From the president: Equine veterinary medicine—profession or trade? .... III
Florida academician, Pennsylvania industry veterinarian join AAEP board ..... IV
Two sides of the same scoop: Ice cream, a draft horse and societal expectations .......................................................... VIII

Highlights of Recent Clinically Relevant Papers
S. WRIGHT .......................................................... 618

Editorial
How to write a clinical case report
P. R. MORRESEY ............................................. 620

Case Reports
Perisuspensory abscessation in eight horses with hindlimb cellulitis
T. VYETROGON and M.-S. DUBOIS .............................. 624
Surgical resection of a squamous cell carcinoma in the perianal region of a 23-year-old crossbred American Paint gelding using sharp surgical excision, laser excision and chemotherapy
L. POORE, Y. SMIT, N. DUNCAN and J. WILLIAMS .................. 627

Clinical Commentaries
Cellulitis: Any change?
E. N. ADAM ............................................................................. 625
Cutaneous squamous cell carcinoma (SCC): “What's the problem?”
D. C. KNOTTENBELT and J. S. CROFT .............................. 635

Review Article
Radiotherapy for the treatment of periocular tumours in the horse
A. R. HOLLIS ................................................................. 647

Original Articles
Infections caused by multidrug-resistant bacteria in an equine hospital (2012–2015)
J. N. VAN SPIJK, S. SCHMITT and A. SCHOSTER ................. 653
The use of pneumatic impact lithotripsy and a retrieval pouch to create a closed system for removal of cystic calculi in standing male horses
N. P. DE BERNARDIS, K. A. SEABAUGH, J. ISMAY and M. MUDGE .................. 659
Transrectal ultrasonographic examination of the sacroiliac joints of the horse: Technique and normal images
A. TALLAJ, V. COUDRY and J.-M. DENOIX .......................... 666

Correspondence
Additional ideas concerning the veterinary-farrier relationship
R. A. MANSMANN ......................................................... 672

Advertisers’ Index ................................................................. 634

Cover photo by Dr. Steven Berkowitz.
From the president: Equine veterinary medicine—profession or trade?

By Jeffrey T. Berk, VMD, MRCVS

Although the situation is not unique to the equine veterinary profession, it seems like we as equine vets struggle with finding the right equilibrium between serving our clients in a way that is best for them and their horses versus being used as vendors to accomplish the purposes that our clients have determined for us. Sometimes those things are one and the same, and sometimes they are not. When they are not, we are forced to ask ourselves some hard questions.

As we look at this conflict that has been ingrained in equine veterinary practice, some of the answers may be found in examining the difference between a profession and a trade. In scouring all the resources I could find on what distinguishes a profession from a trade, I came across a few points that resonated with me and many AAEP members that I’ve spoken with over the last year.

We are all aware of some of the features that the individual professions share—training, accreditation, licensing, etc.—but some other features jumped out at me. One was autonomy: professionals have control over and, correspondingly, ultimate responsibility for their own work. Professionals tend to define the terms, processes and conditions of the work to be performed for clients.

Another feature that defines a profession is that members of a profession can exercise discrimination in choosing clients rather than simply accepting any interested party as a customer. In veterinary medicine, this is the basis for the veterinarian-client-patient relationship. Professionals are bound to a code of conduct or ethics in their relationships with clients, colleagues and the public. In one resource, I found the following: “A profession is charged with a substantial degree of public obligation by virtue of its specialized knowledge.”

Regarding the many disciplines that make up equine performance activity, the public grants these sports a “social license to operate,” which is the public’s way of saying that they think we’re doing an adequate job of guardianship of the equine participants of the sport. The public is not necessarily singling out the equine veterinary profession—we would be lumped in with trainers, riders, judges and stewards, racetrack operators and owners—but because we are professionals, we are held to a higher standard by the public who expects us to lead in addressing any issues that have been identified as detrimental to the health and welfare of horses.

Currently, horse racing is being highlighted by many media outlets as requiring leadership to address perceived inadequacies in the management of horses. It is likely that other equine sports and disciplines will attract the same level of scrutiny at some point, so in addition to occupying a leadership role, the AAEP will also need to communicate on a regular basis to both the AAEP membership and the public our ongoing efforts as well as an honest assessment of progress toward the goals with a targeted timeline. Here are some examples:

- Regarding bisphosphonates, the AAEP assembled a working group of AAEP-member veterinarians (racetrack and sport horse practitioners, equine surgeons, equine researchers, regulatory vets and laboratory analytic specialists) in March 2018 to study the use of bisphosphonates and collate the information in order to make a recommendation to the board of directors. This resulted in the board-approved statement which was the basis for the Thoroughbred sales companies in America banning the use of bisphosphonates in sales horses and several racetracks instituting “house rules” banning the use of bisphosphonates in horses racing there. (Please note that this addresses off-label use of bisphosphonates in horses under four years of age and does not impugn its use in older horses as labeled.)

- The AAEP Horseracing Integrity Act Task Force was charged with studying HR 1754, evaluating the AAEP position on the bill (the board approved a shift from “oppose” to “monitor”), and identifying weaknesses in the bill that, if amended, could lead to AAEP support of a national bill. It was unanimously agreed by this group that national uniformity of racing medication is of paramount importance, and we are in the process of finalizing our recommendations for amendments to the bill. We are in regular conversation with both the crafters of the bill at The Jockey Club as well as the legislators (Rep. Andy

continued on page IV
Florida academician, Pennsylvania industry veterinarian join AAEP board

Following a month-long vote by the membership that concluded Oct. 9, Drs. Amanda House and Sarah Reuss were elected to three-year terms on the AAEP board of directors. Each was installed during the Dec. 10 President’s Luncheon at the 65th Annual Convention in Denver, Colo.

Amanda House, DVM, DACVIM
Dr. House is a clinical professor and director of student affairs at the University of Florida College of Veterinary Medicine in Gainesville, Fla.

Dr. House joined the faculty in 2007 and is the director of the Practice-Based Equine Clerkship program, which enables veterinary students to have an ambulatory practice clinical rotation with private practitioners. She also served as an AAEP Student Chapter faculty advisor from 2008-2015. Dr. House received her veterinary degree from Tufts University and completed an internship and large animal internal medicine residency at the University of Georgia’s Veterinary Teaching Hospital prior to joining the University of Florida.

A past president of the Florida Association of Equine Practitioners, Dr. House serves on the AAEP’s Infectious Disease Committee, as moderator of the Infectious Disease Round and on the Mentorship subcommittee. She previously served on the Horse Owner Education, Member Engagement, and Professional Conduct and Ethics committees.

Sarah Reuss, VMD, DACVIM
Dr. Reuss, of Philadelphia, Penn., is a professional services veterinarian with Boehringer Ingelheim. She transitioned from academia to industry in 2016 with Merial, which was subsequently acquired by Boehringer Ingelheim.

For six years prior, Dr. Reuss had been a clinical assistant professor and chief of the Large Animal Medicine Service at the University of Florida College of Veterinary Medicine, where she served on the Admissions and the Internship and Residency Evaluation committees and as a faculty advisor to the AAEP and AVMA Student Chapters.

Upon earning her veterinary degree from University of Pennsylvania, Dr. Reuss completed an internship at Equine Medical Center of Ocala and a large animal internal medicine residency at Texas A&M University. She joined University of Florida following a stint in general practice at McKinlay and Peters Equine Hospital. Dr. Reuss is a member of the AAEP’s Member Engagement Committee and previously served on the Educational Programs Committee.

From the president, continued

Barr [R-KY], Rep. Kurt Schrader [D-OR] and Rep. Ted Yoho [R-FL]) on Capitol Hill, the latter two of whom are veterinarians with constituents who have impressed upon them the importance of this issue.

- The Medication Task Force has been charged with reviewing and updating our medication guidelines with regard to racehorses, sport horses and sales horses. After that is accomplished by the three subgroups, the revised document will be presented to the board of directors for approval. That is Phase One. Phase Two is then to take these guidelines to industry stakeholders who have the power of implementation and enforcement and work with them to institutionalize our recommendations. Unfortunately, the AAEP as an association can only make recommendations—we are not a regulatory body—so we need to partner with the industry to attempt to make the changes that we seek.

- The AAEP Foundation (now known as The Foundation for the Horse), working in conjunction with Grayson-Jockey Club Research Foundation and the Racing Medication and Testing Consortium, has solicited research proposals relative to the study of and testing for bisphosphonates. Currently, there are 10 proposals being considered for potential funding by this trio of organizations, and the selection process that will determine which projects receive funding will be completed by the end of December.

The AAEP is not a trade union. It is an association of professionals who are trying every day to make a positive difference in the lives of their equine patients and clients. It is your association and, as such, the leadership and staff of AAEP are at your disposal to assist you as you are confronted with the hard decisions that a professional is required to make.
AAEP News December 2019

5 things to know about AAEP this month

1. Embarking on its second quarter-century of improving the welfare of horses, the AAEP Foundation has been renamed The Foundation for the Horse.

2. Watch Performance Horse Committee videos examining the role of medication in the care of sport horses at aaep.org/resources/performance-horse-medication.

3. If you’d like to get more involved with AAEP in 2020, complete the Volunteer Interest Form accessible at aaep.org/dashboard.


5. 2021 Milne Lecture nominations are due Jan. 31. Request a nomination form from Carey Ross at cross@aaep.org.

Nominate a distinguished researcher for the 2021 AAEP Milne Lecture
Deadline to nominate is January 31

The Frank J. Milne State-of-the-Art Lecture is a traditional highlight of each year’s annual convention, and you can help determine the 2021 honoree by nominating an accomplished researcher.

The Milne Lecture was created in 1997 to recognize an individual with a distinguished career in research and discovery, and who has presented and published their findings in a specific area of equine health. The lecture is intended to honor the accomplishments of the presenter and provide a meaningful learning experience to the AAEP membership. The lecture is a perspective on the state-of-the-art in the presenter’s area of expertise.

The award recipient will be determined by a subcommittee of the AAEP Educational Programs Committee in February 2020 and will then be presented to the board of directors for approval. The selected individual will deliver their lecture and receive their award at the AAEP’s 2021 Annual Convention in Nashville, Tenn.

Nominees should be an expert in their field with a track record of accomplishment and the ability to relate the topic to the audience. A nomination form must be completed and include qualifications and accomplishments of the nominee.

A Milne Lecture nomination form may be requested from Carey Ross, scientific publications coordinator, at cross@aaep.org. Completed forms must be returned to her by Jan. 31, 2020.

Share your research and reserve your spot at 2020 convention in Vegas

With thousands of practitioners “descending” from Denver with new solutions for patient and personal wellbeing, it’s time to prepare for 2020 by submitting papers to be considered for presentation during the 66th Annual Convention in Las Vegas, Nev., Dec. 5–9. The presenting author of selected papers will receive complimentary registration and a stipend to support travel to the meeting.

Eligible for consideration are scientific papers, “how-to” papers, review papers, abstracts ≤ 250 words and The Business of Practice papers. All paper presentations are limited to 15 minutes with an additional 5 minutes for Q&A.

Papers must be submitted by 3:00 p.m. ET on March 16 at https://s3.goeshow.com/aaep/annual/2020/AAEP_paper_submission.cfm. Authors should visit the site in advance to set up a profile and provide paper and author information before uploading the paper when it is finished. Complete considerations and ethical guidelines are available in the General Instructions area of the site.

Dr. Virginia B. Reef delivers the 2018 Milne Lecture on the topic of equine cardiovascular complexities.
Help equine rescue and retirement facilities apply for free vaccines
2020 UHVRC application deadline is February 1

AAEP members affiliated with 501(c)(3) equine rescue and rehabilitation facilities in the United States should work with those facilities now to complete the application for complimentary vaccines from the Unwanted Horse Veterinary Relief Campaign (UHVRC) by the Feb. 1 deadline.

The UHVRC is a non-profit partnership between Merck Animal Health and the AAEP to safeguard the health and facilitate the adoption of rescue horses. Since its inception in 2008, the UHVRC has provided more than 32,000 doses of core vaccines for horses in need.

The UHVRC provides qualifying equine facilities with Merck Animal Health vaccines to protect against eastern and western equine encephalomyelitis, equine herpesvirus (EHV-1 and EHV-4), West Nile virus, equine influenza and tetanus. Eligible facilities must coordinate an application with an AAEP-member veterinarian and adhere to the AAEP Care Guidelines for Equine Rescue and Retirement Facilities.

Visit uhvrc.org and click the “Get Involved” button to download the application.

Give yourself the gift of tropical CE to start 2020
Register for AAEP’s Resort Symposium by January 10

Enjoy a midwinter Caribbean getaway that is equal parts practical CE and vacation when the AAEP’s 22nd Annual Resort Symposium heads to the Ritz-Carlton, Aruba, Jan. 23–25.

The meeting offers 15 CE hours and will help you administer effective sedation and restraint; triage, treat and manage field emergencies; provide preventative care for neonates and geriatric horses; and protect client horses from the threat of infectious and contagious disease.

After half-day educational sessions, recharge for the year ahead on Aruba’s soft white beaches; or discover the island’s natural splendor by joining colleagues for optional group excursions that include an off-road UTV expedition, kayaking, air-conditioned vehicle tour and catamaran snorkel sail.

The registration deadline for this unique educational opportunity is Jan. 10. Register and view the educational program at aaep.org/meeting/resort-symposium.

Thanks to Boehringer Ingelheim and IDEXX for their sponsorship support of the 22nd Annual Resort Symposium.
At the AAEP’s 22nd Annual Resort Symposium, you’ll lower your stress amid Aruba’s natural splendor and raise the level of care you provide to client horses during practical half-day sessions devoted to:

**Field procedures and emergencies** with Dr. Stephanie Caston  

**Effective sedation and restraint techniques** with Dr. John Hubbell  

**Preventative medicine and biosecurity strategies** with Dr. Tracy Norman

*RACE-approved CE credits: 15*

Sponsored by

Register by Jan. 10 at [aaep.org/meetings](http://aaep.org/meetings)
Two sides of the same scoop: Ice cream, a draft horse and societal expectations

By Mary Scollay, DVM

This past summer while traveling with friends, I came across a field where several Amish families had set up a roadside market selling crafts, jams, baked goods and ice cream. Remarkably, the ice cream churn was powered by an enormous draft gelding on a treadmill. The horse stood quietly until the farmer chirped at him, whereby he began to plod uphill in a rhythmic and determined manner, the treadmill turning the linkage attached to a churn. Out came the iPhones and we all snapped away at this innovative partnership that resulted in—voila—ice cream. Anything that results in ice cream is a good thing, right?

Several weeks later, a friend alerted me to a post on Facebook that appeared to be of that same horse in that same location, but the Facebook post decried the exploitation of the horse, his enslavement and forced servitude, and the cruelty inflicted in his loss of liberty and free will. How is it possible that two people who observed exactly the same thing reached conclusions so profoundly different? I saw a well-fed horse, for all appearances sound and in good health. He was not fearful of his handler nor did he demonstrate reluctance to perform his task. So, what did the Facebook poster see that I didn’t? And what did I see that she didn’t?

The horse’s inherent needs—safety, food and social interaction—have not changed, but the lens through which a non-agrarian public sees and interprets them has. An evolving societal ethos imposes additional expectations with respect to the stewardship of the horses we care for. In some cases, the expectation is beneficial to the horse; in other cases, benign with no discernable effect; but in some cases, a well-intentioned but ill-informed public can put horses at risk, and that can represent a substantial challenge to the equine practitioner.

Some years ago, a dog trainer opined to me that the biggest contributing factor to pet abandonment was the miscommunication that arises when “people treat dogs like other people, while failing to recognize that dogs treat people like other dogs.” A similar conclusion could be drawn with respect to our relationship with the horse—failed understanding results in unmet or unreasonable expectations. There is a role for the equine veterinarian in recognizing and resolving that conflict—to better meet the needs of the horse.

All aspects of equine ownership and management benefit from ongoing self-examination, but external evaluation is also critical to avoid “because we’ve always done it that way” as the sole defense of the status quo. As equine veterinarians, we should be able to defend our practices—or consider changing them. So, the question is not what we as veterinarians can do, but rather what we should do.

Ethics is the contemplation of the “should,” not the “can”; and the “should” includes context that requires consideration. Keeping the arthritic 30-year-old mare comfortable enough to ramble around the pasture may engender a different “should” than the lame performance horse that the owner wants to finish out the show season rather than give an early layoff—and the “should” is impacted by societal expectations that the veterinarian needs to be aware of. Which is not to say that the veterinarian is required to accede to the societal ethos if, as the advocate for the horse, they believe to acquiesce will result in a failure to meet the horse’s inherent needs. The veterinarian has a role as educator in fulfilling their duty as advocate for the horse.

It’s worth noting that evolution of public sensibility about the role of animals is neither new nor static. In the 1930s, Seabiscuit, generally acknowledged to have been chronically continued on page IX
New name, same commitment: AAEP Foundation is now The Foundation for the Horse

The AAEP Foundation, which has distributed more than $6 million in support of its mission. This total includes a cumulative disbursement of $1.4 million in 2018-2019, which is reflective of The Foundation’s growing influence and impact on horse welfare nationally and internationally.

The Foundation’s priorities are to support education through much-needed veterinary student scholarships and educational programs that improve the care of horses; equine research in pursuit of new treatments and cures that improve patient management and prognosis through exceptional science; and benevolence programs such as working equid welfare administered by “Equitarian” veterinarians, disaster preparedness training and relief efforts for horses in need, and initiatives aimed at improving the lives of horses at risk or in transition.

For additional information about The Foundation for the Horse or to make a gift online, visit foundationforthehorse.org.

Your year-end gift makes a difference

When disasters strike, and horses are in peril. When horses become a burden to their owners. When working equids in developing countries lack the basics. When veterinary students are financially overwhelmed. When equine research is disturbingly underfunded.

Through Education, Research and Benevolence, The Foundation for the Horse improves the welfare of the world’s horses and working equids.

Your year-end gift to The Foundation for the Horse is tax-deductible, and it has a lasting impact. You can make a year-end gift in one of three ways:

- By phone: (859) 233-0147
- By mail: 4033 Iron Works Parkway, Lexington, KY 40511
- Online: foundationforthehorse.org

Your generous gift today, added to the gifts of others, will change the landscape for horses.

Two sides of the same scoop, continued

unsound, became a national symbol of overcoming adversity and inspired a population struggling to rise out of the Great Depression. Today, there would be nothing heartwarming about the prospect of a lame horse being sent out to race. A May 15, 1968, Associated Press article reported, “Dancer’s Image was feeling frisky today, just three days before the 93rd running of the Preakness, following the tapping of his bothersome right front ankle last night.”

Again, it’s not hard to say that within the current ethos that practice would be insupportable. But both events, each in the context of the time, were acceptable.

The passage of a few decades affords clarity that can be difficult to achieve in the moment. All of which makes me wonder if, in 30 years, someone sees that same photo of the horse on the treadmill, what will be their response?
Although semi-retired after selling her ownership stake in Genesee Valley Equine Clinic in Scottsville, N.Y., in December 2017, Dr. Ann Dwyer continues to influence the welfare of horses through her part-time practice and her commitment to various educational programs as a lecturer on ophthalmology and practice management topics and as vice chair of the Cornell University College of Veterinary Medicine Advisory Council.

Dr. Dwyer’s lifetime of compassion for the horse and concern for its well-being began as a child in pony club and will continue in perpetuity as a member of The Foundation’s Halina Leonard Legacy Society. Dr. Dwyer recently discussed her bequest, which she said was one way of giving back for all that the horse has provided.

Is there an important moment, person or special reason connected with AAEP that influenced your decision to include The Foundation in your estate plans?

My decision to include The Foundation in my estate plan grew from my service on the AAEP board of directors (2006-2008) and executive committee (2010-2014). I experienced firsthand the influence that AAEP and its Foundation have on the welfare of the horse and the industry in general during my year as AAEP president (2013).

When you think of The Foundation, what key words or phrases come to mind?


What legacy do you hope to leave through your estate gift?

Horses and the horse industry have provided me with a fascinating and rewarding career. I have enjoyed giving back through service as an educator and AAEP volunteer. My estate gift will be a way to keep on giving in the future.

From your perspective, how has the work of The Foundation influenced the welfare of the horse?

Many, many ways. Through scholarship support for future veterinarians. Through disaster relief for all kinds of situations that jeopardize equine lives and welfare. In recent years, The Foundation has escalated their support of research that is improving the ability of veterinarians to optimize equine health. The establishment of the Equine Disease Communication Center was a keystone effort. The EDCC has become a central resource for accurate communication of evolving disease situations; the entire industry relies on the information it transmits on a daily basis.

What advice would you like to share with other members about this?

Think hard about what horses have done for you in your life. Consider a donation to The Foundation every year as a way to give back, and also keep The Foundation in mind when you make an estate plan. You can also consider making a donation to The Foundation in memory of patients you have cared for, to honor clients or friends in the industry, or to celebrate a milestone in your career or in the career of someone you have mentored.

How would you describe The Foundation to someone who isn’t familiar with it?

The mission of The Foundation is to improve the welfare of horses. This non-profit organization does so in a variety of ways: benevolence, research, education and disaster relief. You have the option to designate the area you would like to support. If you make a contribution of any amount to The Foundation, 100% of the funds you give will work for The Foundation mission as administrative costs are not taken out of donor funds.

Could you talk about the considerations that went into your estate gift to The Foundation and the importance of estate planning in general for equine practitioners?

No matter your age, you should have a will! Even if you are very young, you should have some kind of plan for what will happen after you are gone. Setting up a will does not have to be expensive or complex. As your life changes, any designations that you have chosen can be modified.

As life evolves, our situations become more complex. If you serve clients, own a business, have a role in a governmental or educational institution, and/or have a family, other people depend on you. An estate plan is essential to provide continuity for any of these roles, as well as delivering any philanthropic intent you have for your personal legacy. A carefully constructed estate plan will optimize the impact your life will have on the people, animals, institutions and the causes that are important to you.

Interested in joining the Halina Leonard Legacy Society? Contact Dr. Paul Ransdell, senior development officer, at (859) 233-0147 or pransdell@aaep.org.
Dr. Glenn Anderson, former AAEP board member, dies at 70

Dr. Glenn F. “Andy” Anderson, founder of Equine Veterinary Associates in Broken Arrow, Okla., and a longtime volunteer leader with AAEP, passed away Oct. 21 after a courageous battle with brain cancer. He was 70.

After graduating first in his veterinary school class of 1975 from Oklahoma State University, Dr. Anderson completed an internship in Littleton, Colo., before returning home to Broken Arrow to open Equine Veterinary Associates. He practiced for 40 years and mentored many young veterinarians in the art of equine medicine.

Dr. Anderson served on the AAEP board of directors from 1995-1998 and was heavily involved in AAEP committee service through the years. He chaired the Farrier Liaison and Purchase Exam committees and served on the Abstract Review, Biological & Therapeutic Agents, Drugs & Medications, Horse Show, and Public Relations committees.

Members in the News

Dr. Jill Lancaster named president of Georgia VMA
Dr. Jill Lancaster, who provides relief medicine and surgery services in central Georgia, was sworn in as president of the Georgia Veterinary Medical Association during its annual fall conference in Atlanta on Oct. 20.

A 2004 graduate of the University of Georgia, Dr. Lancaster has served on the GVMA board of directors since 2008 and as a member of the executive board and Advocacy Committee since 2013.

