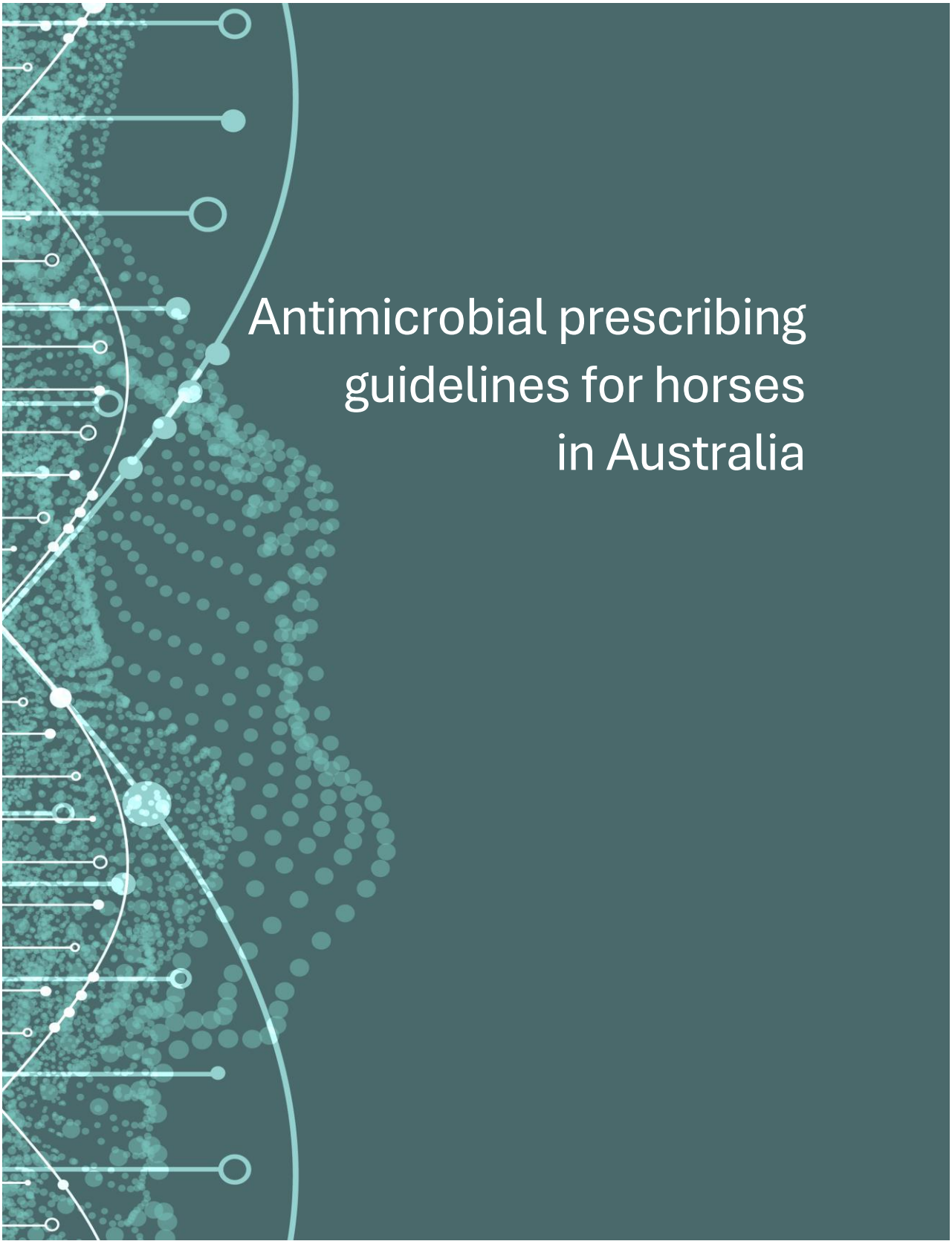

Antimicrobial prescribing guidelines for horses in Australia

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Foreword – antimicrobial prescribing guidelines for horses

Antimicrobial resistance (AMR) is a significant and ongoing threat to human and animal health. Loss of the shared resource of effective antimicrobials jeopardises our ability to manage common infections, an ability that we take for granted in the modern era but one that has not been available at other times in history. There is strong global focus and increasing global coordination to jointly manage this threat and maintain availability of safe and effective antimicrobial medicines for the benefit of both humans and animals.

The consequences of resistant infections in humans include additional investigations, more complex and expensive treatments, longer hospital stays and increased mortality. This increases costs to the healthcare sector and society and the impacts on affected individuals and their families. In animals, resistant infections result in poor animal health and welfare and impacts on production and performance. Resistant bacteria in animals can also transfer to people through direct contact, the environment or the food chain.

The single most powerful contributor to the development of AMR is the inappropriate use of antimicrobials. This includes underuse, overuse, and misuse, and applies to the use of antimicrobials in human health, animal health and in agriculture. The veterinary sector will always be closely scrutinised to ensure that we are using these medicines appropriately. In Australia our strong regulatory systems and well-educated veterinary workforce place us in good stead, by global standards, to minimise development of AMR through veterinary antimicrobial use. However, each practitioner has a role to play in continued stewardship of antimicrobial medicines.

These prescribing guidelines have been developed to help equine practitioners make responsible prescribing decisions, and I thank all those involved in developing this resource. I encourage equine practitioners to use the guidelines and continue efforts to eliminate unnecessary use of antimicrobials. Our profession has an important role to play in maintaining effectiveness of these medicines for the benefit of our own patients and society.

Dr Beth Cookson
Australian Chief Veterinary Officer

Expert panel members

Lead Authors

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Lead author and editor all sections

Laura completed her veterinary degree at Murdoch University in 2003 and worked in mixed practice for 2 years before undertaking an internship at Sydney University. After a residency in Large Animal Internal Medicine at the University of Wisconsin Madison, Laura became a specialist 2010 and returned to Australia at University and private specialty practice, and completed a Masters in Public Health. Laura completed her PhD in 2017 at the University of Melbourne investigating antimicrobial stewardship in veterinary practice. After her PhD she continued researching this topic at Melbourne Veterinary School. In 2019 she was awarded a prestigious ARC Discovery Early Career Researcher Award. She is an international leader in implementation of veterinary antimicrobial stewardship programs and in big data analysis of clinical notes. Laura is co-investigator on several national and international grants, has over 40 publications, 4 book chapters and over 30 conference presentations. Laura was EVA's education chair for 5 years from 2017-2022, was treasurer in 2023 and is president in 2024/25.

Dr Leanne Begg BVSc, DipVetClinStud, MS, MANZCVS, DACVIM
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Leanne graduated from the University of Queensland in 1987. She completed an internship at the University of Sydney, Camden in 1988 and received a Diploma in Veterinary Clinical Studies. She was employed at the Randwick Equine Centre from 1989 to 1991and became a partner in the practice in 1991. Leanne completed a residency in Equine Medicine at Michigan State University from 1991 to 1994. In 1994 she received a Masters Degree from Michigan State University and completed examinations to become a Member of the Australian College of Veterinary Scientists in Equine Medicine. In 1995, Leanne completed examinations to become certified as a Diplomate of the American College of Veterinary Internal Medicine in Large Animal Medicine and became registered as a Specialist in Equine Medicine. She returned to Australia in 1994 to the Randwick Equine Centre, where she has been Gai Waterhouse's stable veterinarian for the last 22 years and consults on medical cases at the REC Specialist Equine Centre.

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BVSc, MVS, PhD, FASM, MASID, Grad Cert Higher Ed

Jacqui is Professor of Veterinary Microbiology and Infectious Diseases and Head of School and Dean at the Sydney School of Veterinary Science, University of Sydney. She is a registered practicing veterinarian and is passionate about practical research projects and education programs for veterinary professionals, animal breeders and animal owners. Her main research areas include: 1) Development of diagnostics and treatments for companion animal viral diseases; 2) Q fever; 3) Multidrug resistant (MDR) Staphylococcus species; 4) Infection prevention and control in veterinary practices; 5) Chronic renal disease in domestic and wild felids and 6) Factors influencing antimicrobial prescribing behaviour of vets and health professionals.

Professor Glenn Browning
BVSc (Hons I), DipVetClinStud, PhD, FASM

Glenn Browning is Distinguished Professor in Veterinary Microbiology, Director of the Asia-Pacific Centre for Animal Health and Director of Research at the Melbourne Veterinary School at the University of Melbourne. He completed a Bachelor of Veterinary Science with First Class Honours at the University of Sydney in 1983, a postgraduate Diploma of Veterinary Clinical Studies in Large Animal Medicine and Surgery at the University of Sydney in 1984 and a PhD in Veterinary Virology at the University of Melbourne in 1988. He was a Veterinary Research Officer at the Moredun Research Institute in Edinburgh from 1988 to 1991, investigating viral enteritis in horses, then joined the staff of the Faculty of Veterinary Science at the University of Melbourne, and has been a member of teaching and research staff there since 1991. He teaches in veterinary and agricultural microbiology. He is a Life Fellow of the Australian Veterinary Association, a Fellow of the Australian Society for Microbiology and past Chair of the International Organisation for Mycoplasmology. He is a co-author of 320 peer reviewed research papers and book chapters, has edited two books on recent progress in understanding the mycoplasmas, and has co-supervised 66 research higher degree students. His research interests include the molecular pathogenesis and epidemiology of bacterial and viral pathogens of animals, the development of novel vaccines and diagnostic assays to assist in control of infectious diseases, and antimicrobial stewardship in veterinary medicine.

Dr Stephen Page BSc(Vet)(Hons), BVSc(Hons), DipVetClinStud, MVetClinStud, MAppSci(EnvTox), MANZCVS(Pharmacology)

Stephen is a consultant veterinary clinical pharmacologist and toxicologist and founder and sole director of Advanced Veterinary Therapeutics– a consulting company that provides advice on appropriate use of veterinary medicines to veterinarians, veterinary organisations (Australian Veterinary Association, World Veterinary Association, World Organisation for Animal Health), state and national government departments and statutory bodies (APVMA, Department of Agriculture, Department of Health, US Environmental Protection Agency), and global organisations (OIE, FAO, Chatham House). He is a member of the AVA Antimicrobial of Resistance Advisory Group (ARAG), a member of the ASTAG committee on antimicrobial prioritisation; in 2017 he became President of the ANZCVS Chapter of Pharmacology, and is a member the World Veterinary Association Pharmaceutical Stewardship Committee. He has more than 100 publications on which he is author or editor, including chapters on antimicrobial stewardship, clinical pharmacology, adverse drug reactions, use of antimicrobial agents in livestock, and antimicrobial drug discovery and models of infection. He has been a teacher and facilitator of courses at the University of Sydney on food safety, public health and antimicrobial resistance since 2003. He is regularly invited to speak nationally and internationally at a broad range of conferences and symposia, especially on the subjects of antimicrobial use, antimicrobial stewardship and risk assessment. He gave his first presentation on veterinary antimicrobial resistance and stewardship at the AVA Conference in Perth in 2000 and remains passionate about improving the use and effective life span of antimicrobial agents.

External Contributing authors

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Chapter 2.3 Purpura Haemorrhagica
Chapter 3.6 Strangles

Charlie El-Hage is a member of the Australian and New Zealand college of veterinary and Australian Equine Parasitology Advisory Panel. After working locally and internationally in mixed and large animal veterinary practices, he returned to the University of Melbourne where he worked as an equine clinician then later as a lecturer whilst completing his PhD. Now an Honorary Fellow, he has maintained an active interest in various areas including equine related microbiology, welfare, immunology, toxicology, endocrinology, parasitology and theriogenology. He is currently supervising PhD students in a variety of fields and has published original research and reviews on subjects including Strangles, Equine Influenza, Ross River virus infection of horses, Pasture Associated Stringhalt, reproductive loss due to Equine Psittacosis.

Professor James Gilkerson BVSc, BSc(Vet), PhD
Chapter 3.6 Strangles
Chapter 3.7 Upper Respiratory Viruses

A veterinarian with an interest in infectious diseases James completed his veterinary studies at the University of Sydney, where he was awarded a BVSc, a BSc (Vet) and a PhD. James is currently a Professor of Veterinary Microbiology and Director of the Centre for Equine Infectious Disease at the University of Melbourne. James is particularly interested in equine infectious diseases, but has recently become involved in the National Centre for Antimicrobial Stewardship at the University of Melbourne. James' research interests also include poultry infectious diseases and an increasing amount of wildlife work. Professor Gilkerson is a Past-president of Equine Veterinarians Australia and the Victorian Division of the AVA. He was awarded the 2008 Australian Veterinary Association President's Prize and in 2009 was made a Fellow of the Australian Veterinary Association. In 2020 James was awarded the Spirit of SAEVA award by the South African Equine Veterinary Association for his outstanding contribution to equine veterinary science.

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Chapter 3.5 Sinonasal and guttural pouch mycosis
Chapter 4.58 Fungal pneumonia

After graduating from the University of Melbourne in 1997, Allison spent 2 years in mixed practice in Gawler, SA, before travelling to the USA to undertake a residency in Large Animal Internal Medicine at the Ohio State University. She completed her Masters of Science and was awarded Diplomate status of the American College of Veterinary Internal Medicine (ACVIM) in 2002. She then became a faculty member at Auburn University in Alabama and competed a fellowship in Emergency and Critical Care and obtained Diplomate status in 2007. Allison worked as a specialist and taught veterinary students at Auburn University for 12 years, being promoted to professor. In 2014 she returned to Australia and spent some time in mixed practice, on the Veterinary Practitioners Registration Board of Victoria before commencing an academic position at The University of Queensland and completing her PhD in Sweden. Allison is an active ANZCVS -Equine chapter member, being treasurer in 2020-2022 and president in 2023.

Gary Muscatello BVSc, GradCertUnivTeach, PhD
Chapter 4.4 Rhodococcal pneumonia in foals

Gary is a Senior Lecturer in Veterinary Microbiology and ONE Health, at the University of Sydney. He is recognised as an authority in *Rhodococcus equi* pneumonia epidemiology completing his PhD in this area at the University of Melbourne in 2005. Publishing over 20 original papers and review articles over the past 25 years in this area Gary's activities have contributed to improved understanding of disease management and diagnoses as well as proposing various disease prevention strategies for the Thoroughbred industry.

Gary has given keynote presentation on the epidemiology of *R. equi* disease at the last three *Rhodococcus equi* Havemeyer workshops and is a frequent chair and presenter at the Australian Society of Microbiology annual conferences as well as the Equine Veterinary Australia Bain Fallon annual lectures. Currently he's research team are exploring bacteriophages as an alternative to antibiotic therapy to manage *R. equi* risk in the face of the emerging threat of multi-drug resistant strains.

Prof. Dr. Denis Verwilghen DVM, MSc, PhD, DES, DECVS, DEVDC(Equine), MRCVS
Chapter 5.1 General dentistry
Chapter 5.2 Sinusitis

Denis Verwilghen is the Clinical Director and Senior Surgeon at Goulburn Valley Equine Hospital, a subsidiary of the University of Melbourne. After graduating from the University of Ghent (Belgium) in 2003, he began his career in equine practice in Ireland and the Netherlands. In 2004, he returned to academia for a residency in equine surgery at the University of Liège, where he completed a Masters degree on osteochondrosis and IGF-I (2006), a DES in Large Animal Surgery (2009), and a PhD on developmental orthopaedic disease.

He became a Diplomate of the European College of Veterinary Surgeons in 2010, and in 2022, of the European Veterinary Dental College (equine section). Denis has held senior academic and clinical roles across Europe and Australia, including Head of Equine Surgery at Uppsala University, Associate Professor at Copenhagen University, and Director of the Camden Equine Centre (Sydney). He also ran a global consultancy, Equinespecialists, providing surgical and dental services worldwide.

Denis has published extensively on equine surgery, asepsis, orthopaedic biomarkers, and dentistry, with over 85 peer-reviewed papers, 7 book chapters, and more than 100 national and international conference presentations.

Gaby van Galen DVM, PhD, DECEIM, DECVECC
Chapter 6.1 Acute Colitis (adult horses)
Chapter 16 Immunisation

Gaby's interests and expertise lay in equine internal medicine and emergency and critical care. She has a special clinical interest in critically ill patients such as horses with acute colic or diarrhea, acute neuromuscular disorders and sick neonatal foals, and the use of thoracic and abdominal ultrasonography in those patients. She is author or co-author of over 70 international peer reviewed scientific publications and book chapters, and has given numerous presentations at national and international congresses.

Gaby started her career as an equine intern in private practice in the Netherlands immediately after graduation from the University of Ghent, Belgium in 2003. Following this internship she commenced a residency program in equine internal medicine at the University of Liege, Belgium and passed the exam of the European College of Equine Internal Medicine in 2009. In 2011 she left Liege and has since taken up clinical academic positions at the University of Uppsala, Copenhagen and Sydney, and has briefly managed together with her husband a private hospital in Germany. In 2017, she also became Diplomate of the European College of Emergency and Critical care. In January 2022, she returned to Australia and joined the Goulburn Valley Equine Hospital.

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Section 7 Endotoxaemia

Jenni graduated from Murdoch University in Perth, Australia and then completed an equine internship at the Equine Medical Center of Ocala, Florida and residency in large animal medicine at the University of Pennsylvania's New Bolton Center, after which she became board certified in large animal internal medicine. She returned to Australia and completed a PhD in equine systemic inflammation at the University of Melbourne, alongside becoming a Senior Lecturer in equine medicine and equine medicine clinician at the University of Melbourne's Equine Centre. She is now a Senior Lecturer in Veterinary Biosciences, and continues a strong research interest in equine sepsis.

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Section 8 Neonates

Rosemary is an Equine Internal Medicine Specialist at Scone Equine Hospital, NSW. She is a 2008 Bachelor of Veterinary Science graduate of the University of Sydney. Following graduation, she worked in rural mixed practice in NSW prior to joining Scone Equine Hospital as the 2010 Equine Medicine and Critical Care intern. She stayed on for a second breeding season at SEH before heading back to the field for 18 months as a mixed animal, equine and small animal locum rotating between practices in Taree, Denman, Scone and Sydney. Rosemary moved to the United States in 2013 to undertake a combined residency program in Large Animal Internal Medicine (Equine focus) and Masters degree in Biomedical Sciences at Auburn University. She gained Membership of the Australian and New Zealand College of Veterinary Science in the field of Equine Medicine in 2012 and became a Diplomate of the American College of Veterinary Internal Medicine (Large Animal Internal Medicine) in 2016.

Rosemary returned to Australia in 2016 and headed first north to work in private performance horse practice in Queensland and then west for a year as an Equine Registrar at Murdoch University in Perth, before returning to SEH in 2018. She enjoys the variety and challenge that an equine medicine caseload provides and has particular interest in neonatology, nutrition and ophthalmology, as well as mentoring new graduates and contributing to the profession through continuing education endeavours.

Benjamin Reynolds BVSc, DACVO
Section 13 – Ophthalmology

Benjamin graduated as a veterinarian from James Cook University winning numerous academic awards during the degree. Benjamin won the prestigious International Society of Veterinary Ophthalmology Scholarship in 2018, which allowed him to undertake advanced ophthalmology training at North Carolina State University while working at one of Brisbane's largest veterinary hospitals as a rotating intern.
Benjamin joined the Eye Clinic for Animals, in Sydney, as an intern in 2019, and after completing that was fortunate enough to stay to undertake an American Board of Veterinary Ophthalmology residency program, which was completed in early 2023. During the residency period, Benjamin underwent further training via an externship at the University of California, Davis and co-authored ophthalmology textbook chapters and published in numerous international veterinary journals.

Cameron J G Whittaker BVSc, MANZCVS, DVCS, DACVO
Section 13 Ophthalmology

Cameron graduated from Sydney University in 1989. After spending time in mixed animal practice, he completed an Internship at Sydney University in 1992 and then a residency in veterinary ophthalmology at the University of Florida, USA. He was granted Diplomate status of the American College of Veterinary Ophthalmologists in 1996. He then worked at Ohio State University as an Assistant Professor before returning to Australia in 1997 to join Eye Clinic for Animals. Since that time Cameron and the ECA team have provided specialist ophthalmology services to both small and large animals in Sydney and regional areas of NSW.
Cameron has also served on the NSW Division of the AVA and for over 20 years has provided ophthalmic lectures and practical sessions to students at Sydney University.

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Section 14.1 Burns/Thermal injuries

Edwina graduated with a Bachelor of Veterinary Science from the University of Sydney in 2005 and worked as a junior associate veterinarian at Morphettville Equine Clinic before commencing an internship at Agnes Banks Equine Clinic. She worked as a seasonal veterinarian at Newmarket Equine Hospital, UK in 2007 and completed an internship in equine theriogenology at Virginia Tech, USA in 2008. Edwina returned to the University of Sydney in 2010 and graduated with a Master of Pharmacy in 2012. She commenced a residency in Equine Internal Medicine and a Doctorate of Veterinary Studies at Charles Sturt University in 2013 with a primary research focus on equine parasitology. She was awarded the CEVA Animal Health Scholarship in 2014 and ANZCVS Fellowship Training Scholarship in 2015 and successfully completed the fellowship exams in Equine Medicine in 2017. In 2019, Edwina completed a 6 month internal medicine fellowship at Hagyard Equine Medical Institute in Kentucky, USA. She was employed as a registered specialist and Senior Lecturer in Equine Medicine at Charles Sturt University for 4 years after completing her residency. Edwina relocated to Melbourne in 2022 and is now a Regulatory Veterinarian and the anti-doping manager at Racing Victoria.

Jennifer Clulow BScAgr, BVMS, PhD, DACT
Section 15 Reproduction

Jen is a registered specialist in Veterinary Reproduction with a special interest in all aspects of Equine Reproduction including stallion and mare fertility as well as artificial reproductive technologies such as artificial insemination, embryo transfer and in vitro fertilisation technologies. Jen's areas of research include sex sorting of stallion spermatozoa, development of a long term liquid storage extender for stallion sperm and improving fertility in the aged broodmare. Jen has extensive experience in Equine Reproduction, having worked in some of the world's largest equine veterinary hospitals including Goulburn Valley Equine Hospital, Scone Equine Hospital, Hagyard Equine Medical (USA), Colorado State University (USA) and Equiception (NL). Jen is a passionate educator of veterinarians and students and is currently an Associate Professor in Theriogenology at Charles Sturt University, Wagga Wagga.

Chelsie A. Burden, DVM, MS, DACT
Section 15 Reproduction

Chelsie is the resident veterinarian at Blue Gum Farm in Euroa, VIC. Her primary responsibilities include reproductive management of broodmares and stallions, neonatal care and routine health care of all resident horses. The farm is at the forefront of thoroughbred breeding in Victoria with a record of producing and selling high-class racehorses.

Chelsie grew up in rural Kansas, where she was exposed to every animal her parent's hobby farm could entertain. Originally aspiring to be a doctor when she grew up, plans took a definitive turn after assisting with a caesarean section on a heifer when she was 9 years old. It was veterinary medicine from that moment on. Chelsie graduated from Kansas State University College of Veterinary Medicine in 2011. She completed an internship at Oklahoma City Equine Clinic followed by a residency and master's degree at the Colorado State University Equine Reproduction Laboratory. Chelsie became board-certified with the American College of Theriogenologists in 2015.

Chelsie transitioned to Australia (Goulburn Valley Equine Hospital) following her residency and continued working between the southern and northern hemisphere breeding seasons employed at Claiborne Farm in Kentucky, Haras Al Boraq in Morocco, and the University of Florida before settling in Australia in 2017. Chelsie continued to work primarily in equine reproduction with a focus on the problem broodmare and assisted reproductive technology.

Aside from her professional life, Chelsie credits her partner Ty and his two boys for truly keeping her in Australia. They are a wholly supportive family that like a little adventure. With their two corgis at foot, they enjoy taking every opportunity to explore regional Victoria together.

Kellie Thomas BFA, GradCertWEP, BVetBiol/BVetSci (Hons I)
Project Manager

Kellie is a small animal general practice veterinarian who is undertaking a PhD in antimicrobial stewardship under the supervision of Professors Jacqui Norris and Jane Heller. She is a co-founder and current vice president of the not-for-profit the AMR Vet Collective, a foundation that works to connect practicing veterinarians with the current best evidence on antimicrobial stewardship across all types of veterinary practice. She has completed a rotating internship at the University of Sydney and conducted multiple continuing education presentations and workshops focusing on AMS, including the simple clinical and diagnostic skills and workplace systems that support AMS in practice. She has also been a guest lecturer in the Veterinary Science program at Charles Sturt University.

Contents

Introduction: Overview of systemic antimicrobials used for horses

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Antimicrobials are commonly used to treat equine infections, but complications with therapy are also relatively common. Antimicrobial-associated diarrhoea (Section 6), immune-mediated diseases and nephrotoxicity (Table 1) have been reported as sequelae of antimicrobial therapy in equine practice. This does not indicate that clinicians should avoid using these drugs, only that knowledge of the potential for adverse effects is critical when deciding on the most appropriate antimicrobial to use and can assist in avoiding serious side-effects, wherever possible, or at least in detecting and responding to them early.

The growing problem of antimicrobial resistance also affects equine veterinarians with increasing frequency. Antimicrobial stewardship and responsible prescribing are essential for a future in which effective antimicrobials are available, as it is unlikely that new antimicrobials will become available for use in horses. Australia's conservative regulatory approach has prevented the registration of antimicrobials (such as 4th generation cephalosporins) that are available elsewhere, and the antimicrobial development pipeline is struggling to attract investment, so few new antimicrobial agents, let alone novel classes, are currently in development.

Resistant pathogens of concern in horses include extended-spectrum β-lactamase (ESBL) producing *Enterobacteriaceae*, methicillin-resistant *Staphylococcus aureus* (MRSA) and multi-resistant *Salmonella* species, while pathogens with high levels of intrinsic and acquired resistance are also common causes of disease, including *Pseudomonas* species, *Klebsiella* species, *Enterococcus* species and *Acinetobacter* species. The limited antimicrobial options available for these pathogens make treatment of cases associated with them extremely challenging.

In Australia, antimicrobial importance is assigned by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG). Antimicrobials are categorised as low-, medium- or high importance based on the consequence to human health if resistance to them was to develop in human pathogens and the number of antimicrobial treatment options available. It is essential that high-importance antimicrobials, such as ceftiofur, enrofloxacin, rifampicin, amikacin and polymyxin B, are used prudently in horses and use should be based on culture and antimicrobial susceptibility testing. Some veterinary boards (e.g. Victoria) require veterinarians to have antimicrobial stewardship protocols in place.

These guidelines comprehensively outline how numerous diseases in horses are linked to bacterial infection. However, systemic inflammation caused by viral or fungal infections, bacterial toxins, tissue damage, or neoplasia can mimic the clinical signs of bacterial infection. Interpreting haematological findings, and fibrinogen and serum amyloid A (SAA) levels, can pose challenges, as they may change in response to both infectious and non-infectious inflammatory conditions. Leukopaenia is frequently observed in association with inflammation, often originating from the gastrointestinal tract, yet it does not necessarily signify the presence of infection or the need for antimicrobial therapy. Similarly, leukocytosis can occur in inflammatory, infectious, and neoplastic conditions, or because of corticosteroid administration, and thus has limited diagnostic value. Complementary examinations can be performed to strengthen the suspicion of a bacterial infection and, if possible, a culture of an appropriate sample or a polymerase chain reaction (PCR) assay can confirm infection. However, it often takes time to perform these tests and obtain results. Given the urgency of treatment in many scenarios, clinicians must often rely on professional judgement to determine the likelihood of bacterial infection.

