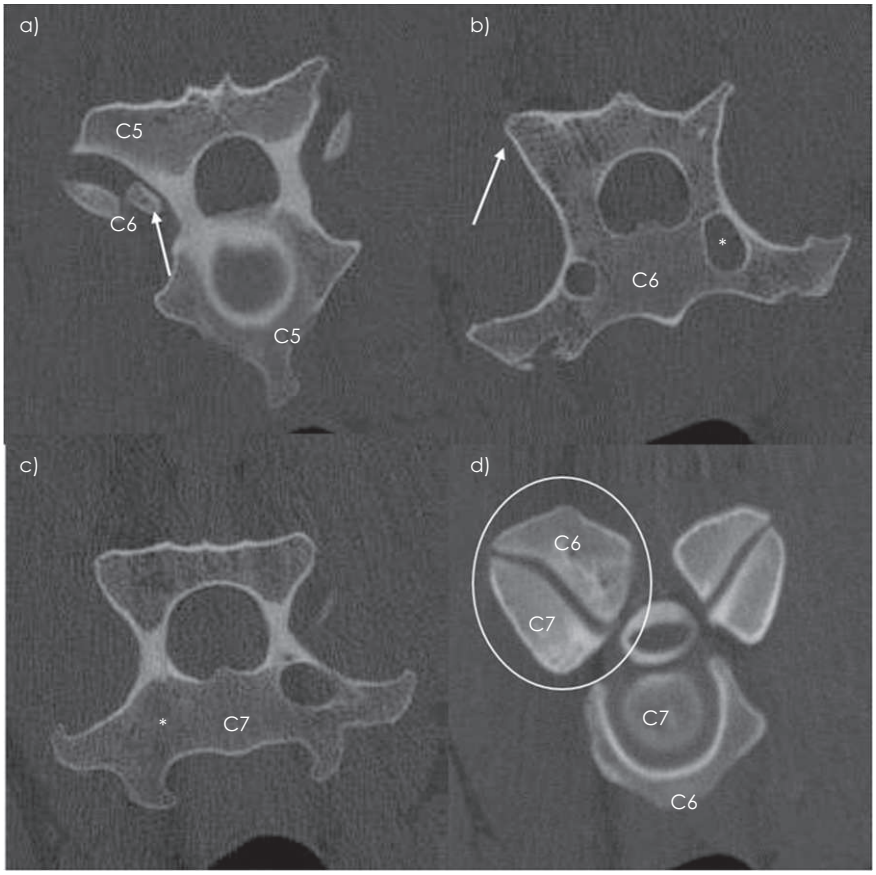

Fig 8: Transverse plane computed tomography images from a 9-year-old Warmblood gelding with a 2-month history of sudden stops followed by extension of the head and neck in a low position during ridden work, unwillingness to lateroflex the neck and hindlimb hypermetria. Left is to the left. a) A smoothly margined ovoid fragment (arrow) within the left C5–C6 articular process joint. b and c) Malformation with anomalous shape and asymmetry of the C6 and C7 vertebrae. b) C6 was asymmetric with the left side facet processes (arrow) larger than the right. The right side lateral foramen (asterisk) was larger than the left. c) The left side C7 lateral foramen was missing (asterisk). d) Larger left side C6–C7 articular processes (encircled) than the right. There was limited evidence of osteoarthritis.

diagnosis to clinical findings in this study. Further studies are needed to establish this association and determine the clinical significance of specific imaging findings. All cervical vertebrae were not examined in all 180 horses (**Fig 4**) for various reasons, for example if the horse had been referred for a suspected lesion of the cranial or mid-cervical vertebrae or due to individual anatomical variations that limited the examination.

Computed tomography and CT myelography were only performed in a static neutral-extended position and may have yielded false-negative results in horses with spinal cord compression only present under dynamic conditions. Kinematics and anatomical variations affect the intervertebral foramina dimensions, dural diameter and spinal cord position within the vertebral canal at specific vertebral levels, and the optimal myelographic criteria for each region in neutral, flexed and extended positions have not been fully determined (van Biervliet *et al*. 2004). Neck flexion may increase the detection of spinal cord compression at mid-cervical levels with the disadvantage of a higher frequency of false-positive diagnoses. The neutral neck position enhances the detection of compression at C6–C7 compared to the flexed position; however, the number of false-positive diagnoses also increase (van Biervliet *et al*. 2004). Accordingly, the static neck position utilised in the present study would be more likely to result in detection of compression at the caudal cervical vertebrae, with the risk of false-positive diagnoses at this level and false-negative diagnoses at the mid-cervical level. A false-positive compressive diagnosis has been associated with CT myelography, based on subsequent histopathology of the spinal cord (Moore *et al*. 1992). Histopathology was not routinely performed in the present study, and its role as the gold standard for confirmation of spinal cord compression has been questioned since functional neurologic deficits may be observed prior to histopathological evidence of spinal cord affection (Moore *et al*. 1992; Mitchell *et al*. 2012). Nevertheless, CT in a static position may provide supporting findings for the diagnosis of dynamic instability as it enables visualisation of predisposing pathology, for example APJ malformation, malarticulation or OA, thickening of the medial articular capsule of APJs and ligamentum flavum. Computed tomography is a novel imaging modality for detection of pathology of the equine cervical spine, and APJ disease has

been classified as OA throughout the text. Further subclassifications should be employed in future studies.

In conclusion, CT and CT myelography provided diagnostic quality images of the complete cervical spine in horses with few procedure-related complications. The most common site of pathological findings was the C6–C7 and C5–C6 articulations, and approximately 90% of the lesions were located caudal to C5. Further studies are needed to correlate specific CT findings to gross pathology, histopathology, clinical presentation and significance.

Authors' declaration of interests

No conflicts of interest have been declared.

Ethical animal research

Computed tomography examinations were performed as part of clinical investigations.

Owner informed consent

Client confidentiality has been maintained throughout the study. Explicit owner informed consent for participation in the study was not obtained.

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Authorship

All authors contributed to the preparation of the manuscript and gave their final approval of the manuscript.

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References

van Biervliet, J., Scrivani, P.V., Divers, T.J., Erb, H.N., de LaHunta, A. and Nixon, A. (2004) Evaluation of decision criteria for detection of spinal cord compression based on cervical myelography in horses: 38 cases (1981–2001). *Equine Vet. J.* **36**, 14-20.

Claridge, H.A.H., Piercy, R.J., Parry, A. and Weller, R. (2010) The 3D anatomy of the cervical articular process joints in the horse and their topographical relationship to the spinal cord. *Equine Vet. J.* **42**, 726-731.

Dennison, S.E., Drees, R., Rylander, H., Yandell, B.S., Milovancev, M., Pettigrew, R. and Schwarz, T. (2010) Evaluation of different computed tomography techniques and myelography for the diagnosis of acute canine myelopathy. *Vet. Radiol. Ultrasound* **51**, 254-258.

Down, S.S. and Henson, F.M.D. (2009) Radiographic retrospective study of the caudal cervical articular process joints in the horse. *Equine Vet. J.* **41**, 518-524.

Fürst, A.E. (2019) Vertebral column and spinal cord. In: *Equine Surgery*, 5th edn., Eds: J.A. Auer, J.A. Stick, J.M. Kümmerle and T. Prange, Elsevier Inc, St. Louis. pp 864-895.

Grant, B. and Paterson, J. (2006) How to perform a myelogram in less than 30 minutes. *Proc. Am. Assoc. Equine Practnrs.* **59**, 74-77.

Hahn, C.N., Handel, I., Green, S.L., Bronsvoort, M.B. and Mayhew, I.G. (2008) Assessment of the utility of using intra- and intervertebral minimum sagittal diameter ratios in the diagnosis of cervical vertebral malformation in horses. *Vet. Radiol. Ultrasound* **49**, 1-6.

Janes, J.G., Garrett, K.S., McQuerry, K.J., Pease, A.P., Williams, N.M., Reed, S.M. and MacLeod, J.N. (2014) Comparison of magnetic resonance imaging with standing cervical radiographs for evaluation of vertebral canal stenosis in equine cervical stenotic myelopathy. *Equine Vet. J.* **46**, 681-686.

Kristoffersen, M., Puchalski, S.M., Skog, S. and Lindegaard, C. (2014) Cervical computed tomography (CT) and CT myelography in live horses: 16 cases. *Equine Vet. J.* **46**, *Suppl*. **47**, 11.

Levine, J.M., Adam, E., MacKay, R.J., Walker, M.A., Frederick, J.D. and Cohen, N.D. (2007) Confirmed and presumptive cervical vertebral compressive myelopathy in older horses: a retrospective study (1992–2004). *J. Vet. Intern. Med.* **21**, 812-819.

Levine, J.M., Ngheim, P.P., Levine, G.J. and Cohen, N.D. (2008) Associations of sex, breed, and age with cervical vertebral compressive myelopathy in horses: 811 cases (1974–2007). *J. Am. Vet. Med. Assoc.* **233**, 1453-1458.

Levine, J.M., Scrivani, P.V., Divers, T.J., Furr, M., Mayhew, I.J., Reed, S., Levine, G.J., Foreman, J.H., Boudreau, C., Credille, B.C., Tennent-Brown, B. and Cohen, N.D. (2010) Multicenter case-control study of signalment, diagnostic features, and outcome associated with cervical vertebral malformation-malarticulation in horses. *J. Am. Vet. Med. Assoc.* **237**, 812-822.

Mitchell, C.W., Nykamp, S.G., Foster, R., Cruz, R. and Montieth, G. (2012) The use of resonance imaging in evaluating horses with spinal ataxia. *Vet. Radiol. Ultrasound* **53**, 613-620.

Moore, B.R., Holbrook, T.C., Stefanacci, J.D., Reed, S.M., Tate, L.P. and Menard, M.C. (1992) Contrast-enhanced computed tomography and myelography in six horses with cervical stenotic myelopathy. *Equine Vet. J.* **24**, 197-202.

Mullen, K.R., Furness, M.C., Johnson, A.L., Norman, T.E., Hart, K.A., Burton, A.J., Bicahlo, R.C., Ainsworth, D.M., Thompson, M.S. and Scrivani, P.V. (2015) Adverse reactions in horses that underwent general anesthesia and cervical myelography. *J. Vet. Intern. Med.* **29**, 954-960.

Nelson, B.B., Goodrich, L.R., Barrett, M.F., Grinstaff, M.W. and Kawcak, C.E. (2017) Use of contrast media in computed tomography and magnetic resonance imaging in horses: techniques, adverse events and opportunities. *Equine Vet. J.* **49**, 410-424.

Powers, B.E., Stashak, T.S., Nixon, A.J., Yovich, J.V. and Norrdin, R.W. (1986) Pathology of the vertebral column of horses with cervical static stenosis. *Vet. Pathol.* **23**, 392-399.

Reed, S., Grant, B. and Nout, Y. (2008) Cervical vertebral stenotic myelopathy. In: *Equine Neurology*, 1st edn., Eds: M. Furr and S. Reed, Blackwell Publishing Professional Ltd., Iowa. pp 283-298.

Ricardi, G. and Dyson, S.J. (1993) Forelimb lameness associated with radiographic abnormalities of the cervical vertebrae. *Equine Vet. J.* **25**, 422-426.

Rombach, N., Stubbs, N.C. and Clayton, H.M. (2014) Prevalence of osseous pathology in the articular process articulations in the equine cervical and cranial thoracic vertebrae. *Equine Vet. J.* **46**, *Suppl*. **47**, 10.

Sleutjens, J., Cooley, A.J., Sampson, S.N., Wijnberg, I.D., Back, W., van der Kolk, J.H. and Swiderski, C.E. (2014) The equine cervical spine: comparing MRI and contrast-enhanced CT images with anatomic slices in the sagittal, dorsal, and transverse plane. *Vet. Q.* **34**, 74-84.

Withers, J.M., Voute, L.C., Hammond, G. and Lischer, C.J. (2009) Radiographic anatomy of the articular process joints of the caudal cervical vertebrae in the horse on lateral and oblique projections. *Equine Vet. J.* **41**, 895-902.

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Original Article

A novel dynamometer for the standardisation of the force applied during distal forelimb flexion tests in horses

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Keywords: horse; flexion test; lower forelimb; dynamometer; lameness examination

Summary

Variability in the technique employed for flexion tests may produce different responses and veterinary assessments. We propose a novel custom-designed dynamometer and compare the results with the literature. Ten horses were enrolled in the present study, with a total of 20 forelimbs. The horses were found to be healthy based on orthopaedic and radiographic examination of the distal forelimb region, performed on both limbs. Lower forelimb flexion tests were performed by applying three different forces (75, 100 and 120 N), measured with a dynamometer, for one minute, with a time interval of 48 h between each test. Each horse was trotted before and after the flexion test. The experiment was videotaped, and the responses were assessed randomly and blindly by three experienced equine veterinarians. None of the horses responded with a lameness grade exceeding 1/5 on a numerical 6-point scale. Two out of three veterinarians detected a increased degree of lameness between the minimum and the maximum force applied, while one veterinarian showed no change in the interpretation of the flexion test for all three applied forces. A mild agreement was detected between veterinarian A and B, applying a force of 100 N, and between A and C, with 120 N; a moderate agreement was found between veterinarian A and B, with 120 N. The chi-square test showed that the results observed were only like the expected ones for 100 N. With a force of 100 N, there is no relationship between intensity and the evaluation of lameness; consequently, 100 N could be used to achieve a real standardisation of the lameness score. The use of the dynamometer was found to be easy and practical. It also enabled the applied force and the manipulation technique to be objectified.

Introduction

Flexion tests are an important part of gait assessment and are routinely used during lameness examinations (Dyson and Greve 2016). The force applied during the flexion test is aimed at stressing the joints and soft tissue structures in the lower limb, in order to emphasise a painful reaction by exacerbating a pre-existing lameness (Verschooten and Verbeeck 1997). The correct evaluation of the results of flexion tests requires the horse to be observed while trotting in a straight line on a firm surface, directly after the flexion (Ross 2011a, 2011b).

This longstanding clinical tool highlights the presence of lameness and in some instances predicts the likely source of pain (Ross 2011a, 2011b). However, variations in the technique used for the flexion test, the degree of flexion, duration of flexion, intensity of force applied to the flexed limb and potential horse-to-horse variability can all influence the post-testing response (Keg *et al.,* 1997a, 1997b; Dyson and Greve 2016; Giusto *et al*. 2016). According to the literature, there is little agreement on the duration of limb flexion time before trotting, which can range from 15 s to 3 min (Armentrout *et al*. 2011; Davidson 2018).

In addition, the force applied during flexion can vary considerably between practitioners and may account for variable results (Ramey 1997; Keg *et al.,* 1997a, 1997b). Some studies have been conducted to make the technique repeatable and objective in terms of duration and force applied (Keg *et al*. 1997a; Ross 2011a, 2011b).

The flexion test is not an accurate diagnostic tool since it is unable to stress a single joint without also exerting force on other joints or adjacent soft tissue (Ross 2011a, 2011b; Davidson 2018). The repeatability of testing between examiners is not very consistent, although individual repeatability is reportedly good (Keg *et al*. 1997b; Starke *et al*. 2012; Davidson 2018).

Nevertheless, flexion tests are still an integral part of the lameness examination. They are used in prepurchase examinations, or during orthopaedic examinations in equestrian competitions and events (Baxter and Stashak 2011). In fact, the flexion test is historically part of the overall lameness examination. It is also an inexpensive and noninvasive technique that reveals hidden sources of pain that might lead to the decision to conduct further specific diagnostic tests (Davidson 2018).

Our aim was to measure the exact force needed to exacerbate latent pre-existent pain in horses showing no signs of lameness. We used a dynamometer to measure the exact force applied by the clinicians.

Materials and methods

This study was authorised by the Ethics Committee of the University of Pisa (D.L. 116/92).

Ten Standardbred mares were included, aged between 6 and 9 years (median age: 7.5 years), with a body mass of between 452 and 587 kg (median value: 520 kg). None of

the horses were involved in sports activities, but were used as recipients for embryo transfer. All the mares were housed in collective paddocks 24 h a day, fed hay ad libitum and 1 kg of feed/per day[1] and were barefoot.

All the animals were considered healthy on the basis of a complete physical examination, and nonlame following an orthopaedic assessment. The horses were examined at walk, trotting in straight lines and in circles, on both right and left reins. The examinations were performed both on hard and soft surfaces. All mares underwent a radiographic examination of their distal fore limbs which comprised, latero-medial and dorso-palmar views of the fetlock and the digit. The mares' hooves were trimmed one week prior to the study-period.

Three experienced operators were involved, each with a specific task, which was the same throughout the study. The tasks were as follows: operator 1 led the horse during the test, operator 2 performed the flexion test, operator 3 recorded the tests with a digital camera from the same points of view (Sony DCR-HC18E PAL, Carl Zeiss lens, nightshot plus, touch screen,)[2].

The lower limb flexion test was performed by exerting a force on the dorsal hoof-wall, applying counter pressure on the distal radius of the horse using the upper arm of the examiner. Care was taken to keep the metacarpus in a vertical position (**Fig 1**).