Professional Rodeo Cowboys Association honors Dr. Eddie Taylor
Dr. Eddie Taylor, attending veterinarian at La Fiesta de los Vaqueros in Tucson, Ariz., for the past 32 years, has been named 2019 PRCA/Zoetis Veterinarian of the Year for his commitment to the health and welfare of rodeo livestock. The ceremony took place Dec. 4 at the PRCA Awards Banquet in Las Vegas, Nev.

Dr. Taylor, who received his veterinary degree from Oklahoma State University in 1985, was instrumental in designing the animal care unit as well as the animal care and emergency procedures at the Tucson rodeo, for which he also leads the annual review of animal welfare procedures. He has served in the same capacity at other ProRodeo competitions, including the Prescott Frontier Days, Coors Showdown Rodeo and RAM Turquoise Circuit Finals Rodeo.

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The Vetlexicon service from AAEP Media Partner, Vetstream Ltd, provides evidence-based, peer-reviewed clinical information designed to aid critical decision making at the point of need. Collaborating content from over 1,000 of the world’s leading veterinary professionals and academics, Vetlexicon consists of articles, images, videos, surgical techniques, formulary, exclusive owner factsheets and more.

There are a host of benefits to this service, including staying ahead of veterinary knowledge and competition, improving trust and client communications, and uniting staff in the delivery of the best quality of care.

You can try Vetstream’s Vetlexicon service with a free, no-obligation, 30-day trial. Sign up at aaep.org/vetstream. After your free trial, you will receive a 20% discount on your Vetlexicon subscription.
Welcome new members, and congratulations recent graduates

**New Members:**

Seongjue Ahn, DVM, Lexington, KY  
Nicole Arcy, DVM, Dearborn, MI  
Laura Britton-Thompson, DVM, Fort Collins, CO  
Marcello Cabrera, DVM, Cotia, Sao Paulo, Brazil  
Stephane Cuiller, DVM, Meslay Du Maine, France  
Paul T. Fornstrom, DVM, Pine Bluffs, WY  
Christine Hardy, DVM, Fort Collins, CO  
Carey Harms, DVM, Penn Valley, CA  
Jennifer Hodge-Adams, DVM, Russell, ON, Canada  
Robert Holt, DVM, Lynden, WA  
Cassie Holtz, DVM, Roscoe, SD  
Sandy Larson, DVM, Jordan, MN  
Lori A. Miller, DVM, Waller, TX  
Mary Lynn Neumeister, DVM, Dubuque, IA  
Thomas Josef O’Brien, BVSc, Athens, GA  
Karen Pimentel, DVM, Saskatoon, SK, Canada  
Tara Riddick, DVM, MS, Summerdale, AL  
Jose Miguel Rivera Martorell, DVM, Lexington, KY  
Andres F. Sanchez Teran, DVM MSc, Sherwood Park, AB, Canada  
Kristi Sandman, DVM, DACVS, Dubuque, IA  
Elizabeth Shafer, DVM, Prospect, KY  
Brian Silva, DVM, Gooding, ID  
Ruth Stewart, MRCVS, Starkville, MS  
Kelly Stoneburner, DVM, Waynesboro, VA  
Debra Taylor, DVM, Ashland, AL  
Rasmus Ulf Westgren, DVM, Farhult, Skane, Sweden  
Robin E. Zack, DVM, Canandaigua, NY

**Recent Graduates:**

Alyssa Ball, DVM, Edmond, OK  
Alexandria Bridges, DVM, Bixby, OK  
Alyssa Butler, DVM, Phoenix, AZ  
Taylor Clawson, DVM, Las Vegas, NV  
Ashley Davenport, DVM, Newnan, GA  
Samantha Eder, DVM, Versailles, KY  
Emmaline Farrell, DVM, Richland Center, WI  
Emily Matheson Max, DVM, Columbia, SC  
Brittany Miller, DVM, Littleton, CO  
Ann E. Oakes, DVM, Three Forks, MT  
Jared Dwayne Oldham, DVM, Lander, WY  
Samantha Pomroy, DVM, Paradise, NL, Canada  
Natalie Wilson, DVM, Chatham, VA  
Rachel Marie Ziesmann, DVM, Oconomowoc, WI

AAEP Educational Partner Profile: Boehringer Ingelheim

About the equine business of Boehringer Ingelheim

As the global leader in equine health, Boehringer Ingelheim’s main goal is to improve equine patients’ health and quality of life. We are dedicated to providing the latest product technology for the treatment and prevention of disease in horses. Learn more about our product portfolio and what we can offer the veterinary community by visiting www.bi-vetmedica.com/species/equine.html.

About Boehringer Ingelheim Animal Health USA, Inc.

Boehringer Ingelheim is the second largest animal health business in the world, with net sales of almost $4.7 billion (3.9 billion euros) worldwide in 2018, about 10,000 employees and a presence in more than 150 markets. We have pioneered advancements in vaccines, parasite-control products and therapeutics that limit pain and slow disease, and we aim to create the future of animal wellbeing for pets, horses and livestock by focusing on prevention.

About Boehringer Ingelheim

Improving the health of humans and animals is the goal of the research-driven pharmaceutical company Boehringer Ingelheim. The focus in doing so is on diseases for which no satisfactory treatment option exists to date. The company therefore concentrates on developing innovative therapies that can extend patients’ lives. In animal health, Boehringer Ingelheim stands for advanced prevention.

Family-owned since it was established in 1885, Boehringer Ingelheim is one of the pharmaceutical industry’s top 20 companies. Some 50,000 employees create value through innovation daily for the three business areas: human pharmaceuticals, animal health and biopharmaceuticals. In 2018, Boehringer Ingelheim achieved net sales of around $20.7 billion (17.5 billion euros). R&D expenditure of about $3.8 billion (3.2 billion euros), corresponded to 18.1 per cent of net sales.

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Highlights of recent clinically relevant papers

Contrast radiography of the DFTS

This multicentre retrospective study by Abigail Kent and colleagues in the UK aimed to evaluate contrast radiography of the digital flexor tendon sheath (DFTS) in diagnosing intraheal tendon pathology.

Medical records from three equine hospitals were reviewed. Horses were included in the study if they were diagnosed with lameness localised to the DFTS and had both contrast radiography and subsequent tenoscopy under general anaesthesia performed to confirm a diagnosis of a manica flexoria (MF) tear, deep digital flexor tendon (DDFT) tear or palmar/plantar annular ligament (PAL) constriction. For contrast radiography, 5–7 mL of sodium meglumine diatrizoate or iohexol was injected with 10 mL mepivacaine hydrochloride into the DFTS. Horses were then walked for 4–5 strides before a lateromedial radiograph of the distal limb was taken. Radiographs were reviewed by four operators blinded to case details. Sensitivity, specificity and interobserver variability were calculated for each pathology.

A total of 206 horses met the inclusion criteria. Contrast tenography was a sensitive test for MF tears and specific for DDFT tears, but there was a poor agreement between evaluators when diagnosing PAL constriction from contrast radiographs. Ponies and cobs were significantly more likely to be affected with MF tears, whereas Thoroughbreds, Warmbloods and draught breeds were more likely to have DDFT tears.

These results indicate that contrast radiography of the DFTS may offer an accurate diagnosis of certain DFTS pathologies.

Equine infectious keratitis

In this study, Minna Mustikka and colleagues retrospectively described laboratory findings, treatment and outcome associated with equine infectious keratitis in Finland.

Medical records of horses diagnosed with infectious keratitis at the University of Helsinki Equine Hospital over a 11.5-year period were reviewed.

Of the 47 cases included in this study, keratomycosis was diagnosed in 27 eyes and bacterial keratitis in 20 eyes. Aspergillus flavus was the most frequent fungal isolate (9/17, 53%), followed by Cylindrocarpon sp. (3/17, 18%) and Aspergillus fumigatus (2/17, 12%). Susceptibility was tested for 10/11 Aspergillus sp. isolates; all were susceptible to voriconazole while only two were susceptible to amphotericin B. Cylindrocarpon sp. isolates were resistant to both agents. Streptococcus equi subsp. zooepidemicus was the most frequent bacterial isolate (9/19, 47%), followed by other streptococci (4/19, 21%). All 13 streptococci sp. isolates were susceptible to penicillin, and all tested isolates (n = 11) were also susceptible to chloramphenicol. Mean duration of medical treatment was longer in fungal keratitis (38 days) than in bacterial keratitis (25 days). Globe-sparing surgery in addition to medical therapy was performed in 26 eyes. Recovery was achieved in 66% (31/47) of all cases and in 59% (16/27) of cases with keratomycosis and 75% (15/20) of cases with bacterial keratitis.

Although Aspergillus sp. and S. zooepidemicus were the most frequently encountered isolates, cytology, culture and susceptibility testing are essential to differentiate bacterial and fungal keratitis and guide the clinician to choose the most efficient treatment.

MicroRNA fingerprint biomarkers

Serum and whole blood microRNA (miRNA) fingerprints have been proposed as a new class of noninvasive human cancer biomarkers. In this study, Lucia Unger and colleagues in Switzerland compared equine sarcoid (ES) disease-specific serum and whole blood miRNA fingerprints and correlated them with miRNA expression in sarcoid tissue.

After high-throughput sequencing, miRNA differential expression analysis between six ES-affected and five control horses was carried out in serum and whole blood using a DESeq algorithm, accounting for the influence of haemolysis and the white blood cell count. Target gene, pathway prediction and enrichment analyses were conducted using TarBase, mirPath and GeneCodis. Four of 11 serum samples were haemoylsed and were excluded; in the remaining serum samples, 9 miRNAs were found to be differentially expressed in serum of ES vs. control horses. In whole blood, all 11 samples showed normal white blood cell counts and 19 miRNAs were found to be differentially expressed. A total of 2/9 serum and 7/19 whole blood differentially expressed miRNAs were also highly expressed at the tissue level, and their predicted target genes were associated with cancer pathways. Serum and whole blood miRNA expression allowed discrimination between ES and control horses and merits further validation in a larger study cohort. The use of whole blood might be superior because it has higher miRNA content and is less influenced by pre-analytical variables compared with serum. Concurrent dysregulation of single miRNAs in tissue and blood suggests a possible biological function of circulating miRNAs.

Inflammatory bowel disease

In this retrospective study, Constanze Fintl and colleagues in Norway and Sweden evaluated the immunohistological changes to the interstitial cells of Cajal (ICC), enteric neurons and glial cells in the small intestine of horses with inflammatory bowel disease (IBD).

Immunohistochemistry was performed on ileal samples collected at post-mortem from eight normal control horses and from 14 horses with clinical signs of IBD. The duration of illness ranged from 3 weeks to 6 months, with two horses having received corticosteroid therapy prior to euthanasia. Tissue sections were labelled with anti-CD117 (c-Kit), anti-TMEM16 (TMEM16), anti-protein gene product (PGP9.5) and anti-glial fibrillary acidic protein (GFAP). Images were then analysed to quantify the presence of ICC, neuronal and enteroglial networks.

ICC networks were significantly reduced in the myenteric plexus region in horses with IBD compared with the controls for both markers. All IBD cases had villous atrophy and lymphoid hyperplasia of the mucosa and submucosa, but the myenteric ganglia typically appeared normal and free from inflammatory cell infiltrate. The authors concluded that disruption to ICC networks may contribute to the clinical signs of IBD.
Biannual equine influenza vaccination

This knowledge summary by Emma Shipman considers the PICO question ‘In three day event horses, does biannual routine influenza vaccination compared to annual routine influenza vaccination reduce performance levels?’

There is no evidence that biannual equine influenza vaccination compared with annual booster vaccination in 3-day event horses is associated with reduced performance.

A group of five studies published over an 11-year period from one veterinary hospital were evaluated. In adult Warmblood horses, there is weak evidence that exercise in the 28-day period post-booster vaccination for equine influenza and equine herpes viruses 1 and 4 (EHV1 and 4) is associated with changes in physical and clinical pathophysiological parameters including total red blood cell (RBC) count, neutrophil and lymphocyte count, fibrinogen concentration and serum proteins. These changes occurred at variable time points in the 14 days post-exercise, and values were not outside the published reference ranges for the reporting laboratories where published. Athlete performance of the horses was not evaluated.

No recommendations for equine influenza vaccination protocols in 3-day event horses can be made from the evidence.

Post-operative reflux after small intestinal surgery

In this retrospective study, Carrie Jacobs and colleagues in the United States aimed to determine whether perioperative variables can be used to differentiate a medical vs a surgical reason for post-operative reflux (POR) after small intestinal (SI) surgery in horses.

Medical records of horses >1 year of age that underwent SI surgery and developed POR over an 8-year period were reviewed. Surgical reasons for POR were defined as an anastomosis complication, mechanical obstruction or nonviable intestine identified at repeat celiotomy/necropsy. A medical reason for POR was presumed when the POR improved with medical treatment or when no surgical reasons were identified at repeat celiotomy/necropsy. Perioperative variables were analysed and used to develop a logistic regression model.

Post-operative reflux after SI surgery was reported in 51 horses. After initial SI surgery, 14 horses had surgical reasons for POR diagnosed at repeat celiotomy or necropsy. Thirty-seven horses were considered to have medical reasons for POR because their POR resolved with medical management or functional ileus was diagnosed at repeat celiotomy/necropsy. A greater volume and a greater duration of POR were not associated with a surgical reason for POR. Rather, a post-operative (PO) fever and the timing of colic in the PO period were associated with a surgical reason for POR.

Horses that developed a fever and colic in the PO period after SI surgery were more likely to have a surgical reason for POR. These findings may provide guidance for clinicians when they are making decisions about repeat celiotomy in horses with POR after SI surgery.

Long-term outcome after stifle arthroscopy

In this retrospective study, Annette McCoy and colleagues in the United States reported the outcome of horses engaged in Western performance disciplines after stifle arthroscopy and identified prognostic factors for return to performance.

Medical records were reviewed for 82 horses involved in athletic performance/training for various Western performance disciplines and undergoing arthroscopy for lameness localised to the stifle. Telephone interviews with the owners were conducted ≥2 years post-operatively. Preoperative and intraoperative findings as well as post-operative treatment were analysed for their association with return to athletic performance as the primary outcome of interest.

The most common disciplines represented were cutting (n = 38), Western pleasure (n = 13) and reining (n = 13). Approximately 40% (32/82) of horses returned to intended use after surgery. Increased age, higher degree of lameness, longer duration of lameness and the presence of partial thickness cartilage lesions decreased the odds of returning to athletic performance. Post-operative therapies (intra-articular: stem cells, corticosteroids, interleukin-1 receptor antagonist protein and hyaluronic acid/poly sulfated glycosaminoglycans; systemic: nonsteroid anti-inflammatory drugs, hyaluronic acid/poly sulfated glycosaminoglycans and oral joint supplements) did not affect the odds of returning to intended use.

The prognosis of Western performance horses undergoing stifle arthroscopy is as guarded as that previously reported in horses of other disciplines.

S. WRIGHT
EVE Editorial Office

References
Editorial

How to write a clinical case report

Summary
A case report should communicate a novel occurrence, manifestation or management of a case. The goal is to add to the body of knowledge of an existing or newly recognised condition, whether as documentation of a single clinical episode, or as part of a series of clinically similar events.

Introduction
The publication of case reports has decreased somewhat in the recent literature. They have received criticism for being anecdotal, or for emphasising bizarre or spurious occurrences. Therefore, they have been considered to have potential to mislead their readership. Instead, it could be argued they should be considered to be at the forefront of recognising the unexpected. Evidence-based medicine reports have somewhat supplanted case reports in the relaying of information; they focus on determining the best evidence to guide clinical decision-making, whether this be a particular therapy or diagnostic test. Ultimately, the randomised clinical trial is considered the best way to determine whether a particular intervention is of clinical benefit.

In their defence, case reports remain an excellent complement to evidence-based medicine. Through the development of medicine both veterinary and medicine, case reports have provided a way of relaying clinical experience and disseminating knowledge, and in some cases, have provided pivotal observations changing medical understanding and practice. They are essentially a written ‘case rounds’, using history and presentation of actual cases to teach management in a primary role as clinician, using realistic scenarios with medical evidence of disease, and detailed decision-making based upon available clinical information. They are, in practice, a dress rehearsal for the reader when faced with a similar presentation. Case reports allow recognition of unexpected or rare clinical occurrences, or new observations not found in standardised textbooks. They challenge the reader’s conventional focus on recall of rote-learned manifestations and management of diseases.

What is a case report?
Case reports tend to fall into three categories: an unusual or novel condition that has not been reported in the literature that is, recognition and description of a new disease; a rare complication of a previously known or routinely managed disease condition; or a new management approach to a common and important clinical syndrome.

What makes a good case report?
Case reports demand a clear focus and explicit documentation as to why they are deserving of publication, and justify the time taken to read and understand them. The most important single message the author wishes to convey should be clearly spelled out. If the case report supports current thinking, this should be stated. If the case report runs counter to current dogma, it should detail how it challenges established thinking. Where a new recommendation arises from the case relating to diagnosis or treatment, this can be highlighted using aspects of the case progression as supporting evidence. If a rarity that could have otherwise been missed is the subject of the report, how this presentation could have been missed and how to avoid missing it in the future should be explained.

Should I attempt to write and publish a case report?
The process of collating case information, searching the relevant medical literature, and writing in an organised scientific manner is a time-consuming endeavour. The process will greatly aid the author in developing deeper medical understanding. The skills developed during this process are then useful during research of other topics of interest or provide a skill set enabling further clinical reporting. Contribution to the body of knowledge may also provide the author both personal and professional benefits.

Getting started
Search the veterinary literature
Of utmost importance is determining whether a similar case observation has previously been reported. The author should search PubMed, Medline, Ovid, Agricola, CAB abstracts and Google Scholar for related case material. Existing case reports and case series may provide supporting information for the case in question, or may negate the necessity of reporting the current episode if sufficiently similar case documentation has already occurred. The author must remember to survey journals in the equine veterinary space that may not be listed in the above databases.

Collect all relevant documentation related to the case
While case documentation and clinical information is current and accessible, this material should be stored in a permanent fashion so as complete information is available later. This will minimise interruption during the write-up phase of the case report. The lack of critical information may prevent complete reporting of case progression or reduce the quality of the report for the reader.

Choose a target journal for the final report
While this may seem to be a decision to be made once the report is near completion, it is important to make this decision early in the case report process. Journals vary greatly in requirements for structure and content of the case report, have different formats for references that make up the bibliography, and differ in how references are indicated within the text of the manuscript. The use of a reference managing program integrated into a word processing
program is extremely useful, allowing not only an orderly insertion and modification of reference citation into the text, but easy changing of formatting should this be required. The requirements for publication of each potential target journal must be carefully read as there may be fees for publication once the manuscript is accepted.

What are the steps to writing a good case report?

It is important to be succinct and only relate those points which are germane to the reporting of the clinical progression of the case. Case reports should not be expansive, and report only the facts of the case with an appropriate supportive literature review accompanying its procedural aspects. Journals may set a word limit that is important to adhere to as this will promote concise reporting and reduce the time taken to complete the editorial process.

The structure of case reports and case series will differ from that of clinical research reports. The format of introduction, materials and methods, results and discussion widely used for scientific reporting is not readily applicable to relaying of clinical case material. A suitable case report format would include the following broad categories:

1 Preamble
A summary paragraph, designated summary, should open the case report. This is in essence an abstract of the article to follow. As detailed later in this section, this is best written after the completion of the case report proper. This is then followed by an opening section, designated introduction. A brief summary of the relevant literature and initial justification for production of the case report can be made in this section. As closure to the introduction, the author can summarise in one sentence the essence of the case report, where the importance and perhaps the unique nature of the case should be clearly stated to the reader.

2 Body of the case report
The following sections do not necessarily require their own heading or separation unless this improves reader understanding. Instead, they should be systematically included in the body of the text of the report and flow logically in order from start to finish. If a case series is being produced, for each patient the following information should be provided and separated into individual ‘case presentations’.

Signalment and history
A brief description of the signalment of the cases should open the case report. Immediately following this, a chronological report of relevant case history should be provided. Next, the history of the presenting condition should be detailed. If the case was examined over multiple visits with previous treatment episodes before the beginning of the reported occurrence, these can be separated as ‘presentation episodes’ within the history.

Examination findings
Physical examination findings should be presented in a systematic fashion compatible with the initial work-up of the case. Vital signs, auscultation findings, palpation findings and visual assessment (mentation, body condition, cutaneous or other grossly visible organ system lesions) can be detailed in this section.

Diagnostic work-up and findings
Following the initial assessment, more advanced tests to narrow the differential diagnosis will be performed. Findings of clinical pathology, microbiology, ultrasonography, radiography, advanced imaging (computed tomography, magnetic resonance imaging) and specific serological, pathological, immunological and endocrinological testing can be reported in this section.

With this information, a working diagnosis or definitive diagnoses as a basis for the ensuing treatment plan can be stated.

Treatment plan
A complete listing of all treatments (both generic and proprietary name where applicable), dose rates administered (in units of the International System, SI), route of administration and treatment intervals should be given. The author should ensure all medications are referenced in the footnotes as per journal instructions.

Outcome
Progression of the case should be relayed in chronological format. At treatment termination, degree of clinical resolution and any follow-up, or the results of any necropsy evaluation, should be detailed as the final part of the body of the case report.

Images
It is important to only include images of high quality and high relevance. Captioning should be succinct and directly relate to the passage of text within the case report where the image will elaborate on details to improve understanding. Highlighted areas and regions of interest within the images should be clearly indicated and match the associated captioning.

3 Discussion
This is in some way the most impactful section of the case report. Rationale for reporting the case can be explained. The case is compared with similar or supporting articles in the literature, with both case reports and primary research articles being referenced. This allows the pathophysiology, outcome and relevance of the case to the general population to be put into context for the reader. This section is also a primer for further reading and a resource for future authors during their literature search in any case presentation related to the report which may also reference it. If limitations exist in the case report they can be stated and placed in context within the case progression and existing literature. The closing paragraph should briefly detail any conclusions arising from the case report which add to the reader’s knowledge base.

4 Acknowledgements
It is important to acknowledge individuals with an impactful role on the progression of the case or those essential in preparation of the manuscript, if not listed as authors (see author criteria mentioned below). This includes individuals who have provided technical or writing assistance. Any funding sources must also be included in this section.

5 References
Wherever possible, original literature should be cited to support statements made in the introduction and discussion. Excessive referencing is to be avoided, with only the most relevant
supporting literature being quoted. It is vitally important for the author to ensure the integrity of the references quoted within their manuscript. Continuing errors can occur throughout the scientific literature when references are sourced in the bibliography of other publications without checking the accuracy of these citations.

6 Summary/abstract
It is easiest and most appropriate to write the summary/abstract that will precede the case report last, once all details of the case are logically relayed and the discussion of relevant literature is written. This enables the author to make a succinct overview of the case and its relevance in a few sentences to both attract and inform potential readers. The abstract should condense the case report while maintaining the important information. As this may be the only part of the report that potential readers access from an electronic database during a literature search, it should seek to inform and stimulate interest in accessing the entire case report. Information pertaining to search engine optimisation can be found at Wiley Author Services https://authorservices.wiley.com/author-resources/index.html

7 Abbreviations and keywords
The first use of an abbreviation should be spelled out in the case report. Subsequent entries should consistently use the abbreviation. Depending on the target publication, a table of all abbreviations used may be required in the early part of the manuscript.

A list of keywords may be requested for submission alongside the case report. These will be used as search criteria for any resulting publication.

8 Title and title page
The title of the case report is the initial contact with the reader. It should be concise, inform the reader of the content, and maintain relevance to the subject.