The traditional concept that “a course of antibiotics needs to be finished to avoid development of resistance” is obsolete and not supported by evidence. In fact, the opposite is true – longer courses of antimicrobial therapy may have a greater impact on development of resistance than shorter courses. In most cases, a short duration of antimicrobial therapy, ranging from a single dose (for example pre-operatively) to a course from 24-72 h, is sufficient, with long-term therapy rarely required. Studies from human medicine have shown marked reductions can be made in the duration of therapy of bacterial infections without compromising clinical cure rates. Despite this growing evidence, limiting the duration of antimicrobial therapy in proven infections can be challenging for clinicians. Fear of treatment failure often leads to prolonged use of antimicrobials, even in patients that appear to have recovered clinically. In the past, return to normal haematological parameters or normal concentrations of acute phase proteins have been used as markers for safe discontinuation of antimicrobial treatment. “Treatment to clinical cure” is the new mantra - return to normothermia, improved appetite, return of normal demeanour and a declining trend in inflammatory markers may be better indicators that further treatment is not necessary. More evidence is urgently needed.

It has also been common practice to initially treat systemically ill horses with injectable antimicrobial drugs for 48-72 h, followed by oral treatment. In most cases, this is not necessary. An alternative approach is stopping antimicrobial treatment after 48-72 h and monitoring the patient closely for another 24 h. Should signs of infection re-occur, such as recurrence of a fever, a decrease in appetite or change in demeanour, treatment can be easily re-initiated – but this is rarely necessary because recurrence is rare.

Many non-antimicrobial therapies can be used effectively to combat and control infection. Debridement, lavage, local drainage and cleaning, and use of non-antimicrobial substances that have antimicrobial properties (e.g. honey), can be more effective than systemic antimicrobial therapy and, in many instances, also combat formation of biofilms.

Many of the recommendations in these guidelines represent extra-label or off-label use. Veterinarians should be aware of the regulations in their state or territory.

Table 1. Antibiotic Pharmacotherapy by Class. Adapted from EVA & Australian Veterinary Prescribing Guidelines Pocket Guide for Antimicrobial Use in Horses.

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Pharmacologic considerations
Beta-lactams	Low	**Procaine penicillin**	IM	22,000 IU/kg (22 mg/kg) q12h	Diarrhoea. Procaine reaction: Inadvertent intravascular administration of procaine resulting in CNS excitation and frantic, uncontrollable behaviour that generally resolves in minutes. Penicillin hypersensitivity reactions: urticaria, anaphylaxis, immune mediated haemolytic anaemia. Local injection reactions (swelling, in rare cases abscessation)	Drug of choice for streptococcal infections. Excellent anaerobic activity (except *Bacteroides* spp.). Often combined with gentamicin for broad spectrum coverage. Distributed widely in plasma but poor penetration of biological membranes as low lipid solubility. Does not penetrate abscesses or sites of tissue necrosis well. Time dependent. Always draw back to check for blood before injecting procaine penicillin and keep penicillin refrigerated to reduce risk of procaine reaction. Rotation through injection sites and splitting injection of large volumes over two sites also reduces risk. Long-acting penicillin formulations are not suitable for use in horses as they are not long acting and do not reach therapeutic concentrations. Racing withhold period: 21 days
	Low	**Benzyl penicillin**	IV	22,000 IU/kg (13 mg/kg) q4-6h		
			IU	5 million IU for Streptococcus zooepidemicus	Secondary bacterial infection, fungal infection. Irritating to endometrium, dilute with at least 60 ml saline.	Uterine lavage and ecbolics are the primary focus of endometritis therapy. Uterine fluid/exudate may inactivate or dilute antibiotics. Inactivated in solutions with pH <5.5 or >8. Only mix with gentamicin immediately before use. Do not mix with sulphonamides or sodium bicarbonate.
	Low	**Ampicillin sodium**	IV/IM	20 mg/kg q 6-8 h	Ampicillin trihydrate irritant when injected IM.	Distributed widely in plasma but poor penetration of biological membranes as low lipid solubility. Does not penetrate abscesses or sites of tissue necrosis well. Time dependent.
	Low	**Amoxycillin-clavulanate**	PO	30 mg/kg q 8 h ONLY IN FOALS <4 MONTHS OF AGE	Severe antimicrobial-associated diarrhoea in animals >4 months when administered orally. No information on injectable form but anecdotally has been used without inducing diarrhoea	Broad spectrum of activity. Distributed widely in plasma but poor penetration of biological membranes as low lipid solubility. Used in areas where TMS resistance is high as an alternative oral antimicrobial for use in foals. Time dependent.

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Pharmacologic considerations
					in a small number of horses.	
	High	**Ceftiofur**	IM/IV	2.2-4.4 mg/kg q 12-24 h (Up to 10 mg/kg IV q 6 h has been used in neonatal foals)	Diarrhoea Muscle soreness Hypersensitivity - urticaria, anaphylaxis.	Should be reserved for multi-drug resistant infections. Does not cross blood-brain barrier. Ceftiofur is rapidly metabolised to desfuroylceftiofur, to which most coagulase positive *Staphylococcus* species are resistant (may appear susceptible in vitro but not in vivo). Time-dependent.
Aminoglycosides	Medium	**Gentamicin**	IM/IV IU	Foals <2 weeks: 12 mg/kg q 36 h Adults and foals >2 weeks: 6.6 - 9.7 mg/kg q 24 h 1-2 g buffered with equal volume of 7.5% bicarbonate or diluted in large volume of saline (e.g. 60 ml)	Nephrotoxic. Muscle soreness if given IM. Hypersensitivity reactions (rare). Ototoxic Chondrotoxic when administered intra-articularly (see IVRP/IS guidelines). Irritates endometrium or induces depigmentation of vulvar skin if not buffered. Secondary bacterial infection, fungal infection.	Generally drug of choice for suspected or confirmed Gram negative infections. No activity against anaerobes. *Streptococci* and *enterococci* are intrinsically resistant. Inactivated by purulent material. Must penetrate bacteria to assert their effect, which is enhanced by drugs that interfere with cell wall synthesis – e.g. penicillin. Low activity against intracellular bacteria such as *Salmonella* species. If kidney function is reduced, avoid if possible, or increase inter-dosing interval. Concentration dependent.
	High	**Amikacin**	IV	Foals: 25 mg/kg q 24 h Adults: 10 mg/kg q 24 h	Nephrotoxic (less than gentamicin). Chondrotoxic when administered intra-articularly (see IVRP/IS guidelines).	Should be reserved for documented gentamicin resistant, amikacin susceptible infections. No activity against anaerobes. *Streptococci* and *enterococci* are intrinsically resistant. Inactivated by purulent material. Can be used IA but gentamicin resistance is uncommon in organisms found in septic joints, so amikacin should not be used as first-line choice. Concentration dependent.
Tetracyclines	Low	**Doxycycline**	PO	Foals: 10 mg/kg q 12 h	Extreme caution is needed with the adult dose as safety data is not available and there	Once daily dosing is only useful for highly susceptible organisms in adults, twice daily dosing is required for most infections and

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Pharmacologic considerations
				Adults: 20 mg/kg q 12 - 24 h	is a risk of colitis. The original dose of 10 mg/kg (shown to be inadequate) has been associated with colitis so a higher dose may present more of a risk. Bone/tooth discolouration. DO NOT GIVE IV – FATAL. Anecdotally associated with tendon laxity in neonatal foals.	always in foals. Excellent broad-spectrum activity, good anaerobic coverage but variable for *Bacteroides* and *Clostridium* spp. Drug of choice for *Lawsonia intracellularis* infection. Doxycycline bioavailability reduced by feeding; withhold feed before and shortly after dosing. Doxycycline is primarily excreted in bile, so is safer than other tetracyclines in horses with renal dysfunction. Lipophilic and distributed well into pulmonary, peritoneal and synovial fluid and concentrated in urine. Penetrates uterine fluids and achieves concentrations above MIC for common pathogens in the late-term foetus. May not reach adequate concentrations in soft tissue. Time dependent.
	Low	**Oxytetracycline**	IV	6.6 mg/kg q 12 h	Hypotension and collapse if administered rapidly IV. Renal tubular necrosis - especially with high doses for neonatal foals with contracted tendons but can also occur following the recommended dose in adult horses. Bone/tooth discolouration. Diarrhoea. Very irritant if extravascular or intramuscular.	Excellent broad-spectrum activity, good anaerobic coverage, but variable for Bacteroides and Clostridium spp. Drug of choice for *Lawsonia intracellularis* infection. Lipophilic and distributed well into pulmonary, peritoneal and synovial fluid and concentrates in urine. High dose oxytetracycline causes tendon relaxation in foals with congenitally contracted tendons (not acquired) and is most efficacious when given in the first 3 days of life (44 mg/kg IV given once or possibly repeated 24 h later). Care in foals that are, or may be, dehydrated due to renal effects; consider administration in 1 L isotonic solution. Care should also be taken, as induction of excessive laxity is possible. Time dependent.
Sulphonamides	Medium	**Trimethoprim-sulphonamide**	PO/slow IV/IM	Foals: 24 mg/kg q 12 h Adults: 30 mg/kg q 12 h	Diarrhoea. Thrombocytopaenia and haemolytic anaemia with prolonged use (rare). Rapid IV administration can tremor and collapse.	Excellent broad-spectrum activity. Inactivated by purulent material. Excreted in urine so useful for urinary tract infections. Resistance is frequent in many regions, especially those with high horse densities. Highly lipophilic and distributes widely including across blood-brain barrier.

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Pharmacologic considerations
					Concurrent administration of detomidine can result in dysrhythmia, hypotension and death. Concurrent administration of procaine penicillin is antagonistic to sulphonamides. Irritant if given IU.	Time dependent. Should not be combined with rifampicin as metabolism of TMS is increased by as much as 150%.
Macrolides	Low	**Erythromycin**	PO	25 mg/kg q 6 h	Severe diarrhoea in adults, variable diarrhoea in foals. Altered thermoregulation in foals (hyperthermia), which seems more common with erythromycin. Can cause fatal diarrhoea in mares co-housed with treated foals.	Generally only used in foals with *Rhodococcus equi* infection, in combination with rifampicin. Can be used in young foals with *Lawsonia intracellularis* infection but not first line choice. Highly lipophilic and distributed widely, including intracellularly. Eliminated via bile. Time dependent. Erythromycin has prokinetic properties but can no longer be recommended for this purpose because of the risk of inducing antimicrobial resistance.
		Clarithromycin	PO	7.5 mg/kg q 12 h		
		Azithromycin	PO	10 mg/kg q 24 h		
Ansamycin	High	**Rifampicin**	PO	5 mg/kg q 12 h	Body fluids turn orange.	Only use in combination, resistance can develop within hours when used as monotherapy. Antagonistic to gentamicin and trimethoprim-sulphonamide.
Fluoroquinolones	High	**Enrofloxacin**	PO/slow IV	7.5 mg/kg q 24 h	OCD in young horses. DO NOT USE IM, IA, IU or as IVRP as causes necrosis and fibrosis. Oral paste has been associated with severe oral ulceration. Diarrhoea. Fluoroquinolones have also induced tendonitis in juveniles.	Should be reserved for multi-drug resistant infections. Generally avoided in horses < 4 years of age and during pregnancy. Synergism with beta-lactams and aminoglycosides. Lipophilic with high concentrations in liver, spleen and kidneys. Moderate penetration of skin, muscles, heart, stomach, uterus, mammary gland, bone and bladder. Lower concentrations in CSF and eyes. Concentration dependent.

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Pharmacologic considerations
	High	**Marbofloxacin**	IV PO	2 mg/kg q 24 h 3.5-4 mg/kg q 24 h	May be less associated with arthropathy than enrofloxacin, but risk remains.	Should be reserved for multi-drug resistant infections. Broad spectrum – especially active against Gram negatives. Limited activity against streptococci, no activity against *Enterococcus* and many anaerobes.
Nitroimidazoles	Medium	**Metronidazole**	PO/IV	Foals <2 weeks: 10 mg/kg q 12 h Foals >2 weeks: No PK/PD data but 15-20 mg/kg q 8 h common Adults: 15-20 mg/kg q 8 h or 25 mg/kg q 12 h Rectal administration route	Inappetence. Can cause neurological signs.	Excellent activity against anaerobes. Generally used in combination with penicillin and gentamicin for broad spectrum coverage where anaerobes are suspected to be contributing (pleuropneumonia, peritonitis). Indicated in cases where *Bacteroides* spp. or *Clostridium* spp. may be involved. Widely distributed and penetrates tissues well. Time dependent.
Polypeptides	High	**Polymixin B**	slow IV	1000-5000 U/kg q 8-12 h	Nephrotoxic	Generally only used systemically for its anti-endotoxic properties, and not for its antimicrobial properties. Care should be taken as endotoxic patients often have impaired renal perfusion. Co-administration with gentamicin may also increase risk of nephrotoxicity, Anti-endotoxic dose is 5000 U/kg. Most effective when given before endotoxin release.
Streptogrammins	High	**Virginiamycin**	PO	5g/100kg q 24 h	High importance antimicrobial - banned for equine use in United Kingdom in 2014	Founderguard – label claim for reduction in fermentative acidosis in the hindgut and may aid in the prevention of pasture-associated laminitis. Management strategies should be used rather than this highly important antimicrobial.
Other	Low	**Sodium Iodide**	IV	20-40 mg/kg q 24 h	Iodinism	Generally used for chronic fungal or bacterial infections where antimicrobial penetration may be poor.

Many of the recommendations in this guide represent off-label use of antimicrobials. Compliance with the legal requirements of your jurisdiction is your responsibility.

Section 1 – Surgical prophylaxis

Contents

Chapter 1: Surgical antimicrobial prophylaxis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Antimicrobial drugs should not be used as an alternative to atraumatic and aseptic surgical techniques.
2. Intravenous prophylactic antimicrobial administration should be given within 60 min of first incision.
3. Shorter durations of antimicrobial prophylaxis will drive less antimicrobial drug resistance.

There are a plethora of data from human surgery and emerging data from veterinary surgery supporting the use of shorter duration surgical antimicrobial prophylaxis (1). Antimicrobial drug use drives antimicrobial drug resistance, and this is a problem in animal and human health. Inappropriate use, especially prolonged surgical antimicrobial prophylaxis, is detrimental to the patient and increases the costs associated with surgery without yielding any reduction in rates of surgical site infections (SSIs). Antimicrobials disrupt the intestinal microbiome, which is critical to immune function and tissue healing. Antimicrobial use has also been associated with acute diarrhoea in horses, and this can have a high fatality rate.

There are three components of surgical antimicrobial prophylaxis. They are:

1. Antimicrobial drug and dose selection
2. Drug administration time relative to surgery
3. Duration of prophylaxis.

1. Antimicrobial drug and dose selection

Antimicrobial drugs should never be used to replace meticulous atraumatic and aseptic surgical techniques. Clean surgical procedures should not require prophylaxis and clean contaminated and contaminated procedures should only require perioperative prophylaxis. Dirty and infected procedures require therapeutic, not prophylactic, antimicrobial therapy (Table 1.1).

Table 1.1 National Research Council's risk index for surgical infection (2)

Clean	Non-traumatic, uninfected. No break in aseptic technique, no inflammation encountered. Elective, primary closure, without use of a drain.
Clean-contaminated	Controlled entry of a hollow muscular viscus, minor break in aseptic technique.
Contaminated	Open, fresh traumatic wound. Incision into a site with acute, non-purulent inflammation. Major break in aseptic technique.
Dirty	Pus encountered during surgery. Perforated viscus found. Traumatic wound with devitalised tissue, foreign material or faecal contamination, or surgery of more than 4-hours' duration.

2. Drug administration time relative to surgery

Prophylactic antimicrobial administration should be timed so that serum and tissue concentrations exceed the minimal inhibitory concentration (MIC) for the organisms likely to be encountered for the duration of the surgery. Antimicrobials cause maximum suppression of infection if given before bacteria gain access to the tissue. Antimicrobials given at a time that does not result in sufficient tissue concentrations during surgery, such as post-operatively, do not reduce the risk of surgical site infection. Specific recommendations depend on the agent and route of administration.

- Intravenous antimicrobials: Administer 30-60 mins prior to surgery
- Intramuscular procaine penicillin: 3.5 h prior to surgery (3)
- T_{max} for individual drugs given by different routes can be used to assess optimal timing to achieve peak blood concentration at the time of first incision.

If repeat dosing is required for prolonged procedures, the dosing interval can be calculated as twice the elimination half-life of the antimicrobial.

- Benzyl penicillin: 80 min
- Ampicillin: 2 hours
- Oxytetracycline and procaine penicillin: redosing not required due to long elimination half-life

Small reductions in arterial blood pressure have been documented following intravenous sodium penicillin in healthy horses (4, 5), so care should be taken when administering benzyl penicillin to unwell horses, particularly those with endotoxaemia and dehydration, or other conditions that cause or predispose to hypotension.

3. Duration of prophylaxis

Table 1.2 provides a guide for recommended durations of prophylaxis for specific procedures.

Table 1.2. Guidelines for surgical prophylaxis (reproduced with permission from the Australian Veterinary Prescribing Guidelines at the Asia-Pacific Centre for Animal Health, University of Melbourne)

Surgical contamination level	Mitigating factors	Antimicrobial recommendation	Duration of therapy
Clean	None	None	N/A
	Field castration (6, 7)	None	N/A
	Routine elective arthroscopy (8, 9)	None	N/A
	Laparoscopy (10)	None	N/A
	Laparoscopy for ovariectomy with ovary >12cm (11)	Penicillin & gentamicin	Perioperative only
	Only if surgical site infection would be a major threat to the patient (i.e. central nervous system surgery)		No evidence, in other species preoperative only

Surgical contamination level	Mitigating factors	Antimicrobial recommendation	Duration of therapy
	If surgical duration > 90 min	Penicillin (or ampicillin) & gentamicin	No evidence, in other species preoperative only
	Implant		No evidence, 7 days common in companion animals
Clean contaminated	Colic	Penicillin & gentamicin	Stop within 24 h
Contaminated	Likely anaerobic	Penicillin, gentamicin & metronidazole	No evidence, 24-48 h is common in human medicine
	Significant bowel leakage	Penicillin, gentamicin & metronidazole	
Dirty		Choose drug appropriate for infection	Treat till infection cured

Treatment

1. Assess patient signalment and risk factors.

2. Classify procedure (Table 1.1).

3. Is surgical prophylaxis indicated (Table 1.2) If so, identify the appropriate agent, dose, route and timing of administration to reach MIC for target tissues.

4. Ensure procedural planning so that the agent is given at the appropriate time (IV within 30-60 min of surgery, procaine penicillin IM 3.5 h prior to surgery).

5. Cease prophylactic medication as soon as possible after surgery (Table 1.2).

Other factors to consider that reduce the risk of intraoperative infection include clipping the patient's hair less than 4 hours before surgery (12) and minimizing the number of people in the surgical theatre (13).

Antimicrobials used

- Benzyl penicillin at 22,000 IU/kg (12 mg/kg) IV and gentamicin at 6.6mg/kg IV within 60 min of first incision.
- Procaine penicillin G at 22,000 IU/kg (22 mg/kg) IM 3.5 hours before surgery and gentamicin at 6.6mg/kg IV within 60 min of first incision.

Reference List

1. Southwood LL. Surgical antimicrobial prophylaxis: Current standards of care. Equine veterinary education. 2023;35(11):607-16.
2. Australian Commission on Safety and Quality in Health Care. Approaches to Surgical Site Infection Surveillance. Sydney: ACSQHC; 2017.
3. Uboh CE, Soma LR, Luo Y, McNamara E, Fennell MA, May L, et al. Pharmacokinetics of penicillin G procaine versus penicillin G potassium and procaine hydrochloride in horses. Am J Vet Res. 2000;61(7):811-5.
4. Hubbell JA, Muir WW, Robertson JT, Sams RA. Cardiovascular effects of intravenous sodium penicillin, sodium cefazolin, and sodium citrate in awake and anesthetized horses. Vet Surg. 1987;16(3):245-50.
5. Henderson ARP, Valverde A, Marchiori J, Tisotti T, Torrent A, Côté N, et al. Effect of rapid and slow intravenous injection of sodium penicillin on arterial blood pressure in isoflurane-anesthetized horses during surgery. Vet Anaesth Analg. 2025;52(2):200-7.
6. Busk P, Jacobsen S, Martinussen T. Administration of perioperative penicillin reduces postoperative serum amyloid A response in horses being castrated standing. Vet Surg. 2010;39(5):638-43.
7. Kilcoyne I, Watson JL, Kass PH, Spier SJ. Incidence, management, and outcome of complications of castration in equids: 324 cases (1998-2008). JAVMA. 2013;242(6):820-5.
8. Weese JS, Cruz A. Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital. Can Vet J. 2009;50:185-8.
9. Borg H, Carmalt JL. Postoperative septic arthritis after elective equine arthroscopy without antimicrobial prophylaxis. Vet Surg. 2013;42(3):262-6.
10. Desmaizières L-M, Martinot S, Lepage OM, Bareiss E, Cadoré J-L. Complications associated with cannula insertion techniques used for laparoscopy in standing horses. Veterinary Surgery. 2003;32(6):501-6.
11. Röcken M, Mosel G, Seyrek-Intas K, Seyrek-Intas D, Litzke F, Verver J, et al. Unilateral and bilateral laparoscopic ovariectomy in 157 mares: a retrospective multicenter study. Vet Surg. 2011;40(8):1009-14.
12. Mayhew PD, Freeman L, Kwan T, Brown DC. Comparison of surgical site infection rates in clean and clean-contaminated wounds in dogs and cats after minimally invasive versus open surgery: 179 cases (2007-2008). JAVMA. 2012;240(2):193-8.
13. Eugster S, Schawalder P, Gaschen F, Boerlin P. A prospective study of postoperative surgical site infections in dogs and cats. Vet Surg. 2004;33(5):542-50.

Section 2 - Cardiovascular

Contents

Chapter 1: Bacterial endocarditis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Fever and heart murmur are usually present.
2. Blood culture is important for diagnosis and to direct antimicrobial therapy.
3. Echocardiography is important to identify valve thickening, heart chamber size and degree of valvular regurgitation.

Bacterial endocarditis is an uncommon, life-threatening cardiac disorder in horses characterised by bacterial invasion of the endothelial surface of the valves or the wall of the heart, resulting in fibrinous clots or vegetations that impede normal cardiac function. Although bacterial endocarditis can affect horses of all ages, it is predominantly found in animals less than 3 years of age (14).

Cases generally present for evaluation of fever of unknown origin. Clinical signs usually consist of fever with an audible heart murmur (grade 3/6 or louder) on either side of the thorax, with or without tachypnoea, tachycardia, cardiac arrhythmia or signs of congestive heart failure. Vegetative lesions are most commonly found on the mitral valve, followed by the aortic valve. Lesions on the tricuspid valve are less common and pulmonary valve lesions are rare.

Common bacterial isolates are *Streptococcus* spp., *Actinobacillus* spp. and *Staphylococcus* spp. (14, 15), but *Serratia marcescens (16)*, *Pseudomonas* spp. and *Escherichia coli* (17) have also been implicated. Cardiac arrhythmias may result from direct extension of the inflammatory lesion into the myocardium or may be secondary to thromboembolic myocardial ischaemia.

Diagnostics

Echocardiography can be used to detect thickening of the heart valves. Blood culture is indicated to identify bacteria present and direct antimicrobial therapy. Multiple blood cultures (5 collected at least 12 hours apart) may improve the likelihood of detecting a pathogen. Delaying therapy to allow adequate sample collection is recommended because the identity of the pathogens involved is unpredictable, as is their antibacterial susceptibility, and long durations of therapy are required.

Haematological analysis reveals leukocytosis, with a mature neutrophilia and elevated fibrinogen and Serum Amyloid A (SAA). An electrocardiogram is required if an arrhythmia is detected by auscultation, but this is rare.

Cardiac troponin I has been established as a sensitive and specific marker of myocardial injury (18). Although this is not always present, it could be useful for diagnosis and to monitor the response to treatment.

Treatment

Broad spectrum antimicrobial therapy is indicated until culture and susceptibility results are available. Resolution of clinical signs, decrease in the size of the lesion on echocardiographic examination and a reduction in leukocytosis, hyperfibrinogenaemia and SAA should determine the duration of therapy, which is likely to be several weeks.

Antimicrobials used

- Benzyl penicillin (22 000 IU/kg (12 mg/kg) IV q 6 h) and gentamicin (6.6 mg/kg IV q 24 h)
- Procaine penicillin G (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 12 h)

Prognosis

Guarded to poor. Sterilisation of lesions can be difficult to achieve.

Marked chamber enlargement, severe deformation of the valve leaflets, severe valvular regurgitation and signs of congestive heart failure are grave prognostic indicators.

Chapter 2: Bacterial pericarditis

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Uncommon disease but found secondary to pleuropneumonia.
2. Echocardiography important for diagnosis.
3. Drainage of pericardial effusion under ultrasonographic guidance.

Pericarditis in uncommon in horses and can be secondary to pleuropneumonia or haematogenous spread of bacteria. The pathogens involved reflect these primary diseases. The clinical presentation includes fever, tachycardia and jugular distension. Heart sounds can be heard over a wider than normal area of the thorax, but sounds can be muffled or pericardial friction rubs can be heard. Pericarditis was found more frequently following exposure to Eastern tent caterpillars in the USA but has not been associated with exposure to the processionary caterpillars present in Australia (19).

Diagnostics

Echocardiography is required to visualise fluid in the pericardial sac. Thickening of the pericardium with fibrin, coating the visceral and parietal pericardial surfaces, can be evident. An electrocardiogram (ECG) might reveal electrical alternans, where a regularly repeating change in P, QRS and T morphology is present due to regular movement of the heart in the pericardial fluid. Haematology reveals an inflammatory leukogram with elevated fibrinogen and Serum Amyloid A (SAA) concentrations.

Sample collection is often possible when there is moderate to severe accumulation of fluid. Fluid analysis reveals high total protein concentrations and elevated white cell counts with a predominance of neutrophils. Culture and susceptibility testing should be pursued in every case, as the identity of the pathogen is unpredictable and may not be consistent with pathogens cultured from the pleural space or tracheal washes.

Treatment

Drainage of the pericardial fluid under ultrasonographic guidance is critical in cases where fluid accumulation is moderate or severe. Collection of fluid for bacterial culture and susceptibility testing and cytological examination should be pursued whenever possible.

Broad spectrum antimicrobial therapy is indicated until culture and susceptibility results are available and can be guided by cytological findings. Non-steroidal anti-inflammatory drugs are an important component of medical treatment of pericarditis (flunixin meglumine 1.1 mg/kg IV q 24 h or 0.5 mg/kg IV q 12 h).

Monitoring of pericardial thickening and cardiac chamber dimensions is advisable as pericardial constriction appears to be an important fatal sequela of equine pericarditis that may develop insidiously, one or possibly up to two years after diagnosis (20).

There are no published studies on which to base the duration of therapy, but it is typically 2-3 weeks, or until resolution of the pericardial effusion.

Antimicrobials used

- Benzyl penicillin (22 000 IU/kg (12 mg/kg) IV q 6 h) and gentamicin (6.6 mg/kg IV q 24 h) until culture and susceptibility results are available
- OR procaine penicillin G (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h) until culture and susceptibility results are available

- Therapy is generally administered for 2-3 weeks or until concomitant pleuropneumonia has resolved.

Prognosis

Sprayberry and Slovis (21) followed a small group of young thoroughbred horses and found a reasonably good prognosis, with some attaining a high level of athletic performance, after successful treatment of pericarditis. This study was dominated by cases associated with Eastern tent caterpillars, which are not present in Australia, so the prognosis may vary with other primary causes of disease.

Chapter 3: Purpura haemorrhagica

Authors: Laura Hardefeldt, Charlie El Hage, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, & Leanne Begg

Key issues

1. Severe disease that often requires intensive care.
2. Aseptic, non-infectious and not contagious.

Purpura haemorrhagica (PH) is a non-septic, immune-mediated vasculitis that occurs as a rare complication of strangles (or vaccination against it), due to a type 3 hypersensitivity reaction. Typically, disease develops 2-4 weeks after infection with *Streptococcus equi*, although it may occur more quickly following vaccination (within a week). Although rare, vaccination with agents containing the SeM protein or avirulent *S. equi* are associated with an increased risk of PH. Occasionally PH may occur secondary to infection with another infectious organism. It appears to be caused by deposition of immune complexes on blood vessel walls following antigenic stimulation.