The force applied was measured through a dynamometer which was custom-made for our research group (**Fig 2**). The device has an ergonomically designed handle and a second concave-shaped element to hold the hoof. The two elements slide against each other in a vertical direction on a Teflon track to reduce friction. To limit the oscillations of the force produced by small movements of the animal or the operator, a spring is located between the two sliding elements, through which the force applied by the operator passes as far as the horse's hoof. The force is measured using a button load cell, with a maximum capacity of 1000 N, whose signal is read and reported in kilogrammes by a calibrated display with a special screen which the operator can continuously monitor during the test.

The study was performed as described by Busschers and Van Weeren (2001) and Giusto *et al*. (2016). In brief, the flexion test was performed by applying three different force intensities (75, 100 and 120 N) in a randomised manner for one minute. On the same horse, the flexion tests were performed bilaterally on the same day with a one-hour interval between flexions. Immediately after each flexion test, each horse was trotted on a hard surface in a straight line, for approximately 12–15 m (Ross 2011a, 2011b). For each different force, the tests were performed at 48 h intervals. This schedule was followed strictly for each horse, in order to standardise the study procedure.

Fig 1: Flexion execution technique.

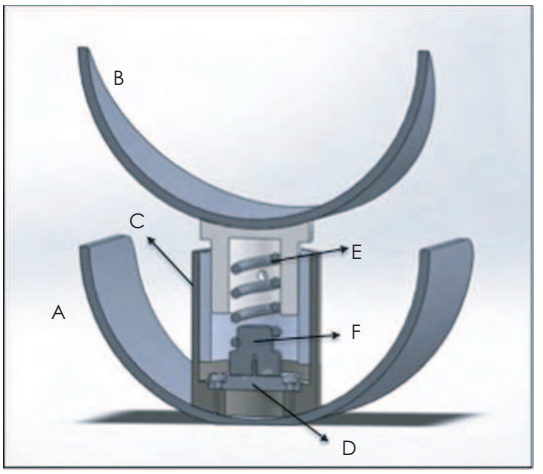

Fig 2: Dynamometer (Prof Bertini L and collaborators, Department of Civil and Industrial Engineering, University of Pisa). a) handles, made of stainless steel; b) hoof holding element, made of stainless steel; c) Teflon track; d) load cell; e) Spring; f) Spring track.

The videos were assessed by three experienced veterinarians to evaluate the presence or absence of response and, if present, the grade of lameness on a numerical 6-point scale (0–5) (**Table 1**). Each test (video) was assessed three times by each assessor randomly and blindly.

As the maximum lameness degree detected was 1/5 on the numerical 6-point scale, the data distribution was considered not normally distributed and hence nonparametric statistical testing was applied. The Kruskal–Wallis and Dunn's test as post hoc were used to test variations in lameness scores in relation to the force applied.

TABLE 1: The 6-point scale (0–5) for the assessment of lameness (Ross 2011b, modified)

Grade	Explanation
0	Lameness is not perceptible while the horse is trotted in a straight line and on a hard surface
1	Lameness is difficult to observe, and it is inconsistent at times while the horse is trotted in a straight line and on a hard surface
2	Lameness is observable but it is not consistently apparent while the horse is trotted in a straight line and on a hard surface
3	Lameness is consistently observable, while the horse is trotted in a straight line and on a hard surface
4	Severe lameness obvious at walk
5	Lameness produces minimal weight bearing in motion and/or at rest or complete inability to move

This test was performed for each veterinarian. The significance level was set at P value <0.05.

Cohen's kappa coefficient was carried out to test the agreement among the veterinarians in terms of the evaluation of the lameness score for each force applied. The agreement was considered mild if $0 \leq k \leq 0.40$; moderate if $0.41 \leq k \leq 0.60$; good if $0.61 \leq k \leq 0.80$; and excellent if $0.81 \leq k \leq 1$. No agreement was considered if $k < 0$, while if one observer gave the same answer on the lameness score, it is impossible to estimate Cohen's kappa coefficient and then we will indicate the data with ne (not estimable).

Finally, a chi-square test was performed to determine if the standardisation of the force applied could objectify the assessment of the lameness score. P was set at <0.05. The chi-square test was applied by comparing the observed data with the expected data (data are counts calculated using probability theory), obtained by calculating the frequencies as if the factors were independent. If a statistical difference is found between the expected and the observed data, it means that there is no relationship between the variables. If no statistical difference is found, the observed results assume the null hypothesis (H_0) is true, that is, no statistical difference between observed and expected data.

The statistical analysis was performed using a commercial software (GraphPad Prism 5®[3] , San Diego, CA, U.S.A.).

Results

Twenty limbs were flexed, and 120 videos were obtained, 60 before and 60 after the flexion test. The results are reported in **Table 2**.

After the flexion test using 75 N force intensity, 4/20 (20%) forelimbs were judged as lame by at least one veterinarian, and 0/20 (0%) forelimbs were considered lame by all three veterinarians.

After the flexion test using 100 N force, 15/20 (75%) forelimbs were judged as lame at least by one veterinarian, and 1/20 (5%) forelimbs were considered lame by all three veterinarians.

After applying 120 N force, 17/20 (85%) forelimbs were judged as lame by at least one veterinarian, and 2/20 (10%) forelimbs were considered lame by all three veterinarians.

Veterinarians A (P = 0.0189) and C (P < 0.0001) detected a higher degree of lameness (0 vs. 1) between the minimum and maximum force applied (75 N vs. 120 N), while veterinarian B (P = 0.8963) did not note any changes in the lameness score when increasing the force applied. On the other hand, the interpretation of the test by all three veterinarians did not vary between the minimum (75 N) and medium intensity (100 N).

Cohen's kappa coefficient revealed a mild agreement in scoring lameness between veterinarian A vs. B for the 100 N force and moderate for the 120 N force, a mild agreement was also found between A vs. C for the 120 N force applied (**Table 3**).

The chi-squared test revealed whether or not the intensity of the force could be associated with the possibility of detecting lameness. If the observed data are statistically equal to the expected data, it means that there is no relationship between intensity and the evaluation of lameness. On the contrary, statistically different values indicate that there is a relationship between force intensity and lameness detection. In particular, the presence of lameness was less than expected when the 75 N force was applied (P < 0.001), while more than expected when the 120 N force was used (P = 0.010). The frequencies of observed and expected results were similar (P = 0.588) when the 100 N force was applied (**Table 4**).

Discussion

The flexion test is routinely applied during orthopaedic examinations for prepurchase insurance and/or when assessing lameness (Busschers and Van Weeren 2001). In

TABLE 2: The evaluation of lameness on a numerical 6-point scale (0–5) obtained by three veterinarians on 20 flexed forelimbs

	Veterinarian A			Veterinarian B			Veterinarian C		
Legs	75 N	100 N	120 N	75 N	100 N	120 N	75 N	100 N	120 N
1	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
2	0/5	1/5	1/5	0/5	1/5	1/5	0/5	1/5	1/5
3	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
4	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	0/5	0/5
6	0/5	0/5	0/5	1/5	0/5	0/5	0/5	1/5	1/5
7	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
8	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	0/5
9	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
10	0/5	0/5	0/5	1/5	1/5	1/5	0/5	1/5	0/5
11	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5
12	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5
13	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
14	0/5	0/5	1/5	0/5	0/5	0/5	0/5	1/5	1/5
15	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
16	0/5	0/5	1/5	0/5	0/5	0/5	0/5	0/5	1/5
17	0/5	0/5	1/5	0/5	1/5	1/5	0/5	0/5	1/5
18	0/5	0/5	1/5	0/5	1/5	1/5	0/5	0/5	0/5
19	0/5	0/5	0/5	0/5	0/5	0/5	0/5	1/5	1/5
20	0/5	1/5	1/5	1/5	0/5	0/5	0/5	0/5	1/5

TABLE 3: The evaluation of the agreement among the veterinarians in their assessment of the lameness score in relation to the three forces applied

75 N			100 N			120 N		
A vs. B	A vs. C	B vs. C	A vs. B	A vs. C	B vs. C	A vs. B	A vs. C	B vs. C
ne	ne	−0.08	0.23	−0.034	−0.071	0.47	0.083	−0.15

$K < 0$: no agreement; 0–0.40: mild agreement; 0.41–0.60: moderate agreement; 0.61–0.80: good agreement; 0.81–1: excellent agreement; ne: not estimable.

TABLE 4: The observed and expected results regarding the assessment of the presence/absence (yes/no) of lameness and the P values obtained

	Observed				Expected			
	No	Yes	Total		No	Yes	Total	P value
75 N	56	4	60	75 N	44	16	60	<0.001
100 N	42	18	60	100 N	44	16	60	0.588
120 N	35	25	60	120 N	44	16	60	0.010
Total	133	47	180	Total	133	47	180	

these cases, the use of the flexion test can elicit a pain response in an apparently sound horse, which may highlight a possible subclinical problem (Busschers and Van Weeren 2001).

Various research teams have studied which structures might be responsible for a positive distal limb flexion test, and the metacarpophalangeal joint seems to be the primary cause of a positive response (Meijer *et al*. 2001; Kearney *et al*. 2010; Davidson 2018).

The flexion test technique does not achieve a clear standardisation and many different values have been recommended over the years (Busschers and Van Weeren 2001; Davidson 2018). Today, most clinicians apply a standard flexion test time of 60 s, as proposed by Marshall *et al*. (2012).

However, to the best of our knowledge, no specific and univocal references concerning the force intensity of the flexion test have been adopted (Ramey 1997; Verschooten and Verbeeck 1997; Keg *et al*. 1997a, 1997b; Busschers and Van Weeren 2001; Davidson 2018). In fact, flexion tests performed on the same horse by different veterinarians may trigger different responses related to the force applied (Giusto *et al*. 2016). The aim of the present study was to standardise the intensity of the force applied during the flexion test, using a dynamometer.

The dynamometer is simple to use since it is made of a light and manageable material. Operationally the dynamometer was found to be user friendly for all the operators. The screen location did not affect the flexion technique; thus, the test was performed according to the standard procedure. The fact that the dynamometer is small and does not make any audible sounds, means that it does not disturb the horse during the test thereby does not compromise the outcome. These findings suggest that a dynamometer could be beneficial during monitoring and maintaining the intensity of the force during the flexion test, as also reported by others (Giusto *et al*. 2016).

Video recordings were chosen as a means to evaluate lameness because they were easy to use and enabled the clinicians to assess all the horses in different work-sessions.

The statistical analysis showed differences in the interpretation of lameness between two of the three veterinarians in relation to the intensity of the force applied. In particular, two out of three veterinarians detected a higher degree of lameness (0 vs. 1) between the minimum and maximum applied force, while one veterinarian did not detect changes in lameness degree when increasing the force applied.

A mild to moderate agreement regarding the assessment of lameness score in relation to the intensity was also reported between veterinarians A vs. B or C in relation to the force applied. In particular, veterinarian A showed a mild agreement with veterinarian B when 100 N was used; instead, when 120 N was used, veterinarian A showed a moderate agreement with veterinarian B and mild agreement with veterinarian C. However, when 75 N was used, no agreement was found between veterinarian A and veterinarians B and C. On the other hand, no agreement was found between veterinarians B and C for any force level applied.

These results might be explained considering that agreement even between experienced evaluators tends to be low when grading mild lameness (Keegan *et al*. 2010). Moreover, the lameness assessment by an expert veterinarian might be subjectively influenced by personal experience (Fuller *et al*. 2006).

Finally, the statistical analysis on observed and expected results showed that the veterinarians underestimated or overestimated the lameness score when 75 N or 120 N was applied, respectively. On the other hand, 100 N enables a real assessment of the lameness score. Thus, our data seem to be partially in line with previous studies in which the standardisation both of the force applied and the time of application seemed to reduce the number of operator-related variations (Giusto *et al*. 2016; Dyson and Greve 2016; Davidson 2018).

Our study has some limitations. Firstly, we did not perform a quantitative lameness assessment to standardise the lameness analysis before and after the flexion test. Many accurate systems to quantify lameness have been developed (Marshall *et al*. 2012). Moreover, it might be useful to assess the movement asymmetry after the flexion test. Modern gait analysis systems can measure small amounts of asymmetry, allowing the clinician to identify, not only the effect of flexion force on the lameness score, but also the effect of flexion force on movement asymmetry.

In further studies, a quantitative gait analysis system could thus be used, coupled with the dynamometer, in order to reduce variations among observers, in particular during the evaluation of low-grade lameness, and to better standardise the use of the dynamometer in the flexion test, as proposed by Marshall *et al*. (2012).

Secondly, only nonlame animals were enrolled in this study. Further studies are needed to investigate whether a dynamometer would be useful in the standardisation of a flexion test in lame horses with a lameness score higher than 1/6.

Conclusions

Our dynamometer was effective in standardising the force applied as it identified 100 N as the force that achieves a real assessment of lameness score. However, the interpretation of flexion tests is basically subjective and there is considerable variation between observers. The dynamometer could help clinicians in monitoring and maintaining the intensity of the force during the flexion test. This would help standardise the manipulation technique and consequently objectify assessments during equine lameness tests (Busschers and Van Weeren 2001; Giusto *et al*. 2016).

Authors' declaration of interests

No conflicts of interest have been declared.

Ethical animal research

The study was authorised by the Ethics Committee of the University of Pisa (D.L. 116/92).

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Authorship

M. Sgorbini and M. Cacini conceived and designed the project. M. Cacini and V. Vitale executed the experiment. I. Nocera, M. Sgorbini and L. Gracia-Calvo analysed the data. All the authors interpreted the data, wrote and critically revised the manuscript and approved the final version.

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References

Armentrout, A.R., Beard, W.L., White, B.J. and Lillich, J.D. (2011) A comparative study of proximal hindlimb flexion in horses: 5 versus 60 seconds. *Equine Vet. J.* **44**, 420-424.

Baxter, G.M. and Stashak, T.S. (2011) Examination for lameness. In: *Adams and Stashak's Lameness in Horses*, 6th edn., Ed.: G.M. Baxter, Blackwell Publishing, Ltd., UK, pp 113-183.

Busschers, E. and Van Weeren, P.R. (2001) Use of the flexion test of the distal forelimb in the sound horse: repeatability and effect of age, gender, weight, height and fetlock joint range of motion. *J. Vet. Med.* **48**, 413-427.

Davidson, E.J. (2018) Lameness evaluation of the Athletic horse. *Vet. Clin. North Am. Equine Pract.* **34**, 181-191.

Dyson, S.J. and Greve, L. (2016) Subjective gait assessment of 57 sports horses in normal work: a comparison of the response to flexion tests, movement in hand, on the lunge, and ridden. *J. Equine Vet. Sci.* **38**, 1-7.

Fuller, C.J., Bladon, B.M., Driver, A.J. and Barr, A.R. (2006) The intra-and inter-assessor reliability of measurement of functional outcome by lameness scoring in horses. *Vet. J.* **171**, 281-286.

Giusto, G., Caramello, V., Comino, F., Bellino, C. and Gandini, M. (2016) A pressure-sensitive glove for standardization of the force applied during distal forelimb flexion tests in horses. *J. Equine Vet. Sci.* **43**, 77-81.

Kearney, C.M., Van Weeren, P.R., Cornelissen, B.P.M., den Boon, P. and Brama, P.A.J. (2010) Which anatomical region determines a positive flexion test of the distal aspect of a forelimb in a nonlame horse? *Equine Vet. J.* **42**, 547-551.

Keegan, K.G., Dent, E.V., Wilson, D.A., Janicek, J., Kramer, J., Lacarrubba, A., Walsh, D.M., Cassells, M.W., Esther, T.M., Schiltz, P., Frees, K.E., Wilhite, C.L., Clark, J.M., Pollitt, C.C., Shaw, R. and Norris, T. (2010) Repeatability of subjective evaluation of lameness in horses. *Equine Vet. J.* **42**, 92-97.

Keg, P.R., Van Weeren, P.R. and Back, W. (1997a) Influence of the force applied and its period of application on the outcome of the flexion test of the distal forelimb of the horse. *Vet. Rec.* **141**, 463-466.

Keg, P.R., Van Weeren, P.R., Schamhardt, H.G. and Barneveld, A. (1997b) Variations in the force applied to flexion tests of the distal limb of horses. *Vet. Rec.* **141**, 435-438.

Marshall, J.F., Lund, D.G. and Voute, L.C. (2012) Use of a wireless, inertial sensor-based system to objectively evaluate flexion tests in the horse. *Equine Vet. J.* **44**, 8-11.

Meijer, M.C., Busschers, E. and Van Weeren, P.R. (2001) Which joint is most important for the positive outcome of a flexion test of the distal forelimb of a sound horse? *Equine Vet. Educ.* **13**, 319-323.

Ramey, D.W. (1997) Prospective evaluation of forelimb flexion tests in practice: clinical response, radiographic correlation, and predictive value for future lameness. *Proc. Am. Assoc. Equine Practnrs.* **43**, 116-120.

Ross, M.W. (2011a) Manipulation. In: *Diagnosis and Management of Lameness in the Horse*, 2nd edn., Eds: M.W. Ross and S.J. Dyson, Elsevier Saunders, USA. pp 80-88.