The title page should be placed at the front of the report. It contains names, qualifications and contact information (institution, postal address, email address) for all authors. The corresponding author should be clearly identified.

The author list should only include those individuals who have contributed significantly to the production of the case report. An author is qualified by his/her contribution to the conception and design of the case report, gathering and interpretation of case information, and drafting and/or revision of the resulting manuscript. Their approval should be sought prior to submission of the final draft.

9 Declarations page
All authors must declare their contributions to the production of the manuscript. Ensure that complete author information (name, qualifications, affiliations, contact information) is included in this section if required. Any conflicts of interest should be noted here.

10 Covering letter
This should be written once the case report is complete. Accompanying the submission of the case report manuscript, this letter should be addressed to the chief editor and clearly detail why the case report is worthy of publication. Whether due to the introduction of new or novel information on existing or unreported case occurrences, or untoward case outcomes or medication-related events during case management, it is important to capture the attention of the chief editor at this initial point of contact.

Submitting for publication
Once the case report is completed in a style matching the requirements of the target journal, a checklist of requirements for the target journal should be compared with the case report submission package. Only when requirements are complete should the submission process begin.

The review process
Once submitted, the target journal will seek to assess the manuscript. This is most often by a peer review process, where individuals deemed knowledgeable in an area relevant to the disease or techniques within the case report will assess the case report for content, grammar, adherence to journal requirements and ultimately suitability for publication. There may be several iterations of this process, with revisions recommended and requested of the author before each review cycle begins anew. Considerable time may elapse during this process prior to final acceptance.

Should the manuscript be rejected for publication in the target journal, close attention should be paid to the reasons for this, as these may indicate the case is not suitable for publication. Alternatively, knowledge gained during this process may enable further revision of the case report and submission to another journal in the desired field. Under no circumstances should the manuscript be simultaneously submitted to more than one journal.

Common errors in submitted manuscripts
While considerable effort is expended by the authors in the creation of a manuscript, attention to the requirement of the target journal is sometimes lacking. This may substantially delay the peer review process and reduce the timeliness of acceptance for publication should the subject matter ultimately be deemed worthy of print.

Commonly occurring errors fall into the following categories

Language and grammar
The publication language of Equine Veterinary Education is English, particularly British English. The journal requires spelling that is correct for this language. This includes the use of digraphs -ae and -oe, also -our, -ce, -se and -re (in place of -or, -se, -ze and -er respectively) in contrast to American English where these are not standard spellings. As Equine Veterinary Education is an international journal, many manuscripts are submitted by authors where English is not their native language, rather, English is a second language, or a common language between peoples who share no other common language communication. This often greatly increases the work of the primary reviewers and editors to assess manuscripts. The consultation by authors of a native English speaker during compilation of the manuscript is encouraged. Advice and assistance with English language writing can be obtained from Wiley Editing Services http://wileyedittingservices.com/en/
**Formatting**
The requirements of the journal must be strictly observed but are often an oversight. Page size, margins, type font, font size, indenting and line spacing must be correct. If requested, line numbering must be included to aid the review process. Word or character count must be observed.

**Structure**
Case presentation should generally adhere to a layout compatible with that detailed previously in this article. There should be an introduction; a broadly inclusive body of the case report detailing clinical presentation, diagnostics, treatments and outcomes; a concise discussion reviewing and relating literature relevant to the case; and a list of relevant references. Regardless of author writing style, it is important to have a logical flow of information and conclusions, and to have case details and supporting references consistently in the correct location.

**Referencing**
Within text citations and the format of the bibliography varies between journals. The correct format as detailed in the journal requirements must be consistently used during manuscript preparation. Should resubmission to a journal other than the initial target be required, ensure that reference format is changed to meet the new requirements.

References should be accurate and complete, however, depending on the source either online or from print, information can be missing: incorrect author name(s), incorrect journal name, absent year of publication, or missing page numbers (start, finish). Anecdotal information should always be stated to be such in the text (e.g. personal communication) and sparingly used.

**Footnotes**
All proprietary equipment and consumables should be referenced in the text and listed as footnotes at the end of the case report prior to the reference section. Omissions and incomplete information for manufacturers is a common deficiency.

**Units of measure**
The International System of Units, abbreviated SI, should be used for all reported numerical values of the patient. These are derived from, and are an extension of, the metric system. Clinical pathological values that are in US conventional units must also be converted to SI.

**Supporting material**
Images should be of high quality and of sufficient quantity to illustrate key points of the case. Image parameters (e.g. pixel count/density, dimensions) will be detailed in the author instructions to ensure adequate quality post publication. Excessive numbers of images are discouraged. Captions should be succinct and areas of interest clearly indicated. Included images should match their description in the body of the text, be numerically complete, and be in the correct order.

**Summary**
Publication of case reports and case series provides a means of disseminating clinical information of novel presentations, deviations from expected presentations and outcomes, and adverse reactions to established treatment modalities and therapeutics. While they may be criticised as the lowest form of clinical evidence, they are often referenced as foundation reports on newly recognised conditions and therapies. Production of a good case report requires considerable effort and time. Language and grammar must be correct for the journal and its audience. Comprehensive case information must be concisely relayed and put in context with the existing literature which is reviewed as part of the discussion. Journal requirements for format and structure must be adhered to exactly.

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**References**


Case Report

Perisuspensory abscessation in eight horses with hindlimb cellulitis

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Keywords: horse; cellulitis; racehorse; abscess; suspensory

Summary

This study reports a distinct presentation of cellulitis, which involved formation of perisuspensory abscessation in eight horses. Medical records of horses presented for cellulitis unresponsive to medical treatment were reviewed. Cases in which perisuspensory abscesses were diagnosed were included, and different data were retrieved from the medical records. Racing data were obtained from two databases, and horses were considered able to return to their intended use if they had entered a race at least once after their hospitalisation. Eight horses met the inclusion criteria. Seven were thoroughbreds (six racehorses and one yearling) and one standardbred racehorse. In all cases, the cellulitis had been ongoing for several days prior to referral. All horses were treated with broad-spectrum antibiotics and nonsteroidal anti-inflammatory drugs, and some were also administered corticosteroids. Horses were referred because of a lack of response to therapy, with marked worsening of lameness and/or limb swelling within 24 h prior to referral. A single hindlimb was affected in all cases (five left hind and three right hind). All horses presented with moderate to marked pitting oedema around the metatarsus, extending from immediately distal to the hock to the fetlock, that was warm and painful on palpation. Careful visual examination revealed that, in addition to generalised swelling of the limb, three horses had a more localised swelling (‘bulging profile’) at the junction of the middle and distal thirds of the metatarsal area on the medial and/or lateral aspect of the limb (Fig 1). For the remaining five horses, a similar localised swelling developed within 3–5 days of hospitalisation, once the generalised swelling had partially subsided. This corresponded upon ultrasonographic examination to either a hypoechoic or heteroechoic fluid pocket between the suspensory ligament and third metatarsus, extending around one or both branches of the suspensory ligament. All horses were treated with broad-spectrum antibiotics, anti-inflammatory drugs, topical therapies and regional perfusions; however, only partial improvement of clinical signs was observed with medical therapy alone. Full resolution of clinical signs was obtained in all cases once the abscess was surgically lanced and drained. The procedure was performed standing under sedation and local anaesthesia in seven horses and under brief general anaesthesia in one horse, due to the uncooperative nature of that patient. After clipping the area and performing routine skin preparation, a 1–2 cm vertical skin incision was made under ultrasonographic guidance. The subcutaneous tissues were bluntly separated with haemostatic forceps until the abscess cavity was penetrated (approximately 0.5–1.5 cm deep). Purulent material was removed, and the pocket lavaged with diluted povidone–iodine. The affected limb was kept bandaged and the abscess cavity was flushed with diluted povidone–iodine solution once daily for the remainder of the hospitalisation. A sample of the purulent material was obtained in all eight cases and submitted for microbial culture and sensitivity testing. In all cases, Staphylococcus aureus was cultured. Six out of eight isolates showed at least some level of antimicrobial resistance, with penicillin and trimethoprim sulfonamides being most commonly involved. None of the isolates showed resistance to gentamicin or enrofloxacin. The antibiotic therapy for each case was adjusted according to the sensitivity pattern, once the results were available. Short-term complications included skin necrosis in two cases and mild impaction colic in two cases and were successfully treated. All horses were discharged from the hospital within 4–13 days and were sound upon discharge. All thoroughbreds (n = 7) were able to return to their intended use, and the standardbred was unraced prior to the cellulitis event and remained unraced afterwards.

Key points

- Abscess formation should be included in the differential diagnosis while dealing with a case of cellulitis that is not responsive to the usual medical therapy within a few days, especially in a racehorse.
- All abscesses were diagnosed by ultrasonographic examination and were located between the cannon bone and suspensory ligament, and extended around one or both suspensory branches. Full resolution of clinical signs was only achieved once surgically lanced and drained.
- Staphylococcus aureus was cultured in all cases and was commonly resistant to penicillin and trimethoprim sulfonamides. None of the isolates showed resistance to gentamicin or enrofloxacin.
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Pilchuck Equine Veterinary Hospital, Seattle, WA
21 – 22 Aug  Ultrasound-Guided Orthopedic Injection Techniques & Therapies
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Clinical Commentary

Cellulitis: Any change?

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Anecdotally, limb cellulitis is a ‘fairly common’ entity encountered in equine practice. It is therefore, quite surprising that we grapple with a paucity of data on the prevalence of this disease, which can range from mild to life-threatening.

There are a few clinical reports that exist in the literature giving us insight into those cases that present to clinics and teaching hospitals (Markel et al. 1986; Adam and Southwood 2006, 2007; Fjordbakk et al. 2008; Putnam et al. 2014). Looking for common threads across these reports can provide valuable clinical information, provided we guard against over-interpretation and wandering from the path of evidence-based medicine. However, with that said and given the dearth of data, we must derive what insight we can from the published data.

In this edition of EVE, Vyetrogan and Dubois (2019) present a case series from which we can learn much. These authors describe a group of eight horses that developed hindlimb cellulitis and abscess formation at the bifurcation of the suspensory ligament. All cases were treated aggressively medically but ultimately needed surgical drainage and went on to do well post-operatively. While this might seem like a very specific presentation, when considered against the backdrop of previous reports, this report has much to offer and remind us of.

This cohort of horses composed of Thoroughbreds (n = 7) and a Standardbred (n = 1), all presented with one limb affected, and all cases were hindlimbs. In much of the previously reported equine limb cellulitis literature these same features are also found: Thoroughbreds are over-represented, one limb was affected, and hindlimbs more commonly involved than forelimbs. Intuitively, we might hypothesise that highly strung bloodstock may be more apt to cause themselves damage by kicking and be more challenging to bath and dry their limbs appropriately but we have little data to test that hypothesis. In the human literature, a landmark study found that risk factors identified with limb cellulitis included the presence of interdigital Staphylococcus aureus and/or a beta-haemolytic Streptococcus spp. (OR: 28.97) and dermatophytosis (OR: 3.86; ‘Athlete’s Foot’) (Björnsdóttir et al. 2003). Prospectively, developing cellulitis if the patient had a previous episode carried an odds ratio of 31.04. In another human study, again looking at risk factors, the authors concluded that ‘increased emphasis on weight loss, smoking cessation, and improved foot hygiene in the homeless might decrease recurrences of lower extremity cellulitis’ (Lewis et al. 2006). Thankfully, in our equine populations, we do not have quite the same considerations but the caution on skin hygiene is noteworthy, as is the high risk of developing subsequent episodes of the syndrome. In the veterinary literature, there is a report relating bathing practices to Staphylococcal skin scald-like syndrome in greyhounds (Love and Davis 1980). In that paper, skin maceration and chapping from imperfect bathing and drying practices were highlighted, as well as the use of communal equipment.

The case series presented here obtained cultures from each horse, all of which yielded Staphylococcus aureus. This has been a consistent finding in the cellulitis literature of both horses and humans, although polymicrobial infections are also noted. Whatever the inciting organism(s) is (are) what is notable is that all of the horses described in this report had already been treated with systemic antimicrobial drugs prior to presentation and sample collection. The authors’ comments on the patterns of antimicrobial resistance make for thoughtful reading.

Previous treatment with antimicrobial agents raises an important fundamental issue. That being that the choice of an appropriate antimicrobial drug, although clearly important, is dependent on the basic premise that to be effective the drug must be delivered to the infection site successfully.

Vyetrogan and Dubois’ group of cases were aggressively treated with antimicrobial drugs delivered both systemically and via regional limb perfusion. Regional limb perfusion is considered a gold standard for the delivery of high levels of antimicrobial agent to tissues in the distal limb. However, in spite of these techniques, the infection continued and abscessation developed. This serves to remind us that local tissue damage caused by the elaboration of bacterial exotoxins and inflammation, can confound treatment even with an appropriate antimicrobial drug choice.

Coagulase positive Staphylococcus spp., namely S. aureus, S. intermedius and S. hyicus, are all adept at synthesising a range of devastating exotoxins (Spaulding et al. 2013). One such group of toxins, the exfoliatins, causes severe exudative dermatitis giving rise to the disease’s colloquial name when affecting swine: Greasy Pig Disease. In humans, they can cause horrific Scalded Skin Syndrome. In addition to exfoliatins, leucocidins and superantigens are produced. Leucocidins are pore-forming toxins, cytotoxic to leucocytes and greatly contribute to the invasive nature of infection. Superantigens are the stuff of nightmares and have been studied as agents of biological warfare. They are produced by Staphylococcus spp. and Group A Streptococcus spp, among others. Superantigens nonspecifically activate T lymphocytes and cause widespread pro-inflammatory cytokine release, often leading to toxic shock syndrome and necrotising lesions. Indeed, in terms of the care of cellulitis cases, in the light of cryotherapy research in laminitis studies (Godman et al. 2016; Dern et al. 2018), cryotherapy becomes a logical choice for the possibility of reducing inflammation and
enzymatic activity, which may reduce bacterial protein synthesis.

The elaboration of highly pathogenic exotoxins from both Staphylococcal and Streptococcal organisms is well entrenched in our collective veterinary psyche. However, the sole reliance on antimicrobial drugs to combat such infections may also be well entrenched. In horses, beyond antimicrobial-related colitis, we rarely consider antimicrobial therapy as having a negative effect. However, in the canine literature, an investigation into isolates of Streptococcus canis causing cellulitis and necrotising fasciitis was performed some years ago (Ingrey et al. 2003). This study revealed that enrofloxacin, even at low concentrations, was able to induce superantigen expression from the encoding bacteriophage in virulent strains of S. canis. Enrofloxacin, even with EU usage restrictions, may be a product that warrants further study in this regard.

The overarching and most refreshing features of this case study are the repeated ultrasound examination of these horses and the deployment of surgical drainage, instead of changing antimicrobial drugs when the case was not progressing satisfactorily. The diligent re-examination of these horses with ultrasound imaging is an imperative component of the management of cellulitis and nowhere more evident is that than in this paper. It is not easy to patiently ultrasound the exquisitely painful hindlimb of a potentially fractious horse. Without evaluating a control group, it is difficult to speculate as to the outcome of these horses had they received only medical treatment. However, the timely surgical intervention in these cases resulted in resolution of the infection and a return to intended use.

Surgical drainage of lesions on horses with cellulitis is not altogether new. Fjordbakk et al. (2008) mentioned it in a previous publication where it was performed in 14 of the 63 cases reported. In an older report, clinicians interviewed informally were reluctant to pierce the skin of a cellulitis limb for a culture sample, let alone perform surgical drainage (Adam and Southwood 2007). As such, it is refreshing in these more recent reports that surgical intervention was employed and in this series was successful.

From the study published in 2007 (Adam and Southwood 2007) and subsequent observations by the primary author clinically, a critical factor in the management of cellulitis cases is to get the horse weight bearing and comfortable as quickly as possible. This and older reports bear witness that contra-lateral limb laminitis is a significant factor in survival. With the improved awareness of pain control measures, the employment of transdermal opioid patches, and use of continuous intravenous infusions and, with hindlimb pain, the use of epidural catheters getting the horse comfortable is a realistic goal.

Given the many factors that relate to a disease that is all too common but for which there is a deficit of data, this report empowers us. It implores the reader to diligently re-evaluate the horse with ultrasound and to critically monitor comfort level and the progress of medical therapy. It empowers us, with ever-greater access to better quality imaging tools, to carefully employ image-guided surgical techniques to bring about a swifter resolution to a problem that might otherwise readily defeat us.

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

Ethical animal research
Not applicable to this clinical commentary.

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None.

References
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Case Report

Surgical resection of a squamous cell carcinoma in the perianal region of a 25-year-old crossbred American Paint gelding using sharp surgical excision, laser excision and chemotherapy

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Keywords: horse; equus caballus; intralesional chemotherapy; laser excision; neoplasia; papillomavirus 2; perianal; squamous cell carcinoma; surgical excision

Summary
A 25 year-old American Paint gelding was referred to the Onderstepoort Academic Veterinary Hospital with an ulcerated lesion of nonpigmented skin at the right lateral aspect of the perianal region. An infiltrating squamous cell carcinoma was suspected. Surgical excision and ablation with sharp surgical excision and a diode laser was performed although complete excision was not possible due to the tumour location. Intralesional chemotherapy was performed at the completion of the surgical excision and continued in the post-operative period. Histological examination of the excised lesion confirmed a diagnosis of squamous cell carcinoma and revealed incomplete resection margins at the medial, dorsal and ventral aspects of the surgical site. The surgical site healed uneventfully and a re-examination at 6 months post-surgery revealed the healing to have normal clinical parameters with no perianal lesions.

Introduction
Tumours of the equine skin represent up to 65% of skin lesions in the horse (Schaffer et al. 2013) and account for 50% of all equine neoplastic lesions in general (Baker and Leyland 1975). Squamous cell carcinomas (SCCs) are malignant neoplasms of epithelial origin and are one of the most commonly diagnosed skin tumours in the horse (Valentine 2006; Schaffer et al. 2013; Knowles et al. 2016). Squamous cell carcinomas occur in various areas of the equine body and are especially common at mucocutaneous junctions (Sundberg et al. 1977; Newkirk et al. 2014). Reported locations in the horse have included the eye, skin, external genitalia, urogenital tract, oesophagus, stomach and nasal cavity (Sundberg et al. 1977; Valentine 2006; Van Den Top et al. 2010; Newkirk et al. 2014). Squamous cell carcinoma in the perianal region of horses has been rarely reported (Wilson 1994; Arnold et al. 2018). In humans, certain papillomaviruses have been identified as the causative agents of SCCs of genital and other mucosal and cutaneous regions (Sykora and Brandt 2017). Equus caballus papillomavirus 2 (EcPV2) has relatively recently been associated with most genital squamous cell carcinomas in horses (Sykora and Brandt 2017). A single anal SCC was tested and found to be EcPV2 positive (Bogaert et al. 2012), however, the association of EcPV2 in perianal SCCs is as yet unreported. Treatment of squamous cell carcinoma in horses usually depends on the size and locality of the lesion (Arnold et al. 2018). At easily accessible locations, a sole surgical therapy may allow the entire tumour to be removed (Dietz 2006). If the anatomical site is difficult to access, surgery infrequently provides satisfactory results (Hewes and Sullins 2006; Arnold et al. 2018).

Chemotherapy has been described as a suitable treatment for neoplasms of the skin and external genitalia in horses (Fortier and Mac Harg 1994; Paterson 1997; Hewes and Sullins 2006). Successful outcomes have been reported with small lesions or in addition to surgical reduction (Hewes and Sullins 2006; Arnold et al. 2018).

There are few previous reports of perianal squamous cell carcinoma in the horse, with no previous reports of combination therapy using sharp surgical excision, laser excision and intralesional chemotherapy.

This paper reports the successful treatment of a perianal squamous cell carcinoma in a horse with surgical and laser excision and intralesional chemotherapy under standing sedation.

Case details
A 25-year-old American Paint gelding weighing 375 kg was presented to the Onderstepoort Veterinary Academic Teaching Hospital (OVAH), University of Pretoria, for evaluation of an ulcerated mass of non-pigmented skin of the right perianal region. The owner had reported that the mass had increased in size gradually over 12 months (Figs 1 and 2) with ulceration shown in the last 4 weeks of this period, prompting referral. The pony had shown no dyschezia, weight loss or change in demeanour during the previous 12-month period.

General physical examination at presentation revealed normal clinical parameters and mentation with no evidence of right hindlimb regional lymphadenopathy or obvious lymph node metastasis. Palpation of the perianal region revealed a nonpainful, irregular, ulcerated cutaneous mass of 4 cm in diameter in the hairless, nonpigmented skin of the right mid-perianal region. The adjacent skin lateral to the lesion was thickened and the subcutaneous tissue exposed below the ulcer had a granular appearance. A squamous cell carcinoma was suspected and surgical excision was discussed with the owner. In view of the proximity of the medial aspect of the lesion to the right anal wall, a combination of sharp surgical excision, laser excision and...
Chemotherapy was planned, under standing sedation and with epidural anaesthesia.

A peripheral venous blood sample obtained on the day of admission revealed no haematological abnormalities. The gelding was admitted to the hospital and feed withheld for 6 h prior to surgery, but with water allowed ad libitum.

Prior to surgery, faeces were manually removed from as far proximally in the rectum as possible and the perineum was aseptically prepared. An intravenous catheter (Extended Use Milocath, Mila International®) was aseptically placed in the left jugular vein and pre-operative medication included intramuscular procaine penicillin [13 mg/kg bwt; Benzyl penicillin®], intravenous gentamicin sulphate [6.6 mg/kg bwt; Genta 50®] and intravenous flunixin meglumine [1.1 mg/kg bwt; Finadyne®].

The gelding was restrained in a metal crush and sedated with intravenous detomidine hydrochloride [10 μg/kg bwt; Domosedan®] and butorphanol tartrate [0.1 mg/kg bwt; Torbugesic®]. An epidural catheter (Epidural pain management kit; Mila International®) was placed into the first intercoccygeal space and lignocaine hydrochloride [0.2 mg/kg bwt; 2% Lignocaine®] and xylazine [0.2 mg/kg bwt; Rompun®] were administered intrathecally.

In preparation for the surgical procedure, all entrances to the surgical suite were locked and laser warning signs placed on doors leading to the surgical suite. Personnel in the surgery room wore dedicated laser safety glasses.

The lateral, ventral and dorsal borders of the lesion were resected using sharp surgical incision with borders of 2 cm achieved. The medial border was resected using a diode laser [980 nm Diode Laser System, Diodevet®] due to the proximity to the anal wall. Laser incision was performed with the laser in a continuous mode and 30 W of power. An initial skin incision was completed and traction was placed on the lesion with towel clamps. After removal of the mass, subcutaneous tissue and skin margins, the entire surgical site was ablated in two directions with the diode laser at 90 degrees to each other (Fig 3). Ablation was considered complete when the tissue was dark yellow to brown and appeared dessicated.

Finally, cisplatin [1 mg of cisplatin per cubic centimetre of tissue; P&U Cisplatin®] was injected into the medial, ventral and dorsal borders of the incision site. These injections were conducted according to occupational safety and health administration guidelines. Protective eyewear was worn by all personnel in the surgery room and additional gloves were worn by the clinician administering the cisplatin.

Fig 1: The mass approximately 12 months prior to presentation.

Fig 2: The mass at presentation.