Painful pitting oedema results from a necrotising vasculitis. The head, limbs and trunk are most frequently affected with petechiation and ecchymoses of the mucous membranes. Severe oedema can result in exudation from the skin surfaces, and sloughing of the skin may occur. The vasculitis can affect other sites, including the gastrointestinal tract (resulting in colic), lungs (resulting in respiratory distress) and muscles (resulting in infarcts or muscle pain). Fever, tachycardia, tachypnoea, anorexia and depression are also frequently present. Renal dysfunction is common.

Secondary complications are common and can include laminitis and thrombophlebitis. Rarely, serious or even fatal haemorrhage can occur.

Diagnostics

In horses with evidence of PH, haematological and plasma biochemical analysis may reveal a leukopaenia or leukocytosis, anaemia, thrombocytopaenia, hyperfibrinogenaemia, hypo- or normoproteinaemia, and increased concentrations of muscle enzymes.

A presumptive diagnosis is generally made based on the history, clinical signs and exclusion of other causes of oedema. Elevated titres of IgA and IgG against *S. equi* are supportive of a diagnosis. Very high SeM-specific antibody titres (greater than 1:12,800) are strongly suggestive of PH secondary to strangles infection or vaccination. Skin biopsies can confirm leukocytoclastic vasculitis but are rarely performed.

Treatment

The objective of treatment is to reduce inflammation. Tapering doses of corticosteroids are used – typically dexamethasone, with initial dose of 0.1–0.2 mg/kg IM or IV for 3-5 days and then reducing the dose by half every 3-5 days over 2–4 weeks. Antimicrobials may be necessary where bacterial infection is concurrent or considered likely. Other supportive care such as hydrotherapy, supportive bandaging, IV fluids and non-steroidal anti-inflammatory drugs are usually required.

Antimicrobials used (include recommended dose rates/duration)

- None if uncomplicated
- If secondary infection is concurrent, broad-spectrum antimicrobials are indicated. Benzyl penicillin 22,000 IU/kg IV q 6 h and gentamicin 6.6 mg/kg q 24 h is a reasonable choice. Penicillin should not be used IM in these cases if muscle pain is present and care should be taken to ensure renal function is sufficient to tolerate gentamicin use.

Trimethoprim/sulphadiazine (30 mg/kg IV or PO q 12 h) would be a reasonable alternative in cases where gentamicin is contraindicated, or IV penicillin is cost prohibitive.

Prognosis

The case fatality rate is ~10%. Relapse in clinical signs is common if corticosteroids are withdrawn too quickly. Anecdotally, treatment of relapsed disease is more difficult than treatment of horses in their first episode.

Further reading

Pusterla N, Watson JL, Affolter VK, et al., Purpura haemorrhagica in 53 horses. Veterinary record. 2003;153(4):118-21. (22)

Waller AS, Sellon DC, Sweeney CR, et al.,. Streptococcal Infections. Equine Infections Diseases. 2013. p. 265-e4. (23)

Chapter 4: Thrombophlebitis

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Aseptic skin preparation should be performed prior to placement of an indwelling catheter.
2. Aseptic technique should be ensured when handling and using an indwelling intravenous catheter.
3. Use of good intravenous injection technique, possibly with use of a disposable catheter when administering large volumes or potentially irritant substances if an indwelling catheter is not present, may reduce the risk of thrombophlebitis.

Thrombophlebitis is the inflammation of blood vessels in association with thrombus formation. It occurs most commonly due to perivascular injection of irritant substances and can be septic or non-septic.

Septic thrombophlebitis is characterised by heat, swelling, pain on palpation and exudation at the site of venepuncture or around indwelling intravenous catheter sites. Ultrasound is a useful tool to help differentiate between non-septic and septic forms of thrombophlebitis. In non-septic thrombophlebitis there is usually thrombus formation in the vein, without visible fluid pockets or associated perivascular inflammation.

Staphylococcus spp. are the most common organisms cultured from catheter tips in septic thrombophlebitis (24), but *E. coli*, *Streptococcus zooepidemicus* and *Actinobacillus equuli* have all been cultured from cases in Australian horses (25).

The catheter material influences the degree of irritation to the vein and increases the likelihood of thrombosis and sepsis. Polyurethane catheters are less traumatic than those made of polytetrafluorethylene (Teflon) (24). Over-the-wire catheters are generally more flexible than over-the-needle catheters and are thought to cause less injury to the vascular endothelium (26). As a general rule, an over-the-needle Teflon catheter should be replaced after three days, and a polyurethane over-the-needle catheter should be replaced after five days, but replacement should occur earlier if signs of thrombophlebitis develop (26).

Over-the-wire catheters can be left *in situ* for up to 30 days if good aseptic technique is used during placement. Bacterial endocarditis is a rare, but possible, complication of septic jugular vein thrombophlebitis.

Because of the poor vascularisation that results from thrombosis, septic foci can be difficult to resolve.

Diagnostics

Pain, heat and swelling at the site of intravenous injections or of an indwelling catheter, and fever are usually present with septic thrombophlebitis.

Ultrasound can help to establish the extent of the thrombus and the presence of cavitation, which may be indicative of sepsis. Non-septic thrombophlebitis can also occur and can be differentiated clinically by the lack of heat and pain at the site of thrombosis and the absence of cavitation.

Removal of the catheter and culture of the catheter tip are recommended.

Treatment

Anti- inflammatory drugs used systemically (phenylbutazone 4mg/kg PO q 24 h or 2 mg/kg PO q 12 h or meloxicam 0.6mg/kg PO q 24 h) and hot-packing can aid resolution of the inflammation.

Broad spectrum antimicrobial therapy is indicated in cases of septic thrombophlebitis until the results of culture and susceptibility testing are available.

Surgical resection of the jugular vein has been described for refractory cases (25).

Antimicrobials used

- Procaine penicillin G (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h)
- OR trimethoprim-suphadiazine (30 mg/kg PO q 12 h)
- There is no evidence to guide a specific duration of therapy, but the poor vascularisation probably necessitates therapy of 10-14 days.

Prognosis

Most cases resolve with antimicrobial and anti-inflammatory therapy. Some may require surgical resection.

Bacterial endocarditis is a very rare complication and has a poor prognosis.

Chapter 5: Vasculitis

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. In Australia, vasculitis most commonly occurs secondary to bacterial or viral infections or endotoxaemia.
2. Clinical signs are painful-dependent-pitting oedema, sometimes with fever and petechial haemorrhages.

Vasculitis can involve the arteries, veins or capillaries. Primary disease can occur because of direct damage to the vessel walls by an infectious agent, such as equine arteritis virus. This virus does occur in Australia, but disease associated with it has never been reported, suggesting that the virulence of Australian strains is low. Equine viral arteritis is a notifiable disease in Australia. More commonly in Australia, vasculitis occurs secondary to a bacterial or viral infection or endotoxaemia (27). Vasculitis secondary to infection with *Streptococcus equi* subsp *equi* is most common (see purpura haemorrhagica).

Vasculitis can also occur secondary to infection with equine herpesvirus 1 (EHV-1) (28) and, rarely, equine herpesvirus 4 (EHV-4), where there is also an immune-mediated pathogenesis. EHV-1 infection increases the procoagulant activity of peripheral blood mononuclear cell tissue factor (TF). The increase occurs during the acute infection and is most marked at the onset and end of viraemia. Tissue factor is an activator of the coagulation cascade during viral infection.

Diagnostics

Horses are usually febrile. The presence of painful, pitting oedema is consistent with the diagnosis. Haematological analysis is useful to determine white cell counts and neutrophil counts. When secondary to endotoxaemia, neutropaenia is common. When secondary to bacterial or viral infection, leucocytosis and neutrophilia are common.

Oedema due to low oncotic pressure should not be painful on palpation. In addition, normal serum albumin and protein, in association with a normal hydration status, rule out decreased oncotic pressure as cause of distal limb oedema.

Diagnosis of the primary disease should be attempted but may not be possible for viral aetiologies. Horses with endotoxaemic vasculitis are generally very unwell, with leukopaenia and neutropaenia. Plasma fibrinogen and SAA concentrations may be elevated during the initial stages, but this is dependent on the stage of disease. EHV-1 and EHV-4 can be diagnosed by isolation of virus from nasopharyngeal swabs or the buffy coat in blood samples collected into EDTA tubes, or by nucleic acid amplification (PCR testing). A rising serum antibody titre can also be used, but results are usually not known until after completion of the clinical course of disease.

Treatment

Anti-inflammatory therapy is indicated with flunixin meglumine at 0.25mg/kg IV q 8 h (anti-endotoxic dose) up to 1.1mg/kg q 12 h for full anti-inflammatory effect (0.5 mg/kg IV q 12 h is common).

Antimicrobial drugs are not indicated for treatment of vasculitis unless they may be required to treat the primary disease process (for example, procaine penicillin in the case of *Streptococcus equi* subsp *equi* infection – see purpura haemorrhagica; Section 2, Chapter 3).

Corticosteroids are indicated for treatment of immune-mediated diseases like purpura haemorrhagica (dexamethasone 0.1 – 0.2mg/kg IV q 24 h; prednisolone 0.10 - 0.2mg/kg PO q 24 h)

Antimicrobials used

- Not indicated for treatment of primary vasculitis.
- If secondary to *Streptococcus equi* subsp *equi* infection, then procaine penicillin G (22 000 IU/kg IM q 12 h, generally for 3-5 days) may be used concurrently with corticosteroids.

Prognosis

Can be guarded depending on the degree of vascular damage that occurs.

Reference List

1. Maxson AD, Reef VB. Bacterial endocarditis in horses: ten cases (1984-1995). Equine veterinary journal. 1997;29(5):394-9.
2. Henderson B, Diaz M, Martins C, Kenney D, Baird JD, Arroyo LG. Valvular endocarditis in the horse: 20 cases (1993-2020). Canadian veterinary journal. 2020;61(12):1290-4.
3. Ewart S, Brown C, Derksen F, Kufuor-Mensa E. Serratia marcescens endocarditis in a horse. JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION. 1992;200(7):961-3.
4. Buergelt CD, Cooley AJ, Hines SA, Pipers FS. Endocarditis in six horses. Veterinary pathology. 1985;22(4):333-7.
5. Nath LC, Anderson GA, Hinchcliff KW, Savage CJ. Serum cardiac troponin I concentrations in horses with cardiac disease. Australian veterinary journal. 2012;90(9):351-7.
6. Cawdell-Smith AJ, Todhunter KH, Perkins NR, Bryden WL. Exposure of mares to processionary caterpillars (Ochrogaster lunifer) in early pregnancy: An additional dimension to equine amnionitis and fetal loss. Equine veterinary journal. 2013;45(6):755-60.
7. Reimer J. Management of equine pericarditis. Equine veterinary education. 2013;25(7):334-8.
8. Sprayberry KA, Slovis NM. Sales performance and athletic outcome in young Thoroughbreds with pericarditis. Equine veterinary journal. 2017;49(6):729-33.
9. Pusterla N, Watson JL, Affolter VK, Magdesian KG, Wilson WD, Carlson GP. Purpura haemorrhagica in 53 horses. Veterinary record. 2003;153(4):118-21.
10. Waller AS, Sellon DC, Sweeney CR, Timoney PJ, Newton JR, Hines MT. Streptococcal Infections. In: Sellon DC, Long MT, editors. Equine Infectious Diseases. St Louis: Elsevier Saunders; 2013. p. 265-e4.
11. Müller CDVS, Lübke-Becker A, Doherr MG, Gehlen H. Influence of Different Types of Catheters on the Development of Diseases of the Jugular Vein in 45 Horses. Journal of equine veterinary science. 2016;46:89-97.
12. Russell TM, Kearney C, Pollock PJ. Surgical Treatment of Septic Jugular Thrombophlebitis in Nine Horses. Veterinary surgery. 2010;39(5):627-30.
13. Divers TJ. Prevention and treatment of thrombosis, phlebitis, and laminitis in horses with gastrointestinal diseases. The Veterinary clinics of North America Equine practice. 2003;19(3):779-90.
14. Knottenbelt DC. Vasculitis: just what does it mean? Equine veterinary education. 2002;14(5):247-51.
15. Wilson ME, Holz CL, Kopec AK, Dau JJ, Luyendyk JP, Soboll Hussey G. Coagulation parameters following equine herpesvirus type 1 infection in horses. Equine veterinary journal. 2019;51(1):102-7.

Section 3 – Upper Respiratory

Contents

Chapter 1: Arytenoid Chondritis

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Arytenoid cartilage infection is thought to be secondary to trauma and extension of mucosal bacterial or viral infection.
2. Can progress to deformation of cartilage and granuloma formation, requiring surgical resection.
3. Mixed bacterial infections common.

Arytenoid chondritis is a performance limiting upper airway disease most commonly reported in young thoroughbred horses (29). The aetiology is thought to be secondary to trauma to the arytenoid cartilage, with subsequent extension of mucosal bacterial or viral infection into the cartilage. The cartilage infection often progresses, to result in permanent enlargement or deformation of the arytenoid cartilage, requiring arytenoidectomy or resection of a granuloma. Clinical signs include insidious and progressive onset of respiratory noise, exercise intolerance and/or coughing. Bacterial cultures from the infected cartilages and granulomas have revealed mixed infections, with 58% growing Gram-positive bacteria, 54% Gram negative bacteria and 33% anaerobic bacteria (1). *Streptococcus* spp. were the most common (32%), followed by members of the *Enterobacteriaceae* (13%). Susceptibility of bacteria often varies substantially by geographic area, so local data should drive decision making. Ceftiofur and enrofloxacin are high importance antimicrobials and should not be used as first line therapy.

Diagnostics

Endoscopy of the larynx is the most widely used diagnostic tool, but ultrasonography of the larynx is useful to determine the extent of the chondropathy.

Culture of the cartilage resected during arytenoidectomy or removal of the granuloma is important. Culture of the surface of these lesions during upper airway endoscopy is not considered useful.

Treatment

Broad spectrum antimicrobial therapy is indicated. Penetration into the infected cartilage is an issue, as vascularisation is poor. Penicillin and gentamicin are recommended, but oral therapy is often used as longer courses of intramuscular antimicrobials can be poorly tolerated by yearlings. Antimicrobial therapy is usually required for at least five to seven days, when some improvement of the endoscopic appearance is expected. If there is no improvement apparent on repeat endoscopic examination, arytenoidectomy or resection of the granuloma should be considered if there is an impediment to the airway and a future athletic career is anticipated. Culture and susceptibility testing should be

performed on the resected infected cartilage and granuloma. The total course of treatment can be weeks, depending on rate of resolution of these lesions.

Anti-inflammatory therapy with phenylbutazone (2 g IV or PO q 24 h for the first five days of treatment) is a useful adjunctive therapy.

Antimicrobials used

- Procaine penicillin G (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h)
- OR oxytetracycline (6.6 mg/kg IV q 12 h)
- OR trimethoprim-sulphadiazine (30 mg/kg IV or PO q 12 h)

Prognosis

Reduction in the lesion size and improvement in arytenoid movement after antimicrobial therapy is encouraging. The prognosis for performance following arytenoidectomy is considered guarded due to the propensity of recovered horses to aspirate.

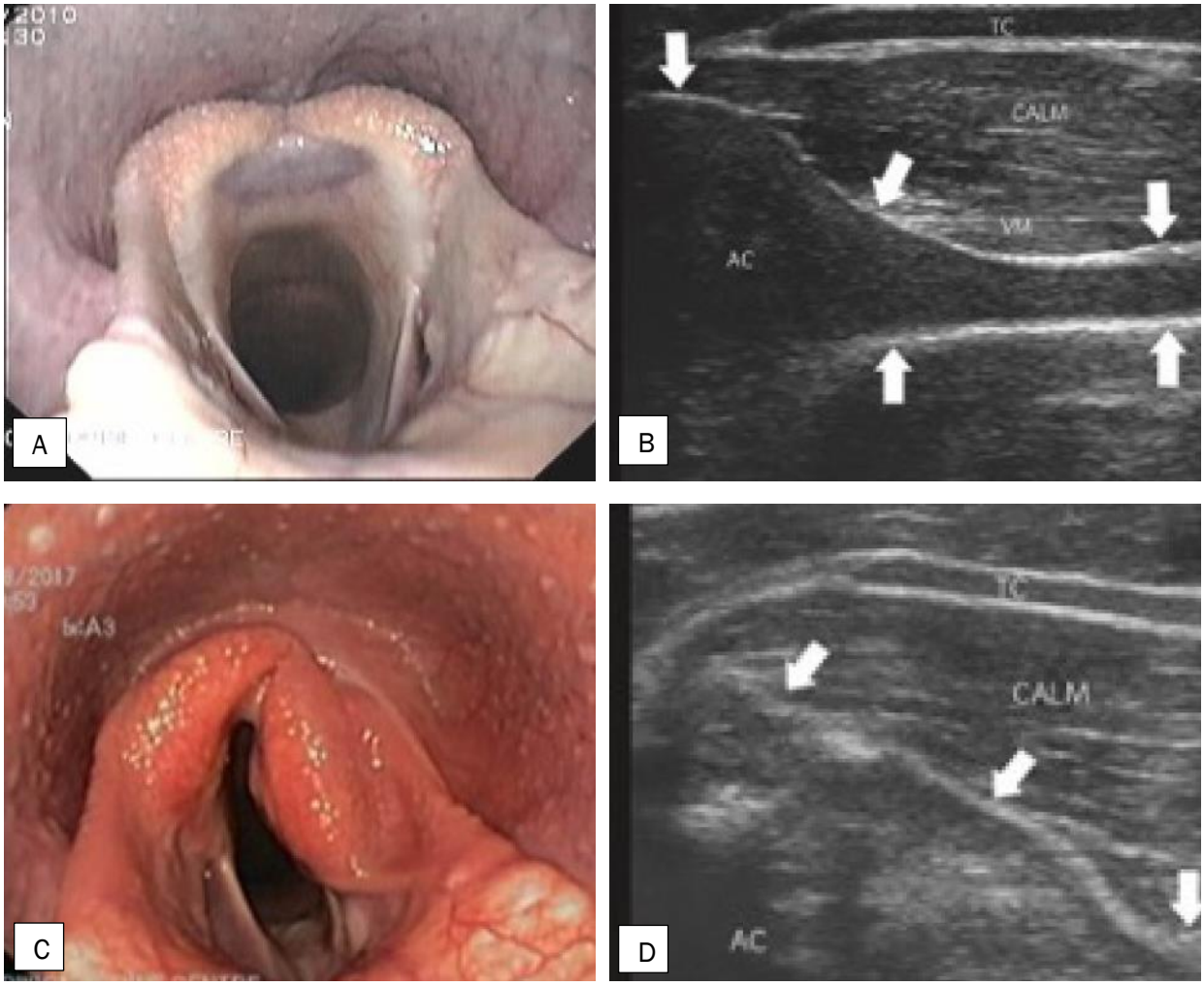

Figure 3.1: A. Normal video endoscopy image and (B) ultrasound of equine larynx.
C. Video endoscopy image and (D) ultrasound image of arytenoid chondropathy.
(Images courtesy of Dr Jonathon Lumsden, 2024.)

Chapter 2: Epiglottitis and epiglottic entrapment

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Mucosal lesions can resolve with rest and anti-inflammatory therapy.
2. Cartilage involvement necessitates broad-spectrum antimicrobial therapy.
3. Epiglottic entrapment requires surgical intervention.

Epiglottitis can occur with ulceration of the epiglottis and in severe cases can lead to exposure of the epiglottic cartilage (Figure 3.2. Image A). Mucosal lesions most result from trauma and this allows extension of mucosal bacterial and viral infection into the cartilage. Epiglottic entrapment is a cause of exercise intolerance and inspiratory and expiratory noise. The epiglottis becomes enveloped by the aryepiglottic fold (Figure 3.2 Image B).

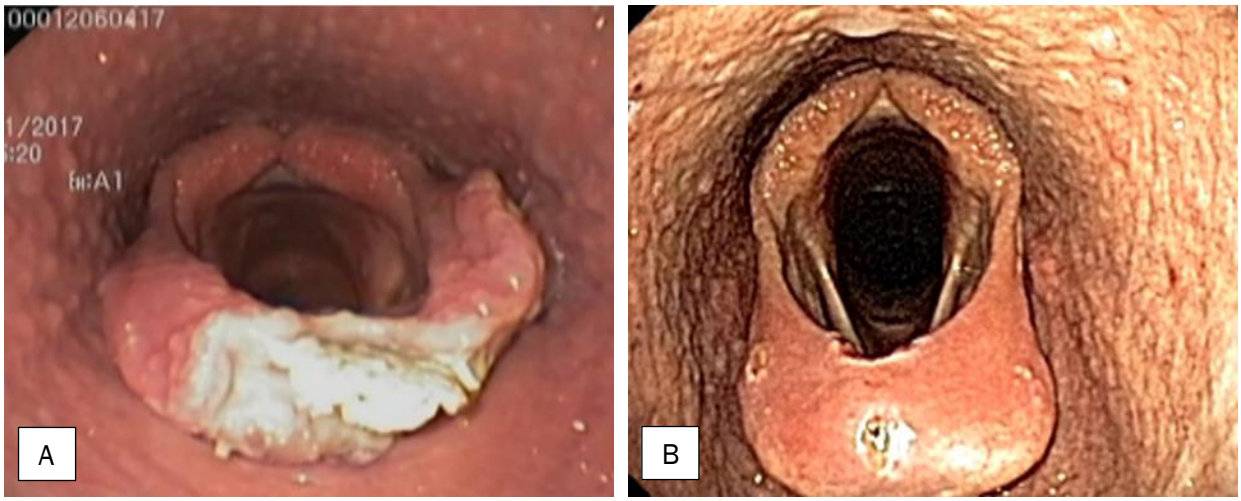

Figure 3.2: A.. Epiglottitis in a horse B. Epiglottic entrapment in a horse.
(Images courtesy of Leanne Begg.)

Diagnostics

Both conditions are diagnosed by endoscopy. With epiglottic entrapment, the distinct serrated margins of the epiglottis and the dorsal epiglottic vascular pattern are obscured by a fold of aryepiglottic mucosa. Cartilage involvement is diagnosed when there is thickening and disfigurement of the cartilage of the epiglottis.

Treatment

Mucosal lesions are best treated with rest and anti-inflammatory drugs. If the epiglottic cartilage is exposed, broad spectrum antimicrobial therapy is indicated.

Epiglottic entrapment requires surgical division of the aryepiglottic fold, which is usually performed standing if it is permanently entrapped but needs to be done under general anaesthesia if it is only intermittently entrapped.

Antimicrobials used

- In cases with exposed epiglottic cartilage, procaine penicillin (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h) for a minimum of 7 days or until clinical resolution is apparent on repeat endoscopic examination.

- OR trimethoprim-sulphadiazine (30mg/kg PO q 12 h) for a minimum of 7 days or until clinical resolution is apparent on repeat endoscopic examination.

Prognosis

Epiglottitis generally has a good prognosis after antimicrobial therapy unless infection of cartilage leads to disfigurement and compromise of epiglottic function.

Epiglottic entrapment has a good prognosis for future athletic performance following surgery.

Chapter 3: Pharyngeal cyst/ subepiglottic cyst

Authors: Leanne Begg & Laura Hardefeldt

Key issues

1. Pharyngeal cysts are congenital cysts that usually occur under the epiglottis (subepiglottic) and are usually identified when investigating respiratory noise.

Subepiglottic cysts are an uncommon cause of respiratory noise in young horses. They are usually present from birth but are diagnosed as horses begin to exercise, when they may cause exercise intolerance or respiratory noise. Large cysts are diagnosed earlier in foals, as they lead to coughing, dysphagia and food aspiration.

Diagnostics

Subepiglottic cysts are diagnosed by upper airway endoscopy.

Treatment

Subepiglottic cysts are removed by surgical resection.

Antimicrobials used

- Subepiglottic cysts do not require antimicrobial therapy other than peri-operative therapy. There is no evidence for duration of therapy but some surgeons advocate for 3 days post-operatively due to the proximity to the epiglottal cartilage. Upper airway surgery in other species (dogs, humans) are generally performed with perioperative (<24h therapy) surgical prophylaxis alone or without surgical prophylaxis.

Prognosis

Subepiglottic cysts have a good prognosis following surgical resection.

Chapter 4: Pharyngeal lymphoid hyperplasia

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Pharyngeal lymphoid hyperplasia is not considered a cause of poor performance.

Pharyngeal lymphoid hyperplasia (PLH) usually occurs in young horses. These follicles are lymphoid tissue that spreads over the larynx. Hyperplasia occurs with lymphoid stimulation. They are usually considered of little significance and not a cause of poor performance.

Diagnostics

PLH is diagnosed by endoscopy (Figure 3.3).

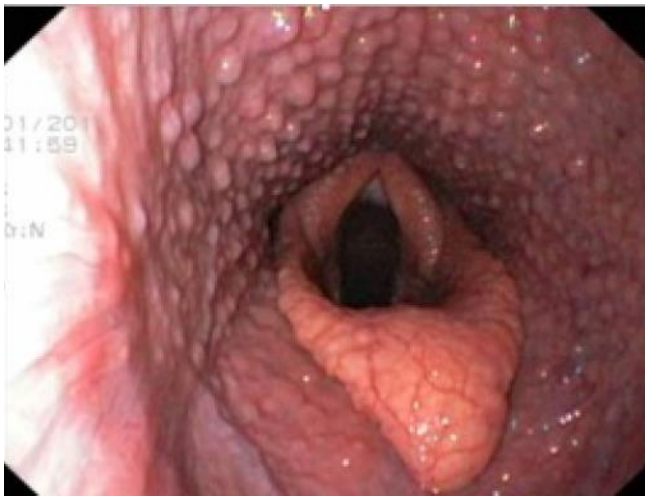

Figure 3.3. Pharyngeal lymphoid hyperplasia in a young thoroughbred.
(Image courtesy of Leanne Begg.)

Treatment

No treatment is recommended for pharyngeal lymphoid hyperplasia. Rest and anti-inflammatory drugs may be indicated if it is severe.

Antimicrobials used

- Antimicrobial therapy not indicated for pharyngeal lymphoid hyperplasia.

Prognosis

Excellent.

Chapter 5: Sinonasal and guttural pouch mycosis

Authors: Leanne Begg, Allison Stewart, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Sinonasal and guttural pouch mycoses are both uncommon in Australia.
2. *Aspergillus* species are the most frequent cause of guttural pouch mycosis.
3. Histopathological examination and culture are required for diagnosis, although care should be taken with guttural pouch mycosis as exsanguination is possible.

Fungal infections of the upper respiratory tract are rare but do occur in the tropical and subtropical regions of Australia. Aspergillus species are the fungi most commonly isolated from sinonasal mycotic infections in cold climates (30), but three cases of cryptococcal infection have been described in Australia (31, 32, 33) and Conidiobolomycocosis is also seen. Clinical signs include dyspnoea, abnormal respiratory noise and decreased airflow through the nares, a unilateral or bilateral nasal discharge that may be malodorous, and bony swelling over the sinuses.

Clinical signs of guttural pouch mycosis include unilateral or bilateral epistaxis, nasal discharge and dysphagia. Epistaxis occurs because of the erosion of the guttural pouch mucosa by the fungal plaque, resulting in haemorrhage from the internal carotid, occipital or maxillary arteries. Severe haemorrhage can result in exsanguination and death (34). Aspergillus species are the fungi most commonly isolated from cases of guttural pouch mycosis (35).