Ross, M.W. (2011b) Movement. In:*Diagnosis and Management of Lameness in the Horse*, 2nd edn., Eds: M.W. Ross and S.J. Dyson, Elsevier Saunders, USA. pp 64-80.

Starke, S.D., Willems, E., Head, M., May, S.A. and Pfau, T. (2012) Proximal hindlimb flexion in the horse: effect on movement symmetry and implications for defining soundness. *Equine Vet. J.* **44**, 657-663.

Verschooten, F. and Verbeeck, J. (1997) Flexion test of the metacarpophalangeal and interphalangeal joints and flexion angle of the metacarpophalangeal joint in sound horse. *Equine Vet. J.* **29**, 50-54.

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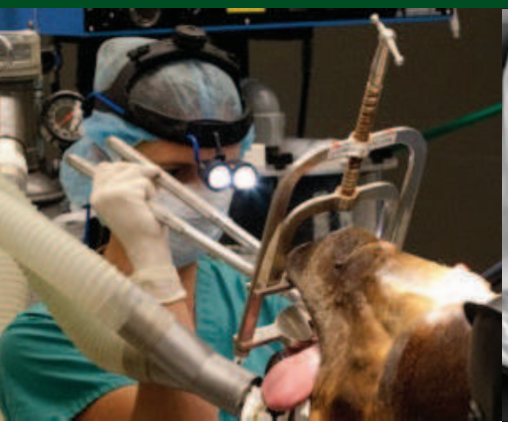
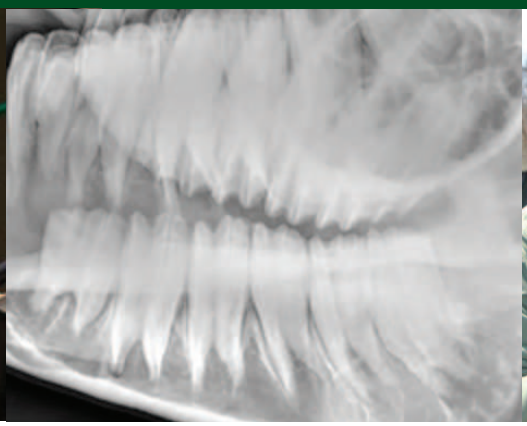


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Original Article

Intraoperative depression of the bulla of the maxillary septum as a method of improving sinus drainage without epistaxis in horses

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Keywords: horse; sinus surgery; anatomy

Summary

Current methods of creating sinus drainage and allowing egress of a sinus pack at the end of surgery create significant haemorrhage. Given that haemorrhage is already a concern in some sinus surgeries, the method described allows for a significant reduction in blood loss. The objective was to describe a method of enlarging the nasomaxillary aperture in horses to allow egress of a sinus pack, and subsequent endonasal treatment, without incurring significant haemorrhage. The bulla of the maxillary septum is depressed using a gloved finger (through a sinus flap or trephine hole) or using a long curved Peine instrument under sinoscopic control before fenestration. No major operative or post-operative complications have been encountered. Satisfactory widening of the nasomaxillary aperture has been accomplished in all cases, although at times, when the bulla is under the floor of the dorsal conchal sinus, it can be difficult to compress. It is imperative that this procedure be performed before fenestration. If performed after fenestration, the most rostral edge of the fenestration can be difficult to identify, and this becomes an impediment to widening the nasomaxillary aperture. Enlarging the nasomaxillary aperture with a finger or blunt instrument allows improvements in sinus drainage without the complication of severe epistaxis. Depression of the bulla of the maxillary septum, before surgical fenestration into the rostral maxillary and ventral conchal sinuses, allows opening of the nasomaxillary aperture with minimal haemorrhage. Thereafter, the sinus pack can be egressed via this route, which is also large enough to perform sinus lavage and post-operative treatments endonasally without the risk of disturbing the external surgical site.

Introduction

Surgery of the equine sinus is a common procedure. Historically performed under general anaesthesia, these are now frequently performed under standing sedation and local analgesia (Barakzai and Dixon 2014). Given that some of these procedures require tamponade to stem haemorrhage and frequently need post-surgical flushing, it is advantageous to leave an access portal for post-operative management. In some cases, the sinus packing is exited via a small hole left in the bone flap when it is replaced at the end of surgery or through the skin overlying a trephine defect.

The most common method of exiting the sinuses with the packing is to fenestrate the medial wall of the ventral conchal sinus into the nares. Even if the surgical procedure has been relatively blood-free, this procedure creates immediate and significant haemorrhage. To overcome this problem but maintain good post-operative drainage from infected sinuses, or to facilitate post-operative management, the balloon sinoplasty procedure was developed (Bell *et al*. 2009); and more recently Bach *et al*. (2019) reported on using a combination of electrocautery and sharp surgery to perform a transnasal conchotomy and surgical enlargement of the nasomaxillary aperture (SENMAP). Following these procedures, the packing can be passed through the widened nasomaxillary aperture into the middle and ventral meati and down the nostril. It is then securely fastened to the ipsilateral external nares to prevent the horse from aspirating or rubbing the packing out.

Both of the aforementioned reports require specialised equipment, significant skill, and an in-depth knowledge of sinus anatomy (Tatarniuk *et al*. 2010; Brinkschulte *et al*. 2014). Further, the SENMAP procedure will create haemorrhage by virtue of the fact that the ventral floor of the dorsal conchal sinus is removed, unless electrocautery is utilised. This report describes a technique by which the nasomaxillary aperture can be opened, in a manner similar to that of the SENMAP procedure, but without using specialised equipment or creating haemorrhage. The resultant opening will allow for packing material to egress the sinus systems, as well as leaving an access point for endoscope guided flushing, debridement and further sinus treatment if necessary.

Instrumentation and surgical technique

Upon entry into the dorsal conchal and frontal sinuses using a standard frontomaxillary bone flap, trephine, or sinoscopically, the surgeon can usually identify the frontomaxillary opening. Rostrally, this is comprised of caudal edge of the floor of the dorsal conchal sinus. Immediately under that is the bulla of the maxillary septum (Brinkschulte *et al*. 2014; **Fig 1a,b**). Between these structures is the nasomaxillary opening (also known as the canalis sinonasalis caudalis) which leads to the nasomaxillary aperture in the middle meatus of the nares (Tatarniuk *et al*. 2010; Brinkschulte *et al*. 2014). The anatomical position of this bulla varies both between and within horses. At times, it is quite large and appears to prolapse around the edge of, and upward into, the dorsal conchal sinus. At others, the caudal extent of this structure lies immediately below the caudal edge of the dorsal conchal sinus or rostral to it (which can present a surgical challenge). The bulla is usually thin and depressible to the touch. By using the index, or middle, finger to reach

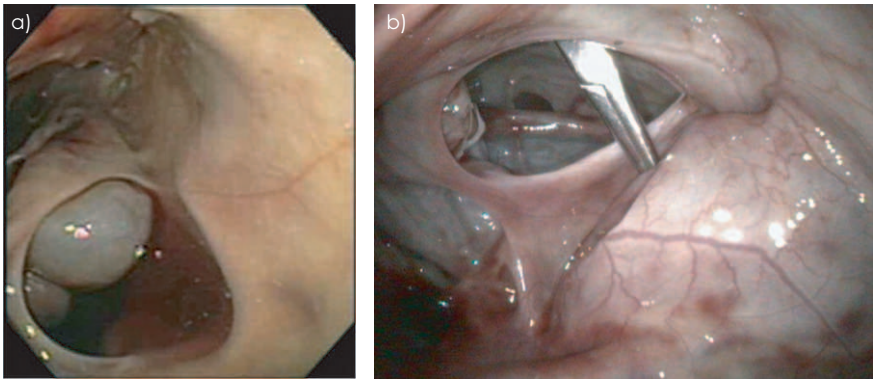

Fig 1: a) A photograph of the bullae of the maxillary septum under the caudal aspect of the floor of the dorsal conchal sinus in a cadaver specimen opened using a frontomaxillary bone flap. Rostral is top left with lateral to the right of the image. b) A sinoscopic image taken using a low maxillary sinus instrument portal and looking rostrally. The bulla of the maxillary septum is slightly depressed (right hand side of image), while the underside of the caudal aspect of the dorsal conchal sinus can be seen as it comprises the rostral margin of the frontomaxillary opening. The instrument is being passed into the nasomaxillary opening via the frontomaxillary opening under visual guidance from the surgeon who gained access to the sinus using a frontomaxillary bone flap.

down into the sinus, the bulla can be depressed while advancing the finger rostromedially into the nasal passages (**Fig 2a–c**). At this point, the nasal septum can be felt, and the gloved finger identified endoscopically in the middle meatus of the nose (if deemed necessary). In the case of a sinoscopic approach to the sinus (Perkins 2009b), the

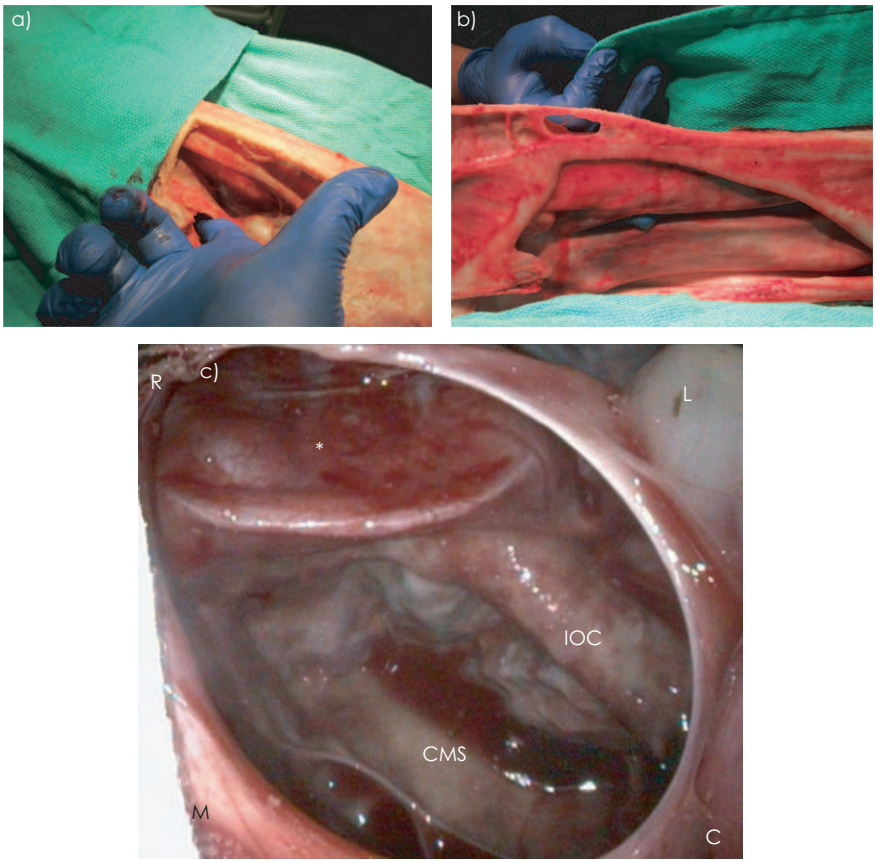

Fig 2: a) A photograph showing manual depression of the bulla of the maxillary septum after approaching the sinus using a frontomaxillary bone flap. The surgeon's finger is advanced rostrally and medially through the nasomaxillary opening into the middle meatus of the nose. b) A cadaver specimen with the nasal septum removed showing the surgeons finger within the middle meatus of the nose, having passed it via the nasomaxillary opening in Fig 2a. c) A sinoscopic view of the depressed bulla of the maxillary septum (*) immediately after removal of the surgeon's finger. The caudal maxillary sinus (CMS), infraorbital canal (IOC), rostral (R), caudal (C), lateral (L), and medial (M) are denoted in the picture.

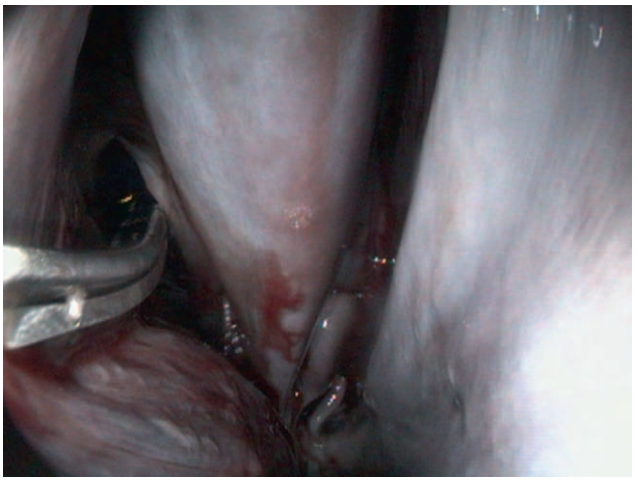

Fig 3: An endoscopic image taken from within the right nostril of a cadaver specimen. Note the presence of the surgical instrument in the nasal cavity having been passed through the widened nasomaxillary opening.

manoeuvre may be performed using a long curved surgical instrument (a curved Carmalt, Ochsner, or Peine clamp) under visual guidance using the same hole as the sinoscope, or using a separate instrument portal (**Figs 1b** and **3**).

Once this has been achieved, the depressed bulla may be fenestrated using standard technique (Perkins *et al*. 2009a,b; **Fig 4**) and the remainder of the surgical procedure performed. At the end of the procedure, the sinus pack, if necessary for tamponade, can be passed through the enlarged nasomaxillary aperture using the surgeon's method of choice. The author applies local analgesia topically (20–30 mL mepivacaine hydrochloride) to the sinus and widened nasomaxillary opening which flows down the ipsilateral nostril.

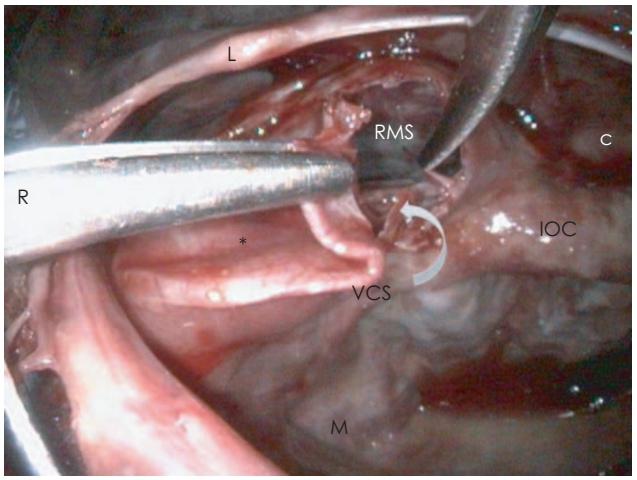

Fig 4: A sinoscopic image illustrating opening of the bulla of the maxillary septum (*) after manual depression allowing access to the ventral conchal (VCS) and rostral maxillary (RMS) sinuses. The infraorbital canal (IOC), rostral (R), caudal (C), lateral (L), and medial (M) are denoted.

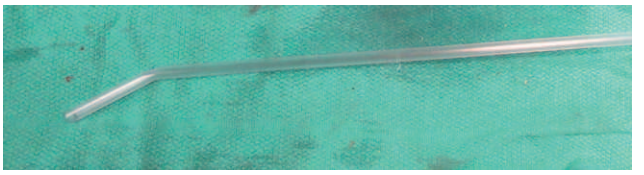

Fig 5: A photograph of a 30 cm manually bent artificial insemination pipette used to extract the end of the roll gauze from the sinus and deliver it to the external nares.

A bent artificial insemination (AI) pipette (or long curved Carmalt or Peine forcep) is passed from the external nares up the nose, through the aperture, and into the sinus (**Figs 5** and **6**). The end of a rolled gauze is sutured to the tip of the AI pipette (or grasped by the jaws of the forcep) which is then withdrawn, pulling the gauze down the nose. The packing material is removed from the pipette and sutured to the external nares. The packing material remaining in the sinus must be carefully arranged such that it will not wad when the pack is removed. Once the packing material is appropriately placed, the sinus flap or trephine hole is closed in routine fashion.