Fig 3: The surgical site in the immediate post-operative period.
Luer-locking syringes were used to minimise spraying of the chemotherapeutic agent through a poorly attached syringe and needle. Sterile swabs were held over each injection site to absorb any excess cisplatin. After administration, all syringes, capped needles, remaining drug, swabs and protective clothing were immediately placed in a chemotherapeutic disposal bag.

The excised mass was submitted for histopathological analysis and margin evaluation.

Post-operative treatment with twice daily intramuscular procaine penicillin (13 mg/kg bwt; Depocillin®), once daily intravenous gentamicin sulphate (6.6 mg/kg bwt; Gentacin®) and once daily flunixin meglumine (1.1 mg/kg bwt; Finadyne®) was administered for a further 4 days. Intercoccygeal intrathecal morphine sulphate (0.2 mg/kg bwt; Morphone Sulphate®) was administered at 12 h intervals for 24 h post-operatively, after which the epidural catheter was removed (Fig 3).

Further intralesional chemotherapy treatment (1 mg of 5-fluorouracil per cubic centimetre tissue; Fluracedyl®) was performed at 2-week intervals for a total of 4 treatments. Prior to each treatment, flunixin meglumine (1.1 mg/kg bwt; Finadyne®) was administered to the patient and a sedation protocol was achieved using intravenous detomidine hydrochloride (10 µg/kg bwt; Domosedan®) and butorphanol tartrate (0.1 mg/kg bwt; Torbugesic®). The tumour site was clipped, aseptically prepared and infiltrated with 2% lignocaine (20 mg of lignocaine per cubic centimetre tissue; 2% Lignocaine®). Using sterile technique, 20 gauge needles were placed in parallel (0.5 cm apart) to provide uniform distribution of 5-fluorouracil at the tumour site and for a 1 cm zone in circumference around the entire surgical site. Five-fluorouracil was administered at 50 mg/cm² with proper handling and disposal according to occupational safety and health administration guidelines. Two pairs of gloves, protective eyewear and a gown was worn by the clinician administering the 5-fluorouracil to minimise skin and eye exposure. Luer locking syringes were used to minimise leakage of the chemotherapeutic agent and all needles were preplaced prior to injection to avoid overlapping needle tracts and to minimise leakage from the injection sites. Sterile swabs were placed over the injection sites to absorb any excess external 5-fluorouracil. After administration, all syringes, capped needles, swabs, protective clothing and remaining 5-fluorouracil were placed in a chemotherapeutic disposal bag.

Fig 4: The surgical site at 2 weeks post-operatively.

Fig 5: The surgical site at 5 weeks post-operatively.

Fig 6: The surgical site at 26 weeks (6 months) post-operatively.
The progress of the surgical site was assessed at 2, 5 and 26 weeks post-operatively and photographic records obtained (Figs 4–6).

At re-examination 26 weeks post-surgery the pony was clinically healthy with no visible lesions of the anus and perianal region [Fig 6]. The owner reported that the horse had not had difficulty defecating, had appeared normal in the post-operative period and had not shown weight loss.

**Histopathological examination**

Histological examination was performed on routinely prepared, labelled sections of surgical edges and the centre of the excised mass, stained with haematoxylin and eosin, using light microscopy. Central and some margin sections revealed invading cords of neoplastic epithelial cells with large nuclei and finely granular chromatin. Abnormal keratinisation and keratin pearl formation were present within the invading cords (Fig 7). There was an associated perivascular reaction consisting mainly of lymphocytes and plasma cells with a scattering of eosinophils. Overlying necrosis and ulceration were evident in some sections and had elicited an inflammatory reaction zone of degenerated leucocytes (neutrophils and macrophages) at the necrotic edge where there were scattered bacterial colonies. Adjacent skin showed carcinoma in situ featuring epidermal hyperplasia, acanthosis, variable basal cell atypia, dyskeratosis and superficial dermal fibrosis (Fig 7). Characteristics that differentiated this lesion from granulation tissue, papilloma, sarcoids and other neoplasms included the histological features of adjacent skin carcinoma in situ, central infiltrative basaloïd-type pleomorphic to anaplastic epithelial cells (Fig 8) with abnormal mitotic figures and overlying ulceration.

A diagnosis of squamous cell carcinoma was made with incomplete resection at the medial, ventral and dorsal margins.

**Discussion**

Squamous cell carcinomas are malignant neoplasms of epithelial origin commonly arising in skin or in organs with stratified epithelium (Garma-Avina 1994; Perrier et al. 2010; Gibbons et al. 2018). Following equine sarcoid, SCC is the second most common tumour type found in the horse (Scott and Miller 2003) and the most common malignant skin tumour of horses (Sykora and Brandt 2017).

Squamous cell carcinomas commonly occur at the eyelids and external genitalia with only rare reports as primary tumours in other locations (Perrier et al. 2010). The location of SCC in this case in the perianal region is extremely unusual with few previous reports (Wilson 1994; Arnold et al. 2018). The difficulty in treating squamous cell carcinomas of the perianal region has been reported, with proximity to the anus and difficulties in performing complete excision emphasised (Arnold et al. 2018). Alternative treatment with immunotherapy and permanent colostomy have been advocated instead of surgical resection (Wilson 1994; Arnold et al. 2018).

Squamous cell carcinoma is common in older horses, as in this case (Howarth et al. 1991; Mair et al. 2000; Van den Top et al. 2008; Knowles et al. 2016), with the mean age of horses with vulva, perianal and anal skin SCCs reported as 19 years (Valentine 2006).

The aetiology of squamous cell carcinoma has been shown to be multi-factorial with genetics of skin pigmentation, ultraviolet light exposure, trauma, chronic irritation, smegma, Equus caballus papilloma virus 2 (EcPV-2) infection and age implicated (Wilson 1994; Elce 2009; Reid 2009; Sykora and Brandt 2017). There were several possible aetiological factors in the current case, with ultraviolet light exposure of the unpigmented skin at the site being the main suspected causative factor although the age and the American Paint breed of the gelding may also have been contributing factors (Valentine 2006; Schaffer et al. 2013). Unfortunately we did not have access to testing of tumour tissue by either PCR or in situ hybridisation for viral DNA of EcPV2, nor antibody for immunohistochemistry for PV. One anal SCC which was tested for DNA was positive for EcPV2 in another study (Bogaert et al. 2012).

The time before referral by the owner, 12 months, was longer than that in the majority of case reports (Scheck 2005; Tomago et al. 2017). Interestingly, however, the two other reports of perianal squamous cell carcinoma had been identified for 12 months and 3 years, respectively, before referral (Wilson 1994; Arnold et al. 2018). The time
delay in the current case was due to lack of owner recognition of the lesion as being possibly neoplastic, despite the age of the pony. The under-recognition by owners of neoplastic disease in older horses, has been previously identified and reported (Ireland et al. 2012). Despite the delay between tumour occurrence and recognition, there was no evidence of metastasis and SCCs have been reported to show slowly progressive development (Howarth et al. 1991; Head et al. 2002).

The histopathological diagnosis in this case was consistent with the clinical presentation and surgical findings. However, whilst the lack of a clean resection margin at the medial aspect of the surgical site was anticipated, the lack of resection margins at the ventral and dorsal aspects of the incision site did not correlate with the surgical findings.

Various treatments of cutaneous SCC have been described, with surgical excision, cryotherapy or without excision, hyperthermia, laser ablation, radiotherapy, immunotherapy, chemotherapy and electrochemotherapy reported (Strafuss 1976; MacFadden and Pace 1991; Burney et al. 1992; Théon et al. 1993; McCauley et al. 2002; Arnold et al. 2018; Spugnini et al. 2017). In future, preventative immunisation against PV-related SCCs may become feasible in horses, as is practiced in humans (Sykora and Brandt 2017).

Surgical excision of squamous cell carcinoma has been recommended at easily accessible sites (Johnson 1998; Dietz 2006). However, in cutaneous locations that are difficult to access, surgical excision alone often does not provide satisfactory results (Hewes and Sullins 2006; Arnold et al. 2018). Tumour recurrence after incomplete tumour removal is a common complication (Théon et al. 1994). Treatment failure has also been shown to alter the biological behaviour of some tumours resulting in more aggressive growth and an increased potential for local extension or metastasis following recurrence (Gunduz et al. 1979; Théon et al. 1994), in view of the location of the tumour in this case, surgical excision alone was not felt to be justified.

Laser excision has been widely reported in the treatment of cutaneous neoplasia in horses (Carstanjen et al. 1997; Martens et al. 2001; McCauley et al. 2002; Mair and Fews 2016). Advantages of this therapeutic modality include reduced damage to the surrounding tissue as laser light is associated with minimal transmission of heat, and therefore little latent thermal necrosis (Palmer 1989, 1990, 1996; Leffell and Thompson 1992; Carstanjen et al. 1997; McCauley et al. 2002). Additionally, coagulation of small blood vessels, lymphatic vessels and nerves by the laser results in reduced intra-operative haemorrhage, post-operative oedema and pain (Palmer 1989, 1990, 1996; Leffell and Thompson 1992; McCauley et al. 2002). These specific advantages were clearly evident in this case.

A further advantage of laser excision is the reduced spread of malignant cells to surrounding tissue when compared with conventional surgery (Carstanjen et al. 1997; McCauley et al. 2002). It was felt that this property of laser excision was particularly important for excision of the medial border of the tumour in this case as obtaining a tumour-free resection margin was not possible.

Chemotherapeutic treatment has been described as a suitable method to treat neoplasms in horses (Théon et al. 1993, 1994; Fortier and Mac Harg 1994; Paterson 1997). Intralesional administration of various chemotherapeutic agents has been reported as an adjunct or alternative to excision of cutaneous neoplasia in horses (Théon et al. 1993, 1994) and was used in this case in conjunction with laser application on the medial margin where a tumour-free resection margin was not possible. Electrochemotherapy has been reported to have been used successfully in a squamous cell carcinoma of an equine foot that was difficult to access and has been recommended when incomplete excision of tumours in horses is not possible (Spugnini et al. 2017). Electrochemotherapy was considered in this case but was not utilised due to lack of availability of a clinical electroporator.

The benefits of intralesional administration of chemotherapeutic agents include minimising adverse systemic effects while providing exposure of tumour cells to high concentrations of the agent (Hewes and Sullins 2006).

Intralesional administration of cisplatin and 5-fluorouracil has been commonly used for treatment of cutaneous tumours in horses and found to be effective against a variety of solid tumours (Loehrer and Einhorn 1984; Théon et al. 1993, 1994, 1997, 1999; Stewart et al. 2006). Reported protocols include multiple treatments, for instance, four treatments administered at 2 week intervals (Théon et al. 1993), which was adopted in this case.

Difficulties associated with intralesional injection of cisplatin include leakage of the cisplatin solution following injection, unpredictability in the stability and consistency of the solution and risk of accidental injection of the veterinarian performing the injection (Hewes and Sullins 2006). None of these difficulties were encountered in this case. The concerns regarding stability of the cisplatin solution were raised by authors using cisplatin in an oil emulsion whilst we used undiluted cisplatin (P&U Cisplatin®). The risks of self-injection were judged to be low in this case as the pony had an excellent temperament and was restrained both physically and chemically during each administration. The first injection was performed under epidural anaesthesia and subsequent injections were performed using standing sedation. Epidural anaesthesia has been widely utilised in surgical conditions of the equine perineum (LeBlanc and Caron 1990; DeRossi et al. 2004; Climent et al. 2009). The placement and use of an epidural catheter in this case was an important component of both the anaesthetic and analgesic components in the intra- and post-operative periods, respectively.

Complications associated with intralesional cisplatin have included tissue oedema, erythema and crusting (Théon et al. 2007). None of these complications occurred in this case.

To avoid the potential complications with intralesional injection of cisplatin, various slow release delivery systems have been implanted at tumour sites (Ike et al. 1992; Suzuki et al. 1995; Ehrhart et al. 1999; Lana et al. 2004; Marr et al. 2004; Withrow et al. 2004). Biodegradable cisplatin-containing beads have been shown to be an effective treatment with or without tumour debulking for cutaneous neoplasms in horses (Hewes and Sullins 2006). Such a slow release system could have been utilised in this case if the temperament of the horse had been challenging or difficulties in administration had been encountered.

The decision to use 5-fluorouracil in the post-operative period was made as it is inexpensive, has relatively few adverse effects and can provide beneficial macroscopic cytodestruction (Puckett and Gilmour 2014). It is an alternative to other intralesional chemotherapy drugs and does not require specialised preparation or equipment to deliver (Puckett
Gilmour 2014). The use of intralesional 5-fluorouracil has been described for treatment of dermatological neoplasia in human patients (Kraus et al. 1998; Longley et al. 2003; Good et al. 2010; Kirby and Miller 2010).

Other potential therapeutic treatment options for this case were radiotherapy and immunotherapy. Radiotherapy as a treatment for equine tumours, has been previously reported (Frauenfelder et al. 1982a, b; Wyn-Jones 1983; Byam-Cook et al. 2006; Montgomery 2014; Hollis 2019) but is infrequently used due to the necessity for special equipment and concerns regarding management of patients receiving radiotherapy (Van Den Top et al. 2010; Hollis 2019). This technique was not available for the current case and would have been cost-prohibitive. Immunotherapy has successfully treated cutaneous neoplasms in horses (Lavach et al. 1985; Vanselow et al. 1988) with autologous dendritic cells reportedly used for perianal SCC (Arnold et al. 2018). Immunotherapeutic techniques would be of benefit to cases similar to the current horse with advantages of safe administration and reduced side effects compared with chemotherapeutic agents (Arnold et al. 2018).

Clinical relevance

To our knowledge, there are no previous reports of a combined treatment approach to perianal squamous cell carcinoma in the horse. Squamous cell carcinoma should be considered in the differential diagnosis of perianal lesions in horses. A combined treatment approach with surgical excision using conventional surgical technique and laser excision with intralesional chemotherapy enabled a full resolution of the squamous cell carcinoma in this case report and is recommended in the treatment of perianal carcinomas in horses where complete excision is difficult or not possible.

Authors’ declaration of interests

No conflicts of interest have been declared.

Ethical animal research

No ethical review was required as this is a case study. The owners of the mare described in the present case gave their consent for publication.

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None.

Antimicrobial stewardship policy

The mare in this case report did not receive quinolones, extended spectrum beta lactam antimicrobials or macrolides.

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Authorship

L. Poore and Y. Smit were responsible for the surgical aspects of this case and post-operative management. N. Duncan and J. Williams were responsible for the pathological assessment and production of the images. All authors gave their final approval of the manuscript.

Manufacturers’ addresses

1. MILA International, Florence, Kentucky, USA.
2. Fresinus Kabi, Midrand, South Africa.
3. Vibac, Centurion, South Africa.
4. MSD Animal Health, Kempton Park, South Africa.
5. Pfizer Animal Health, Sandton, South Africa.
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Cutaneous squamous cell carcinoma (SCC): “What’s the problem?”

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Squamous cell carcinoma (SCC) is a tumour of squamous epithelial cells and therefore, in theory at least, can affect any tissue with a squamous epithelium; these are of course found in the skin but also line the upper respiratory tract, the lower urinary tract and parts of the alimentary tract including the mouth, oesophagus and squamous portion of the stomach.

Much has been written about this relatively common tumour type in horses with many single reports, as in the case described in this edition by Poore et al. (2019), and a modest number of case series. The variety of organs involved and the challenges of diagnosis and management as well as the unpredictability of definitive prognosis continue to perplex and concern practitioners and specialists alike. A broad summary of the detailed nature of this tumour is well-described and fully referenced from a pathological and clinical perspective by Knottenbelt et al. (2015).

Overall results from several tumour surveys both in post-mortem studies and in referrals to pathology services as well as those to specialist centres confirm that squamous cell carcinoma remains one of the most common equine cancers. It is estimated to comprise 7–31% of total neoplasms. Horses of any age can be affected by SCC, with reports in animals as young as one year. However, it is most often reported in mature horses.

The transformation of normal cells to an overt carcinoma is usually a gradual process involving a series of cellular mutations that allow the tumour to pass through a series of developmental stages; these can be easily misinterpreted until late in the progression of the condition. Common carcinogens that have been identified in horses include sunlight and other radiations, chemical exposure and viruses. It is well known that nonpigmented skin is far more likely to be affected by carcinoma and oftentimes the protection afforded from pigmented skin is very clear in horses (Fig 1). This is not always the case, however, and pigmented skin can be affected (Fig 2).

The paper in this edition of Equine Veterinary Education (Poore et al. 2019) describes an unusual carcinoma location in an older horse. Although perianal carcinoma is very rare there are still some features that make the clinical diagnosis easier. The fact that the skin described in this case was nonpigmented and the area ulcerated and destructive is typical (Fig 3) although cannot be said to be pathognomonic; pigmented skin can be affected and some carcinomas are proliferative (Fig 4).

Notwithstanding the relationship between SCC and sunlight (UV) exposure of nonpigmented skin and/or squamous cell mucous membranes (such as the conjunctiva), SCC does occur on pigmented skin and in areas where the sun “doesn’t shine”! In these areas where sunlight exposure is unlikely to play a part in its pathogenesis (Figs 2 and 4), alternative carcinogens have to be considered.

In the case described by Poore et al. in this edition (2019), a carcinoma developed in nonpigmented skin around the anus – it is impossible again to believe that sunshine played a part in its development. Other potential factors suggested to be involved include chronic irritation or infection, cutaneous burns, poor wound healing and parasitic diseases (e.g. habronemiasis, onchocerciasis). In ocular sites, chronic conjunctivitis, chronic nasolacrimal duct obstruction, and congenital or acquired eyelid deformities are all possible risk factors (Rebhun 1998). Seven horses diagnosed with ocular SCC had a documented previous eye injury (Runnells and Benbrook 1942).

Cases of SCC of a deeply invasive nature with a high propensity for local destruction and potential malignancy have been identified at burn wound sites (Schumacher et al. 1986) (Fig 5) and burn sites are probably heavily predisposed to carcinoma development. The reasons for this are not clear but local immune processes and genetic instability of the affected cells may be involved. Exposure of burn sites to strong sunlight can also be contributory (Fig 5a,b).

Squamous cell carcinoma has also been identified in wound sites with some regularity. If this wound healing complication is overlooked it can lead to disastrous consequences (Fig 6). A carcinoma is reported to have occurred in exuberant granulation tissue at the site of a previous injection site abscess over the gluteal region, approximately 2 years following the initial incident (Baird and Freller 1990). An aggressive SCC was also reported to develop in a chronic wound at the site of a neck laceration that had been treated topically with various chemicals; it is thought that the latter may be important in carcinoma pathogenesis (Fessler et al. 1993). Since the number of cases reported in the literature is very small, it is almost impossible to identify specific carcinogens. It is important to remember that any wound that fails to heal should be investigated and there is therefore always clinical justification in submitting excised “granulation tissue” from even the earliest stages of wound management. Early detection gives realistic changes of treatment but any tumour developing at the site of a wound is extremely difficult to manage.

Possibly the commonest site for carcinoma development in horses is the penile skin and to a slightly lesser degree the external and internal laminae of the prepuce. Here, again pigment plays a prominent but not exclusive role in susceptibility to SCC (Fig 4). It has been suggested that viral infection with Equus caballus papilloma virus-2 (EcPV2) or bovine papilloma virus might be in some way responsible since both can often be found associated with SCC in this site. For SCC of the male genitalia smegma is also suggested...
to be a significant aspect of the aetiopathogenesis mainly on the basis of the much higher prevalence in older geldings. It could be considered to be a primary carcinogen of course or even an exacerbating irritant (Brinsko 1998). The penile forms of SCC are a particularly interesting subset of the cancer. A comprehensive and excellent study on the pathogenesis and treatment of penile SCC by Van den Top et al. (2010) confirms that the condition usually starts out with a squamous dysplasia and epidermal hypertrophy. This gradually loses differentiation and ultimately loses its proliferative nature (squamous papilloma) in favour of a more destructive carcinoma. This latter stage results in significant welfare compromise and brings surgical and medical challenges.

The pathogenesis of carcinoma follows an almost classic course in all species and the horse is no exception. The diagram shown here illustrates the development of carcinoma from an early dysplastic information of mildly abnormal cells to a highly malignant and metastatic form. Fortunately, metastasis is not common in the horse. It is, however, an important aspect of the management of
development of a carcinoma requires several important at least, metastatically. The pathogenesis or progression/
Predisposed to carcinoma as a result of lack of pigment but carcinoma development may be subtler than that. (Pictures give an opportunity to thank and pay respects to Aline Schunemann de Aluja, an outstanding contributor to the equine veterinary profession).

carcinoma in all sites. The lack of a strong tendency to metastatic transformation has given rise to a considerable tolerance of the condition and that is probably something of a mistake since there is no doubt that if the tumour is left long enough, malignancy will develop both locally and potentially at least, metastatically. The pathogenesis or progression/development of a carcinoma requires several important circumstances. The “carcinogen” causes a minor genetic mutation resulting in hyperplasia. Under normal conditions such a change would be arrested by cell cycle restriction points that “carry out genetic quality control” before allowing the cell to complete the cycle of replication. The process of restriction and diversion of cells to the options of continuation to replication, repair, diversion to a static (G0) cell or to apoptosis are governed largely by complex relationships within the cell. Viewed simplistically this process is controlled by the p53 family of genes. This and its associated cytokines and mediators therefore act as quality control mechanisms. Here lies one of the weakest points in the process of carcinoma development. The p53 gene is seemingly susceptible to UV light-induced mutation and indeed many other carcinogens, with consequent loss of function or aberrant function. Many studies have indicated that these mutations are critical in the development of a large proportion of human cases of SCC (Brash et al. 1991). Similar P53 impairment has been found in a proportion of SCC cases in horses and in particular those affecting the genitalia (Pazzi et al. 1996), in the majority of carcinoma tumours in most species there is a significant impairment to the P53 function and this imparts both a lack of control on the cell cycle and an inherent genetic instability. The cell becomes increasingly liable to genetic insult and further mutation with relatively less insult. Sequential mutations lead the tumour clone towards malignancy.

From a clinical perspective the mutational changes can be correlated with the genetic changes (Fig 7). The earliest stages are usually manifest as a squamous papilloma or a squamous cell dysplasia (Fig 7). These stages are easily overlooked or misdiagnosed. The sequential mutations within the transformed cell gradually shifts the cell behaviour from a dysplastic, proliferative intraepithelial (in situ carcinoma) state to a state where the tumour breaks through the basement membrane of the epithelium and the threat of local invasion, angiogenesis and potential metastatic tumours develops. Fortunately, almost all SCC cases encountered in the skin of horses are of a less aggressive type at least in the early stages. There is little tendency to metastasis even after aggressive local forms have been allowed to develop. The one exception to this rule is carcinoma of the conjunctiva in the medial canthus whether associated with the nictitans or not. Recurrence at this site following removal of even relatively small, benign and innocuous looking tumours is extremely dangerous; often some vascular or lymphatic (or both) invasion is reported from histology even when a margin is considered to be safe. There is potential for metastatic spread to local lymphatic tissue; for the conjunctiva, caruncle and palpebrum, this is usually the floor of the ipsilateral gullett pouch and then the pharyngeal lymph-nodes – both of these can of course be seen clearly during gullet pouch endoscopy (Fig 8).

Unfortunately, there is still considerable disagreement or at least controversy amongst pathologists as to the best way to classify this disease in a uniform and accepted manner and so the literature remains confused and confusing. It is actually fortunate therefore that the more common forms of squamous cell carcinoma occurring in the skin and in the conjunctiva in particular are only rarely metastatic. It is important, however, always to examine the possibility of extension into a local lymph-node (where this is accessible) (Fig 8) or into remote organs.