Diagnostics

Upper airway endoscopy, including into the guttural pouch, is usually diagnostic for both sinonasal and guttural pouch mycosis. Superficial fungal plaques, as most often seen with Aspergillosis, can be sampled using a cytology brush. For granulomatous masses in the nasopharynx, deep biopsy samples are required. These samples need to be collected with a uterine biopsy instrument as the small endoscopic biopsy instruments are usually too superficial to be diagnostic. Topical adrenaline is useful to control post biopsy haemorrhage.

In cases of guttural pouch mycosis, the diagnosis is generally made by endoscopy alone, in conjunction with the clinical history, because of the risk of haemorrhage from disturbance of fungal plaques on arteries.

Serological testing using latex agglutination to identify cryptococcal capsular antigen (LCAT) may be useful if *Cryptococcus* spp. are suspected based on cytological examination.

When fungal organisms are suspected in sinonasal infections, cytology from impression smears of biopsy samples and histopathology are useful, but fungal culture should also be pursued. This includes cases of sinonasal mycotic infections, which also require imaging studies and are discussed further in Chapter 5.2 Sinusitis (see Section 5 - Dentistry).

Treatment

Surgical treatment of guttural pouch mycosis is traditionally aimed at obstructing blood flow through at-risk vessels by ligation, balloon-tipped catheter placement or transarterial coil embolism, which also results in inhibition of fungal growth, probably because of the reduction in the availability of oxygen (36). Antifungal medical therapy (systemic or topical) is then not required. Laser salpingopharyngostomy into the guttural pouch has been used more recently as an adjunct to treatment of guttural pouch mycosis to alter the guttural pouch environment. This has been shown to specifically alter the oxygen and carbon dioxide concentrations, but not the temperature and humidity,

within the guttural pouch (37) and is an alternative option for treatment when the fungal plaque is not associated with haemorrhage. When lesions are located over major arteries then there is always the risk of sudden fatal haemorrhage. If surgical intervention is not available, and the lesions are not over major arteries then repeated topical therapy with nilconazole or nystatin has been used successfully. When lesions affect cranial nerves and dysphagia results, then horses may need prolonged feeding of gruel via a nasogastric tube and possibly treatment for secondary aspiration pneumonia.

Sinonasal mycotic infections caused by *Conidiobolomycosis coronatus* and *Cryptococcus* spp are usually successfully treated with 1-3 months of oral fluconazole. Antifungal susceptibility testing is warranted for other organisms, including *Aspergillis* spp. Not all laboratories offer this service, so it is worth discussing this with laboratories prior to sample submission. Extensive infiltration can be surgically debulked prior to lavage and oral antifungal therapy. One case of cryptococcal rhinitis in Australia was successfully treated with sinonasal bathing with fluconazole under general anaesthesia (33).

Antimicrobials used

Guttural pouch mycosis

Surgical therapy alone is generally successful for guttural pouch mycosis and reduces the risk of exsanguination.

For superficial lesions:

- Topical enilconazole q 12h (volume chosen according to size of the lesion to ensure that it is completely covered by the drug solution) can be diluted 1:4 to facilitate passage of the solution through the biopsy channel of the endoscope.
- Final concentrations of 0.2- 3% have been reported in the literature without complications (38).
- Treatment is until endoscopic resolution which can take 1.5-5 weeks.

Nystatin or amphotericin B have also been administered via inhalation through a nebuliser twice daily most commonly for 2 weeks. The efficacy and effectiveness of this therapy is unknown as all cases have also been treated with topical therapy (30).

Sinonasal mycosis

Superficial plaques due to *Aspergillus spp.* should be treated based on results of culture and susceptibility

Extensive cryptococcal granulomas, lesions probably benefit from surgical debulking followed by:

- Fluconazole: loading dose 14 mg/kg PO followed by 5 mg/kg q 24h for 1-3 months.
- Duration of therapy is likely dependent on severity of the lesion, but long-term treatment is typically required (several months).
- Lesions should be monitored endoscopically and by reduction in cryptococcal antigen titres (LCAT) (39)
- *Conidiobolmycosis coronatus* granulomas respond well to 1-3 months of oral fluconazole (40).

Prognosis

- Good for guttural pouch mycosis.
- For sinonasal mycosis, reasonable with prolonged treatment, with reports of one to five months needed to see resolution of fungal plaques when medical therapy is used. Recurrence, sometimes years later, is frequently reported.

- Excellent for *Conidiobolomycosis* and *Cryptococcus*.

Further reading

Stewart AJ. Diagnosis and treatment of cryptococcal infections in horses. Equine Veterinary Education. 2020;32(11):576-9.(39).

Stewart AJ. Fungal infections of the equine respiratory tract. Large Animal Internal Medicine 6th Edition 2019. Eds: Smith BP, Van Metre DC, Pusterla N. Elsevier, Philadelphia. 550-559

Chapter 6: Strangles

Authors: Laura Hardefeldt, Charlie El Hage, James Gilkerson, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Persistent infection and shedding continue for 3-6 weeks following clinical recovery
2. Guttural pouches may serve as *S. equi* reservoirs (empyema/chondroids or colonisation)
3. Sequelae may be fatal and include metastatic abscessation of internal organs, Purpura haemorrhagica (see Chapter 2), and immune-mediated myositis (see Chapter 11)
4. Cross-reactivity of serological tests and PCR/culture contamination may reduce specificity of tests for *S. equi*. It is important to interpret results in the full context of the clinical disease and outbreak epidemiology.

Streptococcus equi subspecies *equi (S. equi)* are beta haemolytic Gram-positive cocci. Considered a pathogen of the upper equine respiratory tract*, S. equi* is closely related to *Streptococcus equi* subspecies *zooepidemicus* (*S. zooepidemicus*). Unlike *S.equi*, *S. zooepidemicus* is considered a commensal organism of equine mucosa and an opportunistic pathogen. The genetic similarity between these two bacterial subspecies has clinical relevance, as it may complicate serological testing and agent identification in many assays.

Strangles is a highly contagious upper respiratory tract disease of horses. A proportion of affected horses will establish an infection in the guttural pouch and remain persistent carriers of *S. equi*. Most carriers clear their infection after several weeks, but some remain infectious for months to years. Outbreaks in training yards, agistment facilities and on farms are not uncommon and can be difficult to control. Identification of carriers is challenging, so detection of horses in the early stages is critical, as effective isolation of large groups of animals can be logistically difficult. Unidentified carriers, nose-to-nose contact, fomite transfer on personnel and equipment and in shared water or feeding troughs may perpetuate the outbreak.

Strangles is a notifiable disease in some Australian jurisdictions and practitioners are encouraged to inform and seek advice from their local veterinary authorities.

Infection with *S. equi* in horses generally produces a pyretic episode that precedes clinical signs of upper respiratory tract disease, such as muco-purulent / purulent nasal discharge, pharyngitis and subsequent abscessation of the draining lymph nodes. The severity of the clinical disease may be affected by the age and immune status of the horse. Fever typically occurs 3-14 days after exposure and generally persists until the lymph node abscesses rupture. The substantial pharyngitis results in reluctance to eat and drink. Lymphadenopathy is a typical clinical sign – classically affecting the submandibular and retropharyngeal lymph nodes, although the parotid and cranial cervical lymph nodes are also occasionally involved. Abscesses generally rupture between one and four weeks after infection. Guttural pouch infection and empyema results from abscessation of the retropharyngeal lymph node and subsequent rupture of the abscess into the guttural pouch. Some of these carrier horses develop aggregations of inspissated pus and debris, known as chondroids, which play a role in shielding the bacteria from the immune response and prolonging persistent infection.

Inflammation associated with pharyngitis and formation of lymph node abscesses may cause obstruction of the upper respiratory tract (hence “Strangles”) necessitating temporary tracheotomy.

Although rare, metastatic abscesses can also occur in multiple sites, including the abdomen, and these cases are commonly referred to as “bastard strangles.” There is a clinical impression that the rate of bastard strangles is higher in horses treated with antimicrobials but there is no evidence one

way or the other in the literature. Other complications following strangles infection are also well recognised and include Purpura haemorrhagica (see Section 2, Chapter 3), and immune mediated myositis (Section 11, Chapter 2). Myocarditis is a less commonly reported sequela of strangles infection.

The overall complication rate increases with the duration and intensity of exposure and may be as high as 20%. Overall case fatality rates can be as high as 8.1% to 9.7% in large farm outbreaks.

Diagnostics

Although the clinical signs of strangles are highly indicative, collection of an appropriate sample and identification of the organism is critical, as infection with *S. zooepidemicus* can mimic the clinical signs of strangles. In the early stages of disease an aspirated sample of pus from an abscessed lymph node provides the ideal, least contaminated sample. Swab samples from burst lymph node abscesses may be of some value if samples are collected carefully to minimise contamination with skin commensals. PCR methods have greater sensitivity for detection of *S. equi* than traditional culture methods, as have newer molecular methods, such as isothermal assays such as loop-mediated isothermal amplification (LAMP).

In horses with evidence of clinical disease due to *S. equi*, a complete blood count is non-specific with leukocytosis characterized by a neutrophilia and often hyperfibrinogenaemia. These changes are indicative of a non-specific inflammatory response.

Serial nasopharyngeal swabs and/or guttural pouch washes are often used to detect *S. equi* following resolution of clinical disease. This sampling is important, as shedding of *S. equi* after infection may be a source of infection of new horses and thus prolong the outbreak. A minority of horses may continue to shed the organism, maintaining a carrier state via colonization of guttural pouches (with or without chondroid formation). It is important to allow horses to recover from the acute disease before sampling to identify persistent carriers (Figure 3.4).

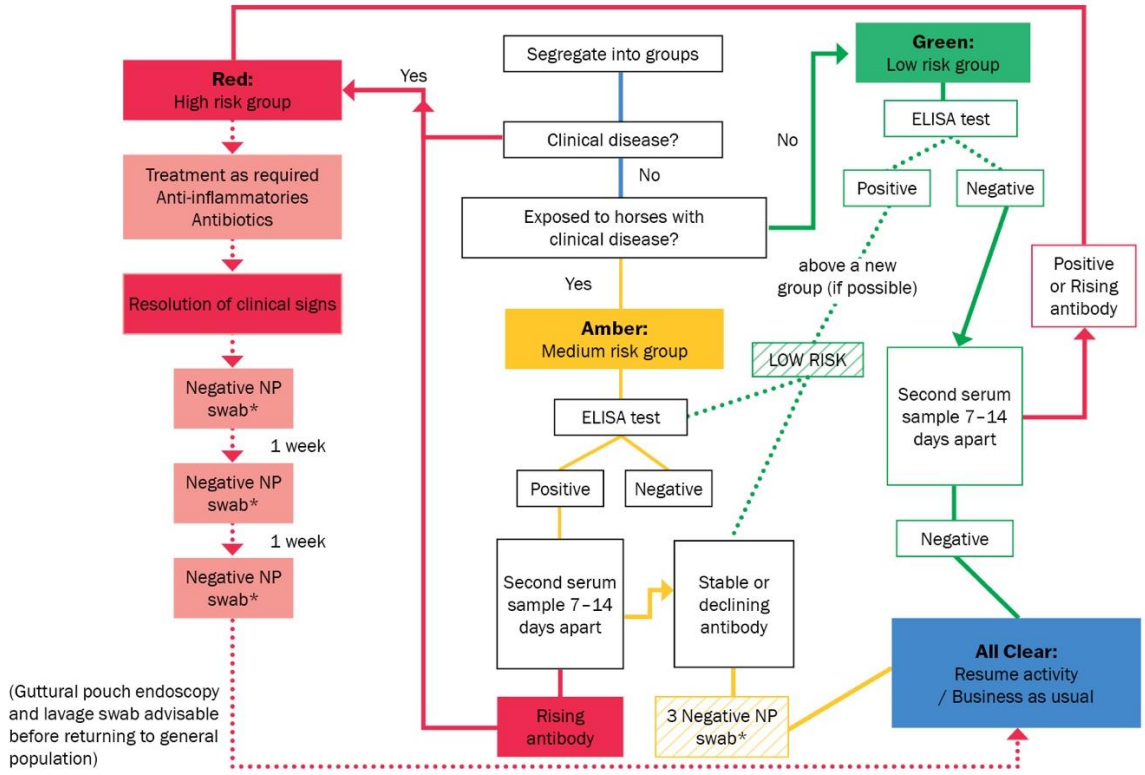

Figure 3.4. Biosecurity approach to Strangles outbreaks on farms (reproduced with permission from J. Gilkerson).

Several commercial ELISAs are available targeting IgG antibodies against surface proteins of *S. equi.* These tests have differing sensitivities and specificities, depending upon the type used and stage of disease. The duplex iELISA is useful to manage an outbreak of strangles, as recent infection can be detected by an increase in antibody levels in paired sera taken 10-14 days apart. Other antibody assays, such as the SeM ELISA assay, may detect antibodies directed against SeM of *S. zooepidemicus* and this cross-reaction leads to reduced specificity of the assay (and false positive results). Microbiological testing of guttural pouch lavages by qPCR or culture can be used to identify sub-clinically infected persistent carriers at the end of an outbreak (Tables 3.1 and 3.2). Sampling for persistent *S. equi* shedding should commence no sooner than 3-4 weeks after the resolution of clinical signs.

The SeM antibody response can be used to detect horses at risk for development of Purpura haemorrhagica, with the recommendation from the USA that horses with strong antibody responses are not vaccinated against *S. equi* until the antibody levels have subsided.

Table 3.1. Tests available for strangles

Test	Sample	Comment
Culture and susceptibility	Nasopharyngeal swab, nasal lavage, lymph node abscess aspirate or abscess swab	Historical gold standard; high % false negatives. b-lactam resistance not recorded in *S. equi*.
Nucleic acid detection (DNA detection by PCR or qPCR)	Nasopharyngeal swab (or nasal lavage or lymph node abscess aspirate) in transport medium	Current gold standard; rapid; highly sensitive and specific; PCR and qPCR superior to culture; qPCR superior to PCR
Serology	Serum	ELISA using 2 antigens; very sensitive and specific; identifies exposure, not carrier status; titres do not correlate with risk of carrier state or with severity of previous clinical disease

(Reproduced with permission from J. Slater)

Table 3.2. Role of *S. equi* tests in the control of strangles outbreaks

Sample	Test	Acute case	Outbreak monitoring	Quarantine and testing	Exposure screening	Carrier detection
Single nasopharyngeal swab (NPS) or single nasal lavage	qPCR* LAMP PCR Culture & susceptibility	Yes	Use for clinical monitoring after initial diagnosis	No	No	No
Serum	IgG serology (duplex iELISA)** SeM ELISA	No	No	Pre- or at arrival (identify & treat possible carriers)	Yes (time to convert, may need 2 samples)	Pre-screen identifies exposure not carriers
3 x nasopharyngeal swabs (at weekly intervals)	qPCR LAMP PCR Culture & susceptibility	No	No	Yes (including as alternative to serology if horse vaccinated)	No	Yes
1 x guttural pouch lavage (GPL)	qPCR LAMP	No	No	Yes (including as alternative to serology if	No	Yes (equivalent sensitivity to 3 x NPS)

Sample	Test	Acute case	Outbreak monitoring	Quarantine and testing	Exposure screening	Carrier detection
	PCR Culture & susceptibility			horse vaccinated)		
Guttural pouch lavage plus nasopharyngeal swab	qPCR* LAMP* PCR Culture & susceptibility	No	No	Yes (including as alternative to serology if horse vaccinated)	No	Yes. Combining GPL and NPS samples maximises likelihood of detection from a single sampling visit, especially when tested by qPCR.

(Reproduced with permission from J. Slater)

*qPCR and newer molecular techniques, including LAMP, are preferred over PCR. Culture and susceptibility are not recommended as sensitivity and specificity are poor.

** the duplex iELISA is preferred for serial serological testing, as SeM ELISA cross reactivity with *S. zooepidemicus* can lead to false positive results. The SeM ELISA is useful in identifying individuals at higher risk of developing *purpura haemorrhagica* in response to *S. equi* vaccination, so may be used to assess vaccination risk after outbreak resolution.

Treatment

Fever without clinical signs in a strangles outbreak may be an indication for antimicrobial therapy if there is certainty that other clinical signs have not commenced. For this condition to be met, horses must be able to be kept isolated and body temperature monitored twice daily to ensure that treatment is commenced immediately following development of fever. Early treatment may reduce formation of abscesses and therefore shedding. However, if abscesses have already started to form, antimicrobial therapy is highly unlikely to result in bacteriological cure and will only delay abscess rupture thereby prolonging the clinical course and that of the outbreak. Procaine penicillin is the drug of choice.

Uncomplicated strangles infection can usually be managed using supportive treatments. Lancing abscesses to establish drainage will hasten recovery, but most abscesses burst and drain, either externally or internally, within one to four weeks. Non-steroidal anti-inflammatories can reduce fever and improve appetite until drainage is established. Bathing and lavage of burst abscesses and non-steroidal anti-inflammatory medications generally results in rapid healing. Despite a perceived indication by many practitioners and lay personnel, the use of antimicrobials is not indicated in uncomplicated cases of strangles and may delay recovery, especially when there is lymphadenopathy (abscess formation) and drainage has not been established.

Antimicrobials are indicated in infected horses with respiratory distress where abscess drainage is not possible or does not resolve airway obstruction. The antimicrobial drug of choice is penicillin given the predictable sensitivity of *S. equi* to this antimicrobial.

Oral antimicrobials are sometimes preferred for logistical reasons and trimethoprim-sulfadiazine (TMS) [30 mg/kg PO q 12 h] has *in vitro* efficacy against *S. equi*, however anecdotal reports of clinical efficacy vary. In emergency situations, penicillin should be used as streptococci are highly susceptible.

Guttural pouch empyema may require repeated lavage with isotonic saline or polyionic fluids. Both topical and prolonged systemic penicillin administration (10 days) have been used successfully to treat these cases. Endoscopic basket removal of any chondroids is preferred over surgery, as complications with surgery are common.

Metastatic abscessation is considered a complication of a small proportion of strangles cases and is commonly referred to as "bastard strangles". Sites of infection include internal abdominal organs, lungs and brain. These cases remain difficult to diagnose and need to be treated on a case-by-case basis. As with all abscesses, drainage is the key to clinical resolution. Considerations influencing antimicrobial selection administration include efficacy against *S. equi* but also include formulation suitable for long-term administration and ability to penetrate tissue (high lipid solubility). Procedures to assist local drainage are indicated, if practical.

Antimicrobials used

- No indication for antimicrobials in uncomplicated infections – effective drainage is sufficient
- For cases with respiratory distress: penicillin at 22,000–44,000 IU/kg IM q 12 h or IV q 6 h for 5-7 days
  Metastatic strangles: penicillin 22,000 IU/kg IM q 12 h (if tolerated long term) or trimethoprim-sulphadiazine at 30 mg/kg PO q 12 h – treatment should continue until the abscesses are no longer visible on ultrasound (which may be several weeks to months). Consideration should be given to attempt surgical drainage if possible.

Prognosis

In uncomplicated cases, the prognosis for clinical recovery is good. However, complications, including death, metastatic abscessation and immune-mediated sequelae, are reported in up to 20% of cases following an outbreak.

It is important to recognise that many horses that recover from clinical infection may become latent carriers of *S. equi*, serving as a transmission risk for in-contact horses.

Further reading

Equine Infectious Diseases second ed. Sellon, D. Long, M(41).

Chapter 7: Upper respiratory tract viruses

Author: James Gilkerson, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Equine herpesviruses and equine picornaviruses usually cause mild and self-limiting upper respiratory tract disease.
2. Abortion and neurological disease can be sequelae of vasculitis associated with systemic EHV-1 infection.
3. Management is key to limiting spread of infection.
4. Vaccination for EHV1 and 4 is useful for increasing herd immunity.

Upper respiratory tract viruses are common, especially in young horses after weaning or when horses are run together in large open groups. As equine influenza is not present in Australia, the equine herpesviruses (EHV 1 and 4) and equine picornaviruses (ERAV and ERBV) are the most common known causes of equine upper respiratory disease (42). Infections can be mild or subclinical, but intermittent fever, mucoid to purulent nasal discharge, and coughing may be present (43). The lungs usually sound normal on auscultation. Unfortunately, laboratory confirmation of the cause of outbreaks of viral respiratory disease is not commonly undertaken in Australia, with practitioners opting to wait and see if horses recover.

The equine herpesviruses are the major viral respiratory pathogens affecting horses in Australia. All herpesviruses establish lifelong latent infections, with reactivation occurring during times of stress. The two endemic alphaherpesviruses, EHV-1 and EHV-4, are both transmitted via the respiratory route, with primary replication in the epithelium of the upper respiratory tract. Replication in the epithelium is associated with the observable clinical signs of rhinitis, such as serous nasal discharge, mandibular lymphadenopathy and occasionally ocular discharge. Infected horses are febrile at this stage. The nasal discharge often becomes mucopurulent, but this is usually self-limiting. Clinical signs last for a variable length of time, with clinical resolution between 2 to 10 days after experimental infection (44). Both EHV-1 and EHV-4 are contagious when horses come into contact with nasal discharge or droplets from the respiratory tract, but transmission requires relatively close contact between affected and susceptible horses. The virus can persist in the environment for several days, especially after abortion where virus loads are high. EHV 1 infections can progress from a local respiratory tract infection to a systemic viraemia, with virus in the bloodstream associated with circulating leukocytes. Systemic EHV-1 infections can cause a vasculitis as a result of infection of the endothelial cells of the arterioles supplying the endometrium, which can lead to abortion in pregnant mares; or the arterioles supplying the central nervous system, causing neurological disease in adults. EHV-1 neurological disease is infrequently diagnosed in Australia. EHV-1 abortions were first reported in Australia in the 1970s and are still a common infectious cause of abortion in Australia. EHV 4 is primarily a respiratory tract pathogen and is the most common cause of upper respiratory disease in weaned foals and yearlings throughout Australia (45). The equine gammaherpesviruses, EHV-2 and EHV-5, are commonly detected in secretions and samples from the respiratory tract, but their role in acute respiratory disease is unclear. Care should be taken when ascribing clinical significance to the detection of these viruses.

Other viruses endemic in Australia that are associated with self-limiting respiratory disease are the equine picornaviruses (equine rhinitis A virus, or ERAV and equine rhinitis B virus, or ERBV). ERAV has been identified as a common cause of, sometimes severe, respiratory disease of performance horses in Canada (46). The equine picornaviruses have been detected in horses with and without clinical signs of respiratory disease, but this is consistent with the serological evidence that horses are

exposed to these viruses by aerosol or direct contact early in life (47). ERAV is associated with more severe respiratory signs, characterized by nasal discharge, pyrexia, and a viraemia that lasts 4 to 5 days.

Diagnostics

PCR testing of respiratory secretions on nasopharyngeal swabs is the diagnostic test of choice. Viral culture and isolation can be performed on swab material but is rarely done. Serology can be undertaken to demonstrate seroconversion, but antibodies to EHV1 and EHV4 will cross-react in neutralisation tests. PCR can be performed on buffy coat cells from blood samples collected in EDTA tubes, or whole blood, to demonstrate viraemia.

Treatment

1. Antibiotics are not indicated unless there is secondary bacterial infection.
2. Non-steroidal anti-inflammatory drugs may be used to control fever (flunixin meglumine 1.1 mg/kg IV or PO q 24 h; phenylbutazone 2 g IV or PO q 24 h; meloxicam 0.6 mg/kg IV or PO q 24 h).
3. Management is important in horses with EHV1 infections to reduce sequelae (abortion in pregnant mares; neurological disease in adult horses). Recommendations include subdividing horses into smaller groups, minimizing stress, barrier nursing of infected horses and vaccination against EHV 1 and 4 to maximise herd immunity.

Antimicrobials used

- Not Indicated.

Prognosis

Good, as viral respiratory infections are usually self-limiting.

Reference List

1. Johnston GCA, Lumsden JM. Antimicrobial susceptibility of bacterial isolates from 33 thoroughbred horses with arytenoid chondropathy (2005-2019). Veterinary surgery. 2020;49(7):1283-91.
2. Pujol R, Tessier C, Manneveau G, De Fourmestraux C. Suspected primary mycotic rhinitis and paranasal sinusitis in seven horses (2013–2019). Equine veterinary education. 2021;33(8):401-.
3. Watt DA. A CASE OF CRYPTOCOCCAL GRANULOMA IN THE NASAL CAVITY OF A HORSE. Australian veterinary journal. 1970;46(10):493-4.
4. Roberts MC, Sutton RH, Lovell DK. A PROTRACTED CASE OF CRYPTOCOCCAL NASAL GRANULOMA IN A STALLION. Australian veterinary journal. 1981;57(6):287-91.
5. Lean NE, Ahern BJ. Antifungal non-invasive soak under general anaesthetic to treat fungal rhinitis in an Australian Quarter Horse gelding at pasture. Australian veterinary journal. 2018;96(8):297-301.
6. Davis EW, Legendre AM. Successful Treatment of Guttural Pouch Mycosis With Itraconazole and Topical Enilconazole in a Horse. Journal of Veterinary Internal Medicine. 1994;8(4):304-5.
7. Ludwig A, Gatineau S, Reynaud MC, Cadoré JL, Bourdoiseau G. Fungal isolation and identification in 21 cases of guttural pouch mycosis in horses (1998–2002). The veterinary journal (1997). 2005;169(3):457-61.
8. Watkins AR, Parente EJ. Salpingopharyngeal fistula as a treatment for guttural pouch mycosis in seven horses. Equine veterinary journal. 2018;50(6):781-6.

9. Jukic CC, Cowling NR, Perkins NR, Eps AW, Ahern BJ. Evaluation of the effect of laser salpingopharyngostomy on the guttural pouch environment in horses. Equine veterinary journal. 2020;52(5):752-9.

10. Kendall A, Bröjer J, Karlstam E, Pringle J. Enilconazole Treatment of Horses with Superficial Aspergillus Spp. Rhinitis. Journal of Veterinary Internal Medicine. 2008;22(5):1239-42.

11. Stewart AJ. Diagnosis and treatment of cryptococcal infections in horses. Equine Veterinary Education. 2020;32(11):576-9.

12. Stewart AJ. Conidiobolus coronatus fungal upper respiratory infections in horses. Equine veterinary education. 2019;31(6):301-2.

13. Sellon DC, Long MT, Eds. Equine Infectious Diseases. 2nd ed. St Louis: Elsevier Saunders; 2013.

14. Gilkerson JR, Bailey KE, Diaz-Méndez A, Hartley CA. Update on Viral Diseases of the Equine Respiratory Tract. The Veterinary clinics of North America Equine practice. 2015;31(1):91-104.

15. Kydd JH, Lunn DP, Osterrieder K. Report of the Fourth International Havemeyer Workshop on Equid Herpesviruses (EHV) EHV-1, EHV-2 and EHV-5. Equine veterinary journal. 2019;51(5):565-8.

16. Gibson JS, Slater JD, Awan AR, Field HJ. Pathogenesis of equine herpesvirus-1 in specific pathogen-free foals: primary and secondary infections and reactivation. Arch Virol. 1992;123(3-4):351-66.

17. Gilkerson J, Jorm LR, Love DN, Lawrence GL, Millar Whalley J. Epidemiological investigation of equid herpesvirus-4 (EHV-4) excretion assessed by nasal swabs taken from thoroughbred foals. Veterinary microbiology. 1994;39(3):275-83.

18. Diaz-Mendez A, Viel L, Hewson J, Doig P, Carman S, Chambers T, et al. Surveillance of equine respiratory viruses in Ontario. Canadian journal of veterinary research. 2010;74(4):271-8.

19. Black WD, Wilcox RS, Stevenson RA, Hartley CA, Ficorilli NP, Gilkerson JR, et al. Prevalence of serum neutralising antibody to equine rhinitis A virus (ERAV), equine rhinitis B virus 1 (ERBV1) and ERBV2. Veterinary microbiology. 2007;119(1):65-71.