The author removes that sinus packing 48 h after surgery. The horse is lightly sedated and the retaining sutures are removed from the external nares. The packing material is wrapped around the hand and withdrawn from the nostril. Typically, the horse will back up rapidly and so a longer lead rope should be used than normal. Additionally, the level of sedation should be such that the horse can move away from the person withdrawing the pack without endangering itself or the veterinary staff. The packing is then checked to ensure that the entire length has been removed from the horse. It is common to have ipsilateral serosanguinous nasal discharge for 24–36 h after pack removal as the wet pack is

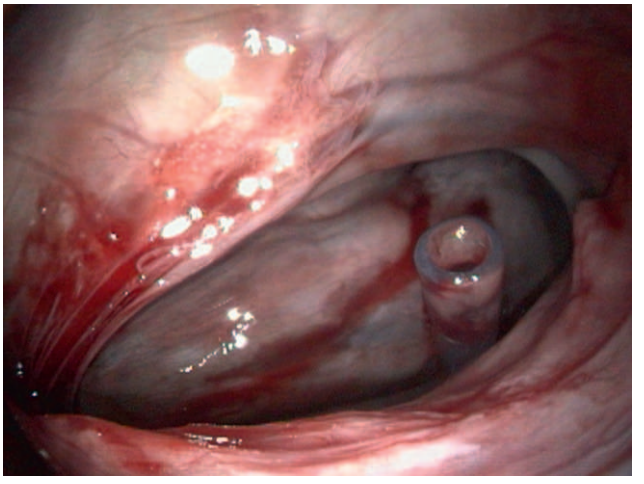

Fig 6: A sinoscopic image of the end of the artificial insemination pipette at the widened nasomaxillary opening, dorsal to the manually depressed bulla of the maxillary septum having been passed up the ipsilateral nostril. Note that this is for demonstration purposes. In a clinical case, the bulla would have been resected prior to passage of the pipette.

compressed and blood constituents are expressed from it during passage through the nasomaxillary opening and nostrils. Further, the presence of the pack may have prevented blood and fluid material which accumulated during surgery from exiting the sinuses. Endonasal treatment of the sinus cavities (further debridement, removal of necrotic or foreign material and flushing) starts 24 h after pack removal by passing the endoscope into the sinus cavities through the widened nasomaxillary opening without any need to disrupt the external surgery site. The frequency of post-surgical treatment is heavily case dependent.

Discussion

Equine sinus surgery is indicated for multiple reasons including, but not limited to, chronic unresolved primary sinusitis, sinusitis secondary to other disease processes such as dental disease, ethmoid haematomata, neoplasia, or cyst formation. Improving sinus drainage after surgery is one of the most important actions before closing the surgical site. This prevents the re-accumulation of purulent or necrotic debris, allows for intraoperative haemorrhage to be cleared from the sinus systems post-operatively, and enables post-operative treatment to be performed endonasally which may result in better cosmesis. The technique described in this paper is fast, usually blood-free, and allows the sinus pack to egress directly in line with the tension applied to the material. Other reported techniques create greater (blunt or sharp fenestration of the wall of the ventral conchal sinus), or lesser (surgical resection of the floor of the dorsal conchal sinus) degrees of haemorrhage; and require the sinus pack to curve around a corner as it exits the sinus. Remaining spicules of bone may be sharp and cause the pack to snag as it is removed. In some cases, cotton fibres may be ripped from the gauze roll during removal and ultimately end up as a gossypiboma which may require an additional intervention to resolve.

It is important to note that depression of the bulla and widening of the nasomaxillary aperture should occur before fenestration (**Fig 2c**) into the rostral sinus system (rostral maxillary and ventral conchal sinuses). The nasomaxillary opening lying above the domed shape of the bulla of the maxillary septum and under the floor of the dorsal conchal sinus (**Fig 7a**) readily accepts a surgeon's finger, or instrument, with very little resistance. The thin bone of the bulla readily collapses as entrance to the middle meatus of the nostril occurs with the finger (**Fig 7b**). Complete collapse of the most rostral extent of the bulla, under the dorsal conchal sinus, enables it to be engaged with curved scissors for resection. If the surgeon begins to resect the bulla before compression, the curvature of the most rostral portion makes it difficult to engage due to the entrance angle of the instrument and the curvature of the bulla as it moves rostrally under the caudal extent of the floor of the dorsal conchal sinus. This unresected bone becomes the main impediment to improved drainage post-operatively.

One oft-mentioned reason for performing standing sinus surgery, as opposed to performing the surgery under general anaesthesia, has been the reported reduction of haemorrhage. The author would contend that other than extirpation of an ethmoid haematoma, or other vascular mass, blood loss during sinus surgery is usually scant, until the egress into the nasal passages is created. At that point, there is significant haemorrhage. In the standing horse, excessive blood loss during inspiration may result in the horse aspirating the blood and coughing or reacting to the feeling of the blood flowing down the nostrils. The reported method of widening the nasomaxillary aperture, while not as rostro-ventral as the procedure of ventral conchal wall fenestration, allows for sufficient sinus drainage without the risk of this complication. This creates a direct communication between the middle meatus of the nose, the conchomaxillary opening (the space between the rostral maxillary and ventral conchal sinuses above the infraorbital canal) and, via the removed bulla of the maxillary septum, the caudal maxillary sinus and its conjoined sinus compartments. In addition to decreasing epistaxis, it allows for removal of the sinus pack placed for tamponade and post-surgical endonasal treatment of the affected sinuses after pack removal. This is done without expensive or custom-made instrumentation, or creating significant haemorrhage, which for the majority of surgery was not a problem.

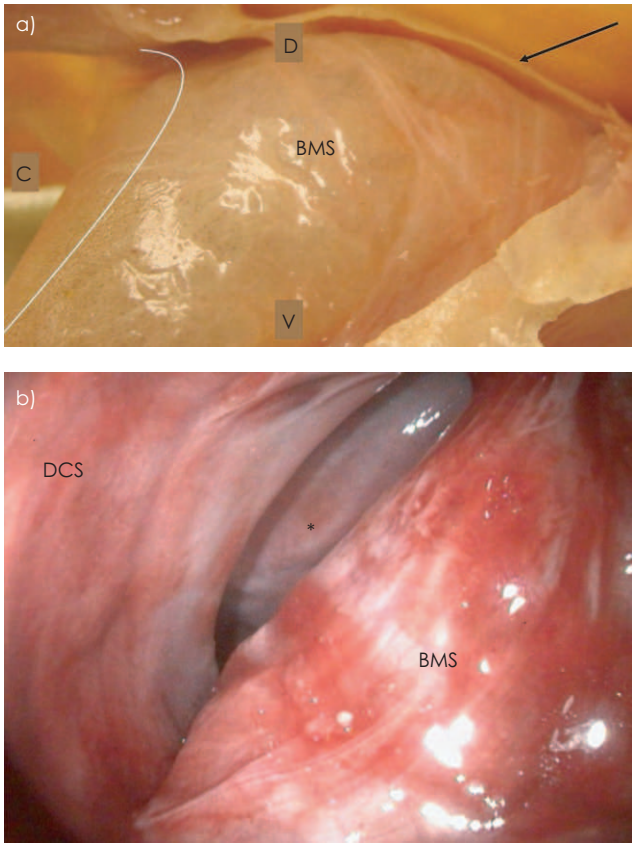

Fig 7: a) A photograph of the medial aspect of the paranasal sinuses, after nasal septum and medial wall removal. The bulla of the maxillary septum (BMS) courses rostro dorsally under the floor of the dorsal conchal sinus (which has been removed) leaving only the margin for orientation (arrow). The caudal extent of this structure is described by the white line which forms the rostral margin of the frontomaxillary opening. D = Dorsal; V = Ventral; C = Caudal. b) A sinoscopic image of an adequately compressed bulla of the maxillary septum (BMS) under the floor of the dorsal conchal sinus (DCS) before excision, showing the entrance into the middle meatus of the nose (*).

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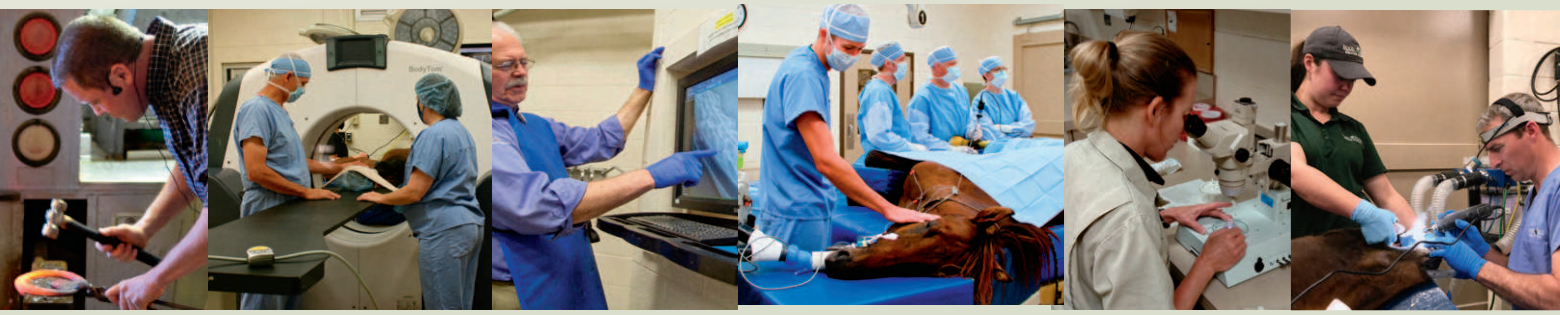

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[1] Data on file: 2020 Equine Pain & Sedation Market Research Study.

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Although this procedure may not work for every patient, it has become the main method by which the nasomaxillary aperture is opened in the author's cases and one which has been used routinely at the end of sinus surgery for the last 10 years. Upon follow-up examination, the only complication noted is that surgically created stomata between sinus and nasal cavities have a tendency to close over time – irrespective of the method of creation. The author would therefore advise surgeons to be mindful of this when creating a drainage portal. If one wishes to have long-term (years) access to the sinus, create as big a stoma as possible, otherwise it may close to the point that endoscopic access cannot be attained.

Author's declaration of interests

No conflicts of interest have been declared.

Ethical animal research

No ethical approval necessary for this article.

References

Bach, F.S., Böhler, A., Schieder, K., Handschuh, S. and Simhofer, H. (2019) Surgical enlargement of the nasomaxillary aperture and transnasal conchotomy of the ventral conchal sinus: Two surgical techniques to improve sinus drainage in horses. *Vet. Surg.* **48**, 1019-1031.

Barakzai, S.Z. and Dixon, P.M. (2014) Standing sinus surgery. *Vet. Clin. North Am. Equine Pract.* **30**, 45-62.

Bell, C., Tatarniuk, D.M. and Carmalt, J.L. (2009) Endoscope-guided balloon sinuplasty of the equine nasomaxillary opening. *Vet. Surg.* **38**, 791-797.

Brinkschulte, M., Bienert-Zeit, A., Lüpke, M., Hellige, M., Ohnesorge, B. and Staszyk, C. (2014) The sinonasal communication in the horse: examinations using computerized three-dimensional reformatted renderings of computed-tomography datasets. *BMC Vet. Res.* **10**, 72-82.

Perkins, J.D., Bennett, C., Windley, Z. and Schumacher, J. (2009a) Comparison of sinoscopic techniques for examining the rostral maxillary and ventral conchal sinuses of horses. *Vet. Surg.* **38**, 607-612.

Perkins, J.D., Windley, Z., Dixon, P.M., Smith, M. and Barakzai, S.Z. (2009b) Sinoscopic treatment of rostral maxillary and ventral conchal sinusitis in 60 horses. *Vet. Surg.* **38**, 613-619.

Tatarniuk, D.M., Bell, C. and Carmalt, J.L. (2010) A description of the relationship between the nasomaxillary aperture and the paranasal sinus system of horses. *Vet. J.* **186**, 216-220.

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Review Article

The use of progestins in equine medicine: A review

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Keywords: horse; progesterone; altrenogest; reproduction; progestin

Summary

Progesterone is in constant fluctuation throughout the lifespan of the horse. As a key regulator of the hypothalamic–pituitary–gonadal axis, progesterone is involved in numerous aspects of reproduction. Synthetic analogs of progesterone, deemed progestins, are widely available to industry to act as progestogenic within the reproductive tract, although few are bioactive in the horse. Utilised to suppress oestrous, delay ovulation, maintain pregnancy, and for behavioural modifications, progestins are a commonly administered class of pharmaceuticals in veterinary medicine. In this review, we discuss the progestins available to equine industry, in addition to assessing efficacy, pharmacokinetics, and potential side effects following administration of each.

Introduction

Progesterone is a key regulator of the hypothalamic–pituitary–gonadal axis and is involved in many aspects of reproduction. Various metabolites of progesterone are seen in circulation at different time points within the lifespan of the horse. Additionally, synthetic analogs of progesterone are available to industry, deemed progestins. These progestins are designed to interact with progesterone receptors to cause progesterone-like biological effects. Several progestins are commercially available for human and animal use, but only altrenogest (Regu-mate®; Merck, USA) has been found consistently progestogenic in horses (Mckinnon *et al.* 2000b; McCue 2003; Storer *et al.* 2009). Altrenogest is a derivate of nortestosterone with a structural relationship to trenbolone and is therefore able to bind to a variety of steroid receptors in addition to its high affinity to progesterone receptors (PR) (Bauer *et al.* 2000; Machnik *et al.* 2007). This ability expands the biological activity of altrenogest beyond that of progesterone. Progestins are used in breeding, racing, and sport stock for a variety of purposes, including the suppression of oestrus, pregnancy maintenance, transitioning from seasonal anoestrus, and behavioural modifications. This review will summarise current use of clinically relevant progestins and include scientific evidence of biological effects.

Progestins available to equine medicine

Progestins are commonly used in equine medicine in a variety of breeds, ages, and genders. Many progestins have been investigated, including medroxyprogesterone acetate (MPA), hydroxyprogesterone hexanoate (HPH), norgestomet, megesteral acetate, melengestrol acetate (MGA), and proligestone, but very limited evidence of pro-gestogenic efficacy (summarised in **Table 1**). In contrast, altrenogest was found both able to activate the progesterone receptor in addition to downstream progesterone-related pathways (Squires *et al.* 1983; McRobb *et al.* 2008). One study found altrenogest, but not hydroxyprogesterone hexanoate, to support pregnancy in ovariectomised mares (Shideler *et al.* 1982). Another found altrenogest to maintain pregnancy following a luteolytic dose of prostaglandin-F_2 alpha ($PGF_2\alpha$), while MPA, HPH, norgestomet, and MGA treatment failed to prevent abortion (McKinnon *et al.* 2000a). Additionally, while proligestone, MPA, and MGA have been investigated for their ability in bringing mares out of seasonal transition, inconsistent results have been noted (Loy and Swan 1966; Van der Holst *et al.* 1985; Lopez-Bayghen *et al.* 2008). In contrast, both progesterone in oil (Loy and Swan 1966) and altrenogest (Webel and Squires 1982) have been found to effectively hasten the time to oestrus and the time to conception in both early and late seasonally transitional mares. Because of this, the majority of this review will focus on altrenogest, with minimal inferences made into other progestins available to industry.

Pharmacokinetics of altrenogest

Altrenogest is a 17a-allyl-17B-hydroxy-estra-4,9,11-trien-3-one compound called allyltrenbolone (**Fig 1**). Although classified as a progestin, altrenogest is more structurally related to that of an androgen. It differs by only two double bonds and an allyl group from the androgenic and anabolic steroid (AAS) nandrolone, while also being structurally related to the AAS trenbolone. While altrenogest has been shown to bind to the androgen receptor with 75% the affinity of dihydrotestosterone (DHT) (Bauer *et al.* 2000), minimal anabolic effects have been noted following altrenogest administration in the horse. This includes no increase in body mass when administered in either intact males or mares (Hodgson *et al.* 2005), although the enlarged clitoris in fillies born to mares treated with altrenogest in late gestation should be noted (Shoemaker *et al.* 1989). It should be noted that trace levels of the AAS trenbolone have been detected in horses receiving altrenogest, leading to restrictions of its use in many performance-related equine organisations.