Equine SCC is not routinely graded by pathologists but a grading system has been suggested by several authors (Schuh 1986; Pérez et al. 1999; Van den Top et al. 2008a,b, 2010):

- Grade I SCC - well-differentiated with numerous dyskeratotic cells and prominent keratin pearls, with obvious intercellular bridges
- Grade II SCC - moderately differentiated with frequent dyskeratosis but only occasional keratin pearls and poorly defined intercellular bridges
- Grade III SCC - poorly differentiated cells with infrequent keratinisation and some atypical mitotic figures and a high mitotic rate

These grades have been clinically and pathologically associated with the depth of invasion in penile, cutaneous and conjunctival carcinoma (Pérez et al. 1999). The grade
and presence of metastasis were not, however, linked in a study of oropharyngeal and nasal SCC (Schuh 1986).

A different grading system, based on the ratios of well-differentiated to anaplastic tumour cells, has also been suggested (Van den Top et al. 2010). This is probably more appropriate to the equine situation and is relatively easy to use.

- **G1 (well-differentiated):** SCC with only minimal basal/parabasal atypia (Fig 9a)
- **G2 (moderately differentiated):** A more disorganised neoplasm with less keratinisation, higher nuclear/cytoplasmic ratios, thicker nuclear membranes, moderate nuclear pleomorphism, occasional clumping of nuclear chromatin, obvious nucleoli and higher mitotic rates (Fig 9b)
- **G3 (poorly differentiated):** Anaplastic cells with other features that are more marked than those found in G2 neoplasms including increased nuclear pleomorphism and higher mitotic activity (Fig 9c)

From a clinical perspective there is probably little to choose between the various systems. Grading does give some indication of prognosis for penile/preputial SCC at least; higher grades are associated with reduced prognosis and increased risk of metastatic spread through lymphatic and haematological routes (Van den Top et al. 2010). In the most malignant form micro-metastasis probably occurs very early and is not always associated with an apparently clinically aggressive primary tumour.

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**Fig 6:** This horse sustained a relatively minor wound over the fetlock region some months previously. The wound appeared to heal relatively normally for the first 3 or 4 weeks and then showed signs of abnormal “granulation tissue”. The wound was managed by surgical debridement and a grafting attempt was made. Nothing responded at all (a) and ultimately a radiograph was taken to try to identify possible causes of incipient wound healing failure (b). The underlying radiographs revealed extensive bone destruction and tissue was then submitted for histology. This revealed a highly aggressive squamous cell carcinoma (c) with undifferentiated cells and a high mitotic index (d) as shown in the histology slides here. Submission of all granulation tissue from nonhealing wounds for histological examination can be clinically justified.

**Fig 7:** Diagrammatic representation of the clinical and pathological events taking place during the progression of a squamous cell carcinoma. It is important to realise, however, that this is a spectrum of change with no clear boundaries between the different ‘phases’ of development. Individual lesions will have variations in the appearance and the pathology. (Drawing by Vicki Martin).

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Squamous epithelia are found in the skin, lining the respiratory tract, the lower urinary tract and parts of the alimentary tract — including the mouth, oesophagus and squamous portion of the stomach. Basement membrane invaded

Stratified squamous epithelial cells

Minor genetic mutation in a single cell

Mild

Moderate

Severe

Squamous dyplasia

Squamous papilloma

Carcinoma in situ

Invasive SCC

Basement membrane

Malignant SCC of sheath with extension to inguinal and sub-iliac lymph nodes

Spread via lymphatics

Spread via blood vessels

Risk of local recurrence after resection: long-term monitoring essential

Early detection and monitoring

Treatment potentially curative

Treatment futile but palliation sometimes possible

SCC in respiratory and alimentary canals can also become extremely aggressive.

Secondaries in regional lymph nodes more common in horse. NB local lymphadenopathy may be of inflammatory origin.

Secondaries in organs unusual in horse, with the exception of gastric carcinoma. SCC in respiratory and alimentary canals can also become extremely aggressive.

Lesions can be productive/ proliferative or erosive/destructive

Cutaneous SCC are mostly less aggressive with little tendency to metastasis. However, SCC of conjunctiva at medial canthus has high risk of local recurrence and spread to ipsilateral gutteral pouch, then to pharyngeal nodes.

Mutations may be arrested by genetic quality control (role of p53 gene)

Further genetic mutation?

Further genetic mutation?

Mutation

Activation

Normal skin

Hyperplasia

Dysplasia

Activation

Early detection and monitoring

Treatment potentially curative

Risk of local recurrence after resection: long-term monitoring essential

Treatment futile but palliation sometimes possible

Development of squamous cell carcinoma

Minor genetic mutation in a single cell

Lesions can be productive/ proliferative or erosive/destructive

Cutaneous SCC are mostly less aggressive with little tendency to metastasis. However, SCC of conjunctiva at medial canthus has high risk of local recurrence and spread to ipsilateral gutteral pouch, then to pharyngeal nodes.

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Lesions can be productive/ proliferative or erosive/destructive

Cutaneous SCC are mostly less aggressive with little tendency to metastasis. However, SCC of conjunctiva at medial canthus has high risk of local recurrence and spread to ipsilateral gutteral pouch, then to pharyngeal nodes.
The most dangerous forms of SCC include the gastric carcinoma, which has a rapidly fatal disseminating and destructive course with haematogenous, lymphatic and transecelomic spread. Carcinoma developing in the alimentary or the respiratory tracts can also become extremely aggressive but most cutaneous forms are fortunately far less liable to metastatic spread. Involvement of the first lymphoid “filter” is however relatively common. It is important to point out that local lymphadenopathy can also be of an inflammatory origin; usually, but not always, the node is then more painful than in neoplastic lymphadenopathy.

The gross appearance of SCC masses varies significantly between horses and different anatomical sites; some authors classify them as productive/proliferative or erosive/destructive. The neoplasms are usually pale and firm due to significant amounts of supporting fibrous tissue. Early well-differentiated tumours often produce keratin and these are identifiable both clinically and histologically. The keratin imparts a very characteristic grey or cream appearance to the surface of the tumour (Figs 9a and 10a). This is usually termed leukoplakia and this is one of the features of the earliest types of preneoplastic or early neoplastic changes in penile and conjunctival carcinoma in particular. Highly destructive carcinoma is unusual but is more associated with palpebral, clitoral and vulvar labial forms of the disease (Fig 11). Many internal carcinoma lesions (such as the pharyngeal, gastric and upper airway carcinoma) take on a very aggressive local invasive and destructive behaviour; this may be associated with avascular necrosis (the tumour “outgrows” its own blood supply) but also local tissue destructive mediators produced by both tumour and its induced inflammatory responses.

Carcinoma tends to occur in older horses but there are equally important predisposing and triggering factors than age alone. Geldings are reported to be five times more likely than stallions, and two times more likely than mares to develop SCC. Penile carcinoma is rare in entire horses but it does occur! Older geldings are more liable to SCC of the penis and preputial skin than entire horses. Nevertheless, penile carcinoma tends to be much more dangerous when it occurs in the younger adult horse. Mares may be affected by vulvar carcinoma and this can be extremely aggressive in both progression and malignancy (Fig 11).

Early diagnosis and intervention results in a cure in many cases especially with the increasingly effective chemotherapy systems now available. Although the clinical diagnosis of carcinoma is usually relatively easy in most cases of moderate or advanced carcinoma early lesions often require further confirmatory tests. Early diagnosis is a fundamental requirement for an improved prognosis – usually the longer the tumour has been present, the poorer the prognosis and the greater the therapeutic challenge. Biopsy provides the most definitive diagnostic: pathologists can invariably make a diagnosis even in very early cases and the addition of immunohistochemistry creates a significant certainty of diagnosis. Cytological diagnosis from impression smears, fine needle aspirations or fluid samples from the peritoneal and pleural cavities may be useful but sufficient numbers of exfoliated cells may not always be present (Brazil 2008). For conjunctival and corneal carcinoma lesions in particular, staining with Rose Bengal is a useful way to identify the extent and location of the tumours (Fig 12). Additionally, the lacrimal occult blood test is a sensitive but less specific test for ulcerative damage to the conjunctiva (Fig 13).

The histological appearance provides excellent information regarding the degree of differentiation of the cells and this is of significant clinical benefit both from a prognostic and therapeutic perspective. The histological report should always contain information about the extent of differentiation of the tumour cells and the integrity of the basement membrane. The number of mitotic figures and the degree of cellular atypia are key pathological features. The extent of vascular or lymphatic invasion also provides a good index for the prognosis (Fig 14). A summary of the suspected carcinogens, the prevalence and the clinical and pathological behaviour of the various forms of cutaneous carcinoma is shown in Table 1.

Of course, treatment is naturally the main focus of the clinical management. As might be supposed the earlier and
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the less aggressive the lesion the better the chances of a “cure”; this basic tenet of cancer medicine is perversely often overlooked by horse owners. Radiotherapy is universally the gold standard for carcinoma treatment but is not available apart from in all but a few specialist centres (Théon et al. 1999; Hollis 2019). It can have dramatic and curative effects (Fig 15).

Leaving aside the challenges of internal SCC or metastatic SCC, there are opportunities to treat many cases effectively. The case described in this edition by

Fig 9: a) Grade 1 SCC showing squamous dysplasia with leukoplakia. This case illustrates the preneoplastic/dysplastic state that is very characteristic of early penile carcinoma. These grey or cream areas are termed leukoplakia and are largely due to cellular hyperplasia of a mildly aggressive form that produces significant amounts of keratin. That is the reason for the appearance. From a clinical perspective, usually the keratin can be peeled off from the surface in many of these lesions and this will leave a slightly haemorrhagic mildly ulcerated surface. At this stage the tumour is intraepithelial or in situ. b) Grade 2 SCC showing proliferative changes with ulceration and infection. c) Grade 3 SCC. This is a highly invasive, destructive carcinoma that had extended to the inguinal and sub-iliac lymph nodes.

Fig 10: a) A proliferative in situ (intraepithelial) carcinoma on the nictitans. Notice the cream-grey pseudomembrane of keratin and inflammatory debris covering the mass itself. b) Although this in situ, intraepithelial carcinoma looks very bad, the large part of the bulk of the tumour is made up of keratin. Of course, this is somewhat unusual in the corneal epithelium because it is a non-keratinising epithelium but this case does illustrate clearly the cellular changes that occur in carcinoma in the early stages in particular.
Poore et al. (2019) was treated with a combination of surgical tumour reduction and chemotherapy. In the case described by Poore et al. (2019) an aqueous solution of 5-fluorouracil was used at 2-week intervals. Although the surgical pathology revealed an unsafe margin, the concurrent use of a chemotherapy program resulted in an apparent complete cure. The major point about this was that the pathology was performed and acted upon.

The value of combined treatment methods cannot be overstated (Plummer et al. 2007). The challenge in this case is the possibility of metastatic development that may only become apparent after some years (Mair et al. 2015) or local recurrence which may also be very delayed; it may look good enough for months or even years to give a degree of optimism but the prognosis should always remain guarded.

Surgical tumour reduction is an important principle of cancer treatment and in some locations is highly effective on its own (Mair et al. 2000; Payne et al. 2009). In effect, the more tumour that can be removed, the less adjunctive measures including topical or local intralesional chemotherapy has to do and therefore the less the doses of chemotherapy required. If the whole tumour is removed with a clear margin there should be no necessity for concurrent or adjunctive chemotherapy or radiation. The prognosis is, however, significantly improved when chemotherapy is combined with sharp surgery, laser surgical excision, cryosurgery or electrochemotherapy; results can be reasonably expected to be good. Examples of this include the removal of the third eyelid affected by a localised conjunctival carcinoma and a distal phallectomy where a penile carcinoma involves the urethral fossa and glans penis. Prospective or expected

Fig 11: This highly destructive carcinoma of the vulva and clitoris developed over a period of 8 months from a mildly erosive vulvar labial carcinoma associated with the ventral labial margin and clitoris. Delays and inappropriate treatment attempts resulted in a hopeless prognosis.

Fig 12: a) and b) The diagnosis of SCC in these two cases was not really equivocal but the use of Rose Bengal stain can be used to add robustness to the diagnosis and confirm its extent. Notice that they both show a characteristic ocular discharge.

Fig 13: The lacrimal occult blood test is useful and simple. A urine haemoglobin dipstick is gently touched onto the accumulated tear drops and examined for blood positive response. In this case an obvious carcinoma was present in the right eye but BOTH were positive. A small, early carcinoma was present in the left eye conjunctiva at the lateral limbus.
“safe margins” for skin tumours are usually established from evidence-based reports but in the case of equine oncology very little is known about any of the major tumours so a sensible balance has to be drawn between the two extremes of wide or narrow margins of excision. The extent of safe margin is also important for local and intralesional chemotherapy! Where a safe margin cannot reasonably and confidently be identified or achieved, concurrent measures can be justified. Surgery can also be followed by cryosurgery or further surgery once the margin has been declared unsafe and this might also have been a choice for Poore et al. (2019) had chemotherapy not been available or practical. Of course, removal of the whole tumour locally does not mean that there is no remote spread – that might have occurred a long while previously. By the time a tumour is visible or palpable, it is usually around 66% of its natural lifespan so events may well have taken place before this point.

Squamous cell carcinoma is generally sensitive to many of the available chemotherapy agents (Knottenbelt et al. 2015). Since margins are impossible to define in most cases anyway and since the tumours can be microscopic and infiltrative, chemotherapy is often a sensible adjunctive treatment. Poore et al. (2019) instigated the chemotherapy with repeated aqueous 5-fluorouracil immediately after the surgery; this is always the pragmatic option to maximise the prognosis. A slow release method based on an emulsion of cisplatin, carboplatin or 5-fluorouracil with sesame oil has been used successfully by several previous authors including Théon et al. (1999) and could probably have been useful in the case described by Poore et al. (2019). Reported case series using intra- or peri-lesional chemotherapy in slow release emulsions have been uniformly impressive. Additionally, topical aqueous mitomycin C has been used also to good effect in conjunctival carcinoma (Malalana et al. 2010).

Topical chemotherapy on its own can also be effective (Patterson 1997; Malalana et al. 2010) provided that cases are suitably chosen but surgical tumour reduction is an effective way of hastening the resolution and enhancing the overall prognosis. Rayner and van Zyl (2006) described the use of topical mitomycin C and achieved a 90% success rate as measured by non-recurrence at 11 months post treatment. Malalana et al. (2010) compared the topical mitomycin C chemotherapy with and without concurrent surgery and concluded that the surgical/chemotherapy option was more likely to result in a cure.

Electrochemotherapy using cisplatin has been used to manage a variety of cutaneous tumours without concurrent surgery and high success rates are reported (Cemazar et al. 2008).

Systemic chemotherapy is in theory at least possible but is not widely practiced and in any case with focal tumours affecting single organs or structures it is probably unnecessary. Nevertheless COX-2 inhibitors such as meloxicam or piroxicam can be justified especially if the tumour COX-2 expression can be confirmed by immunohistochemistry. Daily oral doses of 80 mg of piroxicam (regardless of the size of the horse) have been reported to be helpful (Moore et al. 2003; Iwabe et al. 2009). Piroxicam reduces both direct DNA damage and malignant transformation of cells. It also promotes apoptosis in tumour cells and has a positive effect on cancer cell immunity by

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Fig 14: Three different types of carcinoma. a) This proliferative carcinoma of the nictitans illustrates the intraepithelial (in situ) nature of this tumour type. There are keratin pearls shown here as well (arrows). The solid head arrow is the corneal stroma. b) A histological section of a cutaneous carcinoma with well-differentiated cells and obvious keratin “pearls”. c) An undifferentiated penile carcinoma with no obvious keratin, mitotic figures and an invasive nature. (Pictures courtesy of Lorenzo Ressel [a] and Janet Patterson Kane [b; c]).
The surgical pathology mistake that can be made during treatment is to ignore the pathologist examining the surgical specimens. The biggest mistake that can be made during treatment is to ignore the surgical pathology! The safety of excisional margins is so important that every excised tumour no matter how small should be submitted for examination; this should not be regarded as an optional extra! The case described by Poore et al. had a 6-month local disease free follow-up and it is important to remember that carcinoma at any site including those affecting the conjunctiva and the skin can sometimes recur after a much longer period (Elce et al. 2011). Additionally, and importantly from a prognostic perspective, distant spread in the absence of any local evidence of tumour recurrence can be recognised much later (Mair et al. 2015). Regular, careful and detailed monitoring of all patients is essential and especially when vascular and lymphatic invasion and an unsafe margin are reported from the surgical pathology. The pathology, whether from biopsy or from surgical (excisional) pathology is very important and should never be overlooked and especially not on economic grounds; it is counterproductive, unwise and unprofessional.

The challenges of chemotherapy were also raised by Poore et al. (2019); they noted the need to protect the operators and the handlers of the horse from inadvertent contact with drugs at the site of the procedure and in the urine and droppings. It is important to remember that every chemotherapy agent will have some pro-mutational effects; exposure of humans to the drugs could be considered an unacceptable hazard. The principle of ALARA (as low as reasonably achievable) for exposure to chemotherapeutic agents is no longer acceptable. There should in fact be no exposure at all if proper protection is afforded. Operator and handler safety is paramount and anyone using these chemicals must take special care to ensure human and environmental safety as well as safe disposal of all contaminated materials. Special disposal systems for chemotherapy and hazardous waste are obligatory.

In addition, carcinoma can seed into an operative site from the surface of an exposed ulcerated carcinoma during surgery; this cannot of course be identified by a pathologist examining the surgical specimens. The biggest mistake that can be made during treatment is to ignore the surgical pathology! The safety of excisional margins is so important that every excised tumour no matter how “certain” the excision might seem, should be submitted for examination; this should not be regarded as an ‘optional extra’!

There are many different approaches that can be made to long-term survival. Other treatments that have been reported include photodynamic therapy, cryosurgery and immunotherapy (Arnold et al. 2018). New methods including immunotherapy using dendritic cells and other mediator driven approaches are being explored and may have some future (Arnold et al. 2018).

It is clear that SCC is an eminently treatable tumour in most cutaneous sites provided that the condition is diagnosed early and pursued relentlessly to elimination. There are many different approaches that can be made and it is time that extensive multicentre studies were carried out to compare the various treatment options rather than reliance upon small case series or individual cases.

The long-term prognosis for all forms of carcinoma depends on both local recurrence and distant metastasis. Local recurrence usually reflects a failure of clinical management or, in surgical cases a failure to explore the possibility of an unsafe margin of excision. The lack of a safe margin and the extent of both lymphatic and vascular involvement have to be considered in every case. However, since an exhaustive absolutely certain safe margin can seldom be guaranteed by a pathologist, it is wise to be careful when advising owners of the prognosis. In addition, carcinoma can seed into an operative site from the surface of an exposed ulcerated carcinoma during surgery; this cannot of course be identified by a pathologist examining the surgical specimens. The biggest mistake that can be made during treatment is to ignore the surgical pathology! The safety of excisional margins is so important that every excised tumour no matter how “certain” the excision might seem, should be submitted for examination; this should not be regarded as an ‘optional extra’!

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Perianal carcinoma is very rare in horses but it clearly does occur and although no particular carcinogen can be suggested, any proliferative or ulcerated lesions in this region should be carefully examined. Since SCC is commoner in older horse (Valentine 2006), the advanced age of the horse in the case described by Poore et al. (2019) may have played some part in its aetiopathogenesis. The correct choice of treatment is imperative and the best available combination method should always be employed. Concurrent chemotherapy following any surgical tumour reduction is a sensible option (Fig 16). Fortunately, metastatic spread from cutaneous SCC (apart from some preputial and penile forms) is uncommon although the first lymph node in
Fig 15: SCC is very sensitive to β or γ radiation. The former is usually limited to corneal carcinoma in situ using strontium90 wand plesiotherapy. The latter is conventionally carried out using high or low dose intralesional iridium192 or gold198 brachytherapy. This destructive carcinoma developed in the nasal half of a pigmented lower eyelid. It was treated using low dose brachytherapy with iridium192 and showed a very satisfying and total resolution. The lower right picture was taken at 6 weeks post treatment and the full effect took around 9 months; no recurrence occurred in spite of the pigment loss since the owner was advised to keep the horse out of strong sunlight.

Fig 16: Top: This massive proliferative and invasive carcinoma of the clitoral sinus and vulvar labiae. Middle: It was removed surgically. Bottom: Adjunctive slow release 5 fluorouracil emulsion in sesame oil was infiltrated using a preplanned orthogonal set of 19 g needles. The process was repeated 5 times at 2-week intervals and resulted in a satisfactory resolution – at least in the short term. Long-term follow-up is not available. (pictures courtesy Heather Armstrong)
the chain can be affected. Recurrences and metastasis can become clinically evident months or even years after apparent local resolution and monitoring is essential. EARLY DIAGNOSIS is a fundamental requirement in cancer medicine and every opportunity should be taken to screen horses, clinically at least, as often as possible.

Authors' declaration of interests

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Review Article

Radiotherapy for the treatment of periocular tumours in the horse

A. R. Hollis

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Keywords: horse; equine; radiation; brachytherapy; sarcoid; periorbital

Summary

Periocular tumours are a relatively common problem in the horse, and present some unique challenges. Radiotherapy has long been considered the ‘gold standard’ for the treatment of periocular tumours in the horse, and there are various techniques of delivering this treatment. Although teletherapy and plesiotherapy are occasionally used, the most commonly used technique is interstitial brachytherapy. Low-dose rate interstitial brachytherapy has reported success rates of between 74 and 100% for the treatment of periocular sarcoids, and other tumours can also be successfully treated using this technique. There are significant disadvantages to the low-dose rate brachytherapy approach, and recently, a technique using high-dose rate brachytherapy has been described with a reported success rate of 100% for periocular sarcoid treatment. Electronic brachytherapy is a technique which may provide an alternative to high-dose rate brachytherapy, but its use for the treatment of periocular tumours has not been reported, and the requirement for general anaesthesia is a significant disadvantage.

Introduction

Why use radiotherapy for periocular tumours?

Periocular tumours are a relatively common problem in the horse and present some unique challenges. The most common tumour types in this location are sarcoids and squamous cell carcinomas, although other tumours such as melanomas, mast cell tumours and lymphomas are occasionally reported (Gilger 2017). Their location frequently makes them difficult or impossible to remove via laser surgical excision, and the use of topical creams is complicated by the proximity to the globe and the potential for the creams to cause severe collateral damage. BCG has been widely accepted as a good option for nodular and some fibroblastic sarcoid lesions, with the largest case series reporting success rates as 69% in these lesions, but it is unsuccessful in the treatment of verrucose or occult lesions (Knottenbelt and Kelly 2000), and is currently difficult to access due to manufacturing issues. Intralesional chemotherapy can sometimes be successful, but has health and safety implications and there are few published data on the success of this approach for periocular tumours. One report found only a 33% success rate following cisplatin injection into periocular sarcoids, and stated that accurate injection was extremely difficult (Knottenbelt and Kelly 2000) raising further health and safety concerns should this approach be chosen. Radiotherapy has long been considered the ‘gold standard’ for treatment of periocular tumours, especially periocular sarcoids, although its use has been restricted by the high cost and limited availability of the treatment. Low-dose rate brachytherapy has been used for radiotherapy of periocular sarcoids for over 40 years; however, the availability has become increasingly limited due to the high cost of the sources, practicalities and the health and safety concerns associated with their use. Recently, a technique of high-dose rate brachytherapy has been described which eliminates any operator exposure and therefore many of the health and safety concerns, although this technique remains expensive and very limited in availability (Hollis and Bertato 2018).