Section 4 – Lower Respiratory

Contents

Chapter 1: Bacterial Pneumonia

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Early identification of pathogens is critical for a good response to treatment.
2. Mixed bacterial infections predominate, reflecting the aetiology of the disease.
3. Vaccination against EHV 1 and 4 may be useful to reduce the incidence of viral respiratory disease, but frequent vaccination is required (see section 16 - Immunisation).

Pneumonia not associated with travel is usually associated with other stressors, such as training, racing or mixing in new populations of horses. Initial infection with equine herpesvirus (EHV) 1 or 4 has been implicated as a predisposing risk but is rarely diagnosed. General anaesthesia and oesophageal obstruction are other historical risk factors. Mixed bacterial pathogens predominate, including one or a combination of *Streptococcus equi* subspecies *zooepidemicus*, members of the *Pasteurellaceae*, *E. coli* or anaerobes (48).

Diagnostics

A thorough clinical examination is critical for all horses. Horses with pneumonia typically have abnormal thoracic auscultation (rebreathing examination may be required) and fever identified. Ultrasonography is useful to detect regions of consolidated lung, abscesses and/or pleural effusions (for pleuropneumonia see chapter 9 in this section).

Haematology, serum fibrinogen and serum amyloid A (SAA) are useful for assessing hydration, the presence of endotoxaemia and the response to infection. The most common clinicopathological abnormalities are hyperglycaemia, band neutrophilia, hyperfibrinogenaemia, lymphopaenia and hypoalbuminaemia, reflecting stress and an inflammatory response.

Collection of a sterile tracheal wash for cytology and culture and sensitivity testing is critical.

Treatment

Therapy should be directed by culture and susceptibility results. Empirical use of broad-spectrum antimicrobial therapy is indicated pending results of cytology and culture and susceptibility. If dehydration is detected, oral or intravenous fluid therapy may be indicated. NSAIDs are not usually given, except to control excessive fever (> 39.5 °C), so that the reduction in body temperature can be used as an indication of the response to antimicrobial therapy.

Antimicrobials used

- Procaine penicillin G at 22,000 IU/kg IM q 12 h (21 day withdrawal time for racing) and gentamicin at 6.6 mg/kg IV q 24 h
- Metronidazole (25 mg/kg PO q 8 h) may be indicated when a pleural effusion is present or involvement of anaerobic bacteria is suspected.
- Trimethoprim-sulphonamide (30 mg/kg IV q 12 h) may be useful initial therapy, if there is concern about the withdrawal time for procaine penicillin G.

Prognosis

Good with early identification of infection and appropriate treatment. The case fatality rate was 27% in a recent study (48). Involvement of anaerobic bacteria has been associated with a worsening prognosis, although two recent studies found no difference (48, 49).

Chapter 2: Lung abscess (see Pleuropneumonia)

Chapter 3: Pleuropneumonia

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Early identification and treatment are key for successful outcomes.
2. Prolonged travel, with the head elevated, predisposes to disease.
3. Prophylactic antimicrobial therapy is not associated with a better outcome and is not recommended.

Pleuropneumonia was commonly known as 'travel sickness' or 'shipping fever' because of the association of this disease with land or air travel. Disease can be induced by periods of confinement with the head elevated, with significant increases in bacterial numbers occurring within 6 to 12 hours in most horses (50). Pneumonia results from increased aspiration of oropharyngeal organisms, or reduced clearance of lower airway secretions and contaminating organisms (51). The organisms commonly isolated from these horses are beta-haemolytic streptococci (nearly always *Streptococcus equi* subspecies *zooepidemicus*), *Pasteurella* spp. and *E. coli*, with obligate anaerobes found in large numbers after 5 days, when conditions suitable for the anaerobes develop (51). A delay in diagnosis and initiation of treatment has been associated with failure of horses to recover from pleuropneumonia. Pleural effusion commonly develops early in the course of disease and lung abscessation can occur in more chronic cases, especially if there is a delay in treatment. Antimicrobial prophylaxis with procaine penicillin, prior to confinement with head elevation for 24 to 48 hours, failed to reduce bacterial numbers or prevent accumulation of purulent lower airway secretions (52). Minimising the duration of confinement with head elevation, augmentation of the clearance of accumulated secretions and prompt identification of animals in which airway inflammation has extended into the pulmonary parenchyma remain the best ways of minimising transport-associated respiratory disease (52).

Diagnostics

Sterile tracheal washes (ideally transtracheal washes) for cytology and culture and susceptibility should be performed in all cases. Pleural fluid from both sides of thorax, and fluid from any abscesses, should be submitted for cytology and culture and susceptibility testing, as pathogens can differ between the two thoracic spaces, and between abscesses, because of compartmentalisation of infection in the pleural space.

Thoracic ultrasonography is useful for detecting the presence and volume of pleural effusion and identifying any peripheral abscesses, and for assessing the extent of disease, and monitoring the response to treatment.

Thoracic radiography can be useful for identifying any deep abscesses that cannot be visualised through aerated areas of the lungs on ultrasound. In ponies, young horses and even light breed horses, handheld radiography equipment can yield useful diagnostic images.

Haematology, fibrinogen and Serum Amyloid A are useful for assessing hydration and detecting the response to the infection.

Treatment

1. Broad spectrum antimicrobial therapy is recommended until cytology and culture and susceptibility results are available.
2. Drainage of the pleural fluid is key to success. Indwelling thoracic drains should be used for drainage of the effusion, if present, and any accessible abscesses.
3. Antimicrobial therapy should be continued until serum fibrinogen and Serum Amyloid A concentrations are consistently trending downwards, or until the pleural effusion and abscesses have resolved. Therapy is often prolonged.

Antimicrobials used

Empirical therapy (until culture and susceptibility results are known):

- Procaine penicillin G at 22,000 IU/kg IM q 12 h or benzyl penicillin G at 12,000 IU/kg IV q 6 h
- AND gentamicin at 6.6 mg/kg IV q 24 h
- AND metronidazole at 25 mg/kg PO q 8-12 h

Prognosis

Guarded. Improved with earlier identification and appropriate treatment.

Chapter 4: Rhodococcal pneumonia in foals

Authors: Gary Muscatello, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. *Rhodococcus equi* is a common cause of bronchopneumonia in foals, but subclinical infection is common and rarely requires treatment.
2. Extrapulmonary disease is common, with non-septic polysynovitis most reported.
3. Combination therapy with macrolides and rifampicin is still highly effective in Australia.
4. Multi-drug resistant strains are now common internationally, so active surveillance and judicious treatment regimens are therefore critical.

Rhodococcal pneumonia, caused by *Rhodococcus equi*, is a common condition in foals on many Australian thoroughbred studs and also in foals of other breeds. The disease is seen in foals within the first six months of life, with the bacterial pathogen present in the soil (53). *R. equi* typically accumulates in the foal's environment through a soil-faecal life cycle, with only virulent strains capable of causing disease. Typically, foals are most vulnerable to this pathogen in the first month of life, with inhalation of virulent strains of *R. equi* in dust the most common route of infection (54). The resulting bronchopneumonia is insidious in nature, with foals developing lung abscessation over the course of 2-4 weeks after exposure (54).

Drug resistant *R. equi,* to either macrolides or rifampicin, can occur and has been seen in many countries (55, 56, 57, 58). The prevalence of resistance to macrolides or rifampicin has increased over the past decade in the USA, from a base level of between 1-3% to now close to 20% in Kentucky (59). In Australia there is little published data evaluating the antimicrobial susceptibility of *R. equi* or minimum inhibitory concentrations (MICs), but there are occasional reports by diagnostic laboratories of the rifampicin-resistant strains (personal communications, Anne Blishen). Rifampicin resistance in *R. equi* results from mutations in the *rpoB* gene (56, 60). In the USA, macrolide-resistant *R. equi* contain erythromycin-resistance methylase (*erm*) genes. Strains that contain and express *erm* are resistant to all macrolides, lincosamides and streptogramin B (MLS_B) (59). Two different *erm* genes (*erm*(46) and *erm*(51)) can be acquired, with *erm*(46) frequently seen in isolates from foals. Clonal strains containing *erm* genes and *rpoB* mutations are now becoming prevalent in the USA, probably because of selection pressures imposed by large scale usage of rifampicin/macrolide regimens on farms (61). The presence of macrolide- and rifampicin-resistant *R. equi* (MRRE) represents a significant threat to the ongoing successful use of macrolide/rifampicin therapy to treat infection with *R. equi* in foals. Foals with clinical disease caused by a macrolide **or** rifampicin resistant strain have approximately seven fold higher odds of mortality when treated with macrolide and rifampicin combination therapy compared to those infected with susceptible strains (62). It is likely that clinical cases caused by MRRE strains will be at an even greater risk of therapeutic failure and mortality. Clonal MRRE strains are not restricted to the USA, with a recent study detecting them in Ireland, presumably as a result of international transport of horses (63). These observations point to the need for more surveillance for drug resistant *R. equi* strains in Australia.

The importance of monitoring and selective use of antimicrobials for treatment of *R. equi* pneumonia cannot be underestimated, to reduce selection for drug-resistant strains and, importantly, reduce environmental persistence of these strains in soil. Excessive use leads to environmental persistence of drug-resistant strains (64, 65). Furthermore, MRRE persists in the environment on farms that are using macrolides to treat subclinically affected foals. Reduced use of antimicrobials could potentially eliminate MRRE strains from the horse farm environment, indicating the need for good antimicrobial stewardship, even in the face of outbreaks associated with drug-resistant *R. equi*.

Low rates of treatment of subclinical disease in Australia, and sound clinical decision making based on foal monitoring, has enabled Australian studs to have a relatively low to negligible prevalence of rifampicin- or macrolide-resistant strains of *R. equi*. As there is no vaccine or effective foal-focused prophylaxis available to protect foals from *R. equi* pneumonia, there is a need to continue to manage cases with optimal antimicrobial stewardship at front of mind (66). Reserving treatment for those foals with progressive lesions and clinical signs should reduce antimicrobial usage and hopefully preserve the efficacy of the rifampicin-macrolide combination to treat *R. equi* pneumonia. However, the threat of introduction of MRRE strains through international transport of shuttle stallions and mares needs to be taken seriously and the frequency of culture and susceptibility testing needs to be increased to enhance surveillance for and detection of these drug-resistant strains (63). Environmental monitoring may also assist in gaining a more comprehensive picture of the *R. equi* resistance landscape. Management of clinical cases of *R. equi* pneumonia needs to be guided by sound clinical decision making and judicious treatment with rifampicin-macrolide combination therapy.

Diagnostics

Foals commonly present with fever, an increased respiratory rate and heart rate, abnormal lung sounds on auscultation, dyspnoea in severe cases, and coughing with or without nasal discharge. Extrapulmonary signs occur in ~55-75% of cases, and include enteritis, non-septic polysynovitis, and/or uveitis, amongst others.

Thoracic radiographs reveal a perihilar alveolar pattern consistent with consolidation, as well as discrete abscessation. The presence of nodular lung lesions and mediastinal lymphadenopathy in foals 1–5 months old is highly suggestive of infection with *R. equi*. Thoracic ultrasound can be used to evaluate both the thoracic and abdominal compartments. Ultrasound is best for identifying lesions of the peripheral lung and may miss abscesses that lie deep to aerated areas of lung.

Cytological evaluation of transtracheal wash samples reveals intracellular coccobacilli and can be used to guide appropriate antimicrobial treatment, pending culture results.

Routine complete blood counts and serum biochemistry reveals non-specific abnormalities consistent with infection and inflammation. Hyperfibrinogenaemia, followed by neutrophilic leukocytosis, are the most common abnormalities, but are non-specific and cannot be used to determine the prognosis in a foal. Serum amyloid A, another indicator of inflammation, is poorly correlated with the severity of disease caused by *R. equi* disease.

Thoracic ultrasonography has been used to screen 'at risk' foals prior to the development of overt clinical disease and obtain an early presumptive diagnosis of *R. equi* pneumonia (67). Typically, superficial abscesses can be easily visualised as hypoechoic encapsulated areas of consolidation, and linear hyperechoic artefacts known as 'comet tails' are also more abundant (68). Even though these features are not pathognomonic for *R. equi,* endemically affected farms tend to use thoracic ultrasonography as a tool for the diagnosis of cases.

The widespread adoption of thoracic ultrasonographic screening of foals on endemically affected farms can lead to an increase in observed prevalence of *R. equi* pneumonia, with farms using ultrasonographic screening having two-three fold greater numbers of cases than farms that don't (69). Early subclinical diagnosis is the likely cause of this. The farm's response to these subclinical cases is critical. Treatment of affected foals early and aggressively was once widely supported, but recent evidence suggests that, in many foals with mild to moderate lung pathology, lesions can resolve without antimicrobial therapy (70). Treatment protocols need to be adjusted with this in mind to ensure both the judicious use of antimicrobials and minimal selection pressure for resistance. The goal of clinicians should be to minimise the number of foals receiving antimicrobial treatment by monitoring and selectively treating foals with evidence of progressive lesions and clinical signs. On a large

breeding farm in Germany, a change in treatment criteria to exclude foals with subclinical *R. equi* pneumonia and minor ultrasonographic lesions decreased the number of foals that were treated from 80% to 50% with no impact on mortality (71).

Judicious use of antimicrobial therapy to treat *R. equi* will no doubt reduce selection for resistance to the current dual drug treatment regimen. The decision to treat should be based on data collected through sequential monitoring of the affected foal, with treatment implemented when there is evidence of pathological progression of disease and clinical signs. Monitoring by weekly thoracic ultrasonography, using abscess scoring, has been advocated in Europe (personal communication, Monica Venner). An abscess score is defined as the sum of the diameters of all focal areas of pulmonary consolidation, with diameters with scores greater than 20 cm, accompanied by a fever of > 39.5 °C for more than 2 days or dyspnoea, warranting treatment (71). If foals have an abscess score of less than 20 cm without fever or dyspnoea, ultrasonography monitoring should be performed and, if the abscess score increases by 5 cm within a week, antimicrobial treatment can then be justified (personal communication, Monica Venner).

Treatment

The intracellular location of *R. equi* influences the *in vivo* efficacy of antimicrobials used to treat it. Even though it is susceptible to a range of antimicrobials *in vitro*, there are a limited number of that are clinically efficacious. A combination antimicrobial therapeutic regimen using a macrolide and rifampicin is the treatment of choice.

The initial use of erythromycin and rifampicin to treat cases in the 1980s saw a significant reduction in foal mortality and consequently widespread adoption of this regimen (72). Newer generation macrolides, such as azithromycin and clarithromycin, have replaced erythromycin, based on improved bioavailability within cells, a perceived reduction in adverse effects and the reduced frequency of administration required to maintain therapeutic concentrations in the lungs (73, 74, 75). The combination of a macrolide and rifampicin is synergistic and the use of the two classes of drugs in combination reduces the likelihood of selection for resistance to either drug. Rifampicin (5 mg/kg PO q 12 h) is combined with either azithromycin (10 mg/kg PO q 24 h for the first 5 days and then every 48 h thereafter) or clarithromycin (7.5 mg/kg PO q 12 h). The length of treatment regimens for clinical cases is 2- 4 weeks, depending on their severity.

The efficacy of other drugs for the treatment of *R. equi* pneumonia has been explored in the face of resistant strains. The combination of doxycycline (10 mg/kg orally every 12 h) and azithromycin had comparable therapeutic effects to rifampicin and azithromycin combination therapy in a clinical trial in foals with mild or subclinical disease (76). In cases of rifampicin resistance, treatment using a macrolide and doxycycline combination appears to be safe and effective. Gentamicin was shown to be one of the more active drugs against *R. equi* in *in vitro* intracellular bactericidal assays, but it failed to reach mutant prevention concentrations in the lungs, so the use of this drug for the treatment of *R. equi* pneumonia is not supported by available evidence (77, 78). Gallium maltolate has shown promise in a small field trail, with comparable efficacy in resolving pulmonary lesions compared to clarithromycin and rifampicin therapy (79). However, more extensive efficacy trials in clinical cases are needed to support its use as an alternative treatment option for clinical cases (80). Bacteriophages selective for virulent *R. equi* are also being explored and may have application not only in environmental mitigation but also in foals to aid resolution of pulmonary lesions (81).

Macrolides are associated with adverse effects in foals and their dams. Hyperthermia can occur in foals, so care should be taken in warm-to-hot environments. Treatment of foals is also associated with severe antimicrobial-associated diarrhoea in their dams, presumably as a result of consumption of the drug in foal faeces.

Other supportive care is commonly required and includes judicious use of non-steroidal anti-inflammatories, intravenous fluids and, in some cases, nasal insufflation with oxygen.

Antimicrobials used

- Azithromycin (10 mg/kg PO q 24 h for the first 5 days and then every 48 h thereafter) OR clarithromycin (7.5 mg/kg PO q 12 h)
- AND rifampicin 5 mg/kg PO q 12 h

Prognosis

Survival rate is 60-90%, depending on disease severity and appropriate treatment. Fifty-four percent of thoroughbred or standardbred foals eventually went onto race in one US study (82).

Further reading

Rakowska A, Cywinska A, Witkowski L. Current Trends in Understanding and Managing Equine Rhodococcosis. Animals (Basel). 2020 Oct 18;10(10):1910. doi: 10.3390/ani10101910. PMID: 33081047; PMCID: PMC7603097 (83).

Giguère S, Hernandez J, Gaskin J, Miller C, Bowman JL. Evaluation of white blood cell concentration, plasma fibrinogen concentration, and an agar gel immunodiffusion test for early identification of foals with Rhodococcus equi pneumonia. J Am Vet Med Assoc. 2003 Mar 15;222(6):775-81. doi: 10.2460/javma.2003.222.775. Erratum in: J Am Vet Med Assoc. 2003 Nov 1;223(9):1300. PMID: 12675301 (84).

Passamonti F, Vardi DM, Stefanetti V, Marenzoni ML, Prato S, Cévese P, Coletti M, Pepe M, Casagrande Proietti P, Olea-Popelka F. Rhodococcus equi pneumonia in foals: an assessment of the early diagnostic value of serum amyloid A and plasma fibrinogen concentrations in equine clinical practice. Vet J. 2015 Feb;203(2):211-8. doi: 10.1016/j.tvjl.2014.08.033. Epub 2014 Nov 13. PMID: 25555337 (85).

Chapter 5: Fungal Pneumonia

Authors: Leanne Begg, Allison J. Stewart, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Fungal pneumonia is rare in immunocompetent horses.
2. Fungal elements found in tracheal washes are most likely due to environmental contamination.
3. Systemic treatment with antifungals can lead to a successful outcome.

Fungal pneumonia is rare in horses. There is usually underlying immunocompromise in cases of Aspergillosis, Candidiasis and Pneumocystosis but cases of Cryptococcosis, Histoplasmosis, Blastomycosis and Coccidioides can occur in immunocompetent horses. It has been hypothesised that pulmonary lesions due to *Aspergillus* spp. are most commonly the sequelae of mycotic invasion of the intestinal tract, secondary to severe acute enterocolitis. Septic foals rarely develop *Candida* spp. bacteremia. *Coccidioides immitis*, *Histoplasma and Blastomycosis* spp. have been associated with disease internationally. *Coccidioides immitis* is not present in Australia. *Histoplasma capsulatum* is generally associated with bat caves and bird waste.

Cryptococcal pneumonia due to infection with *Cryptococcus neoformans* is the most common systemic form of cryptococcal infection in the horse but is rare. The most common presentation is multiple, large, pulmonary cryptococcal granulomas, sometimes with a pleural effusion, or less commonly miliary interstitial granulomas distributed evenly throughout the lungs, suggesting haematogenous spread from a primary focus elsewhere. In both presentations granulomas are commonly found in the mesenteric lymph nodes, suggestive of the intestinal tract being the primary focus of infection.

Pneumocystis carinii can infect immunocompromised horses. *P. carinii* cannot be cultured, and diagnosis is based on the cytologic identification of characteristic morphologic features using specimens obtained by bronchoalveolar lavage rather than tracheal wash.

Diagnostics

Transtracheal wash cytology may reveal degenerate neutrophils and yeast cells (*Cryptococcus* spp., *Candida* spp.) or filamentous fungi (*Aspergillus* spp.), depending on the aetiology. The diagnosis should not be based on results of tracheal aspirates alone, as fungal elements are often found in tracheal washings of normal horses because of contamination from the environment. Aspirates from lung abscesses would be a better sample for fungal culture and lead to a definitive diagnosis. Antigen titres are useful for diagnosis and monitoring response to therapy, if available.

Treatment

Long term systemic treatment with an appropriate antifungal is usually required and this may be cost prohibitive. Ideally this should be based on culture and susceptibility results. See Table 4.1 for an overview of antifungal drugs and their common susceptibilities.

Systemic iodide therapy is inexpensive, but toxicity, characterised by excessive lacrimation, a non-productive cough, increased respiratory secretions and dermatitis, can occur (iodination). Although there are a few successful cases reported when iodide therapy was used as primary or adjunctive therapy (86), the overall efficacy of iodides is probably limited and there are more effective treatments now available. Iodides inhibit the granulomatous inflammatory process, but have very little, if any, *in vitro* antifungal activity.

Pneumocystis carinii can be treated with trimethoprim sulphonamides at 30 mg/kg PO q 12 hrs for several weeks or Dapsone (3 mg/kg PO q 12 h). The organism was reclassified from a protozoan to a fungus but lacks ergosterol in its cell wall, therefore antifungals are not effective.

Antimicrobials used

- See Table 4.1 for an overview of antifungal drugs and their common susceptibilities.

Prognosis

Guarded. When fungal infection occurs secondary to irreversible immunocompromise, treatment is usually hopeless.

Table 4.1. Systemic antifungals for use in horses - all use is extra-label.

Drug	Relative cost	Dose	Spectrum	Comments
Amphotericin B	Moderate	0.35 mg/kg in 1 L of 5% dextrose given over 1 h. Increase dose every 3 days by 0.1 mg/kg, until a maximum dose of 0.9 mg/kg is reached, for total course of 30 days (87) Premedication with flunixin meglumine 0.25 mg/kg IV is recommended.	Broad spectrum - *Aspergillus, Candida, Coccidiodes, Sporothrix, Mucor, Rhizopus, Cryptococcus, Sporotrichum, Conidiobolus, Pythium* spp. are generally susceptible. *Trichosporon* and *Pseudallescheria* spp. are often resistant.	Nephrotoxic. Monitoring of renal function with daily urine specific gravity, examination of urine sediment for casts and serum creatinine concentrations is recommended. No adverse effects in pregnancy in humans or laboratory animals. Limited reports of use in horses and no pharmacokinetic data reported.
Fluconazole	Moderate	14 mg/kg PO loading dose, then 5 mg/kg PO q 24 h (88)	Yeast and dimorphic fungi. Effective against Australian strains of *Cryptococcus gattii* in horses (73). *Mucor, Rhizopus, Paecilomyces, Scopulariopsis, Sporathrix, Alternaria,* and *Sporotrichum* spp. are generally	Has been associated with hepatotoxicity in humans, so care should be taken in horses with liver disease. Teratogenic and embryotoxic effects reported in humans and laboratory animals. Not recommended during pregnancy.

Drug	Relative cost	Dose	Spectrum	Comments
			susceptible, as are the algae *Prototheca* spp. *Aspergillus, Fusarium*, *Candida and Histoplasma* spp. are generally resistant.	
Voriconazole	High	4.0 mg/kg/day PO (89)	Drug of choice for invasive *Aspergillus, Candida, Cryptococcus, Scedosporium apiospermum, Bipolsaris*, and *Fusarium*	
Itraconazole	High	5 mg/kg PO q 24 h (90)	Broad spectrum - *Aspergillus, Cryptococcus, Paecilomyces, Scopulariopsis, Sporothrix, Alternaria,* and *Sporotrichum* are generally susceptible. MIC insufficient to treat *Fusarium, Mucor* or *Rhizopus* spp. Some *Candida* species, especially *Candida tropicalis*, are resistant.	Good activity against *Pythium insidiosum* when used in combination with terbinafine. Better bioavailability when administered as a solution, rather than as capsules.
Ketoconazole	Moderate	30 mg/kg PO q 12 h mixed with 0.2 N HCl by nasogastric tube (91)	Dermatophytes, yeasts and dimorphic fungi - *Candida, Scopulariopsis, Cryptococcus, Malassezia, Sporothrix, Microsporum* and *Trichophyton* spp. are generally susceptible.	Hydrochloric acid can cause irritation so should be given by nasogastric tube. Absorption may be improved with fasting.

Drug	Relative cost	Dose	Spectrum	Comments
Griseofulvin	Low	5-10 mg/kg PO q 24 h, after 2 weeks reduce to 5 g/450 kg (92)	Dermatophytes (*Trichophyton* and *Sporotrichum)* are generally susceptible. Systemic treatment using this drug is not recommended as topical therapy with iodine or chlorhexidine is usually effective for dermatophyes.	Contraindicated in the first 4 months of pregnancy. Safety after this is unknown. Monitor liver enzyme activity during treatment. No justification for use in horses now safer and more efficacious antifungals are available.
20% sodium iodide	Low	20-40 mg/kg IV q 24 h or 65-100 mg/kg 1-2 times weekly (93). If iodination occurs, sodium iodide should be withheld for 3-7 days and the dose reduced (typically by 20-50%) when therapy is reinstated.	Used widely to treat a range of fungal infections, but mechanism of activity is unknown. Efficacy is unknown. No longer recommended.	May cause abortion in pregnant mares or goiters in their foals. Itraconazole now preferred for treatment of *Sporothrix* spp.
Ethylenediamine dihydroiodide (EDDI) 80% iodide	Low	1-2 mg/kg PO q 12-24 h for 1 week, then 0.5-1 mg/kg q 12-24 h (94)	*Sporothrix* spp. infections have been successfully treated. Efficacy is unknown. No longer recommended.	
Potassium iodide	Low	10-70 mg/kg PO daily (over 1 or 2 doses) for 1 week then 0.5-1 mg/kg q 12-24 h (93)	Used widely to treat a range of fungal infections but mechanism of activity is unknown. Efficacy is unknown. No longer recommended.	May cause abortion in pregnant mares. Associated with neonatal goiter in humans.

Drug	Relative cost	Dose	Spectrum	Comments
Lufenuron oral suspension	High	5 mg/kg PO q 24 h (92)	Ineffective *in vitro* against *Aspergillus* and *Fusarium* spp.. Has been used to treat dermatophytosis in dogs.	Anecdotal reports of use in fungal endometritis. Caution is advised as no *in vitro* activity against many fungi.
Terbinafine		30 mg/kg PO q 24 h (95)	Broad spectrum. This dose regimen may exceed MIC for *Aspergillus flavus* for 8 hours and, in some horses, *A. niger*.	First pass metabolism is high, which limits utility.

Further reading

Begg LM, Hughes KJ, Kessell A, Krockenberger MB, Wigney DI, Malik R. Successful treatment of cryptococcal pneumonia in a pony mare. Aust Vet J. 2004 Nov;82(11):686-92. doi: 10.1111/j.1751-0813.2004.tb12155.x. PMID: 15977613. (96)

Stewart AJ, Cuming, R. Update of fungal respiratory disease in horses. Vet Clin North Am Equine Pract. 2015: 31(1);43-62. DOI: http://dx.doi.org/10.1016/j.cveq.2014.11.005

Stewart AJ. Fungal infections of the equine respiratory tract. Large Animal Internal Medicine 6th Edition 2019. Eds: Smith BP, Van Metre DC, Pusterla N. Elsevier, Philadelphia. 550-559

Chapter 6: Mycoplasma pneumonia

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Infrequently diagnosed cause of pneumonia in the adult horse and role as a primary pathogen is questionable. May have a role as a secondary pathogen but evidence is unclear.
2. Identified by culture of transtracheal washes.
3. PCR testing on respiratory samples useful, if available.