Pharmacokinetic evaluations have been performed on oral, injectable, and rectal administration routes for altrenogest in order to best predict withdrawal times. Machnik *et al.* (2007) administered oral (PO) altrenogest to 10 adult horses at the routine dose of 0.044 mg/kg. Maximum concentration (C_{max}) was reached within 15–30 min in the majority of horses. When assessing circulating concentrations of altrenogest, the mean maximum concentration was found

TABLE 1: Efficacy of progestins available to the equine industry

	Efficacy/concentration evaluated						
Progestin	Suppression of oestrus	Delay of ovulation	Synchronising oestrus	Transition from anoestrus	Early pregnancy maintenance	Treatment of ascending placentitis	Delay of postpartum oestrus
Progesterone	Strong evidence [100 mg]	Conflicting evidence [100 mg]	Effective w/ estradiol-17B [150 mg]	Conflicting evidence [150 mg]	Strong evidence [150 mg]		Conflicting evidence [100 mg]
Altrenogest	Strong evidence [0.044 mg/kg]	Conflicting evidence [0.044 mg/kg]	Effective w/ estradiol-17B [0.044 mg/kg]	Conflicting evidence [0.044 mg/kg]	Strong evidence [0.088 mg/kg]	Conflicting evidence [0.088 mg/kg]	Conflicting evidence [0.044 mg/kg]
MPA	Ineffective [1600 mg]	Ineffective			Ineffective [1000 mg]		
Norgestomet	Ineffective [1.5–3.0 mg]				Ineffective [15mg]		
HPC	Ineffective [500 mg]				Ineffective [1000 mg]		
MGA	Weak evidence [10–200 mg]				Ineffective [500 mg]		
Proligestone				Weak evidence [150 mg]			
HPH					Ineffective [500 mg]		

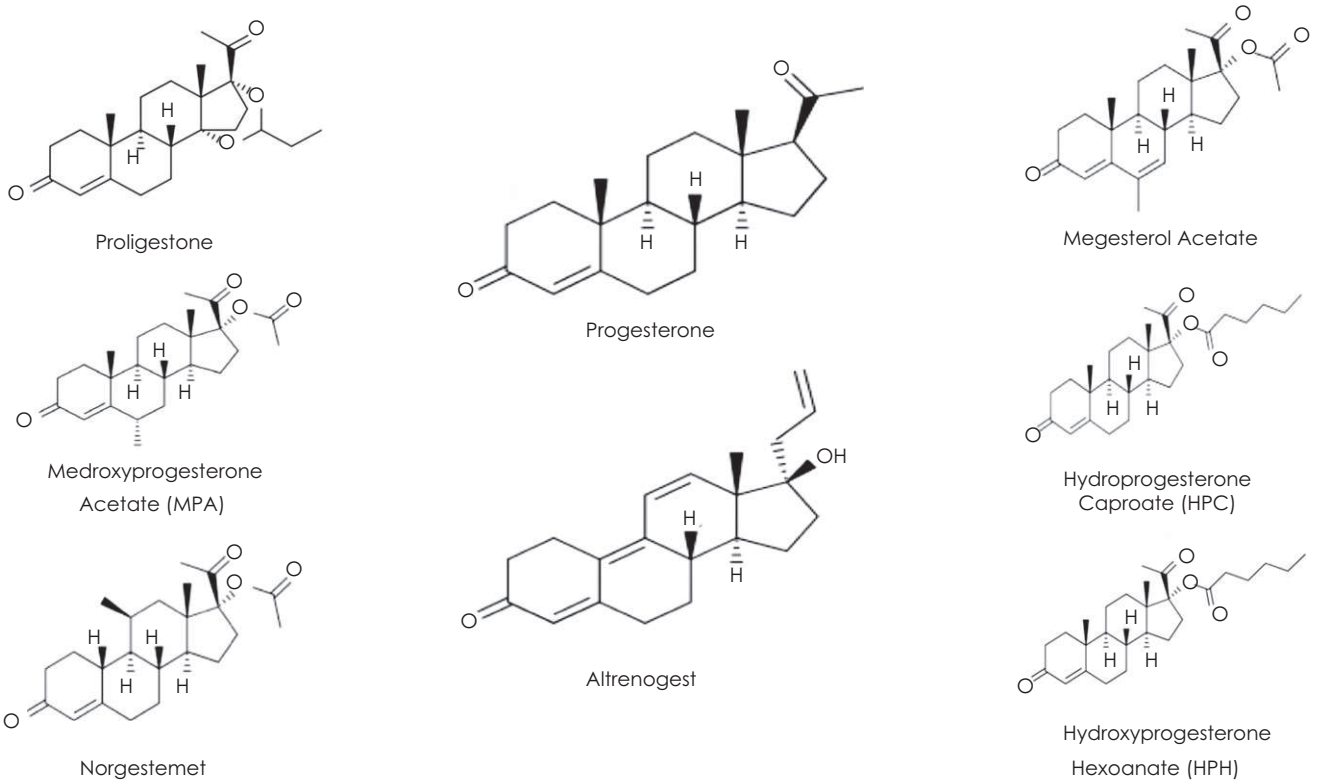

Fig 1: Structure of various progestins available to equine industry.

to be 35 ng/mL on Day 1 and 31 ng/mL on Day 5. Plasma clearance of altrenogest was determined to be 356 mL/h/kg on Day 1 and 264 mL/h/kg on Day 5. In contrast, mean C_{max} values in urine were determined to be 1720 ng/mL on Day 1 and 2107 ng/mL on Day 5. Time to total clearance (with a limit of detection of 2 ng/mL) was determined to be 12 days.

Due to risk of human interaction with oral altrenogest, injectable forms have gained popularity and the pharmacokinetics of which have been investigated. To assess pharmacokinetics, McConaghy *et al*. (2016) administered 0.3 mg/kg altrenogest intra-muscularly (IM) to 12 cycling mares. In this study, the mean circulating concentration of altrenogest was determined to be 33.52 ng/mL, and plasma altrenogest concentrations remained above 0.5 ng/mL for 6.2 days. Additionally, the area under the curve for IM administration was determined to be 5.6-fold higher than the oral product. The authors hypothesised that IM administration developed a depot of product which resulted in a slower absorption rate, and clearance of IM altrenogest may therefore take longer than when administered orally, and the response to a higher dose was not reported. This delayed withdrawal time should be noted when preparing animals for sport or race in restricted jurisdictions.

Pregnant mares are admitted to the hospital for medical or surgical events and may be prohibited from receiving oral medications. Therefore, the pharmacokinetics of intra-rectal altrenogest has also been assessed. Ellis *et al*. (2019) administered 0.088 mg/kg of altrenogest both *per rectum* and *per oral* for 5 days, and altrenogest was detected in circulation as quickly as 15 min following administration. The C_{max} of rectal altrenogest was considerably lower than that of oral (2.54 vs. 16.00 respectively), and clearance of altrenogest was more rapid in the rectal administration group. While rectal administration was found effective in delivering altrenogest to the mare, the bioavailability was found to be only 5.47% that of PO administration. It was concluded that although rectal administration may be a viable option for hospitalised mares, a dosage of 0.088 mg/kg every 4–8 h would be necessary to maintain therapeutic concentrations.

Effects of progestins on the reproductive tract

Nonpregnant mares

Suppression of oestrus

Suppression of oestrus may be desirable in sport, race, and pleasure riding mares, and the administration of a progestin to do so is common in equine practice. Progesterone and altrenogest suppress oestrus in cycling mares through high affinity to the PR (McRobb *et al.* 2008). Progestin administration infers an endometrial and myometrial environment similar to that of the dioestrus or pregnant mare. Loy and Swan performed the pivotal study that found progesterone to effectively suppress oestrus, and the interval to return to oestrus was dependent on the dose administered (Loy and Swan 1966). It was determined that 100 mg progesterone in oil daily was most effective, and mares receiving this dosage returned to oestrus within 3–4 days upon cessation of treatment. Repeat administration of progesterone, either intramuscular or as a slow-release repositol, led to progesterone accumulation within the body that persisted for greater than 10 days after the last administration (Hawkins *et al.* 1979). While the vehicle depends on the compounding agency, progesterone in oil is most commonly suspended in safflower, sesame or corn oil.

Suppression of oestrus was furthered investigated with the synthetic progestin altrenogest. Daily oral treatments with 0.044 mg/kg altrenogest binds sufficiently to PR to suppress oestrus (McCue 2003). Similarly, compounded injectable formulations of long-acting altrenogest suppress behavioural oestrus when administered as recommended by the manufacturers (Storer *et al.* 2009; McConaghy *et al.* 2016). It should be noted that Shideler and co-workers did not observe a negative impact of high-dose (0.22 mg/kg) and prolonged (86 day) altrenogest administration on overall haematologic or biochemical properties of the mare. Additionally, Squires *et al*. (1983) found no effect of long-term altrenogest administration on future fertility potential (Shideler *et al.* 1983). However, it should be noted that long-term use of altrenogest for behavioural purposes is off-label administration, and side effects have been noted, as discussed in this review. Therefore, clinicians should consider the risk to benefit ratio before treatment is initiated (**Fig 2**).

A variety of other progestins have been evaluated in their ability to suppress oestrus in the horse. Many are depots and have the advantage of being administered less frequently for a lengthened period of efficacy. Unfortunately, the administration of MPA (400–1600 mg/day), norgestomet (1.5–3 mg/kg) and HPC (500 mg) had no effect on oestrus suppression (Bristol 1981; Neely 1988; Wiepz *et al.* 1988; Gee *et al.* 2009) (**Fig 1**). Loy and Swan assessed the oestrus suppressing efficacy of various additional progestins in their pivotal study, including MPA (IM and PO; 425–1782 mg/day) and MGA (PO; 10–20 mg/day) (Loy and Swan 1966). Although a small number of mares were assessed, neither progestin consistently suppressed oestrus. It should be noted that while Loy and Swan found no effect of 10–20 mg MGA on oestrus suppression, clinical impressions have found 60–200 mg to suppress oestrus-like behaviour in race mares (Neely 1988). To our knowledge, no other synthetic progestins have been evaluated for their ability to suppress oestrus-like behaviour.

Delay of ovulation

Although progestins have been shown to successfully suppress oestrus in the mare, conflicting results exist for the ability to delay ovulation, the success of which may depend on the phase of the oestrous cycle in which administration began. Canisso *et al*. (2013) found neither oral altrenogest (0.044 mg/kg) or a progesterone-implanted controlled intravaginal releasing device (CIDR; EaziBreed; Pfizer Animal Health) to be effective in preventing ovulation when short-term treatment began in the pre-ovulatory phase. In contrast to this, James *et al*. (1998) found short-term administration of 0.044 mg/kg altrenogest to successfully delay ovulation when administered upon the detection of a 35-mm follicle. Bruemmer *et al*. (2000) attempted to repeat this, but with conflicting results. Initially, it was shown that a double dose of altrenogest (0.088 mg/kg) successfully delayed ovulation by 3.9 days when administered to a pre-ovulatory mare. However, an additional experiment found altrenogest treatment to neither delay ovulation nor improve pregnancy rates in a larger field setting. Interestingly, the use of an injectable sustained-release vehicle utilising varying concentrations of altrenogest (225–500 mg) has been shown to delay ovulation substantially (Storer *et al.* 2009). This was

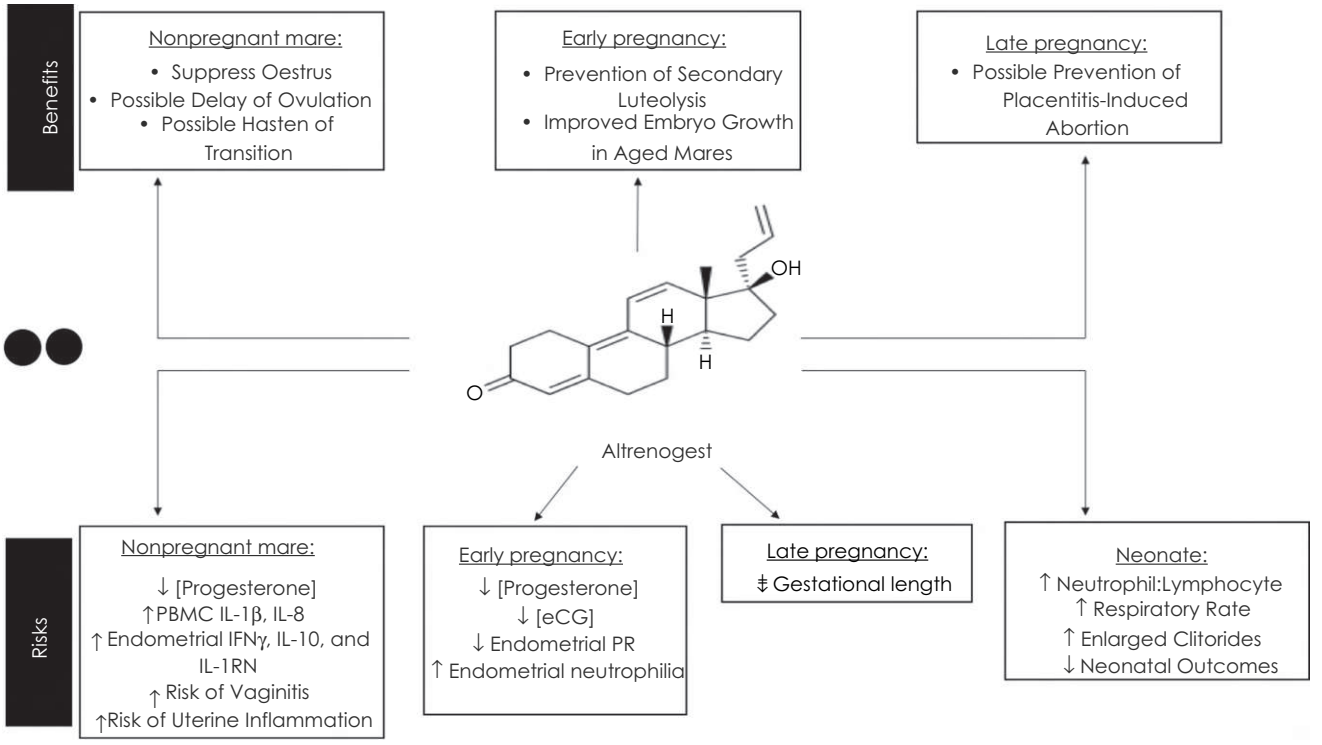

Fig 2: Risk-to-benefit ratio of altrenogest supplementation.

most significant when lactide-glycolide microparticles were added to altrenogest, delaying ovulation by 33.5 days. It should be noted that no effect on ovulation was observed when altrenogest was replaced with MPA (1.0 g) in the same vehicle and microparticle formulation.

Transitional mares

Mares are seasonally polyoestrous long-day breeders and are therefore anovulatory in the months surrounding the winter equinox. A transitionary phase exists between anoestrus and proper cyclicity, the hastening which has been attempted through the administration of exogenous steroids. The proposed rational for progestin treatment is in the perception that inhibiting the release of luteinising hormone (LH) will cause a build-up of the gonadotropin within the pituitary, thereby allowing a released surge upon discontinued treatment for ovulation to be more readily induced. Progestin treatment has been found to hasten the first ovulation of the year, although this is dependent on the stage of transition and the specific progestin administered. Webel and Squires found altrenogest (27 mg) to hasten the duration to first oestrus and interval to conception in late transitional mares (after 15 March, ≥20 mm follicle), although it had no impact on early transitional mares (before 15 March, ≤14 mm follicle) (Webel and Squires 1982). However, Colbern *et al.* (1987) were unable to replicate this utilising a dosage of 0.22 mg/kg altrenogest, which is five times the recommended concentration. Additionally, Alexander and Irvine (1991) found that 150 mg of progesterone in oil had no effect on the timing to first ovulation. Other progestins have been investigated, and 1500 mg of proligestone induced comparable ovulation and pregnancy rates to that of altrenogest in the transitional mare (Van der Holst *et al.* 1985). It should be noted that no control mares were used in this study, and pretreatment follicular status was not assessed. All comparisons were made to previous work on transitional mares, and therefore, extrapolations from this study are difficult to make. Controlled-release intramuscular progesterone (LA P4; BioRelease; 600 mg) was found effective in shortening the duration to first ovulation in late transitional mares, but was also determined ineffective in the early transitional mare (Staempfli *et al.* 2011). The use of an intravaginal progesterone-releasing devices (PRID/CIDR) have been investigated for hastening the first ovulation, but with mixed results. CIDRs impregnated with progesterone were found ineffective in improving pregnancy rates on the first cycle (Cuervo-Arango and Clark 2010), while Newcombe reported 89% of anoestrus mares to ovulate within 10 days following the removal of a progesterone-releasing intravaginal devices (PRIDs) (Newcombe 2002). It should be noted that mild-to-moderate vaginitis is reported in a subset of mares following implantation of the progesterone-releasing devices, and the devices are not approved for equine use in most countries (Crabtree *et al.* 2018). Overall, the efficacy of progestin treatment on shortening the duration to first ovulation is inconsistent and depends on the reproductive status of the mare in addition to the progestin used.

Synchronising oestrous

For simplicity of breeding in addition to proper timing of embryo placement, progestins are commonly used to time both oestrous and dioestrous aspects of the cycle. It should be noted that while progestins suppress the release of LH, the effect on FSH is less evident, resulting in normal development of follicles (Evans *et al.* 1982). Hence, progestin treatment results in a reduction of ovulations, but does not synchronise

follicular growth in treated mares. In order to effectively synchronise oestrous in mares, a combination of progestins (inhibition of LH) and oestrogens (inhibition of FSH) can be used. Originally described by Loy and co-workers, the 'P&E' treatment consisted of 10 days of intramuscular administration of 150 mg progesterone in oil combined with 10mg estradiol-17β (**Fig 3**). This is followed by a luteolytic dose of $PGF_{2}\alpha$ on the tenth day of treatment (Loy *et al.* 1982). It is expected that mares will have a pre-ovulatory follicle 8 days after the cessation of treatment and respond to an ovulatory-inducing agent. This has been repeated by replacing progesterone in oil (150 mg/day) with altrenogest (0.044 mg/kg), and responses were comparable (Squires *et al.* 1992). The use of a PRID has also been assessed for its efficacy in synchronising oestrous, but also required the addition of oestrogen to be effective (Klug and Jochle 2001; Ferreira *et al.* 2015).

Pregnant mares

Progestins are commonly used in equine medicine to maintain pregnancy during early gestation (McKinnon *et al.* 1988a), as well as during late gestation in mares with placentitis (Macpherson 2005; Bailey *et al.* 2010). Although long-term treatment with altrenogest is not recommended by the manufacturer and is therefore considered an 'off-label' application, treatment throughout gestation is commonly used in stud farm practice for maintenance of pregnancy, often without scientific merit to justify the administration. Progesterone is produced by the ovaries from the development of the primary and secondary *corpora lutea* (CL) following ovulation until 120–150 days of gestation when the pregnancy becomes fully dependent on 5α-reduced progestogens from the feto-placental unit, including 5α-DHP and 20α-5P (Ousey 2004; Fowden *et al.* 2008; Conley 2016; Conley and Ball 2019). Pivotal studies demonstrated maintenance of pregnancy in animals ovariectomised after 70 days of gestation, thereby indicating the lack of progestin-necessity in late gestation (Hinrichs *et al.* 1986; Hinrichs *et al.* 1987; McKinnon *et al.* 1988a). Additionally, recent information suggests that the practice of chronic progestin supplementation may be associated with previously unknown side effects, as discussed in this review.