Principles of radiotherapy

How does radiotherapy work?

The effects of radiation are summarised in Figure 1.

- DNA damage
  - Exposure to ionising radiation kills cells by producing secondary charged particles and free radicals in the nucleus. These cause direct and indirect damage to cellular DNA, preventing successful mitosis. Radiation damages normal and tumour cells, but normal cells are able to repair radiation damage to a much greater extent, and can therefore usually repair and function.
Individual responses to radiotherapy may also be dictated by the tumour type, volume and location, with the probability of local tumour control following radiotherapy being inversely proportional to its volume (Theon 1998). Reducing the size of a large tumour may therefore improve efficacy and reduce morbidity where large pericocular lesions are present, with fewer functional and cosmetic effects. In these cases, radiotherapy aims to eradicate any tumour cells left behind after an incomplete excision (Theon 1998). This approach has been successfully used in horses in combination with both low-dose rate brachytherapy (Byam-Cook et al. 2006) and high-dose brachytherapy (Hollis and Berlato 2018).

What happens following radiotherapy?
Following exposure to ionising radiation, cells may undergo apoptosis, autophagy, senescence and/or necrosis. Different tissues have different sensitivity to radiation, which is mainly due to differences in the rate of cell division. Cells that are actively dividing will no longer be able to undergo successful mitosis following exposure to much lower doses of radiation than the dose required to destroy a well-differentiated cell. This means that actively dividing tumour cells may be more likely to be damaged by radiation than less actively dividing tumour cells or normal cells. In addition, most normal cells can repair damage to DNA, although the damage from radiotherapy causes side effects which are usually temporary, but may be permanent (Burcombe et al. 2013). The timing of radiation side effects relates to the speed of cell turnover, with rapidly dividing cells (such as skin) showing damage quickly, and cells with a low rate of turnover (such as bone) showing damage long after the radiation is complete (Burcombe et al. 2013). It also helps to explain the differences in radiosensitivity. Cells with a high rate of turnover, such as corneal cells, are far more radiosensitive than those with a low rate of turnover, such as bone cells.

Radiation side effects
Early effects of radiation can be seen within a few weeks of the completion of a course of radiotherapy. These may include skin erythema, desquamation of the skin and depigmentation of the hair and/or skin (Bentzen 2006). Late effects of radiation may be seen many months or even years after treatment and can include fibrosis and cataract formation. Bone necrosis can be seen many years after radiotherapy and this can be clinically significant, although this appears to be unlikely in equine cases, with no reports of bone necrosis following radiotherapy in the equine veterinary literature. It is imperative to get a balance between therapeutic benefit and the inevitable associated toxicities of exposure to radiation. These side effects appear to usually be mild and self-limiting in equine cases at published dose rates using various forms of brachytherapy in the horse. Interestingly, different human patients will have different levels of tissue reaction and therefore side effects when exposed to the same radiation treatment (Bentzen 2006; Burcombe et al. 2013). This has sparked a field of study known as radiogenomics, which is the study of genetic differences in the response to radiation (Andreassen et al. 2002). This may help to explain some of the individual differences in the response to radiotherapy in horses, although there are very few published data on the side effects and long-term effects seen after any form of radiotherapy in the horse. Reported radiation reactions seen in a series of 115 cases treated with low-dose rate brachytherapy for periorcular tumours included palpebral fibrosis (10.4%), cataract formation (7.8%), and keratitis and corneal ulceration (6.9%) (Theon and Pascoe 1994). Cosmetic effects noted in the same study included permanent epilation (21.7%) and hair dyspigmentation (78.3%) (Theon and Pascoe 1994) (Fig 2).

What are the different forms of radiotherapy?
Table 1 presents summary data of the different forms of radiotherapy reported for use in the horse.

<table>
<thead>
<tr>
<th>Form of Radiotherapy</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teletherapy</td>
<td>The term teletherapy is derived from the Greek ‘tele’ (long) and ‘therapy’ (treatment), and is used to describe a technique where the radiation source is at some distance from the tumour. The treatments are delivered via machines, usually a linear accelerator, although a cobalt-60 unit can...</td>
<td>[See image for a horse showing epilation and hair dyspigmentation, 1 year after treatment with high-dose rate brachytherapy for a fibroblastic sarcoid in the same location.]</td>
</tr>
</tbody>
</table>
Brachytherapy is derived from the Greek ‘brachys’ (short) and ‘therapy’ (treatment), and as the name implies, refers to radiotherapy where the radioactive source is in direct contact with the tumour. There are two main forms of brachytherapy used in horses: interstitial brachytherapy, which usually takes the form of low-dose rate or high-dose rate brachytherapy, or plesiotherapy.

**Plesiotherapy**

Plesiotherapy is where a radiation source is applied directly to the surface of the tumour. The most commonly used source is a strontium-90 probe. Strontium-90 has the advantage of a very long half-life (28.7 years), therefore once a probe has been purchased; it continues to have a similar activity for a very long time, making it potentially quite cost effective. The β radiation produced by the strontium-90 itself is too weak to be of practical use. However, strontium-90 decays to yttrium-90, which produces β radiation at 2.27 MeV as it decays. This β radiation has a very shallow depth of penetration, meaning that very high doses of radiation can be applied to the surface of the tumour without risking exposure of normal underlying tissues. The major disadvantage of this therapy is that it is therefore only suitable for extremely superficial tumours: 60% of the radiation dose is absorbed in the first 1 mm of tissue. Treatment is therefore limited to very superficial corneoscleral, conjunctival and eyelid lesions (usually <3 mm in depth). The radioactive source is usually around 0.8 cm in diameter, and is mounted on a stainless steel shaft which incorporates a Perspex shield to protect the operator’s hand (Fig 4). During treatment, the source is applied directly onto the tumour surface. Depending on the location of the lesion, this may be performed under heavy standing sedation or via general anaesthesia. Corneoscleral and conjunctival lesions require general anaesthesia for an effective treatment to ensure accurate positioning of the probe, but, depending on the horse’s temperament, lesions in some periocular (and other) locations can be safely and effectively treated using sedation alone (Fig 4). The duration of treatment will depend on the current activity of the probe and the size of the lesion to be treated, but is usually only a few minutes. The prescribed tumour dose is defined as the minimum dose in the target volume (which should include a 2 mm margin) and ranges from 80 to 100 Gy (Theon 1998). The radiation surface dose will typically be in the order of 200–250 Gy, depending on the thickness of the area to be treated. Where the treatment area is larger than the size of the probe, a multiple abutting field configuration is required, where the applications are overlapping in the tumour tissue to allow effective treatment. Drawing a measured grid on the surface of the tumour using a marker pen helps to achieve accurate positioning of the probe to the tumour.

**TABLE 1: Summary of the reported use and utility of different forms of radiotherapy for the treatment of periorbital tumours in the horse**

<table>
<thead>
<tr>
<th>Type of radiation</th>
<th>Emission</th>
<th>Penetration</th>
<th>Reported use [periocular region]</th>
<th>Success rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strontium plesiotherapy</td>
<td>Beta (β)</td>
<td>Very low</td>
<td>Squamous cell carcinomas</td>
<td>83–100%* **</td>
</tr>
<tr>
<td>Electronic brachytherapy</td>
<td>X-rays (photons) Gamma (γ)</td>
<td>Low</td>
<td>Ocular B cell lymphoma</td>
<td>One case; 100%†</td>
</tr>
<tr>
<td>Low-dose rate brachytherapy’Iridium wires’</td>
<td>X-rays (photons) Gamma (γ)</td>
<td>Moderate</td>
<td>Sarcomas</td>
<td>78–100%* **‡‡</td>
</tr>
<tr>
<td>High-dose rate brachytherapy</td>
<td>X-rays (photons) or electrons</td>
<td>Moderate</td>
<td>Sarcomas</td>
<td>100%††</td>
</tr>
<tr>
<td>Linear accelerator (teletherapy)</td>
<td>X-rays (photons) or electrons</td>
<td>Very high</td>
<td>None</td>
<td>None reported</td>
</tr>
</tbody>
</table>

Low-dose rate brachytherapy is the traditional method of providing interstitial brachytherapy to periocular tumours in the horse (Fig 5). Iridium-192 wires or seeds can be implanted into the tumour, where they are left for a specified time and are removed when the prescribed radiation dose has been achieved, which will depend on the size of the tumour, the activity of the source and the implantation technique. Implantation involves placing applicators (such as stainless steel needles or nylon catheters) into the tissue, after which the radioactive sources are inserted (‘afterloaded’) manually, using long-handled forceps [Turrel and Koblik 1983]. This can be performed under a short general anaesthesia or standing sedation with local anaesthesia. The radiation is delivered at between 0.3 and 0.5 Gy/h while the implant is in place, with prescribed total doses ranging between 50 and 90 Gy depending on the size, location and type of tumour to be treated and reported success rates of between 74 and 100% [Walker et al. 1986, 1991; Theon and Pascoe 1994; Theon 1998; Knottenbelt and Kelly 2000; Byam-Cook et al. 2006]. Although the technique is relatively simple and the results are impressive, it is not without its problems. There is inevitable operator exposure to radiation at both insertion and removal of the implants. While the implants are in situ, the horse has to be strictly isolated to minimise exposure of personnel to radiation, and this isolation is for several days due to the nature of the treatment. Implants can become displaced and lost, which necessitates exposure of personnel to potentially quite high doses of radiation while attempting to locate the implants, and if the implants are accidently consumed by the horse, it may be some time before they are located in its faeces and the horse can be discharged from the isolation facility. Due to these health and safety concerns and the high cost of the implants, the availability is very low and this technique is not currently available in the UK.

High-dose rate brachytherapy

A technique to more safely enable interstitial brachytherapy has been developed using a remote afterloader and a high-dose rate iridium source. The use of this technique has been briefly described for use in horses under general anaesthesia [Theon 1998]. The technique has since been developed for use in the treatment of periocular tumours under standing sedation [Hollis and Berlato 2018]. A high-activity source is used which dramatically reduces treatment times, and a
remote afterloader completely eliminates any operator exposure. Briefly, radiation catheters are implanted into the tumour (often following debulking of the tumour mass; Fig 6), and orthogonal images are obtained using C-arm imaging and radiodense markers that are inserted into the catheters. These images are used to enable computer-based treatment planning. Following the planning process, the catheters are connected to a remote afterloader which drives the high-dose rate iridium-192 source from a shielded safe into the catheters for treatment according to the predefined plan (Fig 7). The total treatment time is typically 2-6 min, during which time the operators monitor the horse via CCTV from an adjacent shielded radiation bunker. At the end of the treatment, the source is returned to the shielded safe, after which time the radiation catheters can be safely removed. As there is no direct handling of the radiation source, there is no personnel exposure to radiation, and the horse is completely radiation free between treatments. The treatment is delivered in two fractions, given 7 days apart, with a total radiation dose of 25 Gy. Early results are extremely promising (Hollis and Berlato 2018) and there is no reason to believe that the longer term results will be different to those achieved with low-dose rate therapy, as the principles of treatment are identical. To date, 54 treatments have been completed using the current protocol, achieving a 93% success rate using the RECIST criteria (A.R. Hollis, unpublished data) (Figs 8 and 9). However, there is still extremely limited availability, with only one centre in the UK currently offering HDR therapy (Animal Health Trust, Newmarket).

Electronic brachytherapy
A technique involving electronic brachytherapy has been reported for the treatment of an ocular B cell tumour (Bradley et al. 2015). Electronic brachytherapy uses a miniature x-ray source (50 kVp that produces 50 keV x-rays) to deliver radiation rather than a radioactive isotope. This can be via a...
superficial method using a cone applicator or an interstitial technique using applicators. The technique was designed for treating very superficial lesions such as squamous cell carcinoma and basal cell carcinoma in humans, with more invasive and extensive lesions not being considered suitable candidates for this technique (Doggett et al. 2015). Periocular sarcoids are often especially invasive and extensive (Knottenbelt and Kelly 2000), and the use of electronic brachytherapy for these more difficult lesions has not been investigated. Electronic brachytherapy is currently only theoretically possible for horses under general anaesthesia as there is no tolerance for movement of the horse, and the anaesthetist, although shielded with normal x-ray lead gowns, goggles, and a lead shield, will inevitably be exposed to a low level of x-ray exposure during the treatment. Other personnel can be remote from the source during treatment, avoiding unnecessary exposure. Although these are significant disadvantages compared with high-dose rate brachytherapy, the relative portability, affordability and minimal requirements for setting up the system may offer a useful form of brachytherapy for the treatment of periocular tumours if it proves to be successful.

Conclusions
Radiotherapy has long been considered the ‘gold standard’ for the treatment of periocular tumours of the horse, because of excellent long-term success rates despite the difficult location and nature of many of these lesions. There are several methods of delivering radiotherapy to periocular tumours in the horse. Despite the excellent success rates, the high cost and limited availability of any of the techniques are significant disadvantages. High-dose rate brachytherapy eliminates the health and safety and practical disadvantages of low-dose rate techniques, and can be safely and successfully delivered understanding sedation in the horse. Electronic brachytherapy shows promise as an alternative technique, although the requirement for general anaesthesia and the exposure of the anaesthetist to x-rays are significant disadvantages.

Author’s declaration of interests
No competing interests have been declared.

Ethical animal research
Not applicable.

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References

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<table>
<thead>
<tr>
<th>EUROPEAN EDUCATIONAL OFFERINGS</th>
<th>NORTH AMERICAN EDUCATIONAL OFFERINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRANCE</td>
<td>KENTUCKY</td>
</tr>
<tr>
<td>Grosbois</td>
<td>Lexington</td>
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<tr>
<td>October 17-19, 2019</td>
<td>October 8-10, 2019</td>
</tr>
<tr>
<td>Proximal Forelimb &amp; Neck Connec-</td>
<td>Pelvis</td>
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<td>April 16-18, 2020</td>
<td>October 11-13, 2019</td>
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<tr>
<td>Hock &amp; Crus</td>
<td>Sports Medicine Rehabilitation Module</td>
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<tr>
<td>ITALY</td>
<td></td>
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<tr>
<td>Milano</td>
<td></td>
</tr>
<tr>
<td>June 11-13, 2020</td>
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<tr>
<td>Distal Hindlimb up to PSL</td>
<td></td>
</tr>
<tr>
<td>THE NETHERLANDS</td>
<td></td>
</tr>
<tr>
<td>Sporthorse Medical Diagnostic Centre</td>
<td></td>
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<tr>
<td>September 3-5, 2020</td>
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<td>Stifle and Thigh</td>
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<td>October 22-24, 2020</td>
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<td>Pelvis</td>
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Infections caused by multidrug-resistant bacteria in an equine hospital (2012–2015)

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Keywords: horse; antimicrobial resistance; methicillin-resistant Staphylococcus aureus (MRSA); ESBL producing Enterobacteriaceae; nosocomial infection

Summary
Multidrug-resistant (MDR) bacteria are an emerging threat in human and veterinary medicine. There are few reports about infections caused by MDR isolates in horses. The aim of this study was to provide an overview of infections caused by MDR bacteria at the Equine Hospital Zurich between 2012 and 2015. Medical records were searched for horses with confirmed MDR bacterial infection. Multidrug resistance was defined according to human guidelines specific for each pathogen. MDR isolates were most commonly isolated from post-procedural infections (53/110, 48%); followed by musculoskeletal (16/110, 15%) and soft tissue infections (16/110, 15%). Escherichia coli (32/158, 20%) and Staphylococcus aureus (25/158, 16%) were the most common isolates. High resistance rates precluded therapy with commonly used antimicrobial drugs. The overall mortality rate was 20% (22/108) but depended on the localisation of the infection. Antimicrobial treatment prior to development of infection was reported for 89% (91/102) of horses. This study showed that MDR pathogens, mainly E. coli and MRSA, cause a considerable number of infections in horses. A wide range of infections was seen, however, nosocomial infections predominated. These cases are typically hospitalised, pretreated with antibiotics, and suffering from comorbidities putting them at high-risk for acquiring infections caused by MDR isolates. The mortality of such infections was generally low but depended on site of infection.

Introduction
Antimicrobial-resistant bacteria are an emerging threat in human and veterinary medicine (Weese et al. 2015). Antimicrobial resistance is mainly acquired by horizontal gene transfer, allowing its rapid spread within a susceptible bacterial population. At an individual horse level or short-term population level, such as in a hospital population, clonal spread is also an important means of spread of resistance (Barbosa and Levy 2000). Often, bacteria with resistance to three or more antimicrobial categories are called multidrug-resistant (MDR), however, naturally occurring intrinsic resistances present in an entire bacterial species should be excluded from this definition. Pathogen specific guidelines are available for human medicine, however, lacking for veterinary pathogens (Magiorakos et al. 2012).

Few studies on infections caused by MDR bacteria have been published in horses and most often they focused on methicillin-resistant Staphylococcus spp. (MRS) and extended-spectrum β-lactamases (ESBL)-producing Escherichia coli (Anderson et al. 2009; van Duijkeren et al. 2010; Maddox et al. 2011; Dierikx et al. 2012; Walther et al. 2014). Both species have developed resistance towards β-lactam antibiotics, one of the most important antimicrobial classes in veterinary medicine. The majority of these isolates have also acquired resistance to other important antimicrobial categories (Anderson et al. 2009; Walther et al. 2014).

Staphylococcus spp. and E. coli are commensals on the equine mucosal membrane and gut, respectively (Devriese et al. 1985; Corrente et al. 2009; Damborg et al. 2012); however, they are also important pathogens causing a wide range of infections (van Spijk et al. 2016a). An increasing prevalence of equine infections caused by methicillin-resistant Staphylococcus aureus (MRSA) has been reported during the last years (van Duijkeren et al. 2010). Reports of infections caused by ESBL-producing Enterobacteriaceae, mainly E. coli, have also emerged (Dierikx et al. 2012; Walther et al. 2014). Less is known about the role of other MDR isolates such as Acinetobacter baumannii, Enterococcus spp. and Pseudomonas aeruginosa in equine infections (Jokisalo et al. 2010; Herdan et al. 2012; Theelen et al. 2014), but a high rate of multidrug resistance was recently shown in these pathogens isolated from infections in horses (van Spijk et al. 2016b).

Studies in human subjects have repeatedly demonstrated an increased length of hospitalisation, higher costs and a higher mortality of infections caused by MDR isolates compared with similar conditions caused by susceptible organisms (Lautenbach et al. 2001; Tabah et al. 2012). A delay in appropriate therapy is suggested to be the main reason for this association (Tabah et al. 2012; Weese et al. 2015). Information about the outcome of infections caused by MDR isolates in horses is scant (Anderson et al. 2009; Herdan et al. 2012; Walther et al. 2014).

The aim of this study was to report cases with diagnosed infections caused by MDR bacteria in horses at the Equine Hospital of the University of Zurich between 2012 and 2015, in order to provide an overview of their occurrence, clinical presentation and outcome.

Materials and methods
All horses with a bacteriologically confirmed MDR bacterial infection at the Equine Hospital between 2012 and 2015 were included in the study. Multidrug resistance was defined as acquired resistance towards at least one agent in three or
more defined antimicrobial categories and adapted from the definition in human medicine (Magiorakos et al. 2012; van Spijk et al. 2016b). This definition was applicable to Enterobacteriaceae, *S. aureus*, *A. baumannii*, *Enterococcus spp.* and *P. aeruginosa*. Infections due to methicillin-resistant coagulase-negative staphylococci (MR-CNS) were also included in the study, although the above-described definition for multidrug-resistance could not be applied to these isolates.

The following information was collected from the databases of the Equine Hospital and the Institute of Veterinary Bacteriology of the University of Zurich: age, sex, breed, date of admission, number of samples, number of isolates, isolated bacteria and their susceptibility testing results, site of infection, antimicrobial therapy up to 3 months prior to the diagnosis, outcome, and in case of non-survival, the reason for euthanasia.

Diagnoses were classified into 10 groups based on the origin of the samples. Implant infections, infections of incisions and phlebitis were grouped as post-procedural infections. Synovial infections, osteitis and hoof abscesses were gathered to musculoskeletal infections. Soft tissue infections included external abscesses, wounds, cellulitis and infected haematomas. Urinary tract infections contained upper and lower urinary tract infection, and omphalitis. Respiratory tract infections included pathogens isolated from the upper and lower airways. Further diagnoses were sepsis, dental infection, peritonitis, dermatitis and diverse, which included neoplasia infection and otitis. Bacteria isolated from faecal samples were excluded.

Isolates considered as nonpathogenic or contamination were excluded based on information on bacterial species, origin of sample, quantity of growth, the occurrence of mixed cultures and clinical findings. If opportunistic pathogens were isolated, they were only included if a role as causative pathogen seemed reasonable based on clinical findings. When mixed infections occurred in one sample, all isolates were included. When a bacterial strain was isolated more than once from the same site in a horse within 6 months, the isolate was only counted once in the study (persistent infection).

Bacteriological culture, identification and susceptibility testing including the interpretation of results to susceptible or resistant was conducted as described elsewhere (van Spijk et al. 2016b). The automated VITEK® 2 Compact system was used for antimicrobial susceptibility testing and screening for phenotypically methicillin-resistant (pMR) Staphylococcus spp. and phenotypical ESBL-producing (pESBL) *E. coli* and Klebsiella pneumoniae spp. pneumoniae. Interpretation of results referred to the guidelines from the Clinical and Laboratory Standards Institute (CLSI) 2013 and, if information was lacking, guidelines from the European Committee on antimicrobial susceptibility testing (EUCAST 2016) and the U.S. Food and Drug Administration (FDA 2016) were used. Intermediate susceptibility was classified as resistant.

### Results

Between March 2012 and October 2015, 110 infections caused by a total of 158 MDR isolates were diagnosed. There were 21/110 (19%), 36/110 (33%), 30/110 (27%) and 23/110 (21%) infections in 2012, 2013, 2014 and 2015 respectively.

Infection with MDR isolates were reported in 108 horses. Breeds included Warmbloods (56/108, 52%), draught horses (14/108, 13%), Icelandic horses (8/108, 7%), Thoroughbreds (9/108, 8%), ponies (7/108, 6%), donkeys (2/108, 2%) and diverse other breeds (Connymara, Spanish horses, Quarter Horses, Friesian horses: 12/108, 11%). There were 61/108 (56%) geldings, 7/108 (6%) stallions and 40/108 (37%) mares. Age distribution ranged from 1 day to 30 years (median 10 years).

Most infections caused by MDR isolates were post-procedural infections (53/110, 48%), including 37/53 (70%) incisional infections, 13/53 (25%) implant infections and 3/53 (6%) phlebitis. While 52/110 (47%) infections were monomicrobial, 58/110 (53%) infections were polymicrobial (2–6 isolates). Polymicrobial infections caused by different MDR isolate (2–4 MDR isolates) were common (32/58, 55%). Two horses had multiple infections caused by different MDR isolates, simultaneously. One foal had omphalitis caused by MRSA and Enterococcus spp., and an incisional infection caused by pESBL *E. coli* and MDR Enterococcus spp. An adult horse had pneumonia caused by MDR *P. aeruginosa* and an incisional infection after colic surgery caused by pESBL *E. coli*, MRSA and MDR Enterococcus spp.