Mycoplasmas are an infrequently diagnosed cause of pneumonia in the horse in Australia, although many laboratories probably don't attempt to culture them. They can infect the respiratory tract and *Mycoplasma equirhinis*, *M. pulmonis* and *M. felis* have been isolated from horses with respiratory disease in France (97). *Mycoplasma felis* was isolated from a high proportion of a group of young Thoroughbred horses in training in the United Kingdom with lower respiratory tract disease (98). These horses were coughing with exercise and were pyrexic, had distal limb swelling and a mucopurulent exudate evident on endoscopy of their trachea. Morbidity was greater than 85% and seroconversion to *M. felis* was detected in 19/22 horses tested. Large numbers of *M. felis* were isolated from tracheal washes of four affected horses and no evidence of seroconversion to known viral pathogens was present. In Japan (99), *M. equirhinis* was isolated from 40% of 40 cases in an outbreak of respiratory disease in thoroughbred horses with coughing and a fever, and no other common aetiological agents were detected. The prevalence of *M. equirhinis* was not associated with disease severity in the French study and it was not considered to be a primary pathogen (100). However, *M. equirhinis* could play a role in the equine respiratory disease complex and may may act through dysregulation of the host immune response, as is well known in other respiratory complexes (100).

Diagnostics

Culture of the respiratory tract secretions can yield *Mycoplasma* spp., but they are very slow growing and can require specialist culture media. Suspicion of mycoplasmosis can be aroused if cytological signs of infectious lower airway disease are present, but bacterial culture is negative on standard media. PCR of respiratory secretions, if available, is useful for diagnosis. Haematology reveals an elevated white cell count, fibrinogen and Serum Amyloid A, consistent with infection.

Treatment

Antimicrobial therapy based on identification by culture or PCR. Antimicrobial susceptibility testing can be performed but is only available in specialist laboratories. Treatment should continue until resolution of clinical signs and reduction in while cell count, fibrinogen and Serum Amyloid A.

Antimicrobials used

- Tetracycline at 6 mg/kg IV q 12 h.
- Doxycycline 10 mg/kg PO q 12 h.

Prognosis

Good with sufficient course of treatment.

Chapter 7: Equine Asthma

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Antimicrobials are not indicated for treatment as no infectious agents are associated with this disease.
2. Management of environment is key.
3. Inhaled anti-inflammatory therapy is usually successful.

Equine asthma (previously known as Inflammatory Airway Disease or Chronic Obstructive Pulmonary Disease; COPD) is a chronic, non-infectious inflammatory disease affecting the lower airway of horses. The pathogenesis is probably multifactorial, but airborne environmental allergens cause induction and progression of equine asthma. The severity of disease is determined by the responsiveness of the individual to various inhaled allergens in the environment. There is also a possible genetic predisposition, as it is more prevalent in specific breeds and families (101). Viruses and bacteria have been linked to mild to moderate asthma, but a causative relationship is still inconclusive. Equine asthma is sub-classified into mild to moderate, affecting mainly younger performance horses, which may be subclinically affected or show intermittent coughing, poor performance and possibly a nasal discharge (previously inflammatory airway disease), while severe asthma typically occurs in older horses, which have laboured breathing at rest, as well as frequent coughing and exercise intolerance (102) (previously recurrent airway obstruction). Severe asthma is uncommon in Australia, likely due to the means of housing horses. Severe asthma may be seen in horses and ponies fed round bales.

Diagnostics

A thorough clinical examination, with particular attention to body temperature (which should be in the normal range of 37.5 – 38.5°C), cardiac (normal) and lung auscultation (normal or increased lung sounds with possible wheezes present, especially in severe disease). Endoscopy of the upper airway should be normal, but lower airway endoscopy may reveal mucopurulent material in the trachea. Haematology, fibrinogen and Serum Amyloid A should all be within normal ranges. A bronchoalveolar lavage is the diagnostic test of choice, with finding of greater than 5% neutrophils, 2% eosinophils or 2% mast cells, consistent with a diagnosis of equine asthma in most geographic locations. Neutrophils may reach >90% in cases of severe equine asthma.

Treatment

1. Removal of triggering factors is most important. Ideally house the horse outside permanently. Methods to reduce the dust content of bedding should be employed when outdoor housing is not possible. Methods to reduce the dust content of feed should be used in both scenarios.
2. Control of airway inflammation with corticosteroids and possibly provide relief of bronchospasm with bronchodilators.
3. Corticosteroids are ideally given using a nebuliser (aerosolisation of 2,744 µg of ciclesonide q 12 h for 5 days, then 4,116 ug once daily for 5 days; 1,500 µg budesonide q 12 h; fluticasone at 1-6 µg/kg q 12 h – all have a five day withdrawal time for racing), but can be given systemically (prednisolone at 1.1-2.2 mg/kg po q 24 h; dexamethasone at 0.05mg/kg po q 24 h; no information on withdrawal time for racing is available for either of these drugs).

Antimicrobials used

- Antimicrobials are not indicated for treatment of equine asthma.

Prognosis

Good with appropriate management changes and treatment.

Further reading

Kinnison et al, 2022. Mild-moderate equine asthma: a scoping review of evidence supporting the consensus definition. https://doi.org/10.1016/j.tvjl.2022.105865 (103)

Chapter 8: Exercise induced pulmonary haemorrhage (EIPH)

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Elevated pulmonary arterial pressures occur in all horses during strenuous exercise.
2. Some EIPH therefore occurs in most strenuously exercising horses.
3. A significant degree of EIPH can result in poor performance.

Haemorrhage from the lungs during exercise is described as EIPH. It is seen in the majority of thoroughbred and standardbred horses, and in other breeds, after strenuous exercise. The accepted pathogenesis of EIPH is stress failure of pulmonary capillaries because of the high pulmonary arterial pressures occurring in normal galloping horses (104). There is an association between the degree of EIPH and poor performance. The presence of blood in the lungs is thought to result in inflammation in the pulmonary parenchyma or airways. Clinical signs include the presence of blood at one or both nostrils after strenuous exercise, coughing after exercise and a history of poor performance.

Diagnostics

The presence of blood in the trachea on endoscopic examination after exercise or the presence of red blood cells, or more usually haemosiderophages, in bronchoalveolar lavage fluid.

Treatment

1. Furosemide (0.5 -1 mg/kg IV four hours prior to strenuous exercise) may reduce the severity and incidence of EIPH by reducing pulmonary vascular pressure and can be used as a training aid, but has a 54 h withdrawal time for racing (105).
2. Management changes to improve air quality in housing and use of nebulised corticosteroids (ciclesonide at 2,744 µg q 12 h for 5 days, followed by 4,116 µg q 24 h for 5 days; with a five-day withdrawal time for racing) may be useful in cases where there is inflammation associated with pulmonary haemorrhage.

Antimicrobials used

- Antimicrobials are not indicated in prevention or treatment of EIPH.
- Close monitoring of the body temperature of horses following a significant bleed is recommended, but antimicrobials are not indicated unless infection develops.

Prognosis

Horses can compete successfully following a diagnosis of EIPH, but preventative strategies, such as improving air quality, use of anti-inflammatory medications and furosemide in training, can all contribute to a decreased incidence of this condition.

Further reading

Hinchcliff KW, Couetil LL, Knight PK, Morley PS, Robinson NE, Sweeney CR, et al. Exercise Induced Pulmonary Hemorrhage in Horses: American College of Veterinary Internal Medicine Consensus Statement. Journal of veterinary internal medicine. 2015;29(3):743-58.(104)

Chapter 9: Equine multinodular pulmonary fibrosis (EMPF)

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Severe progressive interstitial lung fibrosis in older horses.
2. Association with EHV5.
3. Lung biopsy required for definitive diagnosis.

EMPF is a chronic, progressive, fibrosing interstitial lung disease of adult horses and has been associated with infection with equine herpesvirus type 5 (EHV5) (106), with cases reported in Australia since 2013 (107). Clinical signs include pyrexia, weight loss, depression, respiratory distress with tachypnoea, and coughing. Although infection with EHV5 is ubiquitous in horses, only a small proportion of horses develop respiratory signs and lung fibrosis, suggesting that host-specific factors, such as age and immunological response, could influence the development of EMPF. However, lung fibrosis has been induced in an experimental equine model using EHV5 isolated from affected horses (108). Affected horses have multiple nodules of interstitial fibrosis in their lungs.

Diagnostics

Transtracheal washes and bronchoalveolar lavage are often performed to rule out other pulmonary diseases. Lung radiographs are often the best indicators of progression of the disease and a lung biopsy is required to detect EHV5 by PCR. Bronchoalveolar lavage fluid should be examined for the presence of intranuclear herpesvirus-like inclusion bodies within alveolar macrophages (seen by both light and electron microscopy).

Treatment

Antiviral medications and anti-inflammatory drugs (prednisolone at 1-2 mg/kg PO q 24 h or dexamethasone at 0.02-0.2 mg/kg q 12-24 h IM or IV) are generally used. Successful treatment has been reported with valaciclovir at 40 mg/kg PO q 8 h for 1 week (109). However, a study on horses with EMPF examining the effect of 10 days of valacyclovir treatment on EHV5 viral loads reported no significant changes at the dose commonly used to treat horses (110). In another case series, acyclovir was used (in combination with dexamethasone) in two horses that responded to treatment (and three horses that did not respond) (111). The oral bioavailability of acyclovir in horses is poor, so extrapolation of these “successful” treatment examples into treatment guidelines is impossible.

Antimicrobials used

- Valaciclovir at 27 mg/kg PO q 8 h for 2 days then 18 mg/kg PO q 12 h (112). No evidence of efficacy in EMPF or for EHV5, but this therapy does reduce EHV1 load in experimentally infected horses.
- Acyclovir at 10 mg/kg IV diluted in 1 L isotonic crystalloid fluid given over 1 hour q 12 h, followed by oral treatment at 30 mg/kg PO q 8 h (however, acyclovir is minimally bioavailable orally).
- Continue until resolution of clinical signs and reduction in size of nodules on thoracic radiographs.

Prognosis

The successful treatment of a few cases of EMPF by administration of valacyclovir and corticosteroids has been reported, but the disease is generally considered to have a poor prognosis because of progressing pulmonary fibrosis and impaired respiratory function. Short term survival was 57%, with

only 24% of cases surviving longer than 3 months (113) and only 14% of cases surviving longer than 6 months (114) from discharge in recent studies. The only factor that was associated with increased short-term survival was corticosteroid administration, but corticosteroids have not been associated with long-term survival. Antiviral therapy (valaciclovir and acyclovir) has not been associated with improved short- or long-term survival.

Chapter 10: Acute Respiratory Distress Syndrome (ARDS – includes ALI and NERDS)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning & Leanne Begg

Key issues

1. *Chlamydia psittici* is a possible aetiological agent and is zoonotic, so personal protective equipment (PPE) should be worn when managing affected foals.
2. ALI/ARDS can develop following a wide range of inflammatory and non-inflammatory insults, but intrathoracic disease is the most common cause.
3. Disease progression is rapid and prompt identification of cases and referral to adequately resourced hospitals is critical.

Syndromes of acute respiratory distress, like those seen in humans, have been recognised in animals. ARDS develops as a complication of a primary disease or injury (usually, but not necessarily, thoracic) triggering an overwhelming and uncontrolled inflammatory process in the lungs, resulting in severe pulmonary damage, oedema and respiratory dysfunction. Patients have an acute onset of tachypnoea, hypoxaemia, bilateral infiltrates on chest radiographs, and loss of lung compliance without heart disease. Blood gas analysis is necessary for definitive diagnosis (Table 4.2), but where blood gas analysis has not been performed, some authors refer to the syndrome as acute interstitial pneumonia.

Neonatal Equine Respiratory Distress Syndrome (NERDS): A syndrome of severe respiratory distress occurring over the first 24 hours following birth. Distinct from ARDS, NERDS is a primary surfactant deficiency related to shorter gestation length and the lack of readiness for birth of the foetus. The defining features of NERDS are presented in Table 4.1.

Table 4.2. Definition of NERDS (Neonatal Equine Respiratory Distress Syndrome)

Etiology: Primary surfactant deficiency due to a failure of final foetal pulmonary surfactant metabolism maturation. Diagnosis requires meeting ALL below criteria:
1. Persistent hypoxaemia, progressive hypercapnia a. Hypoxaemia defined as Pa02<60mmHg taken with foal in lateral recumbency while breathing room air
2. Appropriate risk factors present (1 or more of 3 listed below) a. Very early gestational age (< 290 days OR < 88% of average of dam's previous gestation lengths b. Induction of parturition c. Caesarean section
3. Failure to develop normal immediate postpartum respiratory patterns: development/persistence of paradoxical breathing over the firs several hours of life, persistent tachypnoea
4. At ≤ 24 of age, 'ground glass' appearance of lateral thoracic radiographs (standing or lateral recumbency)
5. Absence of evidence of foetal inflammatory response syndrome (FIRS) at birth 1. Normal WCC, differential, and fibrinogen concentration for gestational age
6. Congenital cardiac disease ruled out as cause of tachypnoea

(Reproduced with permission from Wilkins , P (115).)

Acute Respiratory Distress Syndrome (ARDS): There is a disease continuum from Acute Lung Injury (ALI) to Acute Respiratory Distress Syndrome (ARDS). The onset of respiratory distress is acute and known risk factors must be present to make a diagnosis of ARDS. The definition of VetALI/VetARDS is provided in Table 4.2. Pneumonia caused by bacterial, and possibly viral, pathogens is a common predisposing cause, but other risk factors include:

1. Inflammation
2. Sepsis
3. Systemic inflammatory response syndrome (SIRS)
4. Severe trauma (long bone fracture, head injury, pulmonary contusions)
5. Multiple transfusions
6. Smoke inhalation
7. Near-drowning
8. Aspiration
9. Toxins (red maple leaves, especially when wilted, white snakeroot [rare in Australia], perilla mint [rare in Australia])

No single pathogen has been associated with ARDS. Case reports in the literature include infections with *E. coli*, *R. equi*, *Klebsiella*, *Leptospira* and *Streptococcus* spp. Viruses are also commonly implicated, although causation has not been established.

Equine Neonatal ALI/ARDS (EqNALI/EqNARDS): Gas exchange efficiency changes substantially in the equine lung in the first week of life. For this reason, the definition of ALI/ARDS above does not apply to neonatal foals and age-specific definitions are needed. The diagnosis of EqNALI/EqNARDS is essentially identical to VetALI/VetARDS, except that age-specific cut-offs are used for the PaO_2/FiO_2 ratio (cut-offs can be found in Wilkins et al., 2007(115)). Sepsis is probably the most common risk factor for EqNALI/EqNARDS, but in Australia infection with *Chlamydia psittici* should be considered as a differential diagnosis (116). *Chlamydia psittaci* is a zoonotic pathogen and personal protective equipment (PPE) should be worn for the management of foals with suspected or confirmed infection. Perinatal EHV1 infection should also be considered.

Table 4.3. Definition of VetALI/ VetARDS: Veterinary Acute Lung Injury and Acute Respiratory Distress Syndrome

Must meet at least one of each of the first 4 criteria; 5 is a recommended but optional measure
1. Acute onset (<72 hours) of tachypnoea and laboured breathing at rest
2. Known risk factors (see above)
3. Evidence of pulmonary capillary leak without increased pulmonary capillary pressure* (any one or more of the following): a. Bilateral/ diffuse infiltrate on thoracic radiographs (> 1 quadrant/ lobe) b. Bilateral dependent density gradient on CT c. Proteinaceous fluid within the conducting airways d. Increased extravascular lung water
4. Evidence of inefficient gas exchange (any one or more of the following): a. Hypoxaemia without PEEP or CPAPC and known FiO2 i. PaO2/FiO2 ratio 1. ≤ 300 mmHg for VetALI 2. ≤ 200 mmHg for VetARDS ii. Increased alveolar-arterial oxygen gradient iii. Venous admixture (non-cardiac shunt) b. Increased 'dead-space' ventilation

Must meet at least one of each of the first 4 criteria; 5 is a recommended but optional measure
5. Evidence of diffuse pulmonary inflammation a. TTW/BAL sample neutrophilia b. TTW/BAL biomarkers of inflammation c. Molecular imaging (PET)
* No evidence of cardiogenic oedema (one or more of the following): PaOP < 188 mmHg (adult horse) No clinical or diagnostic evidence supporting left heart failure (including echocardiography)
Acronyms: CT = computed tomography; PEEP = positive end expiratory pressure; CPAP = continuous positive airway pressure; PaOP = pulmonary artery occlusion pressure; FiO2 = fraction inspired oxygen; TTW = trans-tracheal wash; BAL = bronchoalveolar lavage; PET = positron emission tomography.

(Reproduced with permission from Wilkins , P (115).)

Diagnostics

The diagnostic test required are largely described above. Thoracic radiographs are useful, especially for foals, but diagnostic quality images can now be obtained in adults, especially in referral hospitals. Arterial blood gas and trans-tracheal washes are also important for making a diagnosis and deciding on treatment.

Treatment

Treatment is aimed at the primary disease, controlling inflammation, improving oxygenation and providing supportive care. Treatment needs to be prompt and is intensive, necessitating referral to a hospital with experience in intensive care.

Oxygen therapy is indicated in any neonate with a PaO2 less than 60 mm Hg or a SaO2 less than 90%. In humans, lung protective mechanical ventilation is a cornerstone of therapy, but is rarely available for treatment of horses in Australia. Continuous positive airway pressure using a commercial human CPAP device has been shown to improve respiratory support compared to oxygen insufflation in healthy sedated foals (117). The impact in diseased foals is unknown. Intranasal oxygen supplementation is the minimal acceptable form of oxygen support. Intratracheal oxygen supplementation could be considered in adults (118), but this has not been described in foals.

Treatment with potent anti-inflammatory drugs is critical and almost all cases are treated with corticosteroids. Dexamethasone (0.03–0.20 mg/kg IV q 12–24 h) and prednisolone sodium succinate (Solu-Delta-Cortef; 0.8–5.0 mg/kg IV q 8–12 h) are most common. Concurrent treatment with both flunixin (0.5-1 mg/kg IV q 12-24h) and corticosteroids is also common.

Given the association with a primary infectious disease, treatment with antimicrobials is warranted. Culture of lung fluid should be attempted. Trans-tracheal washes are generally better tolerated than endoscopy or BAL. Empirical, broad-spectrum antimicrobial treatment is indicated following sample collection. Intravenous benzyl penicillin is preferred over intramuscular procaine penicillin, as absorption can be delayed by the poor perfusion associated with severe disease and dehydration. Gentamicin is commonly used in combination with penicillin. Trimethoprim-sulphonamide may be an alternative if budgetary constraints prohibit use of benzyl penicillin.

Inhaled therapies are also commonly used. Use of nebulised frusemide (1 mg/kg q 8–12 h), bronchodilators, steroids and antimicrobials (gentamicin) have all been reported. The efficacy of these treatments is unknown, given the multi-modal therapy administered to horses with ALI/ARDS and the paucity of data in the literature. Other supportive therapy can include polyionic isotonic crystalloid fluid therapy and plasma (in neonates). Positive inotropes and vasopressors (dobutamine, adrenaline and vasopressin) should also be considered when hypotension is not responsive to fluid therapy.

Antimicrobials used

- Oxytetracycline at 6.6 mg/kg IV q 12 h when infection with *Chlamydia psittici* is possible, with re-evaluation of the need for antimicrobials after 5-7 days.
- In other cases, benzyl penicillin at 12-24,000 IU/kg IV q 4-6 h & gentamicin at 6.6-13.6 mg/kg IV q 24-36 h; with re-evaluation of the need for antimicrobials after 5-7 days.
- Trimethoprim-sulphonamide at 30 mg/kg IV q 12 h; with re-evaluation of the need for antimicrobials after 5-7 days.

Prognosis

Guarded. Survival rates of 60% have been reported in older foals, but they are often lower in neonatal foals. With appropriate treatment, survivors typically stabilise or improve within a few days. When ALI, but not ARDS, is present, the prognosis may be better. Clinicopathological variables on admission have not been useful in formulating a prognosis but may be useful in assessing the response to treatment.

The prognosis in foals infected with *C. psittaci* appears poor, with only 2/15 foals surviving in an Australian case series (116).

While the impact of this condition on future athletic performance is unknown, limited reports suggest that recovered foals can go on to have successful athletic careers.

Further reading

Wilkins P et al., 2007. State-of-the-Art Review Acute lung injury and acute respiratory distress syndromes in veterinary medicine: consensus definitions: The Dorothy Russell Havemeyer Working Group on ALI and ARDS in Veterinary Medicine. J Vet Emerg Crit Care. doi: 10.1111/j.1476 - 4431.2007.00238.x. (115)

Dunkel B, Dolente B, Boston RC. Acute lung injury/acute respiratory distress syndrome in 15 foals. Equine veterinary journal. 2005;37(5):435-40.(119)

Reference List

1. Hallowell KL, Hepworth-Warren KL, Dembek K. An updated description of bacterial pneumonia in adult horses and factors associated with death. Journal of veterinary internal medicine. 2024;38(5):2766-75.
2. Tomlinson JE, Reef VB, Boston RC, Johnson AL. Association of Fibrinous Pleural Effusion with Survival and Complications in Horses with Pleuropneumonia (2002–2012): 74 Cases. Journal of veterinary internal medicine. 2015;29(5):1410-7.

3. Raidal SL, Love DN, Bailey GD. Inflammation and increased numbers of bacteria in the lower respiratory tract of horses within 6 to 12 hours of confinement with the head elevated. Australian veterinary journal. 1995;72(2):45-50.

4. Racklyeft DJ, Love DN. Bacterial infection of the lower respiratory tract in 34 horses. Australian veterinary journal. 2000;78(8):549-59.

5. Raidal SL, Taplin RH, Bailey GD, Love DN. Antibiotic prophylaxis of lower respiratory tract contamination in horses confined with head elevation for 24 or 48 hours. Australian veterinary journal. 1997;75(2):126-31.

6. Muscatello G. Rhodococcus equi pneumonia in the foal – Part 1: Pathogenesis and epidemiology. The veterinary journal (1997). 2012;192(1):20-6.

7. Sanz M, Loynachan A, Sun L, Oliveira A, Breheny P, Horohov DW. The effect of bacterial dose and foal age at challenge on Rhodococcus equi infection. Veterinary microbiology. 2013;167(3-4):623-31.

8. Fenton CS, Buckley TC. Minimum inhibitory concentrations of erythromycin and rifampin for Rhodococcus equi during the years 2007-2014. IRISH VETERINARY JOURNAL. 2015;68(1):23-.

9. Fines M, Pronost S, Maillard K, Taouji S, Leclercq R. Characterization of mutations in the rpoB gene associated with rifampin resistance in Rhodococcus equi isolated from foals. Journal of clinical microbiology. 2001;39(8):2784-7.

10. Takai S, Takeda T, Nakano Y, Karasawa T, Furugoori J, Sasaki Y, et al. Emergence of rifampin-resistant Rhodococcus equi in an infected foal. Journal of Clinical Microbiology. 1997;35(7):1904-8.

11. Burton AJ, Giguere S, Sturgill TL, Berghaus LJ, Slovis NM, Whitman JL, et al. Macrolide- and rifampin-resistant rhodococcus equi on a horse breeding farm, Kentucky, USA. Emerging infectious diseases. 2013;19(2):282-5.

12. Huber L, Giguère S, Slovis NM, Carter CN, Barr BS, Cohen ND, et al. Emergence of Resistance to Macrolides and Rifampin in Clinical Isolates of Rhodococcus equi from Foals in Central Kentucky, 1995 to 2017. Antimicrob Agents Chemother. 2018;63(1).

13. Asoh N, Watanabe H, Tharavichitkul P, Sirisanthana T, Nagatake T, Fines-Guyon M, et al. Emergence of Rifampin-Resistant Rhodococcus equi with Several Types of Mutations in the rpoB Gene among AIDS Patients in Northern Thailand. Journal of Clinical Microbiology. 2003;41(6):2337-40.

14. Huber L, Giguère S, Cohen ND, Slovis NM, Hanafi A, Schuckert A, et al. Prevalence and risk factors associated with emergence of Rhodococcus equi resistance to macrolides and rifampicin in horse-breeding farms in Kentucky, USA. Veterinary microbiology. 2019;235:243-7.

15. Giguère S, Lee E, Williams E, Cohen ND, Chaffin MK, Halbert N, et al. Determination of the prevalence of antimicrobial resistance to macrolide antimicrobials or rifampin in Rhodococcus equi isolates and treatment outcome in foals infected with antimicrobial-resistant isolates of R equi. Journal of the American Veterinary Medical Association. 2010;237(1):74-81.

16. Val-Calvo J, Darcy J, Gibbons J, Creighton A, Egan C, Buckley T, et al. International Spread of Multidrug-Resistant Rhodococcus equi. Emerging infectious diseases. 2022;28(9):1899-903.

17. Riviere JE, Papich MG. Veterinary pharmacology and therapeutics. Tenth edition. ed. Hoboken, NJ: John Wiley & Sons Inc.; 2018.

18. Huber L, Giguère S, Hart KA, Slovis NM, Greiter ME, Dailey CA, et al. Association between antimicrobial treatment of subclinical pneumonia in foals and selection of macrolide- And rifampicin-resistant Rhodococcus equi strains at horse-breeding farms in central Kentucky. Journal of the American Veterinary Medical Association. 2021;258(6):648-53.

19. Sanz MG. Rhodococcus equi–What is New This Decade? The Veterinary clinics of North America Equine practice. 2023;39(1):1-14.

20. Muscatello G. Rhodococcus equi pneumonia in the foal – Part 2: Diagnostics, treatment and disease management. The veterinary journal (1997). 2012;192(1):27-33.

21. Ramirez S, Lester GD, Roberts GR. Diagnostic contribution of thoracic ultrasonography in 17 foals with Rhodococcus equi pneumonia. Veterinary radiology & ultrasound. 2004;45(2):172-6.

22. McCranken JL, Slovis NM, editors. Use of thoracic ultrasound for the prevention of Rhodococcus equi pneumonia on endemic farms. American Association of Equine Practitioners Annual Conference; 2009; Las Vegas, Nevada.

23. Venner M, Astheimer K, Lämmer M, Giguère S. Efficacy of Mass Antimicrobial Treatment of Foals with Subclinical Pulmonary Abscesses Associated with Rhodococcus equi. Journal of veterinary internal medicine. 2013;27(1):171-6.

24. Arnold-Lehna D, Venner M, Berghaus LJ, Berghaus R, Giguère S. Changing policy to treat foals with Rhodococcus equi pneumonia in the later course of disease decreases antimicrobial usage without increasing mortality rate. Equine veterinary journal. 2020;52(4):531-7.

25. Hillidge CJ. Use of erythromycin-rifampin combination in treatment of Rhodococcus equi pneumonia. Veterinary microbiology. 1987;14(3):337-42.

26. Jacks S, Giguere S, Gronwall RR, Brown MP, Merritt KA. Pharmacokinetics of azithromycin and concentration in body fluids and bronchoalveolar cells in foals. American journal of veterinary research. 2001;62(12):1870-5.

27. Womble AY, Giguère S, Lee EA, Vickroy TW. Pharmacokinetics of clarithromycin and concentrations in body fluids and bronchoalveolar cells of foals. American journal of veterinary research. 2006;67(10):1681-6.

28. Suarez-Mier G, GiguÈRe S, Lee EA. Pulmonary disposition of erythromycin, azithromycin, and clarithromycin in foals. Journal of veterinary pharmacology and therapeutics. 2007;30(2):109-15.

29. Wetzig M, Venner M, Giguère S. Efficacy of the combination of doxycycline and azithromycin for the treatment of foals with mild to moderate bronchopneumonia. Equine veterinary journal. 2020;52(4):613-9.