Early pregnancy

Primary luteal deficiency, or the inability of the luteal cells to produce sufficient progesterone concentrations needed to support pregnancy, has been described in other species, but with lesser work in the horse (Allen 2001; Krog *et al.* 2016; El Hachem *et al.* 2017). There is conflicting evidence to both support and reject primary luteolysis as a cause for early pregnancy failure. Deficient progesterone concentrations have been found incompatible with maintenance of pregnancy, but there is limited data to support a primary failure of the CL as a cause of embryonic loss in the horse, and this may be due to the differing types of implantation and placentation (Irvine *et al.* 1990). Interestingly, the laboratory of Betteridge *et al*. (2018) recently described an unexplained decrease in serum progesterone concentrations to supersede early embryonic loss in a subset of mares. In this study, mares were monitored daily via transrectal ultrasonography and daily progesterone measurements. In 6/11 singleton losses, the pregnancy failure was preceded by a decrease in circulating progesterone. It should be noted that mean progesterone concentration was above 4 ng/mL in 5/11 mares which experienced embryonic loss. Additionally, measuring circulating progesterone concentrations in a single blood sample to determine whether the pregnancy is at risk is not accurate unless it is less than 1 ng/mL, as variations in secretion of this hormone occur throughout the day (Perkins *et al.* 1993).

Secondary luteal deficiency can occur as a result of endogenous release of $PGF_{2}\alpha$ associated with systemic or uterine inflammation, endotoxaemia, etc., which is detrimental to the CL if it occurs prior to the time when the feto-placental unit is producing sufficient progestogen to maintain pregnancy. Studies have indicated the progestogenic potential of altrenogest, while no other synthetic progestin has been found as effective outside of progesterone in oil. Shideler *et al*. (1982) found both progesterone in oil (150 mg) and altrenogest (0.044 mg/kg) to support pregnancy following a luteolytic dose of $PGF_{2}\alpha$ in ovariectomised mares when ovariectomy occurred at day 35 of gestation. This was further confirmed by Ball *et al*. (1992b) utilising progesterone in microspheres. It was determined that 1.5–2.25 g/day supported pregnancy maintenance, while 0.75 g/day did not when luteolysis was induced at Day 14 of gestation. Interestingly, Hinrichs *et al*. (1986) found a similar dose-dependent response with altrenogest and concluded that a double dose of altrenogest (0.088 mg/kg) to be more effective in pregnancy maintenance following embryo transfer to ovariectomised recipient mares. In this study, it was determined that the standard dose of 0.044 mg/kg led to

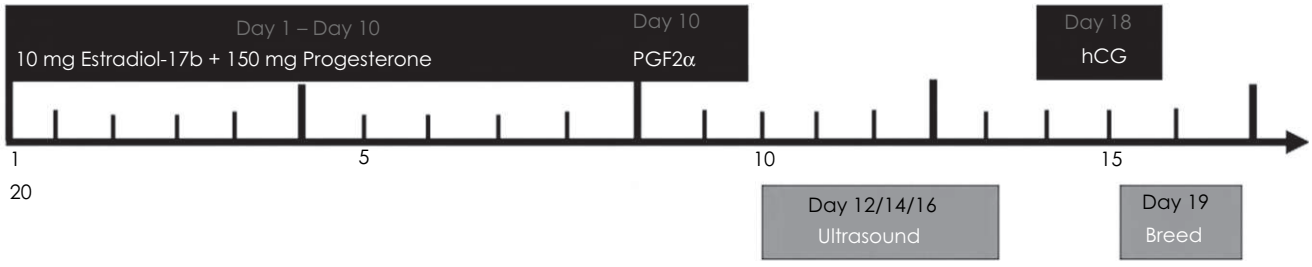

Fig 3: Standard progesterone and oestrogen 'P&E' treatment protocol. Upon the detection of a 25 mm follicle, mares begin standard P&E treatment. This consists of a daily administration of 150 mg progesterone in oil or 0.044 mg/mL altrenogest in combination with 10 mg estradiol-17B. A luteolytic dose of PGF2α is administered on day ten, and transrectal ultrasonography is utilised to assess follicular development. Upon detection of a 35-mm follicle (6–9 days after cessation of treatment), an ovulatory stimulant (hCG) is administered and insemination occurs 24–36 h later.

poor uterine tone and decreased cervical competence. The authors recommended the double dose (0.088 mg/kg) to be utilised during embryo transfer procedures. Dual studies by McKinnon *et al*. (1993) found various other synthetic progestins to fail in pro-gestogenic function, and this included HPC (1000 mg), MPA (1000 mg), HPH (500 mg), norgestomet (15 mg), and MGA (500 mg; **Fig 1**). Only altrenogest-treated mares (0.044 mg/kg) maintained pregnancy following $PGF_2\alpha$ administration on Day 18 of gestation, while the rest of the treatments failed to stop abortion from occurring (McKinnon *et al.* 2000a). Long-acting progesterone (150 mg) compounds have also been shown effective in preventing early pregnancy loss following a luteolytic dose of $PGF_2\alpha$ and can therefore be considered progestogenic (Vanderwall *et al.* 2007). It should be noted that progestin supplementation appears to have no negative effect of embryo retrieval, quality, or transfer success (Parry-Weeks and Holtan 1987; Ball *et al.* 1992a; Knowles *et al.* 1993).

There is no cross-reactivity between altrenogest and progesterone in commercial progesterone assays, so blood samples obtained after recovery from disease will determine whether the CL was lysed (P4 < 1 ng/mL) or is still active (Wynn *et al.* 2018). The results can guide the clinician in the decision to discontinue or continue treatment until the feto-placental unit provides necessary progestogen support to maintain the pregnancy, which occurs at roughly 100–120 days of gestation (Conley and Ball 2019). It should be noted that altrenogest treatment can suppress endogenous production of progesterone and may interfere with the formation of secondary CL (Daels *et al.* 1992; DeLuca *et al.* 2011). Willmann *et al*. (2011b) found altrenogest supplementation to decrease the production of equine chorionic gonadotropin (eCG) in mares greater than 8 years of age. This same study found that while advanced age correlates with a small embryo diameter, treatment with altrenogest resulted in a normal embryo diameter in this population.

Late pregnancy

Treatment with a double dose of altrenogest (0.088 mg/kg) to prevent late term abortion in mares is based on the observation that this treatment prevented pregnancy loss in an experimental protocol in which researchers induced abortion with a synthetic prostaglandin at 90–115 days of gestation (Daels *et al.* 1996). Progestins have been suggested to maintain pregnancy in late gestation by inducing myometrial quiescence, suppressing PGF2α secretion, and through a presumed modulation of cytokines (Bailey *et al.* 2010; LeBlanc 2010; LeBlanc *et al*. 2012; Fedorka *et al.* 2019). Therefore, altrenogest is routinely administered during pregnancy for the prevention of abortion and treatment of ascending placentitis, which is the leading cause of infectious abortion in North America (Hong *et al.* 1993). A study by Bailey *et al*. (2010) found that the combined treatment of antimicrobial (trimethoprim sulphamethoxazole), haemorrheologic (pentoxifylline) and progestin (altrenogest; 0.088 mg/kg) effectively treated experimentally induced ascending placentitis following trans-cervical inoculation with *Strep. zoo*. While none of the untreated mares carried to term, 10/12 (83%) of the treated mares produced a viable foal. Unfortunately, the treatments were not assessed individually, so it is unclear whether altrenogest is effective at preventing abortion when used as a singular therapy. It is important to critically determine whether progestin therapy is effective in the treatment of placentitis in light of recent research demonstrating a withdrawal of the progesterone receptor is associated with premature parturition following experimental induction of disease, indicating that altrenogest supplementation may be of no benefit to the treatment of this disease (El-Sheikh Ali *et al.* 2019). It should be noted that samples were only obtained from inflamed placental tissue at the site of infection, and this may not reflect the remainder of the uterus. Nevertheless, the conclusion is supported by Curcio and co-workers who demonstrated that the addition of altrenogest treatment (0.088 mg/kg) had no effect on gestational length, time from inoculation to delivery, or neonatal outcome in comparison with mares solely treated with antimicrobials and anti-inflammatories. This study found that the addition of estradiol cypionate (ECP) to antimicrobial/anti-inflammatory treatment increased gestational length from induction of disease, in addition to improving neonatal viability (Curcio *et al.* 2017). This study evaluated small group sizes when evaluating the effect of treatment, but the data are further supported by other reports that have found altrenogest to negatively impact gestational length (Neuhauser *et al.* 2008). Future studies are needed to determine whether altrenogest should be considered as an entity in the multimodal approach for treatment of ascending placentitis.

Information is incomplete on the foetal response to altrenogest when administered daily to pregnant mares during late gestation. Mares treated with altrenogest daily from 280 days of gestation to parturition appeared to have decreased gestational length (significant trend) have significantly higher incidence of neonatal medical problems such as neonatal death, maladjustment and respiratory rate and an increased risk of birthing fillies with enlarged clitorides (Shoemaker *et al.* 1989; Neuhauser *et al.* 2008). Furthermore, Palm *et al*. (2010) demonstrated that altrenogest administration (0.088 mg/kg) in late gestation is detectable within both foetal fluid compartments in addition to being detectable at a grossly higher concentration in fetal compared to maternal serum, indicating a heightened concentration in the foetal compartment. Yet, foals born to mares receiving altrenogest in late gestation have been shown to have normal onset of puberty, comparable fertility and reproductive function to controls (Squires *et al.* 1989; Naden *et al.* 1990). Based on these findings, the efficacy and necessity of progestin supplementation in mid- to late-pregnancy needs further investigations.

Post-partum mares

Mares experience the initial postpartum oestrous within 5–20 days post-partum (Gygax *et al.* 1979; Blanchard *et al.* 2004), while the uterus is still undergoing repair from tissue alterations during pregnancy and parturition, a process known as involution. Although uterine involution is not complete until 15 days post-partum, studies have found that mares which ovulate greater than 10 days post-partum are more likely to conceive than those which ovulate earlier (Loy 1980). This is believed to be due to the length of time in which the embryo resides within the oviduct following fertilisation (5.5 days) before migrating to the uterine lumen, at which point involution should be complete. Therefore, studies have investigated the use of progestins to delay

ovulation in order to improve fertility on the first post-partum oestrous, but with conflicting results. McKinnon *et al.* (1988a) and McKinnon *et al*. (1988b) found that altrenogest delayed ovulation and increased pregnancy rates in post-partum mares when administered for the initial 8 days post-partum (McKinnon *et al.* 1988b). It should be noted that altrenogest had no effect on other aspects of uterine involution, including uterine tone, size or retention of fluid. Sigler *et al*. (1989) found altrenogest treatment to delay the time to first ovulation by 10 days when administered post-partum for 15 days (Sigler *et al.* 1989). This study also investigated the effect of altrenogest on other parameters including uterine tone, bacteriology and histology, and milk yield/composition, none of which altered. Additionally, in contrast to the previous study, altrenogest did not improve pregnancy rates.

Progesterone in oil has also been investigated for its potential use to delay ovulation post-partum. Loy *et al*. (1975) found that the administration of 100 mg progesterone from Day 5 to Day 14 post-partum successfully inhibited ovulation in 6/9 mares studied. Additionally, the researchers noted no histological changes in treated mares, and pregnancy was achieved in 66% of treated mares, comparable to other oestrous cycles. Bruemmer *et al*. (2002) attempted to improve this protocol with the addition of estradiol-17β. No delay in ovulation was noted when mares were treated with either 150 mg progesterone in oil in combination with 10 mg estradiol-17β or 300 mg progesterone in oil in combination with 20 mg estradiol-17β, and pregnancy rates were comparable when comparing the treated groups to controls. It was noted that none of the P&E treated mares ovulated prior to 10 days post-partum, while 20% of control mares experienced early ovulation. Additionally, less variability from time to ovulation was noted in treated mares. Overall, while progestin treatment does appear to successfully delay ovulation post-partum, there is conflicting data on its ability to improve pregnancy rates in the first oestrous cycle.

Stallions

Synthetic progestins are commonly administered to intact males for behavioural modifications, due to the progestins ability to suppress LH and therefore testosterone production. In both the young and mature stallion, 0.088 mg/kg altrenogest administered *per oral* was shown to decrease circulating LH and testosterone, total scrotal width, daily sperm output and the percentage of morphologically normal spermatozoa (Squires *et al.* 1997; Johnson *et al.* 1998). In contrast, short-term administration of 0.044 mg/kg altrenogest suppressed aggressive behaviour in mature stallions, but had no noted effects on semen quality (Miller *et al.* 1997). It should be noted that the effects noted in the stallion persisted for greater than eight weeks after the cessation of treatment due to effects on spermatogenesis. Therefore, administration of altrenogest should be avoided in breeding stallion, and if necessary, treatment should be discontinued well in advance of the breeding season.

Potential side effects of progestins on the immune system

Progestins have been shown to effect the immune system in a variety of species, as reviewed by Hall and Klein (2017). In humans, similar synthetic progestins to that of the equine industry are available for the purpose of contraception, many of which have been shown to detrimentally affect the immune system. In the majority of species, progesterone is anti-inflammatory and enacts this function on the immune system through signalling on the PR (Hardy *et al.* 2006; Butts *et al.* 2007; Jones *et al.* 2010; Lei *et al.* 2012). In contrast, synthetic progestins such as MPA and levonorgestrel (LNG) have been shown to increase the expression or production of a variety of pro-inflammatory mediators (Coleman *et al.* 2013; Deese *et al.* 2015; Hall *et al.* 2017; Eastman *et al.* 2018). Additionally, the specific function of each individual progestin appears to be affected by the receptor through which it functions, with MPA activating both the PR and glucocorticoid receptor (GR), while LNG solely activates the PR (Kontula *et al.* 1983; Attardi *et al.* 2007). Through this increase in pro-inflammatory cytokine activation, in addition to recruitment of varying immune cells, women placed on synthetic progestins have been found to be at higher risk for a variety of diseases, including HIV (Lavreys *et al.* 2004a, 2004b, 2004c; McClelland *et al.* 2005; Huijbregts *et al.* 2013; Ralph *et al.* 2015), HSV-2 (Kaushic *et al.* 2003; Gillgrass *et al.* 2005; Quispe Calla *et al.* 2016), chlamydia (Kaushic *et al.* 1998, 2000), gonorrhoea (Xu *et al.* 2013) and even influenza (Hall *et al.* 2016, 2017). It is believed that the increased risk of viral and bacterial infection is due to the pro-inflammatory activation of NFκβ, which binds to the terminal repeat of viral DNA, thereby promoting viral replication as well as increasing bacterial migration to the site of inflammation (Hall and Klein 2017).

A recent study investigated the effect of altrenogest on the immune system of nonpregnant mares and found similar results to those reported in humans (Fedorka *et al.* 2019). *In vitro*, altrenogest caused a dose-dependent increase in the expression of the pro-inflammatory cytokine *IL-1β* in addition to the inflammatory-modulating cytokine *IL-6* in peripheral blood mononuclear cells (PBMCs). This was also noted *in vivo*, where under the dioestrus influence of endogenous progesterone, control mares experienced a decrease in the expression of pro-inflammatory cytokines *IFNγ, IL-1β* and *IL-8*, while the PBMCs of altrenogest-treated mares (0.044 mg/kg) did not decrease in the expression of either *IL-1β* or *IL-8*. Additionally, altrenogest treatment led to an alteration in the expression of a variety of cytokines within the endometrium, including *IFNγ, IL-10* and *IL-1RN,* indicating both a local and systemic effect of altrenogest on the immune system of the mare (summarised in **Fig 4**). This may be clinically relevant, as altrenogest administration in nonpregnant mares has been associated with vaginal candidiasis (Montes *et al.* 2001) and uterine inflammation (Palm *et al.* 2013). Interestingly, it was determined that altrenogest alters the immune system of the nonpregnant mare without activating the GR. As it is structurally a 19-nortestosterone, and more comparable to LNG, the lack of GR interaction is not surprising.