The most common MDR isolates were *E. coli* (32/158, 20%) and *S. aureus* (25/158, 16%). In Figure 1, the prevalence of all MDR isolates is illustrated. The most common MDR isolates differed between organ systems and this is demonstrated in Table 1. Antimicrobial susceptibility testing results of MDR isolates are shown in Table 2. High resistance rates towards commonly used antimicrobial drugs were seen.

All MDR *S. aureus* (25/25, 100%) were phenotypically methicillin-resistant. Phenotypically 26/32 (81%) *E. coli* and 3/4 (75%) *K. pneumoniae* spp. pneumoniae isolates were ESBL producing.

The mortality rate of all horses with infections caused by MDR isolates was 20% (22/108). Out of the 22 horses that were subjected to euthanasia, 17/22 (77%) horses were subjected to euthanasia as a result of the MDR infection. The remaining seven horses were subjected to euthanasia because of colic (4/7), MDR-unrelated sepsis (2/7) and neurological deficits with recumbency (1/7). The mortality based on reason for euthanasia of horses infected by MDR isolates in different organ systems is shown in Figure 2.

Information about antimicrobial therapy prior to MDR infection was available for 102/108 horses; 91/102 (89%) horses were treated with one or more antimicrobial drugs. Common previous given antimicrobials included penicillin, gentamicin, trimethoprim-sulfamethoxazole, marbofloxacin and cefquinome.

![Fig 1: Prevalence of different MDR isolates from infections in horses at the Equine Hospital of the University of Zurich (2012–2015).](image-url)
TABLE 1: Most common MDR isolates per organ system isolated from infections in horses at the Equine Hospital of the University of Zurich (2012-2015)

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Number of MDR isolates</th>
<th>MDR bacteria</th>
<th>n/Total per organ system (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-procedural</td>
<td>n = 81</td>
<td>S. aureus</td>
<td>17 (21%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>14 (17%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNS</td>
<td>13 (16%)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>n = 24</td>
<td>A. baumannii</td>
<td>8 (33%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterobacter cloacae complex</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>n = 22</td>
<td>E. coli</td>
<td>5 (23%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. aureus</td>
<td>4 (18%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterococcus spp.</td>
<td>5 (45%)</td>
</tr>
<tr>
<td>Urinary</td>
<td>n = 11</td>
<td>E. coli</td>
<td>2 (18%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. aureus</td>
<td>1 (9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterococcus spp.</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>n = 4</td>
<td>Enterobacter cloacae complex</td>
<td>2 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. aeruginosa</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Dental</td>
<td>n = 3</td>
<td>Enterococcus spp.</td>
<td>2 (67%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>1 (33%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterococcus spp.</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>n = 2</td>
<td>E. coli</td>
<td>1 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNS</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Skin</td>
<td>n = 2</td>
<td>E. coli</td>
<td>1 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNS</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Diverse</td>
<td>n = 4</td>
<td>P. aeruginosa</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. aureus</td>
<td>1 (25%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proteus mirabilis</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Total</td>
<td>n = 158</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Only MDR bacteria with an occurrence of >15% of all isolated MDR bacteria from the organ system are shown.
A. baumannii, Acinetobacter baumannii; CNS, coagulase-negative staphylococci; S. aureus, Staphylococcus aureus; E. coli, Escherichia coli; P. aeruginosa, Pseudomonas aeruginosa.

Discussion
This study showed that MDR pathogens, mainly MDR E. coli and MRSA, cause a considerable number of infections in horses. A wide range of infections was seen, however, the main group of diseased horses was affected by infections following therapeutic procedures.

Multidrug-resistant E. coli was the most common isolate in this study, causing a wide spectrum of infections. Enterobacteriaceae, including E. coli, Klebsiella spp., Enterobacter spp. and others, are common pathogens in horses (van Spijk et al. 2016a) and are known for their ability to acquire antimicrobial resistance (Vo et al. 2007). Production of ß-lactamase enzymes after acquisition of plasmid-mediated ESBL is the most important resistance mechanism in Enterobacteriaceae leading to extended spectrum ß-lactam resistance. The majority of MDR E. coli seen in this study was phenotypically ESBL-producing. ESBL-producing E. coli have previously been found in diverse clinical samples from horses (Vo et al. 2007; Ewers et al. 2010; Dierikx et al. 2012; Walther et al. 2014). MDR Klebsiella spp. and Enterobacter spp. have so far only been reported in single equine samples and their number was likewise low in this study (Vo et al. 2007; Dierikx et al. 2012).

Methicillin resistance in staphylococci is due to a modification of the penicillin-binding protein (PBP) (Ubukata et al. 1989). Similar to prior studies, MRSA in the present study were mainly responsible for incisional infections, phlebitis and synovial infections (Maddock et al. 2010). Methicillin-resistant coagulase-negative staphylococci have so far not been recognised as important pathogens in horses due to their inferior pathogenicity compared with S. aureus (Devriese et al. 1985). A considerable number of infections caused by these isolates was seen in our population and case reports of MR-CNS causing osteitis and implant infection also reported these isolates to be relevant pathogens (Trostle et al. 2001; Corrente et al. 2009).

Other common MDR isolates seen in our study were A. baumannii, Enterococcus spp. and P. aeruginosa. In addition to their high rates of intrinsic resistance, these species are known for their ability to rapidly acquire resistance to further antimicrobials (Jokisalo et al. 2010; Herdan et al. 2012; Theelen et al. 2014; van Spijk et al. 2016b). Pan-resistant A. baumannii strains are a serious problem in human medicine and MDR A. baumannii have already been isolated from horses (Jokisalo et al. 2010). Enterococcus spp. has been recognised as an increasingly resistant pathogen in foal sepsis and a report of MDR Enterococcus spp. causing septic arthritis was recently published (Herdan et al. 2012; Theelen et al. 2014).

Diverse infections have been caused by MDR bacteria; however, post-procedural infections represented almost half of the presented cases. In contrast, respiratory infections caused by MDR isolates were rarely seen, although respiratory infections are the most commonly diagnosed bacterial infections at our hospital (van Spijk et al. 2016a). Nosocomial infections, defined as hospital acquired infections not present at admission (WHO 2002), caused by MDR E. coli and MRSA were previously reported in horses (Anderson et al. 2009; Walther et al. 2014). Factors which have been shown to be significantly associated with the presence of MDR isolates in human subjects are prior use of antimicrobials, length of hospital stay, stay in the intensive care unit, the presence of co-morbidities, placement of various types of catheters, intubation and mechanical ventilation and a specific therapeutic interventions such as tracheostomy and hydrotherapy (Lautenbach et al. 2001; Falagas and Kopterides 2006). Many of these factors are typically also present in equine cases with nosocomial-acquired post-procedural infections. The previous use of antimicrobial drugs is the most common and consistent factor in all studies evaluating risk factors for the presence of MDR isolates. At least 89% of the horses included in this study were treated with antimicrobials prior to their diagnosis of MDR infection. The presence of several concurrent MDR isolates was common in our cases. Furthermore, in one case a non-MDR Enterococcus spp. together with a MRSA causing an emphyatitis was isolated at clinic entry; later on the same horse developed a surgical site infection with a MDR Enterococcus spp. strain. It is plausible that there was selection for a strain that was present as a coloniser or in the environment due to the selection pressure of antimicrobial
treatment, supporting an influence of antimicrobial therapy on the development of multidrug-resistant infection (Barbosa and Levy 2000).

Antimicrobial treatment of infections caused by MDR isolates is challenging and should always be guided by antimicrobial susceptibility testing results. Newer antibiotics,
like fluoroquinolones, macrolides, imipenem and vancomycin, remain usually effective against many MDR isolates, but their usage should be strictly limited in horses due to their critical importance in human medicine (WHO 2017). Chloramphenicol, a drug that has been avoided in the past because of its adverse effects in human patients, is regaining importance because of its frequent efficacy against MDR isolates (Giguère et al. 2013). In order to reduce the absolute amount of antimicrobials used and their adverse effects, local therapy (i.e. drainage and disinfection) should be considered whenever possible to eliminate the infectious agent and to overcome infections caused by MDR isolates (Weese 2009). The mortality rate of horses in the present study was generally low and comparable with previous results in horses with S. aureus infections (Anderson et al. 2009). The presence of a MDR isolate has been shown to increase the mortality rate of infections in human patients (Tabah et al. 2012). It is debatable whether this is a true association or if the presence of MDR isolates is simply reflecting the presence of co-morbidities. Previous studies in dogs were not able to detect a difference in the mortality of animals with methicillin-resistant and methicillin-susceptible isolates (Faires et al. 2010).

The main limitation of the present study is the lack of a control group. Comparison of outcome between horses with and without MDR isolates and identification of risk factors for their occurrence was not feasible. Attempts to compare incisional infections (the largest group) with and without MDR isolates failed due to a complete lack of incisional infections with non-MDR bacteria (data not shown).

In veterinary medicine, definition of MDR isolates has not been standardised and comparison between published data is therefore difficult. We adapted a definition from human medicine to our field (Magiorakos et al. 2012). Certainly, this approach was limited and a standardised definition for MDR isolates should be agreed upon.

**Conclusion**

This study showed that MDR pathogens, mainly MDR E. coli and MRSA, cause considerable numbers of infections in horses. Most infections caused by MDR isolates were incisional, implant or catheter-related infections. Patients affected by these infections are typically pretreated with antimicrobials, hospitalised and suffered from other morbidities, putting them at high-risk for acquiring infections caused by MDR isolates. Previous antimicrobial treatment was present in a large number of cases, highlighting the importance of prudent use of antimicrobial drugs. The mortality rate of infections caused by MDR was generally low and depended on the diagnosis of the horse. Studies are required to evaluate the impact of MDR isolates on the outcome of equine infections and to determine risk factors for their occurrence.

**Authors’ declaration of interests**

The authors have no conflicts of interest to declare.

**Ethical animal research**

This is a retrospective study which does not fall under Swiss animal use guidelines.

**Source of funding**

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**Authorship**

J. van Spijk contributed to study design, study execution, data interpretation and preparation of the manuscript. S. Schmitt contributed to data interpretation and preparation of the manuscript. A. Schoster contributed to study design, data interpretation and preparation of the manuscript. All authors gave their final approval of the manuscript.

**Manufacturer’s address**

1BioMérieux, Marcy l’Etoile, France.

**References**


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neural network \( n \).
a computer system modeled on the human brain and nervous system.

<script>
function identifiedImage (radiograph, species)

$('#image').click(function() {
    var radiograph = $('#radiograph').val();
    var species = $('#species').val();
    var horse = $('#horse').val();
    var lateralhoof = $('#lateralhoof').val();

    var identified = identifiedImage (radiograph, species);

</script>
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The use of pneumatic impact lithotripsy and a retrieval pouch to create a closed system for removal of cystic calculi in standing male horses

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Keywords: horse; urolith; lithotripsy; surgery; bladder

Introduction

The prevalence of urolithiasis in horses is reported to be 0.04–0.5% (Duesterdieck-Zellmer 2007). Calculi can be located anywhere along the urinary tract but are most commonly located within the urinary bladder (Laverty et al. 1992). Under normal conditions, horses excrete large amounts of calcium carbonate in their urine (Mair and Osborn 1990). This combined with the alkaline nature of their urine contributes to the formation of two different types of uroliths. Type I uroliths, which make up 90% of equine uroliths, are yellow–green spiculated stones that easily fragment. Type II uroliths, which are less common, are grey–white, smooth stones that are more resistant to fragmentation (Schott 2004). Clinical signs associated with cystic urolithiasis include dysuria and haematuria. Cystic urolithiasis is more commonly found in male horses presumably due to their longer, less distensible urethra. If found in mares, calculi can typically be removed whole via manual dilation of the urethral sphincter or urethral sphincterotomy after epidural anaesthesia, although fragmentation with electrohydraulic or pulsed-dye laser lithotripsy has also been suggested (Divers 2008).

In human subjects, if urinary bladder stones cannot pass naturally, they are typically addressed via transurethral cystolitholapaxy, which involves inserting a cystoscope into the urethra and delivering laser energy or shockwave (Li et al. 2015a). The length of the male horse’s urethra in combination with the relatively small diameter of an endoscope makes this procedure difficult in horses. Moreover, when using this technique, the fragments are not contained within a surgical bag so would be more likely to irritate the urinary bladder and would potentially act as a nidus for further stone formation. Pneumatic lithotripsy has been reported to fragment renal and ureteral stones in human subjects but extracorporeal shockwave lithotripsy is more commonly used in management of human urolithiasis (Radojevic et al. 2009; Li et al. 2015b). The ability to break up kidney stones, and less commonly urinary bladder stones, with this technique avoids the need for invasive surgery in human patients (Telha et al. 2016). However, extracorporeal shockwave instrumentation in human subjects uses a generator that encircles the abdomen, so unfortunately, the size of the horse precludes the use of true extracorporeal shockwave lithotripsy in the equine cases.

Multiple techniques have been described for removal of cystic calculi in the horse. Cystotomy techniques require general anaesthesia (Beard 2004; Watts and Fubini 2013) or deep dissection of pararectal tissues (Abuja et al. 2010). Laparoscopic cystotomies have also been described (Lund et al. 2013) as well as laparoscopic-assisted techniques (Roken et al. 2006; Stratico et al. 2012; Vitte et al. 2013). Complications associated with these techniques are rare but can include abdominal incisional dehiscence, peritonitis, uroperitoneum and incomplete removal of the urolith. Intact and manually fragmented uroliths have been removed through perineal urethrotomy (PU) as a standing procedure in geldings (Laverty et al. 1992; Hawkins 2013; Kilcoyne and...
Dechant 2014). Complications associated with PU include stranguria, urine scalding, haemorrhage, urethral stricture, perforation of pelvic urethra and recurrence of cystic calculi (Laverty et al. 1992; Kilcoyne and Dechant 2014).

The use of radial (Foerner and Stanschi 2005; Katzman et al. 2016), ballistic (Koenig et al. 1999) and electrohydraulic shockwave (Koenig et al. 1999; Rocken et al. 2012) have been described in the horse, but all methods of shockwave have notable disadvantages. Ballistic shockwave and radial shockwave in one report (Foerner and Stanschi 2005) involved general anaesthesia, pneumatic radial shockwave in another report involved expensive instrumentation (Katzman et al. 2016) and electrohydraulic shockwave required up to six separate sessions. There are also reports of use of a pulsed-dye laser and holmium:yttrium-aluminium-garnet (holmium:YAG) laser to fragment equine uroliths. Both lasers have the disadvantages of expense, increased surgical time to fragment uroliths and incomplete fragmentation for type II calculi (May et al. 2001; Judy and Galuppo 2002; Grant et al. 2009).

Although anecdotal reports of pneumatic lithotripsy in the horse exist, to the authors' knowledge, there is only one other published report of its use in a group of horses, which uses pneumatic radial shockwave lithotripsy (Katzman et al. 2016). Shockwave lithotripsy uses sound waves to fragment uroliths, whereas the current report goes into greater detail to describe the use of a pneumatic impact lithotrite, which uses direct physical contact of a steel rod to fragment uroliths. This report also details two different types of laparoscopic retrieval bags for removal of cystic calculi through a PU. The goal of this study was to report on the success and benefits of pneumatic lithotripsy in combination with a laparoscopic retrieval bag for removal of cystic stones in male horses. We hypothesised that pneumatic lithotripsy would require a shorter surgical time and lower equipment costs than other described methods for removal of cystic calculi in the horse.

**Materials and methods**

All horses that underwent pneumatic lithotripsy at one of the five participating referral centres for removal of cystic calculi were included in the study. The participating referral centres were Colorado State University (CSU), Sturgis Veterinary Hospital and Equine Center, Ohio State University (OSU), the University of Georgia (UGA) and South Valley Large Animal Clinic. At least one author was physically present for all procedures.

The presence of a cystic calculus was confirmed with transrectal palpation and ultrasonography with or without cystoscopy. Cystoscopy was used if the calculus/calculi could not be well characterised ultrasonographically in terms of size and number. The diameter of the stone was measured ultrasonographically. Feed was withheld from all horses for 24 h prior to surgery. This range is due to differences between institutions, with the longer end of the range hypothesised that pneumatic lithotripsy would require a shorter surgical time and lower equipment costs than other described methods for removal of cystic calculi in the horse.

The surgical end of the pneumatic impact lithotrite was secured within the urethra (Fig 3). The interior of the bag was sterilised with sterile lube (Fig 4). The endoscope was inserted into the bladder via the PU and the bag was deployed. The stone was placed into the bag by one of two methods: (1) transrectal manipulation of the stone (blind, Fig 2) or (2) under endoscopic guidance (endo, Fig 3). The endoscope was removed from the urethra bladder once the urolith was secured within the retrieval bag. The urolith secured in the laparoscopic retrieval bag, the opening of the bag was exteriorised through the PU (Fig 4). The interior of the bag was then lubricated with obstetrical lube (n = 9, Lubrivet13) or sterile lube (n = 2, Surgilube14).

The lithotripsy instrumentation consists of a stainless steel rod (pneumatic impact lithotrite) that is 0.5 inches in diameter, a pneumatic scaler, a regulator with associated air lines and a gas source (Fig 5). The rod is 18 inches long. The surgical end is blunt. The opposite end is designed such that it fits into a pneumatic scaler15 (E in Fig 5). Once mounted into the pneumatic scaler the vibrating action causes the urolith to break apart when in contact. The scaler used vibrates at 4000 beats/min with 0.25 inch strokes. This air scaler requires connection to a gas line with 90 psi.

The surgical end of the pneumatic impact lithotrite was passed into the exteriorised opening of the laparoscopic retrieval bag and the end of the lithotrite was held firmly in contact with the urolith. The urolith was stabilised against the rod transrectally. The urolith was fragmented by activating the lithotrite in short bursts while continuing to stabilise the
urolith transrectally (Fig 6). The fragmentation process was monitored by transrectal palpation and applying gentle traction on the retrieval pouch. Frequently, the lithotrite was removed from the pouch to allow lavage of the fragments from the laparoscopic retrieval bag. The bag was infused with obstetrical lube$^{13,14}$ in sufficient quantity to lavage out the small pieces of the urolith. Sponge forceps were also used to remove larger fragments. The obstetrical lube$^{13,14}$ was infused into the pouch using a 60 mL catheter tip syringe and a 30 cm section of a stallion catheter. Additional fragmentation was performed if necessary. The retrieval pouch was removed from the urinary bladder when a sufficient quantity of the fragments had been flushed from the retrieval pouch opening to allow its passage through the urethra (Fig 7).

Upon removal of the retrieval bag and urolith fragments (Fig 8), a cystoscopic examination was performed to detect if there were any remaining calculi or fragments. If additional calculi were identified, the procedure was repeated until the urinary bladder was free of calculi. If any fragments were present within the urinary bladder, it was lavaged with isotonic fluids. In some cases, fragments were removed using instrumentation (laparoscopic grasping forceps) and direct visualisation with the endoscope. When all calculi had been successfully removed, the urinary bladder and urethral mucosa were assessed with the endoscope. The PU incision was left to heal by second intention.

Fig 1: Laparoscopic retrieval bags (a) Endo Catch™II and (b) thicker Mila bag.

Fig 2: Drawing of laparoscopic retrieval bag positioned through the perineal urethrotomy site and securing the urolith with transrectal manipulation.

Fig 3: A laparoscopic retrieval bag positioned through the perineal urethrotomy site and securing the urolith with endoscopic guidance.
The horses remained hospitalized for a minimum of 1 day post-operatively. They remained on an oral trimethoprim-sulfonamide2,3, (15–30 mg/kg bwt, PO) twice daily for 5 days and received phenylbutazone (Bute Boluses16, 2.2 mg/kg bwt, q 12 h, PO) for 3–5 days following surgery. The PU site was cleaned daily with warm water. Petroleum jelly was applied distal to the incision after each cleaning to prevent urine scald. The owners were instructed to watch for bleeding from the site, abnormal swelling or discharge.

Results

Eleven horses underwent pneumatic lithotripsy (Sturgis (5), CSU (3), OSU (1), UGA (1) and South Valley (1)). The mean age was 15.5 years (range 5–22 years). The horses weighed between 400 and 660 kg. Ten horses had a single urolith and one horse had multiple uroliths present within the urinary bladder. Urolith diameters ranged from 4 cm to 9 cm. Only the largest urolith was measured in the horse with multiple uroliths present. Preoperative medications included antibacterial coverage with a trimethoprim-sulfaonamide (n = 9) or potassium penicillin and gentamicin (n = 2) as well as flunixin meglumine for control of pain and inflammation. All horses received epidurals before the PU was performed and were continued for 5 days post-operatively on a trimethoprim-sulfonamide and phenylbutazone.

All calculi were successfully removed. The urolith was manipulated into the laparoscopic retrieval bag transrectally in eight horses and endoscopy was used in three horses. The Mila retrieval bag was used in six cases and the Endo Catch II laparoscopic retrieval bag was used in five cases. The laparoscopic retrieval bag developed holes in two of the cases and the urinary bladder had to be lavaged to remove all fragments in these cases. The mean surgical time from the start of the PU incision to extraction of the laparoscopic retrieval bag with urolith contents was 68.1 min (range 48–110 min). The mean lithotripsy time (from the time the stone was contained within the bag to when the bag was extracted) was 37.9 min (range 25–60 min) for nine horses. Surgery time was not recorded for two horses.

Follow-up information was available for 10 of the 11 cases (2 months–4 years post-operatively, mean = 497 days, median = 391 days). All 10 horses had returned to full work. Owners reported no recurrence of clinical signs of urinary pathology. At the time of publication, three of the 11 horses had died, two of completely unrelated causes and one of unknown causes. In all cases, the PU sites had healed without complication.

Discussion

This report describes the use of pneumatic impact lithotripsy and a laparoscopic retrieval bag for the removal of cystic
calculi through a PU in the standing gelding and stallion. A total of 11 horses were reported in this study.

The pneumatic impact lithotrite used in the current study is a novel device for manual lithotripsy in horses. The lithotrite is a smooth, steel rod that can be advanced through the PU site into the urinary bladder with little to no resistance. The rod can also be readily palpated transrectally allowing for positioning of the stone against the rod. The vibration of the rod quickly fragments type I uroliths and type II uroliths require slightly more fragmentation. The rod can be sterilised. The pneumatic scaler can also be sterilised using gas sterilisation. The instrumentation requires minimal maintenance in the form of compressor and air tool lubricant after each use. This piece of equipment requires some experience to gain comfort with but once used a few times becomes uncomplicated to manipulate.

The laparoscopic retrieval bag plays an important role in the success of this technique because it contains the urolith fragments and protects the urethra. In previous cases, fragmentation of the urolith into the bladder lumen then required a more extensive lavage of the bladder following lithotripsy. This leads to increased bladder and urethral mucosal irritation. The use of a laparoscopic retrieval bag has been described previously (Menendez and Fitch 2012; Katzman et al. 2016), but in one report the uroliths were less than 5 cm in diameter and in the other a pneumatic impact lithotrite was not used, leading to prolonged surgical times.

The laparoscopic retrieval bag does add a level of technical difficulty. In the two cases where the retrieval bags

Fig 6: Drawing and pictures depicting activation of the pneumatic lithotrite against the urolith while stabilising the urolith transrectally.

Fig 7: The retrieval pouch after removal with fragmented stone inside.