30. Giguère S, Berghaus LJ, Lee EA. Activity of 10 antimicrobial agents against intracellular Rhodococcus equi. Veterinary microbiology. 2015;178(3-4):275-8.

31. Cohen ND, Giguère S, Burton AJ, Rocha JN, Berghaus LJ, Brake CN, et al. Use of Liposomal Gentamicin for Treatment of 5 Foals with Experimentally Induced Rhodococcus equi Pneumonia. Journal of veterinary internal medicine. 2016;30(1):322-5.

32. Cohen ND, Slovis NM, Giguère S, Baker S, Chaffin MK, Bernstein LR. Gallium Maltolate as an Alternative to Macrolides for Treatment of Presumed Rhodococcus equi Pneumonia in Foals. Journal of veterinary internal medicine. 2015;29(3):932-9.

33. Giguère S, Cohen ND. Controversies in therapy of infections caused by Rhodococcus equi in foals. Equine veterinary education. 2018;30(6):336-41.

34. Muscat K, Venturini C, Giles C, Barton M, Muscatello G. Bacteriophages from Australian horse farms targeting Rhodococcus equi. Equine veterinary journal. 2021;53(S56):18-9.

35. Ainsworth DM, Eicker SW, Yeagar AE, Sweeney CR, Viel L, Tesarowski D, et al. Associations between physical examination, laboratory, and radiographic findings and outcome and subsequent racing performance of foals with Rhodococcus equi infection: 115 cases (1984-1992). J Am Vet Med Assoc. 1998;213(4):510-5.

36. Rakowska A, Cywinska A, Witkowski L. Current trends in understanding and managing equine rhodococcosis. Animals (Basel). 2020;10(10):1-12.

37. Giguere S, Hernandez J, Gaskin J, Miller C, Bowman JL. Evaluation of white blood cell concentration, plasma fibrinogen concentration, and an agar gel immunodiffusion test for early identification of foals with Rhodococcus equi pneumonia (vol 222, pg 775, 2003). Journal of the American Veterinary Medical Association. 2003;223(9):1300.

38. Passamonti F, Vardi DM, Stefanetti V, Marenzoni ML, Prato S, Cévese P, et al. Rhodococcus equi pneumonia in foals: An assessment of the early diagnostic value of serum amyloid A and plasma fibrinogen concentrations in equine clinical practice. The veterinary journal (1997). 2015;203(2):211-8.

39. Steiger RR, Williams MA. Granulomatous tracheitis caused by Conidiobolus coronatus in a horse. J Vet Intern Med. 2000;14(3):311-4.

40. Madison JB, Reid BV, Raskin RE. Amphotericin B treatment of Candida arthritis in two horses. Journal of the American Veterinary Medical Association. 1995;206(3):338-41.

41. Mullen KR, Fenn M, Hill JA, Alexander K, Gonzalez-Barrientos CR, Rodrigues-Hoffmann A, et al. Successful management of pneumonia and pyogranulomatous cranial mediastinitis due to Coccidioides species infection with fluconazole in a 3-year-old horse. Equine veterinary education. 2024;36(11):e270-e5.

42. Passler NH, Chan HM, Stewart AJ, Duran SH, Welles EG, Lin HC, et al. Distribution of voriconazole in seven body fluids of adult horses after repeated oral dosing. Journal of veterinary pharmacology and therapeutics. 2010;33(1):35-41.

43. Davis JL, Salmon JH, Papich MG. Pharmacokinetics and tissue distribution of itraconazole after oral and intravenous administration to horses. Am J Vet Res. 2005;66(10):1694-701.

44. Prades M, Brown MP, Gronwall R, Houston AE. Body fluid and endometrial concentrations of ketoconazole in mares after intravenous injection or repeated gavage. Equine veterinary journal. 1989;21(3):211-4.

45. Robinson NE, Sprayberry KA. Appendix 1 - Table of Common Drugs and Approximate Dosages. Robinson's Current Therapy in Equine Medicine. Seventh edition ed: Elsevier; 2015.

46. Baptiste KE. Antimicrobial Drug Use in Horses. In: Dowling PM, Prescott JF, Baptiste KE, editors. Antimicrobial Therapy in Veterinary Medicine. Sixth ed. New Jersey: Wiley-Blackwell; 2024.

47. White SD. Equine Bacterial and Fungal Diseases: A Diagnostic and Therapeutic Update. Clinical Techniques in Equine Practice. 2005;4(4):302-10.

48. Williams MM, Davis EG, KuKanich B. Pharmacokinetics of oral terbinafine in horses and Greyhound dogs: Pharmacokinetics of terbinafine horses and dogs. Journal of veterinary pharmacology and therapeutics. 2011;34(3):232-7.

49. Begg LM, Hughes KJ, Kessell A, Krockenberger MB, Wigney DI, Malik R. Successful treatment of cryptococcal pneumonia in a pony mare. Aust Vet J. 2004;82(11):686-92.

50. Martineau M, Castagnet S, Kokabi E, Tricot A, Jaÿ M, Léon A, et al. Detection of Mycoplasma spp. in horses with respiratory disorders. Equine veterinary journal. 2023;55(5):747-54.

51. Wood JLN, Chanter N, Newton JR, Burrell MH, Dugdale D, Windsor HM, et al. An outbreak of respiratory disease in horses associated with Mycoplasma felis infection. Veterinary record. 1997;140(15):388-91.

52. Uchida-Fujii E, Kinoshita Y, Niwa H, Maeda T, Nukada T, Ueno T. High prevalence of Mycoplasma equirhinis in Thoroughbred horses with respiratory symptoms in autumn 2018. Journal of Veterinary Medical Science. 2021:21-0163.

53. Martineau M, Kokabi E, Taiebi A, Lefebvre S, Pradier S, Jaÿ M, et al. Epidemiology and pathogenicity of M. equirhinis in equine respiratory disorders. Veterinary microbiology. 2023;287:109926-.

54. Gerber V, Tessier C, Marti E. Genetics of upper and lower airway diseases in the horse. Equine veterinary journal. 2015;47(4):390-7.

55. Couëtil LL, Cardwell JM, Gerber V, Lavoie JP, Léguillette R, Richard EA. Inflammatory Airway Disease of Horses—Revised Consensus Statement. Journal of veterinary internal medicine. 2016;30(2):503-15.

56. Kinnison T, McGilvray TA, Couëtil LL, Smith KC, Wylie CE, Bacigalupo SA, et al. Mild-moderate equine asthma: A scoping review of evidence supporting the consensus definition. The veterinary journal (1997). 2022;286:105865-.

57. Hinchcliff KW, Couetil LL, Knight PK, Morley PS, Robinson NE, Sweeney CR, et al. Exercise Induced Pulmonary Hemorrhage in Horses: American College of Veterinary Internal Medicine Consensus Statement. Journal of veterinary internal medicine. 2015;29(3):743-58.

58. Bayly W, Lopez C, Sides R, Bergsma G, Bergsma J, Gold J, et al. Effect of different protocols on the mitigation of exercise-induced pulmonary hemorrhage in horses when administered 24 hours before strenuous exercise. Journal of veterinary internal medicine. 2019;33(5):2319-26.

59. Wilkins PA. Equine multinodular pulmonary fibrosis: Diagnosis and treatment. Equine veterinary education. 2013;25(8):393-7.

60. Spelta CW, Axon JE, Begg A, Diallo ISI, Carrick JB, Russell CM, et al. Equine multinodular pulmonary fibrosis in three horses in Australia. Australian veterinary journal. 2013;91(7):274-80.

61. Williams KJ, Robinson NE, Lim A, Brandenberger C, Maes R, Behan A, et al. Experimental Induction of Pulmonary Fibrosis in Horses with the Gammaherpesvirus Equine Herpesvirus 5: e77754. PloS one. 2013;8(10).

62. Schwarz B, Schwendenwein I, van den Hoven R. Successful outcome in a case of equine multinodular pulmonary fibrosis (EMPF) treated with valacyclovir. Equine veterinary education. 2013;25(8):389-92.

63. Easton-Jones CA, Madigan JE, Barnum S, Maxwell LK, Taylor SD, Arnesen T, et al. Effect of valacyclovir on EHV-5 viral kinetics in horses with equine multinodular pulmonary fibrosis. Journal of veterinary internal medicine. 2018;32(5):1763-7.

64. Wong DM, Belgrave RL, Williams KJ, Del Piero F, Alcott CJ, Bolin SR, et al. Multinodular pulmonary fibrosis in five horses. Journal of the American Veterinary Medical Association. 2008;232(6):898-905.

65. Maxwell LK, Bentz BG, Gilliam LL, Ritchey JW, Pusterla N, Eberle R, et al. Efficacy of the early administration of valacyclovir hydrochloride for the treatment of neuropathogenic equine herpesvirus type-1 infection in horses. American journal of veterinary research. 2017;78(10):1126-39.

66. Craven A, Todd-Donato A, Stokol T, Liepman R, Glasberg I, Wilkins P, et al. Clinical findings and outcome predictors for multinodular pulmonary fibrosis in horses: 46 cases (2009-2019). Journal of veterinary internal medicine. 2024;38(3):1842-57.

67. Easton-Jones CA, Cissell DD, Mohr FC, Chigerwe M, Pusterla N. Prognostic indicators and long-term survival in 14 horses with equine multinodular pulmonary fibrosis. Equine veterinary education. 2020;32(11):41-6.

68. Wilkins PA, Otto CM, Baumgardner JE, Dunkel B, Bedenice D, Paradis MR, et al. Acute lung injury and acute respiratory distress syndromes in veterinary medicine: consensus definitions: The Dorothy Russell Havemeyer Working Group on ALI and ARDS in Veterinary Medicine. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2007;17(4):333-9.

69. Gough SL, Carrick J, Raidal SL, Keane S, Collins N, Cudmore L, et al. Chlamydia psittaci infection as a cause of respiratory disease in neonatal foals. Equine veterinary journal. 2020;52(2):244-9.

70. Raidal SL, McKean R, Ellul PA, Nielsen SG, Quinn CT. Effects of continuous positive airway pressure on respiratory function in sedated foals. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2019;29(3):269-78.

71. Floriano D, Watkins AR, Hopster K. Intratracheal oxygen administration increases FIO2 and PaO2 compared with intranasal administration in healthy, standing horses. American journal of veterinary research. 2022;83(5):450-4.

72. Dunkel B, Dolente B, Boston RC. Acute lung injury/acute respiratory distress syndrome in 15 foals. Equine veterinary journal. 2005;37(5):435-40.

73. Secombe CJ, Lester GD, Krockenberger MB. Equine Pulmonary Cryptococcosis: A comparative literature review and evaluation of fluconazole monotherapy. Mycopathologia. 2017;182(3-4):413-423.

Section 5 – Dentistry

Contents

Chapter 1: General Dentistry

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The use of antimicrobials is not indicated in most dental interventions. Even in more advanced cases of dental or sinus disease (see section 5, chapter 2), where bacterial infection is suspected or confirmed, the use of antimicrobials is not consistently necessary. Conservative or tooth-preserving treatment in horses has become an option in recent years, however, our ability to perform endodontics or periodontal treatments is limited by the often-advanced state of dental disease in horses at first presentation to a veterinarian. Dental extraction therefore becomes the most appropriate option in many cases. Preservation of the tooth may be possible when disease is identified in its early stages and antimicrobials play a limited role in our ability to achieve this.

The surface of the equine oral cavity is colonised by a variety of microorganisms, and ~50% of the oral microflora cannot be cultured using conventional techniques (120). Aerobic and anaerobic bacteria have been detected in both healthy and diseased oral cavities (121), with samples from healthy horses showing lower diversity (122). The dominant aerobic genera in the oral cavity of diseased horses were *Streptococcus* spp. and *Actinomyces* spp. (123). A shift in the oral bacterial flora towards predominantly anaerobic and Gram-negative bacteria has been described in horses with periapical abscesses, necrotic pulps and periodontal disease (122, 124, 125). Bacterial genera isolated from swab samples of extracted teeth largely corresponded to those identified in blood cultures during and after tooth extraction of these same horses (123).

i. **Equine odontoclastic tooth resorption and hypercementosis (EOTRH)** is a disease with an unclear aetiopathogenesis. In horses with EOTRH of the incisors, bacteria from the 'red complex', such as *Treponema* and *Tannerella* spp., were isolated significantly more frequently than in healthy horses (126). However, antimicrobial therapy has not found to be beneficial in reducing the progression of the disease. At present extraction of the affected teeth is the only valid treatment option available (see details on extraction below).

Perioperative antimicrobials for dental extractions. Transient bacteraemia of oral origin has been described after dental surgical manipulation in humans and dogs, and has also been detected during and after oral extraction in horses (123). The clinical significance of this bacteraemia is unclear, as none of the horses in this study developed complications related to the bacteraemia. Nevertheless, transient bacteraemia may lead to sepsis and other serious diseases of individual organs. Only a few case reports describe infectious and sometimes

lethal complications, such as arthritis, endocarditis, meningitis or pneumonia, after tooth removal or sinus surgery in horses (127, 128, 129). The bacteria implicated were those that are usually isolated from the equine oral cavity or infected paranasal sinuses.
The severity of the sequelae caused by bacteraemia raises the question of whether horses should be given an antimicrobial drug prophylactically when teeth are extracted (123).The prophylactic administration of antimicrobials is not generally recommended for people undergoing dental treatment. It is known that tooth brushing, normal chewing and the use of dental floss can lead to bacteraemia, and that the risk increases in the presence of dental disease (130). Pre-existing conditions, such as congenital heart disease or artificial heart valves, are an indication for the prophylactic administration of antimicrobials to human dental patients when the apical or gingival tissue is damaged (130). However, antimicrobial drugs cannot prevent the occurrence of bacteraemia and there is controversy in human dentistry about whether antimicrobials can minimise the incidence, severity or duration of bacteraemia, as there is insufficient research to make a determination (131, 132). However, national and international guidelines no longer recommend their use, except under very limited circumstances (133). Ultimately, it cannot be determined whether the risks and costs of antimicrobial administration outweigh any beneficial effect, even preventing severe diseases like endocarditis (131).

Diagnostics

Comprehensive evaluation of horses suspected of dental disease is crucial. Examination of the oral cavity with the aid of a mirror is the minimal acceptable practice. A better option to detect subtle changes, such as open pulp cavities, small fistulas, dental cracks or other externally unidentifiable pathologies, is the use of oroscopy. Radiography is a crucial addition to the identification of dental pathology, but its sensitivity and specificity is relatively low. Radiography is particularly poor for the identification of apical infections in the early stages, when antimicrobial therapy may be successful. Computed tomography is the gold standard in the identification of early onset dental disease and should be recommended in cases with suspected disease when radiographic signs are absent.

Treatment

Randomised controlled trials comparing treatment of horses with dental disease with or without antimicrobials have not been performed. Our clinical experience and reports from case series show that systemic treatment with antimicrobials alone in horses with deep tooth fractures, open pulps or other serious pathological findings is rarely successful. One study reported only 10% of acute apical infection of the caudal maxillary molars with secondary sinusitis respond favourably to systemic antimicrobial therapy. This appeared to be particularly true in young horses with wide open pulp canals and a good blood supply to the common pulp cavity which are far more likely to respond favourably to antimicrobial treatment than older individuals (134). In these cases, a combination of trimethoprim-sulphonamide and metronidazole is recommended for systemic treatment (135). Horses with chronically diseased teeth can usually only be helped by extracting the affected tooth in order to eliminate the cause of the infection and minimise secondary damage (136).

Apical infection: If identified in very early stages, one week of doxycycline (10 mg/kg PO q12h) or trimethoprim-sulphonamide (30 mg/kg PO q12h) may be attempted. Anti-inflammatory therapy is essential.
Through progression of caries, dental fissures or bacteraemia, bacterial contamination of pulpar tissues is possible but the main insult to pulp tissue is the inflammatory response. Once the inflammatory cascade is initiated the confined nature of the pulp chamber leads to a

compartment syndrome-like scenario. Increasing intrapulpal pressure compromises vascular supply, leading to pulp necrosis. At this stage, even if bacteria are present, the devitalised tissue no longer permits effective antimicrobial penetration. Therefore, systemic antibiotics have little to no therapeutic value once the pulp is necrotic. Clinical outcomes hinge not on pharmacological intervention, but on timely mechanical management—either by decompression, endodontic therapy (where feasible), or extraction. Relying on antimicrobials alone delays definitive care and contributes unnecessarily to resistance selection.
Endodontic treatment (therapy addressing the inside of the tooth thereby preserving the tooth) has become an option with variable to good results but requires referral to an equine dental specialist. Successful treatment of five out of six cases of apical infection caused by patent infundibula has been described (137). An orthograde endodontic technique applied in 700 cheek teeth reported an 80% success rate in 474 follow up cases (138). More recently a 75% success rate in endodontic treatment and restoration of incisor teeth affected with apical disease was shown (139).

ii. **Dental fractures:** In parasagittal uncomplicated (not exposing pulp cavities) fractures, conservative treatment is favoured. This does not include antimicrobials as no vital tissues are exposed. Monitoring of progression is advised.

In case of complicated fractures with fresh exposure of the pulp cavities, pulp capping is recommended. This also is not an indication for the use of antimicrobials.

Teeth with complicated chronic fractures with evidence of apical disease and sagittal fractures with apical communication are best extracted.

iii. **Diastema and Periodontal disease:** In cases of diastema and associated periodontal disease, local treatment is advisable. Debridement of the affected area, diastema widening, occlusal grooves and specific odontoplasty are all treatments that allow for the management of diastema and periodontal disease. Extraction of teeth with an elevated periodontal disease score (140) may be required. Very rarely are antimicrobials required either locally or systemically. Some recurrent cases of periodontal disease associated with diastema may require local antiseptic application.

iv. **Peripheral caries:** Peripheral caries, although including a bacteriological component in their aetiology, are not amenable to be treated with antimicrobials either locally or systemically. The treatment is composed of management of epidemiological factors such as reducing oaten hay in the diet, increasing access to pasture and reducing reliance on concentrate feed and reducing acid (by not feeding silage or acidic water) (141).

v. **Infundibular caries:** Restoration of the infundibular structure is advised, depending on the degree of the caries and the age of the tooth, to reduce progression of the pathology and avoid further sagittal fracture and apical infection. Specialist referral is required. No antimicrobials are indicated.

vi. **EOTRH:** Extraction is currently the only viable option for EOTRH affected teeth. The rationale to provide antimicrobials following extraction is debatable in EOTRH cases as infection is present preoperatively and antimicrobial treatment has not been associated with resolution of disease. In the clinical experience of the authors, antimicrobial treatment is not necessary for an undisturbed healing process unless co-morbidities are present. A maximum treatment duration of 5 days is advised.

vii. **Extractions:** The administration of antimicrobials to horses undergoing classical uncomplicated oral extractions had no effect on outcome or the level of complications (142).

The preoperative use of antimicrobials for dental surgery is indicated only if secondary diseases such as painful, reactive osteitis (e.g. localised bony swelling with ipsilateral lymphadenitis), purulent fistula tracts, sinusitis or meningitis already exist or if there is a very high risk of them developing. In cases with known immunodeficiency or simultaneous application of high dose glucocorticoids, the use of antimicrobials, and in particular bactericidal antimicrobials, is indicated (143). In horses undergoing minimally invasive transbuccal screw extractions, lower rates of complications have been shown when perioperative antimicrobials (discontinued after surgery) are administered (142).

Table 5.1. Recommendation for perioperative antimicrobials for equine dental disease

	Antimicrobial	Dose	Timing	Duration
Healthy horse, uncomplicated oral extraction	None OR			
	Benzyl penicillin OR	22,000 IU/kg (12 mg/kg) IV	30 – 60 minutes before the start of surgery	Re-dose every 80 minutes Discontinue after surgery
	Procaine penicillin	22,000 IU/kg (22 mg/kg) IM	3.5 hours before the start of surgery	Single dose only
Concurrent disease or when using minimally invasive transbuccal extraction (MTE)	Benzyl penicillin OR	22,000 IU/kg (12 mg/kg) IV	30 – 60 minutes before the start of surgery	Re-dose every 80 minutes Discontinue after surgery
	Procaine penicillin	22,000 IU/kg (22 mg/kg) IM	3.5 hours before the start of surgery	Single dose only

In routine cases without co-morbidities horses should be closely monitored post-operatively to detect early signs of complications that could be attributable to bacteraemia or infection, such as fever or tachycardia. The use of serial SAA samples can aid in identification of potential infectious complications. The use of antimicrobials should then be discussed and considered on a case-by-case basis only if problems arise.

Sequestrum formation can follow extraction. In the absence of peripheral signs of wound infection, the administration of antimicrobials is not indicated. Damaged and sequestrating bone requires a long time, sometimes weeks, before demarcating. Once fully sequestrated, removal of the bone fragments will lead to rapid resolution with granulation of the socket and

adequate healing. The negative impacts of long duration antimicrobial treatment in these cases far outweighs the potential and unproven benefits.

viii. **Mandibular draining tracts:** In cases of mandibular draining tracts, administration of antimicrobials is normally unsuccessful. Temporary resolution may be achieved but considering they mostly occur due to chronically infected dental apices, identification of the causative tooth and extraction or endodontic treatment is the only effective treatment option.

Persistent mandibular draining tracts can also develop following extraction of a tooth. Bone sequestration or remaining teeth fragments in the alveolus are common conditions related to a non-healing, recurrent or persistent fistulisation following extraction of a tooth. Repeat oral inspection and imaging, sometimes requiring CT for proper identification may be required to identify the fragments or sequestrum. Antimicrobial treatment is highly unlikely to result in resolution.

If cellulitis accompanies the draining tract antimicrobials should be administered for 3-5 days.

Antimicrobials used

- Procaine Penicillin 22,000 IU/kg IM q12 h or benzyl penicillin 22,000 IU/kg IV q6 h
- Trimethoprim-sulphonamide 30 mg/kg PO q12 h
- Doxycycline 10 mg/kg PO q12 h
- Metronidazole 25 mg/kg PO q12 h
- For duration please see disease specific recommendations above.

Prognosis

Prognosis for dental disease resolution is generally good to excellent but is highly reliant on the appropriate diagnostics and removal of the underlying cause. Ongoing alveolar sequestration following extraction, formation of oro-sinus/nasal/cutaneous fistulas, and ongoing sinus discharge are all complex complications of dental disease which require more complex surgical interventions for resolution.

Prognosis for resolution of apical infection is highly dependent on the cause and the chronicity of the infection. In many cases antimicrobials will fail, particularly considering the pulpar tissue present in the teeth is often necrotic and antimicrobial penetration weak to non-existent.

Chapter 2: Sinusitis

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Key issues

1. Differentiation between primary and secondary aetiologies is key
2. Client communication on possible need for further step-wise diagnostics is advisable upon initial consultation.

There are many causes of sinusitis in the horse. Determining the precise origin can be challenging but crucial for a successful outcome.

Sinusitis can be primary or secondary. Primary sinusitis is caused by infection with bacteria, viruses or fungi without a predisposition or previous illness. In secondary sinusitis there is a clear underlying cause/pathology that will maintain the infection. Secondary sinusitis occurs, for example, as a result of dental disease, paranasal cysts, trauma, fistulas or neoplasia. The diagnosis, and especially the differentiation between a primary and secondary disease of the paranasal sinuses is not always straight forward but crucial to effectively resolve the infection. Extensive and repeated clinical (oral exam, trans-nasal endoscopy) and imaging diagnostics (radiographs, CT) may be required to pin-point an underlying cause.

Oral bacteria can penetrate into the sinus through the, sometimes very thin, alveolar bone and into the maxillary sinuses. Deep periodontal pockets, fractured teeth, open pulps, tooth root abscesses of various origin are some of the more common dental aetiologies.

A shift in the oral bacterial flora towards predominantly anaerobic and Gram-negative bacteria has been described in horses with periapical abscesses, necrotic pulps and periodontal disease (125, 144). However, research using advanced bacteriology techniques could not differentiate between primary and secondary sinusitis based on culture results (145).

In other secondary sinusitis cases, the inciting cause may not be infectious in origin. Sinus cysts are space occupying structures that are not infectious yet cause recurrent irritation of the sinus that results in chronic discharge. Frontal or maxillary fractures can result in presence of small bone sequestrate that act as foreign bodies and also result in discharge, as do neoplastic processes. Treatment should therefore be focused primarily on removing the underlying cause identified.

Diagnostics

Clinical examination is generally not very rewarding in differentiating primary from secondary sinusitis. Elevated temperature, nasal discharge – usually purulent, foetid odour from the nostril, dull percussion of the sinuses are often present for both. Facial swelling over the sinuses may also be present, depending on the underlying cause. On initial presentation, a thorough oral examination should be performed to determine if a clear dental cause of the sinusitis is present (deep periodontal pocket, open pulp(s), fractured tooth, draining tract etc).

Imaging:

Radiology of the sinuses and adjacent teeth maxillary 08 to 11 are required to investigate ongoing sinusitis. This may need to be done after flushing of the sinuses to remove accumulated pus to ensure that extensive fluid lines do not complicate diagnoses of subtle dental causes. Widening of the periodontal ligament space, blunting of the tooth roots, sclerosis of the alveolar bone and a ”halo” around one or more tooth roots are some of the indicators of dental disease. Sensitivity of radiographs for identifying dental disease remains around 75% (146). However, reviews of sinus disease highlight

that the secondary causes of sinusitis are not identified in about half the cases on first radiographic examination (147). Apart from the ability to identify dental causes of sinusitis, radiographs are helpful in diagnosing the presence of masses, cysts or simply the accumulation of inspissated pus (most often in the ventral conchal sinus) within the sinus complex.

Computed Tomography is regarded as the gold standard for diagnosis of sinus disease. The sensitivity and specificity of the CT surpasses that of traditional radiography with scans having shown 97% sensitivity (148). Considering the extensive 3D anatomy of the sinus complex, clients should be offered the option to have a CT performed, particularly in cases of chronic or persistent sinusitis.

Scintigraphy has shown a good sensitivity to differentiate between dental and non-dental related sinusitis (149) but CT is superior as scintigraphy remains relatively nonspecific in terms of other aetiological causes of sinusitis.

Ultrasound has limited value in the workup of sinusitis. Unless secondary sinusitis is suspected to be caused by facial trauma, in which superficial bone sequestration is involved. Ultrasound is useful for rapid identification of a sequestrum but again CT is superior. Cases of suture periostitis can also be the origin of secondary sinusitis and identification of sequestra by means of ultrasound is easily achieved in those cases (150).

Oral **endoscopy** (oroscopy) has become a critical tool in the investigation of the oral cavity. Dental pathologies extending to the occlusal surface can most clearly be visualised with oroscopy. Detailed examination should focus on occlusal surface of pulp cavities, possibly identifying non vital exposed pulp (look for gas bubbles forming at the surface, use probes to identify). Particular attention should be given to the gingival margins as draining tracts can be present along affected teeth.

Trans-Nasal endoscopy will allow identification of drainage from the sinonasal angle. Nasal discharge is often mistaken for sinusitis, however there are many other origins of nasal discharge like rhinitis, nasal foreign bodies, 06-08 apical infections and others. Before investigating sinusitis cases, it is recommended to confirm the discharge is actually originating from the sinus.

Sinoscopy is best performed through a frontal approach with removal of the bulla of the maxillary septum, as this will provide a full overview of the sinus and may aid in diagnostic as well as therapeutic approach. If available, small diameter flexible endoscopes allow for exploration and intervention which can be done through a transnasal approach with relatively successful outcomes (151).

Sampling:

Acquisition of a sinus sample, via trephination with 14G needle, for culture and susceptibility may be useful in some cases. The results of the C&S will not differentiate between primary and secondary causes. Anaerobic culture should be included but is not always available.

A standard process for evaluating sinusitis cases is useful and is provided here (Figure 5.1).