In early pregnancy, altrenogest treatment (0.044 mg/kg) from Day 5 post-ovulation to Day 11 led to a decrease in endometrial expression of the PR (Willmann *et al.* 2011a). Additionally, an increase in the number of polymorphonuclear neutrophils (PMN) was noted within the endometrium following treatment. In late pregnancy, no noted changes were observed in endometrial gene expression of *IL-6, IL-8* or *COX-2* following altrenogest treatment (0.088 mg/kg) from Day 280 to parturition (Palm *et al.* 2013). In this same study, treatment with altrenogest had no effect on the expression of the progesterone,

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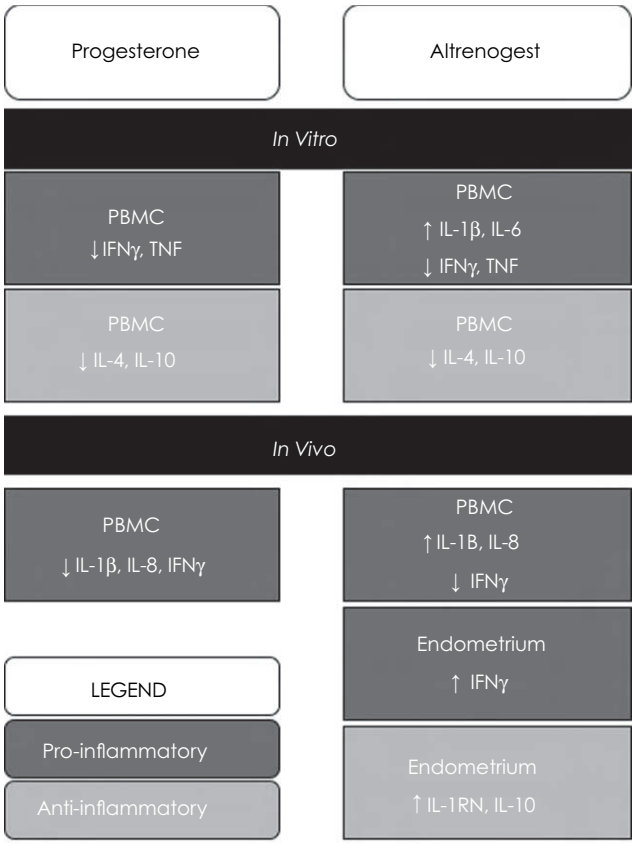

Fig 4: Effect of progestins on immune system of the nonpregnant mare. As previously described by Fedorka et al. (2019).

oestrogen or oxytocin receptors which conflicts with the data seen in the early pregnant mare. This is interesting, as progesterone itself has been found to inhibit the NFκβ pathway, including downstream COX-2 and IL-1β (Lei *et al.* 2015), again indicating a differing pathway of effect for altrenogest. It should be noted that foals born to mares that were treated with altrenogest (0.088 mg/kg) during late gestation up until the day of parturition have been found affected by treatment. This includes an imbalanced neutrophil:lymphocyte ratio, increased cortisol, decreased potassium and decreased calcium within hours after birth (Neuhauser *et al.* 2009). An additional study found neonates born to mares receiving late term altrenogest to have decreased respiratory function and more problems in the perinatal period, including maladjustment and death (Neuhauser *et al.* 2008). It should be noted that this study compared small group sizes and had a higher amount of late-term complications than commonly seen in clinical practice and therefore should be appraised with some concern. These potential side effects are summarised in **Fig 4**.

Conclusion

The use of progestins is a valuable clinical tool in various aspects of equine medicine. Although only progesterone and altrenogest have been found to be consistently progestogenic in the horse, both compounds have been determined to be efficacious in many aspects of reproduction, including oestrus suppression, hastening of transition and early pregnancy maintenance. In the past, progestin treatment has been considered to be without side effects and perhaps overused as an insurance policy of pregnancy maintenance. Recent information suggests that long-term use of altrenogest, particularly during late gestation, may be associated with immune-related side effects in mares and foals. This possibility should be considered when benefits are weighed against risks in clinical situations.

Authors' declaration of interests

No conflict of interests have been declared.

Ethical animal research

Not applicable.

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Authorship

C. Fedorka prepared the manuscript and M. Troedsson gave their final approval.

References

Alexander, S.L. and Irvine, C.H. (1991) Control of onset of breeding season in the mare and its artificial regulation by progesterone treatment. *J. Reprod. Fertil. Suppl.* **44**, 307-318.

Allen, W.R. (2001) Luteal deficiency and embryo mortality in the mare. *Reprod. Domest. Anim.* **36**, 121-131.

Attardi, B.J., Zeleznik, A., Simhan, H., Chiao, J.P., Mattison, D.R. and Caritis, S.N. (2007) Comparison of progesterone and glucocorticoid receptor binding and stimulation of gene expression by progesterone, 17-alpha hydroxyprogesterone caproate, and related progestins. *Am. J. Obstet. Gynecol.* **197**(**599**), e591-e597.

Bailey, C.S., Macpherson, M.L., Pozor, M.A., Troedsson, M.H., Benson, S., Giguère, S., Sanchez, L.C., Leblanc, M.M. and Vickroy, T.W. (2010) Treatment efficacy of trimethoprim sulfamethoxazole, pentoxifylline and altrenogest in experimentally induced equine placentitis. *Theriogenology* **74**, 402-412.

Ball, B.A., Miller, P.G. and Daels, P.F. (1992a) Influence of exogenous progesterone on early embryonic development in the mare. *Theriogenology* **38**, 1055-1063.

Ball, B.A., Wilker, C., Daels, P.F. and Burns, P.J. (1992b) Use of progesterone in microspheres for maintenance of pregnancy in mares. *Am. J. Vet. Res.* **53**, 1294-1297.

Bauer, E.R., Daxenberger, A., Petri, T., Sauerwein, H. and Meyer, H.H. (2000) Characterisation of the affinity of different anabolics and synthetic hormones to the human androgen receptor, human sex hormone binding globulin and to the bovine progestin receptor. *APMIS* **108**, 838-846.

Betteridge, K.J., Raeside, J.I., Waelchli, R.O., Christie, H.L. and Hayes, M.A. (2018) Patterns of conceptus development and of progesterone concentrations in maternal blood preceding spontaneous early pregnancy failure in mares. *Reprod. Fertil. Dev.* **30**, 1066-1076.

Blanchard, T.L., Thompson, J.A., Brinsko, S.P., Stich, K.L., Wendt, K.M., Varner, D.D. and Rigby, S.L. (2004) Mating mares on foal heat: a five-year retrospective study. *Proc. Am. Assoc. Equine Practnrs.* **50**, 525-530

Bristol, F. (1981) *Studies on estrous synchronization in mares*, Pro. Soc. of Therio.

Bruemmer, J.E., Coy, R.C., Olson, A. and Squires, E.L. (2000) Efficacy of altrenogest administration to postpone ovulation and subsequent fertility in mares. *J. Equine Vet. Sci.* **20**, 450-453.

Bruemmer, J.E., Brady, H.A. and Blanchard, T.L. (2002) Uterine involution, day and variance of first postpartum ovulation in mares treated with progesterone and estradiol-17beta for 1 or 2 days postpartum. *Theriogenology* **57**, 989-995.

Butts, C.L., Shukair, S.A., Duncan, K.M., Bowers, E., Horn, C., Belyavskaya, E., Tonelli, L. and Sternberg, E.M. (2007) Progesterone inhibits mature rat dendritic cells in a receptor-mediated fashion. *Int. Immunol.* **19**, 287-296.

Canisso, I.F., Gallacher, K., Gilbert, M.A., Korn, A., Schweizer, C.M., Bedford-Guaus, S.J. and Gilbert, R.O. (2013) Preovulatory progestagen treatment in mares fails to delay ovulation. *Vet. J.* **197**, 324-328.

Colbern, G.T., Squires, E.L. and Voss, J.L. (1987) Use of altrenogest and human chorionic gonadotropin to induce normal ovarian cyclicity in transitional mares. *J. Equine Vet. Sci.* **7**, 69-72.

Coleman, J.S., Mwachari, C., Balkus, J., Sanguli, L., Muliro, A., Agnew, K., Coombs, R.W., Cohen, C.R. and Hitti, J. (2013) Effect of the levonorgestrel intrauterine device on genital HIV-1 RNA shedding among HIV-1-infected women not taking antiretroviral therapy in Nairobi, Kenya. *J. Acquir. Immune Defic. Syndr.* **63**, 245-248.

Conley, A.J. (2016) Review of the reproductive endocrinology of the pregnant and parturient mare. *Theriogenology* **86**, 355-365.

Conley, A. and Ball, B.A. (2019) Steroids in the establishment and maintenance of pregnancy, and at parturition in the mare. *Reproduction* **158**, R197-R208

Crabtree, J.R., Mateu-Sanchez, S., Cooke, C.D., Rogers, I.G., Rendle, D.I. and Wilsher, S. (2018) Investigation into the safety and clinical effects of a new progesterone releasing intra-vaginal device (PRID Delta) in mares. *J. Equine Vet. Sci.* **66**, 123.

Cuervo-Arango, J. and Clark, A. (2010) The first ovulation of the breeding season in the mare: the effect of progesterone priming on pregnancy rate and breeding management (hCG response rate and number of services per cycle and mare). *Anim. Reprod. Sci.* **118**, 265-269.

Curcio, B.R., Canisso, I.F., Pazinato, F.M., Borba, L.A., Feijo, L.S., Muller, V., Finger, I.S., Toribio, R.E. and Nogueira, C.E.W. (2017) Estradiol cypionate aided treatment for experimentally induced ascending placentitis in mares. *Theriogenology* **102**, 98-107.

Daels, P.F., DeMoreas, J., Stabenfeldt, G.H. and Hughes, J.P. (1992) The effect of altrenogest on the development of secondary corpora lutea. *Proceedings of the 12th ICAR*.

Daels, P.F., Besognet, B., Hansen, B., Mohammed, H., Odensvik, K. and Kindahl, H. (1996) Effect of progesterone on prostaglandin F2 alpha secretion and outcome of pregnancy during cloprostenol-induced abortion in mares. *Am. J. Vet. Res.* **57**, 1331-1337.

Deese, J., Masson, L., Miller, W., Cohen, M., Morrison, C., Wang, M., Ahmed, K., Agot, K., Crucitti, T., Abdellati, S. and Van Damme, L. (2015) Injectable progestin-only contraception is associated with increased levels of pro-inflammatory cytokines in the female genital tract. *Am. J. Reprod. Immunol.* **74**, 357-367.

DeLuca, C.A., McCue, P.M., Patten, M.L. and Squires, E.L. (2011) "Effect of nonsurgical embryo transfer procedure and/or altrenogest therapy on endogenous progesterone concentration in mares. *J. Equine Vet. Sci.* **31**, 57-62.

Eastman, A.J., Bergin, I.L., Chai, D., Bassis, C.M., LeBar, W., Oluoch, G.O., Liechty, E.R., Nyachieo, A., Young, V.B., Aronoff, D.M., Patton, D.L. and Bell, J.D. (2018) Impact of the levonorgestrel-releasing intrauterine system on the progression of *Chlamydia trachomatis* infection to pelvic inflammatory disease in a baboon model. *J. Infect. Dis.* **217**, 656-666.

El Hachem, H., Crepaux, V., May-Panloup, P., Descamps, P., Legendre, G. and Bouet, P.E. (2017) Recurrent pregnancy loss: current perspectives. *Int. J. Womens Health* **9**, 331-345.

Ellis, K.E., Council-Troche, R.M., Von Dollen, K.A., Beachler, T.M., Bailey, C.S., Davis, J.L. and Lyle, S.K. (2019) Pharmacokinetics of intrarectal altrenogest in horses. *J. Equine Vet. Sci.* **72**, 41-46.

El-Sheikh Ali, H., Legacki, E.L., Loux, S.C., Esteller-Vico, A., Dini, P., Scoggin, K.E., Conley, A.J., Stanley, S.D. and Ball, B.A. (2019) Equine placentitis is associated with a downregulation in myometrial progestin signaling dagger. *Biol. Reprod*. **101**, 162-176.

Evans, M.J., Loy, R.G., Taylor, T.B. and Barrows, S.P. (1982) Effects of exogenous steroids on serum FSH and LH, and on follicular development in cyclic mares. *J. Reprod. Fertil. Suppl.* **32**, 205-212.

Fedorka, C.E., Ball, B.A., Walker, O.F., Conley, A.J., Corbin, C.J., Lu, K.G., Hanneman, J.M., Troedsson, M.H.T. and Adams, A.A. (2019) Alteration of the mare's immune system by the synthetic progestin, altrenogest. *Am. J. Reprod. Immunol.* **82**, e13145.

Ferreira, J.C., Thompson, D.L. and Boof, A. (2015) Progesterone-releasing intravaginal device in conjunction with estradiol benzoate induces follicular regression in mares. ISER, *J. Equine Vet. Sci.* **35**, 445.

Fowden, A.L., Forhead, A.J. and Ousey, J.C. (2008) The endocrinology of equine parturition. *Exp. Clin. Endocrinol. Diabetes* **116**, 393-403.

Gee, E.K., DeLuca, C., Stylski, J.L. and McCue, P.M. (2009) Efficacy of medroxyprogesterone acetate in suppression of estrus in cycling mares. *J. Equine Vet. Sci.* **29**, 140-145.

Gillgrass, A.E., Fernandez, S.A., Rosenthal, K.L. and Kaushic, C. (2005) Estradiol regulates susceptibility following primary exposure to genital herpes simplex virus type 2, while progesterone induces inflammation. *J. Virol.* **79**, 3107-3116.

Gygax, A.P., Ganjam, V.K. and Kenney, R.M. (1979) Clinical, microbiological and histological changes associated with uterine involution in the mare. *J. Reprod. Fertil. Suppl.* **27**, 571-578.

Hall, O.J. and Klein, S.L. (2017) Progesterone-based compounds affect immune responses and susceptibility to infections at diverse mucosal sites. *Mucosal Immunol.* **10**, 1097-1107.

Hall, O.J., Limjunyawong, N., Vermillion, M.S., Robinson, D.P., Wohlgemuth, N., Pekosz, A., Mitzner, W. and Klein, S.L. (2016) Progesterone-based therapy protects against influenza by promoting lung repair and recovery in females. *PLoS Pathog.* **12**, e1005840.

Hall, O.J., Nachbagauer, R., Vermillion, M.S., Fink, A.L., Phuong, V., Krammer, F. and Klein, S.L. (2017) Progesterone-based contraceptives reduce adaptive immune responses and protection against sequential influenza A virus infections. *J. Virol.* **91**, e02160.

Hardy, D.B., Janowski, B.A., Corey, D.R. and Mendelson, C.R. (2006) Progesterone receptor plays a major antiinflammatory role in human myometrial cells by antagonism of nuclear factor-kappaB activation of cyclooxygenase 2 expression. *Mol. Endocrinol.* **20**, 2724-2733.

Hawkins, D.L., Neely, D.P. and Stabenfeldt, G.H. (1979) Plasma progesterone concentrations derived from the administration of exogenous progesterone to ovariectomized mares. *J. Reprod. Fertil. Suppl.* **27**, 211-216.

Hinrichs, K., Sertich, P.L. and Kenney, R.M. (1986) Use of altrenogest to prepare ovariectomized mares as embryo transfer recipients. *Theriogenology* **26**, 455-460.

Hinrichs, K., Sertich, P.L., Palmer, E. and Kenney, R.M. (1987) Establishment and maintenance of pregnancy after embryo transfer in ovariectomized mares treated with progesterone. *J. Reprod. Fertil.* **80**, 395-401.

Hodgson, D., Howe, S., Jeffcott, L., Reid, S., Mellor, D. and Higgins, A. (2005) Effect of prolonged use of altrenogest on behaviour in mares. *Vet. J.* **169**, 322-325.

Hong, C.B., Donahue, J.M., Giles, R.C. Jr, Petrites-Murphy, M.B., Poonacha, K.B., Roberts, A.W., Smith, B.J., Tramontin, R.R., Tuttle, P.A. and Swerczek, T.W. (1993) Equine abortion and stillbirth in central Kentucky during 1988 and 1989 foaling seasons. *J. Vet. Diagn. Invest.* **5**, 560-566.

Huijbregts, R.P., Helton, E.S., Michel, K.G., Sabbaj, S., Richter, H.E., Goepfert, P.A. and Hel, Z. (2013) Hormonal contraception and HIV-1 infection: medroxyprogesterone acetate suppresses innate and adaptive immune mechanisms. *Endocrinology* **154**, 1282-1295.

Irvine, C.H., Sutton, P., Turner, J.E. and Mennick, P.E. (1990) Changes in plasma progesterone concentrations from days 17 to 42 of

gestation in mares maintaining or losing pregnancy. *Equine Vet. J.* **22**, 104-106.

James, A.N., Vogelsang, M.M., Forest, D.W. and Stott, G.G. (1998) Efficacy of short-term administration of altrenogest to postpone ovulation in mares. *J. Equine Vet. Sci.* **18**, 329-331.

Johnson, M.S., Brady, H.A., Whisnant, C.S. and LaCasha, P.A. (1998) Effects of oral altrenogest on sexual and aggressive behaviors and seminal parameters in young stallions. *J. Equine Vet. Sci.* **18**, 249-253.

Jones, L.A., Kreem, S., Shweash, M., Paul, A., Alexander, J. and Roberts, C.W. (2010) Differential modulation of TLR3- and TLR4-mediated dendritic cell maturation and function by progesterone. *J. Immunol.* **185**, 4525-4534.

Kaushic, C., Murdin, A.D., Underdown, B.J. and Wira, C.R. (1998) *Chlamydia trachomatis* infection in the female reproductive tract of the rat: influence of progesterone on infectivity and immune response. *Infect. Immun.* **66**, 893-898.