Fig 8: A fragmented urolith after removal from the retrieval bag.
developed holes, the bags were in the early stages of development for this procedure and were manufactured of a thinner material. In those cases, fragments were found within the urinary bladder following extraction of the bag and more extensive lavage of the urinary bladder was required to remove the remaining fragments. It is also important that the bag is fully deployed prior to scooping the urolith. Full deployment allows the stone to pass to the most ventral portion of the bag. The opening of the bag is then exteriorised. One laparoscopic retrieval bag has fenestrations at the attachment to the ring. These fenestrations can tear free prematurely. Other models of the laparoscopic bag do not possess these fenestrations and have greater integrity at the ring. Bag strength is also important. As the urolith breaks apart, the fragments assume a grit-like texture, which can create holes within the bag, especially with type II uroliths which are more difficult to fragment.

In this study, two retrieval bags were used. One is the Endo Catch II, which has perforations at the ring so manipulations of the urolith have to be performed delicately in order to not tear the bag at the perforations. It is recommended that when the Endo Catch II bag is used, the urolith is manipulated into the bag by direct visualisation using an endoscope to help prevent this tearing. The authors recommend a thicker laparoscopic retrieval bag which is now commercially available from Mila and does not have perforations that lead to tearing. The design of the Mila bag also allows for it to be retracted and re-deployed as necessary with no damage to the bag, allowing for greater manoeuvrability of the bag.

Rectal perforation due to transrectal manipulation of a urolith has been reported (Laverty et al. 1992). Transrectal palpation and manipulation should always be performed with great care but in the cases included in this study there were no complications with transrectal manipulation of the urolith. Once the urolith has been positioned into the laparoscopic retrieval bag, transrectal manipulation is restricted to the caudal 15–20 cm (estimated) of the rectum. Claes et al. reported that the median distance from the anus for rectal tears was 25–30 cm (Claes et al. 2008).

This technique required less surgical time and was less expensive than other published techniques. Reported surgical times for removal of cystic calculi are 210 min (ballistic shockwave) (Koenig et al. 1999), 125 min (pneumatic radial shockwave lithotripsy) (Katzman et al. 2016), 7 hours (electrohydraulic lithotripsy) (Reichert and Lischer 2013), 70 min (pararectal cystotomy) (Abuja et al. 2010) and 59 min (parainguinal laparocystotomy) (Beard 2004). The average surgical time in this study was 68.1 min. The cost to the client for the procedure was $1000–2400 which varied across the different institutions.

Complications associated with PU for the treatment of cystic calculi have been reported (Holt and Pearson 1984; Laverty et al. 1992; Kilcoyne and Dechant 2014). Kilcoyne and Dechant (2014) reported a high incidence of complications following PU for treatment of urolithiasis (54.5%, 12/22) but this report overstates the risk of complications. Only four of the nine listed complications were directly related to the PU: severe haemorrhage, urethral fistula, urine scald and urethral stricture. Within those cases, the urine scald only occurred in permanent PUs and the strictures only occurred in donkeys (Kilcoyne and Dechant 2014). In this study, no complications associated with the PU were reported.

No complications were observed in this study. Care must be taken to avoid known complications associated with transrectal palpation and PU, but the authors consider the risk of these complications to be low. Additionally, the operator must expect to spend some time gaining experience with the lithotrite and retrieval bag before being comfortable employing their use. The most serious complication that the authors can perceive is if the lithotrite becomes displaced from the stone and then either tears the bag, or worse, traumatises the bladder. For this reason, it is important to rely on transrectal palpation to assure proper placement of the lithotrite against the stone as well as frequent removal of the lithotrite to flush fragments from the bag and reorient the urolith(s).

In conclusion, the reported technique for removal of cystic calculi in the standing horse results in less trauma to the bladder than techniques involving cystotomy or not involving use of a retrieval bag, the shortest mean surgical time of a standing procedure that fragments and removes uroliths, and is a safe, cost-effective alternative to other techniques.

Authors’ declaration of interests

N. De Bernardis, K. Seabaugh and M. Mudge have no conflict of interest. J. Ismay has a patent on this procedure referred to as – Closed System Pneumatic Impact Lithotripsy.

Ethical animal research

The authors believe that this procedure is the best option for patients with urolithiasis. Clients were informed of the risks of the procedure and provided their consent.

Sources of funding

None.

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The authors thank Dr Randy Eggleston DVM, DACVS, at the University of Georgia and Dr Roger Rees DVM at the South Valley Large Animal Clinic for contributing cases to this study. Thanks are also extended to Jeff Vitullo with MILA International for assistance with development of a laparoscopic retrieval bag to the authors’ specifications and to Travis Ismay for development of the lithotrite instrument, for which he shares a patent with Dr. John Ismay.

Authorship

N. De Bernardis performed most of the data analysis and interpretation (calculating average times, compiling data from different cases to summarise procedure and results, performing follow-up, etc.) and prepared the manuscript. K. Seabaugh contributed to the study design, study execution (was present for 4/11 cases), data analysis and interpretation, and preparation of the manuscript. J. Ismay contributed to the study design, study execution (was present for 6/11 cases) and preparation of the manuscript. M. Mudge contributed to the study design and study execution (was...
present for 1/11 cases). All authors approved the final version of the manuscript.

Manufacturers’ addresses

1MWI Veterinary Supply, Boise, Idaho, USA.
2Cameron Pharmacy, St. Matthews, South Carolina, USA.
3Amneal Pharmaceuticals, Glasgow, Kentucky, USA.
4Pfizer, New York, New York, USA.
5Butler Schein Animal Health, Dublin, Ohio, USA.
6Fort Dodge Animal Health, Fort Dodge, Iowa, USA.
7Lloyd Laboratories, Shenandoah, Iowa, USA.
8Zoetis, Florham Park, New York, USA.
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10Boehringer Ingleheim, Ridgefield, Connecticut, USA.
11MILA International, Kentucky, USA.
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13Henry Schein, Kentucky, USA.
14Surgilube, HR Pharmaceuticals, Inc., York, Pennsylvania, USA.
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References

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Dates & Tuition

<table>
<thead>
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<th>Regular Tuition</th>
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*Early tuition rate when registering by 12/31/2019.

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  - Session 5 (final session): fully integrate acupuncture into daily practice

Registration & Dates

Small Animal, Mixed Practice or Equine Acupuncture Tracks are available

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<td>June 4 - 7, 2020</td>
<td>Dec 10 - 13, 2020</td>
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Transrectal ultrasonographic examination of the sacroiliac joints of the horse: Technique and normal images

A. Tallaj*, V. Coudry and J.-M. Denoix

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Keywords: horse; pelvis; sacroiliac joint; transrectal; ultrasonography

Summary
Transrectal ultrasonography of the sacroiliac joints is routinely performed for the diagnosis of the cause of low back pain and lack of power in the hindlimbs. As a result of the localisation of these small joints, performing and interpreting ultrasonographic images requires a good anatomical knowledge. This paper describes an ultrasonographic procedure that allows imaging of the ventral aspect of the sacroiliac joints. A complete screening should be done to evaluate the articular margins. Moreover, the shape of sacral and iliac wings can vary among individuals especially depending on the gender.

Introduction
Sacroiliac lesions have been considered as a cause of poor performance and lack of power in the hindlimbs since the 1980s (Jeffcott et al. 1985; Denoix 1992). In the past, diagnosis has been limited by anatomical location and used to be assumed by exclusion (Erichsen et al. 2002; Haussler 2010). Local analgesia by infiltration of local anaesthetic solution close to the sacroiliac joint has been described (Dyson and Murray 2003; Haussler 2010). Nevertheless, this technique lacks sensitivity due to the ventral location of the lesions (Dalin and Jeffcott 1986a) and specificity due to large diffusion in surrounding tissues (Denoix 2014) and presents a risk of sciatic nerve paresis. Therefore, its use to diagnose sacroiliac pain is limited in routine practice. Radiography is valuable for the diagnosis of pelvic and coxofemoral fractures but is limited for assessing lumbosacral and sacroiliac injuries (Denoix et al. 2005; Bergman et al. 2013). Conversely, nuclear scintigraphy has been found useful in diagnosis of sacroiliac lesions (Tucker et al. 1998; Erichsen et al. 2002; Dyson et al. 2003a,b; Coudry et al. 2006; Denoix et al. 2006) but this modality cannot be used in the field. Chronic osteoarticular changes of the sacroiliac joint are mainly found over the caudomedial margins of the ventral aspect of the joint (Jeffcott et al. 1985; Dalin and Jeffcott 1986a; Dalin and Jeffcott 1986b; Haussler 2004; Denoix 2014). As this part of the joint can be imaged with an adequate ultrasound transducer placed in the rectum, transrectal ultrasonographic examination has become routinely used to diagnose sacroiliac injuries. For more than two decades, the knowledge of the normal images and their variations as well as pathological changes has progressively improved (Denoix 1999).

The purpose of this paper is to describe the ultrasonographic technique for imaging the sacroiliac joints of the horse transrectally and to present their normal ultrasonographic appearance in order to improve the specificity in diagnosing lesions.

Basic anatomy
The sacroiliac joint is a complex joint made of a flat synovial articulation with hyaline cartilage on the sacral auricular surface and fibrocartilage on the iliac auricular surface (Dalin and Jeffcott 1986a; Barone 2000; Degueurce et al. 2004; Haussler 2004, 2010). The joint space is located deep to the iliac wing, between the auricular surface of the iliac wing and the auricular surface of the first transverse process of the sacrum (sacral wing) (Fig 1). The auricular surfaces are usually described as L-shaped with the convex border directed caudoventrally. Sacroiliac joints are stabilised by three sets of strong sacroiliac ligaments (Denoix 1992; Barone 2000; Degueurce et al. 2004). The ventral sacroiliac ligament lies along the ventral margin of the auricular surfaces of the ilium and sacrum and its fasciculi extend mediolaterally (Fig 2). The interosseous sacroiliac ligament is made of several strong fasciculi separated by fat. It joins the dorsal
surface of the sacral wing and the cranioventral surface of the iliac wing (Fig 2). The dorsal sacroiliac ligament is strong and does not have any direct anatomical relationship with the sacroiliac joint space. It inserts on the tuber sacrale of the ilium and is divided in two parts. The dorsal (or funicular) part extends caudally and attaches on the spinal processes of the sacrum (median sacral crest). The ventral (or membranous) part extends ventrally to insert on the transverse processes of the sacrum (lateral sacral crest) (Barone 2000; Degueurce et al. 2004; Denoix 2014). These three sacroiliac ligaments build a strong ligamentous sling to the sacrum and give stability to the sacroiliac joint, allowing only one to two degrees of nutation (or flexion) and counter nutation (or extension) (Denoix 1992; Barone 2000; Degueurce et al. 2004; Haussler 2004). Gluteal muscles, erector spinae muscle and psoas muscles also strongly contribute to stabilise the sacroiliac joints (Denoix 1992). Each sacroiliac joint enables the transmission of power from the corresponding limb to the vertebral axis and the rest of the body (Denoix 1992; Barone 2000), undergoing high biomechanical stresses.

Ventrally, the sacroiliac joint is crossed by the cranial gluteal artery and vein and the truncus lumbosacralis providing the sciatic nerve and the gluteal nerves (Fig 3). These structures are close to the ventral sacroiliac ligament. The ventral ramus of the first sacral intervertebral nerve emerges from the first ventral sacral foramen, adjacent to the medial aspect of the sacroiliac joint (Fig 3). The most lateral aspect of the sacroiliac joint margin is overlaid with the iliopectineus muscle.

In many species including equids, the size and conformation of the pelvis is related to the gender. The pelvic dimensions are reduced in males, females having a larger and rounder pelvic inlet (Barone 2000).

**Equipment and technique**

Ultrasoundographic images of the equine sacroiliac joint are routinely performed with a 7.5 MHz small curvilinear transducer.
(intraoperative) transducer, but satisfying images can be acquired with a 7.5 MHz linear rectal transducer (Fig 4) which is more often available in field practice (Denoix 1998). On thin horses, a higher frequency (e.g. 10 MHz) may improve image resolution. First, the horse is placed into stocks and the rectum is evacuated with all the necessary precautions to preserve the rectal mucosa, after careful approach of the horse’s hindquarters and adequate lubrication. Sedation may be required if the horse is not relaxed enough. Gel is applied to the transducer before starting the rectal examination. No stand-off pad is required. The sacroiliac joint is imaged on parasagittal sections, the transducer facing up and being placed in a horizontal axis (Fig 5). For each clinical case, examination of both sacroiliac joints should be performed. Examination starts dorsally in the median plane with identification of the last lumbar intervertebral disc (L6) or the lumbosacral promontorium which is used as a landmark. In order to move to the sacroiliac joints, the transducer is displaced laterally in a parasagittal plane to image the lumbosacral intervertebral foramen containing the ventral ramus of the sixth lumbar intervertebral nerve (L6) and then moved caudally to image the first ventral sacral foramen filled with the ventral ramus of the first sacral intervertebral nerve (S1). These two rami are the major roots of the sciatic nerve (Fig 3).

Finally, the ventral aspect of the sacroiliac joint is visualised by placing the transducer laterally to the first ventral sacral foramen in a parasagittal direction (Fig 5). The joint space and margins must be screened carefully from the most medial aspect of the ilium neck to the most lateral aspect of the sacral wing (Fig 6). The shape of the margins of the sacroiliac joint changes progressively mediolaterally and will be described in three medial, intermediate and lateral portions of the joint (Fig 6). The process is repeated on the contralateral side. As the transducer must be moved laterally on both sides of the pelvis, it is easier to image the left sacroiliac joint using the right hand and the right sacroiliac joint using the left hand (Denoix 2014).

**Reference ultrasonographic images**

Knowledge of the normal ultrasonographic appearance of the anatomical structures involved in the sacroiliac joint is essential to correctly identify pathological changes. On reference ultrasound scans, the sacral and iliac wing profiles are imaged as two regular and thin hyperechogenic lines, with smooth articular margins of the auricular surfaces (Figs 7, 8 and 9) (Denoix 1998; Denoix et al. 2006, 2007). The sacroiliac periarticular space is filled by a homogeneously echogenic triangular structure, the ventral sacroiliac ligament, which is about 5 to 8 mm thick and wide on sound horses (Denoix 1998; Denoix et al. 2006, 2007). The ventral aspect of the sacroiliac joint is crossed by the cranial gluteal artery and vein, which can be used as anatomical window to allow improvement of image quality (Figs 7, 8 and 9). Females and geldings have a narrower sacroiliac joint space than males with sharper margins (Figs 7a–c, 8 and 9). Similarly, the shape of the sacroiliac joints shows some 13254689

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**Fig 5:** Ventral anatomical view of the root of the pelvis (cranial is to the top). A double-arrow shows the transducer orientation when starting screening the sacroiliac joint transrectally. 1: vertebral body of the sixth lumbar vertebra; 2: vertebral body of the first sacral vertebra; 3: lumbosacral intervertebral disc; 4: sixth lumbar intervertebral foramen; 5: first ventral sacral foramen; 6: sacral wing; 7: iliac wing; 8: intertransverse lumbosacral joint; 9: ventral sacroiliac ligament.

**Fig 6:** Schematic drawing of the ventral aspect of the sacroiliac area (cranial is to the top and medial is to the left). Depending on the transducer position, different parts of the ventral aspect of the sacroiliac joint can be imaged. a: medial part; b: intermediate part; c: lateral part; 1: transverse process of the first sacral vertebra (sacral wing); 2: sixth lumbar vertebra; 3: ilium neck; 4: tuber coxae; 5: minor tuberculum of the femur; 6: sacroiliac joint (partly covered by muscles); 7: iliosacral part of the internal obturator muscle; 8: minor psosas muscle; 9: major psosas muscle, 9a: medial aspect covering the medial part of the iliac muscle; 10: iliac muscle, 10a: medial part, 10b: lateral part.
individual variations (Barone 2000), according to age and body weight (Dalin 1984; Dalin and Jeffcott 1986b). Moreover, the imaged parts of the sacrum and ilium vary and different profiles of the articular margins can be imaged, according to the transducer position (Figs 8a–c and 9a–c).

The medial parasagittal section images the wide base of the sacral wing and cuts the narrow medial border of the iliac wing; on the lateral parasagittal section, the apex of the sacral wing become narrower and the iliac wing wider.

**Discussion**

When undertaking a transrectal examination, attention should be paid to the horse’s behaviour to avoid any rectal laceration. Light sedation can be used if necessary. The practitioner should take care to handle the transducer properly without putting too much pressure on the rectum wall, and to adapt his movements to the horse’s reactions. One finger should be placed at the cranial aspect of the transducer to avoid direct contact between the transducer and the rectum wall (Denoix 2014).

External percutaneous ultrasonographic imaging of sacroiliac joints has been reported several times, especially in the context of therapeutic periarticular injections (Tomlinson et al. 2001, 2003; Kersten and Edinger 2004; Engeli et al. 2006; Cousty et al. 2008; Denoix and Jacquet 2008). The dorsal sacroiliac ligament can be visualised with this approach (Denoix 1998). Lesions of this ligament are uncommon and often observed in the tuber sacrale insertion (Denoix 1998). Although the external approach is indicated for treatment, it does not enable the visualisation of the ventral aspect of sacroiliac joints, which is the area of interest in the diagnosis of sacroiliac osteoarthritis. Osteoarthritis is the most common pathological finding in horses affected by sacroiliac pain (Haussler 2004). The ventral and caudomedial joint margins are the most affected parts of the joint (Dalin 1984; Jeffcott et al. 1985; Denoix 1998; Haussler 2004; Bergman et al. 2013) and can be accurately imaged with adequate equipment and technique.

![Fig 7](image1)

**Fig 7:** Parasagittal ultrasound scans of the intermediate part of the sacroiliac joint (cranial is to the left). Images were acquired with a small curvilinear transducer on a female a), a gelding b) and a male c). 1: sacral wing; 2: iliac wing; 3: ventral sacroiliac ligament; 4: cranial gluteal artery and vein; *: sacroiliac joint space.

![Fig 8](image2)

**Fig 8:** Parasagittal ultrasound scans of the sacroiliac joint of a female (cranial is to the left). Images were acquired with a small curvilinear transducer on three different positions described on Fig 6. The transducer is placed on the medial a), intermediate b) and lateral c) part of the joint. 1: sacral wing; 2: iliac wing; 3: ventral sacroiliac ligament; 4: cranial gluteal artery and vein; *: sacroiliac joint space.
Considering the anatomy and position of the sacroiliac joint, a small curvilinear transducer is ideal to obtain a complete representation of the bone margins thanks to the trapezoidal shape of the ultrasound field. However, images can be acquired with a linear rectal transducer, which is more often available in practice.

Knowledge of normal anatomy and anatomical variations is essential for avoiding overdiagnosis in the identification of findings and lesions. Because of a larger and rounder pelvic inlet (Barone 2000), the sacroiliac joint space of females is narrower and has sharper margins, especially on the sacral wing. According to our daily observations on several hundreds of horses every year, the sacroiliac joint space on males is wider and geldings have an intermediate sacroiliac joint conformation (Denoix 2014).

Transrectal ultrasonographic examination of the sacroiliac joints has nevertheless some anatomical limitations. The interosseous sacroiliac ligament cannot be imaged, because of its dorsal localisation between the sacrum and the ilium. The most lateral part of the joint is also difficult to assess due to the thickness of the iliopsoas muscle covering it. Subchondral bone surface cannot either be assessed with ultrasound.

Despite these limitations, ultrasonography enables a good topographical representation of the equine pelvis and has been validated by other modalities such as CT, MRI as well as measurements of frozen anatomical sections (Tomlinson et al. 2001) and post-mortem studies (Hausel et al. 1999).

Following the ultrasonographic technique described in this paper, a real-time diagnosis of sacroiliac injuries can be easily obtained by the practitioner in the field. Combined with clinical examination and complementary imaging techniques such as nuclear scintigraphy, ultrasonography has contributed to a better knowledge of sacroiliac injuries, and a better management of affected horses.

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

Ethical animal research
Not applicable.

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Authorship
All authors contributed to the preparation of this manuscript.

References


Correspondence

Additional ideas concerning the veterinary-farrier relationship

The editorial in the November 2018 issue of EVE reviewing the Veterinary-Farrier Relationship by Drs Moyer, Werner, O’Grady and Ridley (Moyer et al. 2018) summarised some excellent thoughts on the two professions and how to develop relations and keep them. I applaud them for adding a farrier to improve their previous writing on this topic (Moyer et al. 2012) I would like to add some additional comments since I feel equine practitioners’ and farriers’ relations have markedly improved since the late 1990s and the early 2000s. In the recently published 2018 Farrier Business Practices Report (Zank 2019), 59% of the farrier survey respondents are consulting weekly with veterinarians and only 6% rarely consult with a veterinarian. I also feel that joint veterinary and farrier therapeutic efforts have markedly increased with some good successes in these past two decades. In that same Business Practices report, 94% of farriers responded that they “practice therapeutic shoeing – to correct lameness”. More than two-thirds (70%) of farriers said they encounter horses with thrush on a weekly or monthly basis. At least half of the respondents indicated that they had dealt with white line disease, laminitis, navicular issues or soft tissue injuries within the last month of the survey. Besides the daily working together of equine practitioners and farriers, there are many joint regular local (Mansmann 2002; Freer 2008), regional and even national CE accredited veterinary and farrier meetings that have joint attendance discussing equine medical and mechanical foot topics. At these meetings, farriers, veterinarians and highly respected veterinarians trained as farriers lecture and oversee wet labs. They are all striving to improve common medical language and moderating medical educational levels that were mentioned in the Moyer editorial. Veterinarians and farriers are reading radiographs together to enable a collaborative approach to the foot care of their client’s horses (Cota 2017; Healey 2018). The veterinary-farrier relationship exists at a high and co-operative level at the stall side of horses with foot problems.

It is also critical to note that farriers as healthcare providers see and communicate potentially more frequently with horse owners than do equine veterinarians. The largest detriment to the veterinary-farrier relationship currently is the major veterinary organisations, and maybe veterinary specialty boards and state veterinary medical boards, being perceived as attempting to control equine farriery (Cota 2018a). The AVMA Model Practice Act controversy of 2018 did not need to happen. This was perceived by many farriers as disrespecting their profession and their role in equine health. It puts many equine practitioners in awkward positions trying to explain the situation to their important professional associates. Conflicts between veterinary and farrier associations are not just an American problem (Cota 2018b). If we veterinarians really want to have a decent relationship with farriers and their profession, it is the time to consider the farrier as a true equine healthcare provider. It is a discredit to the AVMA; and maybe the AAEP and other AVMA recognised Specialty boards, that the most read article in the American Farrier’s Journal (AFJ) of 2018 was related to the AVMA’s proposed new Model Veterinary Practice Act. That topic was covered in two other articles in the AFJ and they ranked number 5 and 9 as most read! (Moskov 2019). Besides the veterinary profession needing to consider farriers as a critical part of the equine healthcare team so too do farriers need to consider themselves as an equine healthcare provider. This concept needs to be part of farrier training programs and emphasised in their associations, association meetings and journals. The AAEP, Veterinary Specialty Boards and progressive farrier associations can work together to make this happen. The complexities of equine foot pathophysiology, imaging, medical therapeutics, mechanical shoeing principles and farrier products are only going to get more complex in the future.

More than likely most equine healthcare givers have had the important and necessary combined human medical experiences with orthopaedic surgeons, their nurses, case managers, physical therapists and other related healthcare givers and understand the importance of each in their successful personal medical recovery. It is the time that the veterinary and farrier associations work positively and respectfully together to improve each other’s professional status for the benefit of the horse and their owners. Both healthcare professions together and independently are completely necessary for good horse health.

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References