Kaushic, C., Zhou, F., Murdin, A.D. and Wira, C.R. (2000) Effects of estradiol and progesterone on susceptibility and early immune responses to *Chlamydia trachomatis* infection in the female reproductive tract. *Infect. Immun.* **68**, 4207-4216.

Kaushic, C., Ashkar, A.A., Reid, L.A. and Rosenthal, K.L. (2003) Progesterone increases susceptibility and decreases immune responses to genital herpes infection. *J. Virol.* **77**, 4558-4565.

Klug, E. and Jochle, W. (2001) Advances in synchronizing estrus and ovulation in the mare: a mini review. *J. Equine Vet. Sci.* **21**, 474-479.

Knowles, J.E., Squires, E.L., Shideler, R.K., Tarr, S.F. and Nett, T.M. (1993) Relationship of progesterone to early pregnancy loss in mares. *J. Equine Vet. Sci.* **13**(**9**), 528-533.

Kontula, K., Paavonen, T., Luukkainen, T. and Andersson, L.C. (1983) Binding of progestins to the glucocorticoid receptor. Correlation to their glucocorticoid-like effects on in vitro functions of human mononuclear leukocytes. *Biochem. Pharmacol.* **32**, 1511-1518.

Krog, M.C., Nielsen, H.S., Christiansen, O.B. and Kolte, A.M. (2016) Reproductive endocrinology in recurrent pregnancy loss. *Clin. Obstet. Gynecol.* **59**, 474-486.

Lavreys, L., Baeten, J.M., Kreiss, J.K., Richardson, B.A., Chohan, B.H., Hassan, W., Panteleeff, D.D., Mandaliya, K., Ndinya-Achola, J.O. and Overbaugh, J. (2004a) Injectable contraceptive use and genital ulcer disease during the early phase of HIV-1 infection increase plasma virus load in women. *J. Infect. Dis.* **189**, 303-311.

Lavreys, L., Baeten, J.M., Martin, H.L. Jr, Overbaugh, J., Mandaliya, K., Ndinya-Achola, J. and Kreiss, J.K. (2004b) Hormonal contraception and risk of HIV-1 acquisition: results of a 10-year prospective study. *AIDS* **18**, 695-697.

Lavreys, L., Chohan, V., Overbaugh, J., Hassan, W., McClelland, R.S., Kreiss, J., Mandaliya, K., Ndinya-Achola, J. and Baeten, J.M. (2004c) Hormonal contraception and risk of cervical infections among HIV-1-seropositive Kenyan women. *AIDS* **18**, 2179-2184.

LeBlanc, M.M. (2010) Ascending placentitis in the mare: an update. *Reprod. Domest. Anim.* **45**, 28-34.

LeBlanc, M.M., Giguere, S., Lester, G.D., Brauer, K. and Paccamonti, D.L. (2012) Relationship between infection, inflammation and premature parturition in mares with experimentally induced placentitis. *Equine Vet. J.* **44**, *Suppl*. **41**, 8-14.

Lei, K., Chen, L., Georgiou, E.X., Sooranna, S.R., Khanjani, S., Brosens, J.J., Bennett, P.R. and Johnson, M.R. (2012) Progesterone acts via the nuclear glucocorticoid receptor to suppress IL-1beta-induced COX-2 expression in human term myometrial cells. *PLoS One* **7**, e50167.

Lei, K., Georgiou, E.X., Chen, L., Yulia, A., Sooranna, S.R., Brosens, J.J., Bennett, P.R. and Johnson, M.R. (2015) Progesterone and the repression of myometrial inflammation: the roles of MKP-1 and the AP-1 system. *Mol. Endocrinol.* **29**, 1454-1467.

Lopez-Bayghen, C., Zozaya, H., Ocampo, L., Brumbaugh, G.W. and Sumano, H. (2008) Melengestrol acetate as a tool for inducing early ovulation in transitional mares. *Acta Vet. Hung.* **56**, 125-131.

Loy, R.G. (1980) Characteristics of postpartum reproduction in mares. *Vet. Clin. North Am. Large Anim. Pract.* **2**, 345-349.

Loy, R.G. and Swan, S.M. (1966) Effects of exogenous progestogens on reproductive phenomena in mares. *J. Anim. Sci.* **25**(**3**), 821-826.

Loy, R.G., Hughes, J.P., Richards, W.P. and Swan, S.M. (1975) Effects of progesterone on reproductive function in mares after parturition. *J. Reprod. Fertil. Suppl*. **23**, 291-295.

Loy, R.G., Evans, M.J., Pemstein, R. and Taylor, T.B. (1982) Effects of injected ovarian steroids on reproductive patterns and performance in post-partum mares. *J. Reprod. Fertil. Suppl.* **32**, 199-204.

Machnik, M., Hegger, I., Kietzmann, M., Thevis, M., Guddat, S. and Schanzer, W. (2007) Pharmacokinetics of altrenogest in horses. *J. Vet. Pharmacol. Ther.* **30**, 86-90.

Macpherson, M.L. (2005) Treatment strategies for mares with placentitis. *Theriogenology* **64**, 528-534.

McClelland, R.S., Lavreys, L., Katingima, C., Overbaugh, J., Chohan, V., Mandaliya, K., Ndinya-Achola, J. and Baeten, J.M. (2005) Contribution of HIV-1 infection to acquisition of sexually transmitted disease: a 10-year prospective study. *J. Infect. Dis.* **191**, 333-338.

McConaghy, F.F., Green, L.A., Colgan, S. and Morris, L.H. (2016) Studies of the pharmacokinetic profile, in vivo efficacy and safety of injectable altrenogest for the suppression of oestrus in mares. *Aust. Vet. J.* **94**, 248-255.

McCue, P.M. (2003) Estrus suppression in performance horses. *J. Equine Vet. Sci.* **23**, 341-345.

McKinnon, A.O., Squires, E.L., Carnevale, E.M. and Hermenet, M.J. (1988a) Ovariectomized steroid-treated mares as embryo transfer recipients and as a model to study the role of progestins in pregnancy maintenance. *Theriogenology* **29**, 1055-1063.

McKinnon, A.O., Squires, E.L., Harrison, L.A., Blach, E.L. and Shideler, R.K. (1988b) Ultrasonographic studies on the reproductive tract of mares after parturition: effect of involution and uterine fluid on pregnancy rates in mares with normal and delayed first postpartum ovulatory cycles. *J. Am. Vet. Med. Assoc.* **192**, 350-353.

McKinnon, A.O., Figueroa, S.t.d.M., Nobelius, A.M, Hyland, J.H and Vasey, J.R. (1993) Failure of hydroxyprogesterone caproate to maintain pregnancy in ovariectomised mares. *Equine Vet. J.* **25**, 158-160.

McKinnon, A.O., Lescun, T.B., Walker, J.H., Vasey, J.R. and Allen, W.R. (2000a) The inability of some synthetic progestagens to maintain pregnancy in the mare. *Equine Vet. J.* **32**, 83-85.

Mckinnon, A.O., Lescun, T.B., Walker, J.H., Vasey, J.R. and Allen, W.R. (2000b) The inability of some synthetic progestogens to maintain pregnancy in the mare. *Equine Vet. J.* **32**, 83-85.

McRobb, L., Handelsman, D.J., Kazlauskas, R., Wilkinson, S., McLeod, M.D. and Heather, A.K. (2008) Structure-activity relationships of synthetic progestines in a yeast-based in vitro androgen bioassay. *J. Steroid Biochem. Mol. Biol.* **110**, 39-47.

Miller, C.D., Dickson, D.V., Blanchard, T.L., Thompson, J.A. and Johnson, L. (1997) Effects of a commonly used progestogen on behavior and reproductive function of stallions. *Procedings of Fourth Annual Race Horse Conference*.

Montes, A.J., Montes, L.F., Vaughan, J.T., Wilborn, W.H., Bado, G., Comero, A. and Blaquier, P.C.P. (2001) Vulvo vaginal candidiasis in thoroughbred mares following progestogen administration intravaginal treatment with clotrimazole. *J. Equine Vet. Sci.* **21**, 68-70.

Naden, J., Squires, E.L., Nett, T.M. and Amann, R.P. (1990) Effect of maternal treatment with altrenogest on pituitary response to exogenous GnRH in pubertal stallions. *J. Reprod. Fertil.* **88**, 177-183.

Neely, D.P. (1988) Progesterone/progestin therapy in the broodmare. *Proc. Am. Assoc. Equine Pract*. 203-217.

Neuhauser, S., Palm, F., Ambuehl, F. and Aurich, C. (2008) Effects of altrenogest treatment of mares in late pregnancy on parturition and on neonatal viability of their foals. *Exp. Clin. Endocrinol. Diabetes* **116**, 423-428.

Neuhauser, S., Palm, F., Ambuehl, F., Mostl, E., Schwendenwein, I. and Aurich, C. (2009) Effect of altrenogest-treatment of mares in late gestation on adrenocortical function, blood count and plasma electrolytes in their foals. *Equine Vet. J.* **41**, 572-577.

Newcombe, J.R. (2002) Field observations on the use of a progesterone-releasing intravaginal device to induce estrous and ovulation in seasonally anestrous mares. *J. Equine Vet. Sci.* **22**, 378-382.

Ousey, J.C. (2004) Peripartal endocrinology in the mare and foetus. *Reprod. Domest. Anim.* **39**, 222-231.

Palm, F.M., Schenk, I., Neuhauser, S., Schubert, D., Machnik, M., Schanzer, W. and Aurich, C. (2010) Concentrations of altrenogest in plasma of mares and foals and in allantoic and amniotic fluid at parturition. *Theriogenology* **74**, 229-235.

Palm, F., Walter, I., Nowotny, N., Budik, S., Helmreich, M. and Aurich, C. (2013) Progestin treatment does not affect expression of cytokines, steroid receptors, oxytocin receptor, and cyclooxygenase 2 in fetal membranes and endometrium from pony mares at parturition. *Theriogenology* **79**, 59-68.

Parry-Weeks, L.C. and Holtan, D.W. (1987) Effect of altrenogest on pregnancy maintenance in unsynchronized equine embryo recipients. *J. Reprod. Fertil. Suppl.* **35**, 433-438.

Perkins, N.R., Threlfall, W.R. and Ottobre, J.S. (1993) Pulsatile secretion of luteinizing hormone and progesterone in mares during the estrous cycle and early pregnancy. *Am. J. Vet. Res.* **54**, 1929-1934.

Quispe Calla, N.E., Vicetti Miguel, R.D., Boyaka, P.N., Hall-Stoodley, L., Kaur, B., Trout, W., Pavelko, S.D. and Cherpes, T.L. (2016) Medroxyprogesterone acetate and levonorgestrel increase genital mucosal permeability and enhance susceptibility to genital herpes simplex virus type 2 infection. *Mucosal Immunol.* **9**, 1571-1583.

Ralph, L.J., McCoy, S.I., Shiu, K. and Padian, N.S. (2015) Hormonal contraceptive use and women's risk of HIV acquisition: a meta-analysis of observational studies. *Lancet Infect. Dis.* **15**, 181-189.

Shideler, R.K., Squires, E.L., Voss, J.L., Eikenberry, D.J. and Pickett, B.W. (1982) Progestagen therapy of ovariectomized pregnant mares. *J. Reprod. Fertil. Suppl.* **32**, 459-464.

Shideler, R.K., Voss, J.L., Aufderheide, W.M., Hessemann, C.P. and Squires, E.L. (1983) The effect of altrenogest, an oral progestin, on hematologic and biochemical parameters in mares. *Vet. Hum. Toxicol.* **25**, 250-252.

Shoemaker, C.F., Squires, E.L. and Shideler, R.K. (1989) Safety of altrenogest in pregnant mares and on health and development of offspring. *J. Equine Vet. Sci.* **9**, 69-72.

Sigler, D.H., Ericson, D.E., Gibbs, P.G., Kiracofe, G.H. and Stevenson, J.S. (1989) Reproductive traits, lactation and foal growth in mares fed altrenogest. *J. Anim. Sci.* **67**, 1154-1159.

Squires, E.L., Heesemann, C.P., Webel, S.K., Shideler, R.K. and Voss, J.L. (1983) Relationship of altrenogest to ovarian activity, hormone concentrations and fertility of mares. *J. Anim. Sci.* **56**, 901-910.

Squires, E.L., Shideler, R.K. and McKinnon, A.O. (1989) Reproductive performance of offspring from mares administered altrenogest during gestation. *J. Equine Vet. Sci.* **9**, 73-76.

Squires, E.L., Martin, J.M. and Jasko, D.J. (1992) Reproductive response of mares after treatment with progestogens with and without the additional of estradiol. *J. Equine Vet. Sci.* **12**, 28-32.

Squires, E.L., Badzinski, S.L., Amann, R.P., McCue, P.M. and Nett, T.M. (1997) Effects of altrenogest on total scrotal width, seminal characteristics, concentrations of LH and testosterone and sexual behavior of stallions. *Theriogenology* **48**, 313-328.

Staempfli, S.A., Clavier, S., Thompson, D.L., Burns, P.J., Lyle, S.K. and McKinnon, A.O. (2011) Effect of a single injection of long-acting progesterone on the first ovulation in early and late spring transitional mares. *J. Equine Vet. Sci.* **31**, 744-748.

Storer, W.A., Thompson, D.L., Gilley, R.M. and Burns, P.J. (2009) Evaluation of injectable sustained release progestin formulations for suppression of estrus and ovulation in mares. *J. Equine Vet. Sci.* **29**, 33-36.

Van der Holst, W., van Laar, P.H. and Oldenkamp, E.P. (1985) Prolonged spring oestrus in mares: the use of progestogens with specific reference to proligestone. *Theriogenology* **24**, 609-617.

Vanderwall, D.K., Marquardt, J.L. and Woods, G.L. (2007) Use of a compounded long-acting progesterone formulation for equine pregnancy maintenance. *J. Equine Vet. Sci.* **27**, 62-66.

Webel, S.K. and Squires, E.L. (1982) Control of the oestrous cycle in mares with altrenogest. *J. Reprod. Fertil. Suppl.* **32**, 193-198.

Wiepz, G.J., Squires, E.L. and Chapman, P.L. (1988) Effects of norgestomet, altrenogest, and/or estradiol on follicular and hormonal characteristics of late transitional mares. *Theriogenology* **30**, 181-193.

Willmann, C., Budik, S., Walter, I. and Aurich, C. (2011a) Influences of treatment of early pregnant mares with the progestin altrenogest on embryonic development and gene expression in the endometrium and conceptus. *Theriogenology* **76**, 61-73.

Willmann, C., Schuler, G., Hoffmann, B., Parvizi, N. and Aurich, C. (2011b) Effects of age and altrenogest treatment on conceptus development and secretion of LH, progesterone and eCG in early-pregnant mares. *Theriogenology* **75**, 421-428.

Wynn, M.A.A., Esteller-Vico, A., Legacki, E.L., Conley, A.J., Loux, S.C., Stanley, S.D., Curry, T.E. Jr, Squires, E.L., Troedsson, M.H. and Ball, B.A. (2018) A comparison of progesterone assays for determination of peripheral pregnane concentrations in the late pregnant mare. *Theriogenology* **106**, 127-133.

Xu, L., Dong, B., Wang, H., Zeng, Z., Liu, W., Chen, N., Chen, J., Yang, J., Li, D. and Duan, Y. (2013) Progesterone suppresses Th17 cell responses, and enhances the development of regulatory T cells, through thymic stromal lymphopoietin-dependent mechanisms in experimental gonococcal genital tract infection. *Microbes Infect.* **15**, 796-805.

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Supporting information

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

Supplementary Item 1: Technical setup of the equipment: a Big Bore CT scanner and custom-designed air-cushion table (arrow) that connects to the patient table of the scanner.

Supplementary Item 2: a) CT myelography. Puncture of the atlanto-occipital cistern, b) Aspiration of cerebrospinal fluid, and contrast fluid injection. c) The neck is latero-flexed for 5 min.

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References:
[1] Brendemuehl JP, Kopp K, Altman J. Uterine Inflammatory Response to Frozen Semen is attenuated by Oral Supplementation of a Blend of Omega-3 Fatty Acids (Algal DHA and Flax Seed) in Susceptible and Resistant Mares. Submitted to Theriogenology. [2] Brendemuehl JP, Altman J, Kopp K. Influence of dietary algal N-3 fatty acids on breeding induced inflammation and endometrial cytokine expression in mares bred with frozen semen. J Equine Vet Sci. 2014; 34(1): 123-124. [3] A.M. Adkin, A.V. Muniz, C.J. Mortensen, L.K. Warren. Maternal fatty acid supplementation influences memory and learning ability in yearling and 2-year-old horses. J Equine Vet Sci. 2015; 35: 418-436. [4] A.M. Adkin, L.K. Warren, C.J. Mortensen, J. Kivipelto. Maternal supplementation of docosahexaenoic acid and its effect on fatty acid transfer to the foal (longitudinal study). Equine Vet Sci. 2013; 33: 321-329. t[5] A.M. Adkin, L.K. Warren, and C.A. McCall. Effect of maternal docosahexaenoic acid supplementation on behavior and cognitive development in nursing foals. J Equine Vet Sci. 2013; 33: 321-399.

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