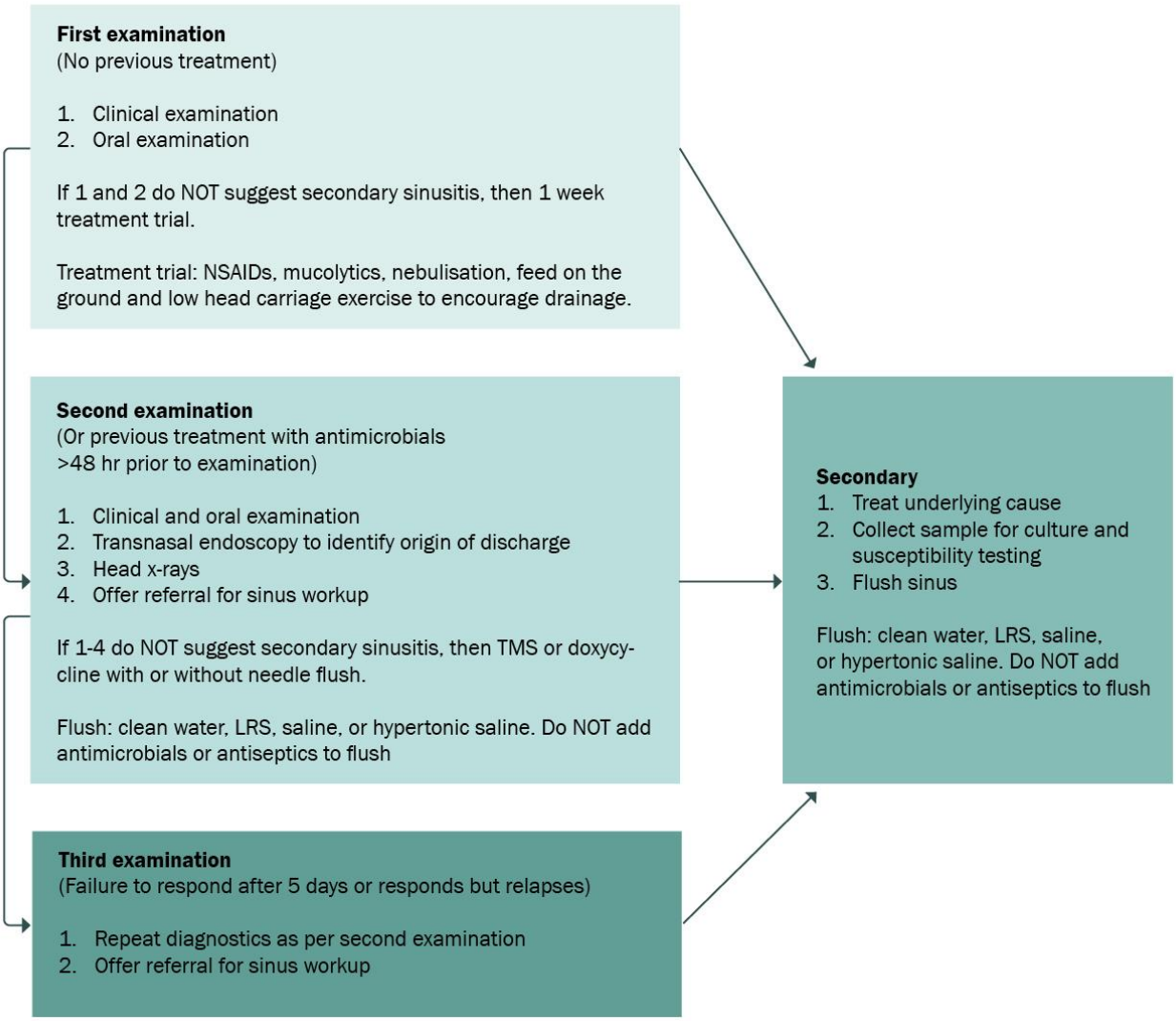

Figure 5.1. Process for investigating equine cases with suspected sinusitis.

Treatment

Initial management of non-specific sinusitis may include NSAIDS, mucolytics and adequate drainage (feed the horse on the ground, low head carriage exercise) for 7 days to assess response (Figure 5.1).

Second-line treatment may include a 5-day course of antimicrobial therapy (typically using trimethoprim-sulfonamide or doxycycline), with or without sinus lavage. However, this empirical approach is only justified if a thorough investigation, including additional or repeated examinations, has failed to identify an underlying or secondary cause (e.g. dental pathology, cysts, neoplasia, foreign body). A lack of clinical response to this therapy, or recurrence of sinusitis following withdrawal of antimicrobials, should prompt a more comprehensive diagnostic work-up (see above).

If a tooth/teeth are found to be the cause of the sinusitis, exodontia is required to remove the source of infection. If another secondary cause is identified, removal of the cause (cyst, sequestrum, fungal plaques, inspissated pus etc) is required to achieve resolution. Discontinue antimicrobials until treatment for underlying cause is undertaken.

Prolonged antimicrobial therapy for sinusitis has been associated with development of inspissated pus or fungal overgrowth within the sinus complex. In these cases, further antimicrobial treatment is contraindicated.

If diagnostics do not identify any underlying causes, initial treatment with antimicrobials may be justified. In case of re-occurrence of disease, continuation of antimicrobial therapy is not advised and repeated and/or more advanced investigations should be pursued.

Antimicrobials used (include recommended dose rates/duration)

- Trimethoprim-sulphonamide – 30 mg/kg PO q12h for 5 days
- OR Doxycycline – 10mg/kg PO q12h for 5 days
- OR Penicillin procaine - 22,000 IU/kg (22 mg/kg) IM q12 for 5 days

Prognosis

Prognosis for sinus disease resolution is generally good but is highly dependent on the aetiology and relies on the appropriate diagnostics and removal of the underlying cause. Ongoing alveolar sequestration following extraction, formation of oro-sinus/nasal/cutaneous fistulas, ongoing sinus discharge etc. are all complex complications of dental and sinus disease, yet none of them will resolve with antimicrobial therapy alone. More complex surgical interventions are usually required. Nasal discharge resolution is not different between cases having received antimicrobials or not, following dental extraction (152).

Reference List

1. Aas JA, Paster BJ, Stokes LN, Olsen I, Dewhirst FE. Defining the Normal Bacterial Flora of the Oral Cavity. J Clin Microbiol. 2005;43(11):5721-32.
2. Bailey GD, Love DN. Oral associated bacterial infection in horses: studies on the normal anaerobic flora from the pharyngeal tonsillar surface and its association with lower respiratory tract and paraoral infections. Vet Microbiol. 1991;26(4):367-79.
3. Kennedy R, Lappin DF, Dixon PM, Buijs MJ, Zaura E, Crielaard W, et al. The microbiome associated with equine periodontitis and oral health. Veterinary research (Paris). 2016;47(1):49-.
4. Kern I, Bartmann CP, Verspohl J, Rohde J, Bienert-Zeit A. Bacteraemia before, during and after tooth extraction in horses in the absence of antimicrobial administration. Equine Vet J. 2017;49(2):178-82.
5. Mackintosh ME, Colles CM. Anaerobic bacteria associated with dental abscesses in the horse and donkey. Equine Vet J. 1987;19(4):360-2.
6. Bienert A, Bartmann CP, Verspohl J, Deegen E. Bacteriological findings for endodontical and apical molar dental diseases in the horse. Dtsch Tierarztl Wochenschr. 2003;110(9):358-61.
7. Sykora S, Pieber K, Simhofer H, Hackl V, Brodesser D, Brandt S. Isolation of Treponema and Tannerella spp. from equine odontoclastic tooth resorption and hypercementosis related periodontal disease. Equine Vet J. 2014;46(3):358-63.
8. Bartmann CP, Peters M, Amtsberg G, Deegen E. Dentogene Sinusitis durch gramnegative Anaerobier beim Pferd. Tierärztliche Praxis Ausgabe G, Grosstiere/Nutztiere. 2002;30:178-83.
9. Verdegaal EJMM, Heer Nd, Meertens NM, Maree JTM, Oldruitenborgh-Oosterbaan MMS. A right-sided bacterial endocarditis of dental origin in a horse. Equine Vet Educ. 2006;18(4):191-5.
10. Bach FS, Bodo G, Kuemmerle JM, Bienert-Zeit A, Hainisch EK, Simhofer H. Bacterial Meningitis After Sinus Surgery in Five Adult Horses. Vet Surg. 2014;43(6):697-703.
11. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on

Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. J Am Dent Assoc. 2007;138(6):739-45, 47-60.

12. Rutherford SJ, Glenny AM, Roberts G, Hooper L, Worthington HV. Antibiotic prophylaxis for preventing bacterial endocarditis following dental procedures. Cochrane database of systematic reviews (Online). 2022;5(5):Cd003813.

13. Hall G, Heimdahl A, Nord CE. Bacteremia after oral surgery and antibiotic prophylaxis for endocarditis. Clin Infect Dis. 1999;29(1):1-8; quiz 9-10.

14. Daly CG. Antibiotic prophylaxis for dental procedures. Australian prescriber. 2017;40(5):184-8.

15. Dixon PM, Parkin TD, Collins N, Hawkes C, Townsend N, Tremaine WH, et al. Equine paranasal sinus disease: a long-term study of 200 cases (1997-2009): treatments and long-term results of treatments. Equine Vet J. 2012;44(3):272-6.

16. Lowder MQ, Mueller POE. Periradicular dental disease in horses. Compend Contin Educ Vet. 1999;21(9):874–6.

17. Tremaine H. Advances in the Treatment of Diseased Equine Cheek Teeth. The Veterinary clinics of North America Equine practice. 2013;29(2):441-65.

18. Pearce CJ. Treatment of maxillary cheek teeth apical infection caused by patent infundibula in six horses (2007–2013). Equine Vet Educ. 2016;28(11):600-8.

19. Lundström T, Wattle O. Description of a technique for orthograde endodontic treatment of equine cheek teeth with apical infections. Equine Vet Educ. 2016;28(11):641-52.

20. du Toit N, Pearce CJ. Long-term follow-up of equine incisor endodontic treatments using an orthograde technique. J Am Vet Med Assoc. 2023;261(S2):S96-S101.

21. Easley J, Dixon P, Toit Nd. Equine dentistry and maxillofacial surgery. 1st edition ed. Newcastle upon Tyne: Cambridge Scholars Publishing; 2022.

22. Jackson K, Kelty E. Recent advances in the treatment and prevention of equine peripheral caries. J Am Vet Med Assoc. 2023;261(S2):S79-S86.

23. Christiansen MS, Rosenmeier JG, Jensen DB, Lindegaard C. Standing equine cheek tooth extraction: A multivariate analysis of the effect of antibiotics on the risk of post-operative complications. Equine Vet J. 2023;55(6):968-78.

24. Potschka H, Richter A, Kroker R. Pharmaka zur Behandlung bakterieller Infektionen. Löscher W, Richter A, Potschka H (Hrsg), Pharmakotherapie bei Haus- und Nutztieren. Stuttgart: Enke; 2014. p. 282-330.

25. Kennedy RS, Dixon PM. The aetiopathogenesis of equine periodontal disease – a fresh perspective. Equine Vet Educ. 2018;30(3):161-8.

26. Beste KJ, Lawhon SD, Chamoun-Emanuelli AM, Duff AH, Coleman MC, Griffin CE, et al. Culture-independent and dependent evaluation of the equine paranasal sinus microbiota in health and disease. Equine Vet J. 2020;52(3):455-63.

27. Townsend NB, Hawkes CS, Rex R, Boden LA, Barakzai SZ. Investigation of the sensitivity and specificity of radiological signs for diagnosis of periapical infection of equine cheek teeth. Equine Vet J. 2011;43(2):170-8.

28. Dixon PM, Parkin TD, Collins N, Hawkes C, Townsend N, Tremaine WH, et al. Equine paranasal sinus disease: A long-term study of 200 cases (1997–2009): Ancillary diagnostic findings and involvement of the various sinus compartments. Equine Vet J. 2012;44(3):267-71.

29. Liuti T, Smith S, Dixon PM. Radiographic, computed tomographic, gross pathological and histological findings with suspected apical infection in 32 equine maxillary cheek teeth (2012–2015). Equine Vet J. 2018;50(1):41-7.

30. Barakzai S, Tremaine H, Dixon P. Use of Scintigraphy for Diagnosis of Equine Paranasal Sinus Disorders. Veterinary surgery. 2006;35(1):94-101.

31. Verwilghen D, Easley J, Zwick T, Uhlhorn M, Grulke S, Simhofer H, et al. Equine Suture Exostosis: A Review of Cases from a Multicenter Retrospective Study. Vet Sci. 2022;9(7).

32. Jehle MC, Biermann NM, Haltmayer E. Trephination versus Minimally Invasive Transnasal Approaches for the Diagnosis and Treatment of Sinus Disease in Horses. 2022. Report No.: 2306-7381.

33. Lydiksen CV, Christensen JI, Rosenmeier JG, Jensen DB, Lindegaard C. Equine dental sinusitis—A statistical analysis of the effect of antibiotics on dental sinusitis following dental extraction. Equine Vet Educ. 2024;36(7):357-65.

Section 6 - Gastrointestinal

Contents

Chapter 1: Acute colitis (adult horses)

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Key issues

1. Disease can result in rapid death due to dehydration and endotoxaemia.
2. Multiple aetiologies that are indistinguishable clinically.
3. Large volume fluid therapy is the key to treatment.
4. Early treatment and recognition of patients requiring referral improves clinical management and probability of survival.

Acute colitis is severe inflammation of the large intestine (specifically the large colon and caecum) and can cause rapid dehydration and death if untreated. The equine large intestine contains a large quantity of bacteria, amongst which anaerobes, Gram-positives and Gram-negative species. When Gram-negative bacteria die, endotoxin, a constituent of their cell wall, is released into the gut lumen. At normal rates of bacterial reproduction and death, only a relatively small amount of endotoxin is released. Absorption of this is mainly prevented by the mucosal barrier (epithelium, enzymes, IgA, and normal microflora) and the small amount that reaches the portal circulation is effectively removed by the liver. However, if there is disruption of the flora and/or the mucosal barrier, significant amounts of free endotoxin can be absorbed into the circulation, overloading the capacity of the liver to remove it. This results in clinical signs of endotoxaemia (see Section 7).

Because most equine diarrhoea is hypersecretory, with loss of fluid and electrolytes into the gut lumen, dehydration occurs rapidly. Fluid losses in diarrhoea can be extremely high (up to 100 L per day), quickly resulting in hypovolaemia. In addition, hypovolaemia also develops due to endotoxaemic shock. Hypovolaemia and endotoxaemia both reduce tissue perfusion and oxygen delivery to the tissues, leading to hyperlactataemia. Common acid-base abnormalities include metabolic acidosis due to electrolyte losses (hyponatraemia) and hyperlactataemia, and metabolic alkalosis due to electrolyte (hypochloraemia) and protein losses. Protein is lost into the gastrointestinal tract via a protein-losing

enteropathy. Progression of endotoxaemia is common, with a systemic inflammatory response syndrome (SIRS) deteriorating into multiple organ dysfunction syndrome (MODS), and eventually multi-organ failure (MOF) and death in severe or untreated cases. Laminitis, thrombophlebitis and acute kidney injury are common sequelae of MODS in patients with colitis. In severe and peracute cases, death can occur before the onset of passing of diarrhoea. Colic is common, especially in the early stages of the disease, before the onset of diarrhoea. Some cases develop neurological signs due to intestinal hyperammonaemia.

The aetiology of acute diarrhoea in adult horses in Australia includes infectious causes (*Salmonella enterica*, *Clostridioides difficile* and possibly *Clostridium perfringens)*, carbohydrate overload, NSAID toxicity (right dorsal colitis), sand irritation, heavy infestations or rapid emergence of cyathostomins, dietary changes, and antimicrobial-associated diarrhoea. Equine proliferative enteropathy could also be a differential diagnosis in horses aged less than one year (see Chapter 5 in this section). Equine coronavirus is a recognised cause of acute diarrhoea and colic, sometimes in conjunction with neurological disease thought to be associated with hyperammonaemia (153), in the USA and Japan, but its significance in Australia is currently unknown. It has been detected in Australia in foals (Bailey, unpublished) and by PCR in the faeces of horses with colitis (154). Further investigation is required to evaluate the significance of a positive coronavirus PCR test in Australian horses with acute diarrhoea. Internationally it can present as individual cases (2) but more commonly is associated with herd outbreaks (1).

The different aetiologies present very similarly, and it is impossible to distinguish them from each other without knowledge of the risk factors of the case and additional testing. The literature would suggest that in up to 50% of cases a definitive diagnosis cannot be reached, despite extensive diagnostic testing.

i. Antimicrobial-associated diarrhoea

Diarrhoea can occur following the use of antimicrobial drugs in adult horses, generally within the first week after initial administration. High-grain diets and the stress of training and performance are also thought to contribute. Oral antimicrobials, such as trimethoprim-sulphonamide and doxycycline have been implicated, but parenterally administered antimicrobials, such as cephalosporins and penicillin, can also result in diarrhoea. Oral administration of penicillins, macrolides (in adults), and oxytetracycline are strongly associated with antimicrobial-associated diarrhoea and these drugs should never be administered orally in adult horses. However, many antimicrobials used in the adult horse have the capacity to alter normal gut flora, regardless of route, and may result in colitis, so clients should be warned of the risks (155). The resulting diarrhoea can be life-threatening. *Clostridioides difficile* and *Salmonella* spp. have been equally implicated in antimicrobial-associated diarrhoea.

Infectious causes of diarrhoea - bacterial

ii. Salmonellosis

(see Chapter 8 in this section).

iii. Clostridial diarrhoea

Clostridial diarrhoea is caused by the Gram-positive, anaerobic, spore-forming bacteria. In adult horses, *Clostridioides difficile* is the most important species. The role of *Clostridium perfringens* remains unclear, although recent detection of novel toxins has renewed speculation about the importance of this pathogen (156). Other species have also been sporadically implicated, including *C. septicum, C. cadaveris* and *C. sordellii*. Previous administration of antimicrobial drugs is common. Any

cause of stress, including hospitalisation, transportation and sudden dietary changes, can predispose to disease. Clostridial organisms are present in the soil and are a normal inhabitant of the gastrointestinal tract of horses. Disease associated with clostridia is mediated by enterotoxins – for *C. difficile*, 2 large molecular weight toxins, toxin A and toxin B, are shed early in the course of disease. Under conducive conditions, *C. difficile* spores germinate, and vegetative forms colonise the intestinal mucosa and produce toxins A and B. Horses may also be infected by direct ingestion of vegetative forms. Both toxins are believed to synergistically damage the mucosal epithelium by different mechanisms. In a 2023 study in Western Australia, *C. difficile* was detected in 38% of horses with gastrointestinal signs and 30% of horses without gastrointestinal signs, underscoring the lack of specificity of culture as a diagnostic tool in clinical cases. Only 55% of cases that carried *C. difficile* harboured a toxigenic strain in this study (157). *C. perfringens* enterotoxicosis is mediated by *C. perfringens* enterotoxin (CPE), alpha toxin (CPA), beta toxin (CPB), beta2 toxin (CPB2) or necrotising enterotoxin (NetF).

Infectious causes of diarrhoea – parasitic

iv. Parasite-associated diarrhoea (cyathostomins)

Cyathostomins are a group of small strongyle parasites. The larvae are pathogenic, but not the adults. Although the incidence of clinical disease associated with parasitism has decreased in recent decades with availability of more effective anthelmintics, small strongyle infestations have been increasingly important due to development of resistance to anthelmintics and the poor efficacy of current anthelmintics against the encysted larval stages. Cyathostomin infection occurs through the faecal-oral route. Larval stages travel to the caecum or colon, where they encyst in the intestinal mucosa and mature, before re-emerging as adult worms. This re-emergence most commonly occurs in winter and early spring (158) and causes physical disruption of the intestinal wall, resulting in diarrhoea. The factors that contribute to the maturation and synchronous emergence of inhibited cyathostome larvae are poorly understood, but removal of adult worms from the intestinal lumen through ageing or anthelmintic treatments is thought to stimulate the inhibited stages to develop. Encysted third-stage larvae may persist in nodules (hypobiosis) for as long as two years. Synchronous larval emergence has been demonstrated to be associated with general dysbiosis of the intestinal flora (158).

v. Diarrhoea associated with diet or dietary change

After sudden access to or an increase in grain (i.e., carbohydrate) feeding, the hydrolytic and/or absorptive capacity of the small intestine is overwhelmed and a portion of the ingested carbohydrate passes into the cecum undigested, where it undergoes rapid fermentation, with increased production of lactate and gas, a decrease in caecal and colonic pH and an increase in endo- and exotoxin production, associated with increased intestinal permeability, favouring increased absorption of endotoxin. High risk changes to diet include sudden introduction to grain feeding or an abrupt increase in the amount of grain concentrate, feeding of large grain meals (even in horses adapted to such feeds), or grazing of lush pasture or first-cut forage with a high content of rapidly fermentable substrate, such as fructan and simple sugars (159).

vi. Right dorsal colitis (NSAID toxicity)

Right dorsal colitis (RDC) has traditionally been thought to be associated with the oral administration of phenylbutazone, but there have also been sporadic cases associated with administration of flunixin meglumine or meloxicam, and a combination of NSAIDs may predispose to disease. The aetiology of RDC and the reason lesions are confined to the right dorsal colon are not fully understood. NSAIDS inhibit cyclooxygenase (COX), in the arachidonic acid pathway, reducing prostanoids, which convey some of the harmful effects of inflammation. However, these enzymes are also part of the physiological

mechanisms for maintaining blood flow to the gastrointestinal mucosa and kidney. A lack of ability to restore mucosal barriers in the face of NSAID therapy was thought to cause RDC, but experimental models have failed to prove this pathogenesis. Further work is necessary to understand this disease. Also unknown is why some horses develop RDC while on treatment with NSAIDs and others do not, regardless of the drug, dose or duration of therapy, although many cases may only show very mild signs or be subclinically affected (160). Horses with inappetence and/or dehydration are thought to be more at risk, so extra care should be taken with these cases. Administration of phenylbutazone at standard doses (6 mg/kg/day) to healthy horses with concurrent 50% water restriction can induce disease in as little as 5 days (161). In clinical cases, gross lesions involve haemorrhage on the serosal surface, along with ulceration of the mucosa and oedema of the colon wall. Full necropsy examination often reveals lesions in other areas, including the oral cavity, stomach and kidneys (162).

vii. Sand-irritation diarrhoea

Sand causes enteropathy by physical irritating the mucosa of the colon, resulting in colitis. Some horses actively eat sand, while others ingest soil and sand accidentally. Underfeeding or inadequate roughage or feeding from a sandy surface have been suggested to predispose to accidental eating of sand. Regardless, it is common for horses on sandy pastures to consume sand, although not all develop enteropathy, and the reason for this individual variation is unknown. It is suggested that underlying colonic pathologies, such as inflammatory bowel disease, can lead to decreased clearance of sand in some cases. Clinical signs can include acute colic, recurrent colic, diarrhoea and unexplained weight loss.

Diagnostics

History is very important when assessing colitis cases. Recent medical treatments, including anthelmintics, NSAIDS and antimicrobials, diet, and a history of any stressful events should be ascertained.

Clinical signs can range from mild to peracute, with sudden death. The classic triad of clinical signs are fever and diarrhoea along with leukopaenia. Haematology and biochemistry are critical to quantify dehydration, electrolyte loss, protein loss and organ dysfunction, as well as acid-base status and coagulation cascade activation. Moderate to severe haemoconcentration is common and may mask hypoproteinaemia and hypoalbuminaemia. Azotaemia is also very common, and it may be difficult to differentiate between renal and prerenal changes, as urine is generally difficult to obtain until fluid therapy is commenced. Monitoring of coagulation factors is valuable in cases where progression to disseminated intravascular coagulation is of concern, although testing is limited in many hospitals.

Lactate can be measured on a hand-held device. These devices are practical and financially viable for use in equine clinics and in ambulatory practice. Normal lactate in mature horses is < 0.7 mmol/L. Measurement can be used for diagnostic and prognostic information, as well as monitoring the response to therapy. In severe shock, lactate may transiently increase following initiation of intravenous fluid therapy due to release from tissues into the circulation with correction of perfusion.

Rectal examination may be useful in early cases to differentiate impending diarrhoea from other causes of colic, such as fluid faecal content passing over an impaction in the pelvic flexure.

Faecal samples should be submitted for PCR or culture for *Salmonella* spp. (see Chapter 8 in this section). PCR assays (not quantitative) for the A and B toxins of *C. difficile* and the genes for enterotoxin of *C. perfringens* are commercially available. However, the latter is of questionable value, as *C. perfringens* enterotoxin is of low virulence. A definitive diagnosis of clostridial diarrhoea can only be made when there is positive culture and demonstration of toxins. This is challenging as clostridial culture requires anaerobic techniques that are not widely available in private diagnostic laboratories,

and the toxin test is not quantitative, so small amounts of toxin, possible from normal flora, can result in a positive toxin test.

Diagnosis of larval cyathostominosis is challenging, as clinical disease can occur before the parasites shed eggs or the larval stages in the faeces. Macroscopic examination of the faeces may be useful if there are large numbers of larvae present (redworms). A serum antibody test has recently been developed (163) that appears to be useful for detecting mucosal and luminal cyathostominosis, but this test is not yet available commercially.

Abdominal ultrasound is a very useful tool for evaluating the colon. Normal colonic wall thickness is 0.3-0.4 cm or less. All causes of colitis can result in thickening of the colonic wall, but thickening does not always occur. Thickening of the colonic wall is not pathognomonic for colitis, as it can also occur in other syndromes, such as colonic volvulus and inflammatory bowel disease. In horses with RDC, there is substantial thickening of specifically the right dorsal colonic wall, with a distinct hypoechoic layer (oedema) bordered by hyperechoic layers on both the serosal and mucosal sides, and the wall typically looks corrugated. A normal right ventral colon differentiates RDC from other causes of colitis, as the colon is generally diffusely thickened in other inflammatory or infectious causes of colitis. Sand is difficult to detect on ultrasound.

Abdominal radiographs are recommended if sand enteropathy is suspected.

Salmonella detection protocols are described in Chapter 8 of this section.

Treatment

Horses with 2 of the 3 classical signs of colitis (fever, diarrhoea and leukopaenia) should be managed in isolation because of the risk of contagious and zoonotic diseases.

Referral of cases that have watery diarrhoea and signs of endotoxaemia (with or without fever), to a facility with 24 h care and isolation facilities is encouraged to provide intensive care and high-volume fluid therapy and improves the probability of a successful outcome.

Overarching treatments:

The main treatment for horses with diarrhoea is symptomatic. Fluid therapy to correct dehydration, hypovolaemia and electrolyte loss is critical, and large volumes are usually required. Fluids can, in mild cases, be administered orally, but in moderate to severe cases oral fluid therapy is not sufficient or can even be contra-indicated (if ileus is present), and intravenous fluid therapy is essential. The water absorptive capacity of the colon (the section of the gastro-intestinal tract that absorbs water) is limited and compromised due to pathology and dysfunction of the colon and due to poor gastro-intestinal perfusion secondary to shock. Hartmann's solution is preferred over normal saline (0.9% NaCl), as normal saline is acidifying, whereas Hartmann's solution is alkalinising because it contains lactate, which is converted to bicarbonate in the liver. This is an advantage in colitis, where metabolic acidosis is the predominant acid-base abnormality. Hartmann's is also polyionic and therefore causes less electrolyte disturbances when given in large volumes than normal saline. Hypertonic saline (7% NaCl at 4 ml/kg IV) can lead to rapid volume expansion in severely hypovolaemic cases, but must be followed with isotonic fluids, either administered orally (via a nasogastric tube or providing free access to them) or intravenously. A resuscitation bolus with isotonic fluids of up to 60-80 ml/kg can be administered if needed. Ongoing fluid requirements can be estimated from maintenance needs, the degree of dehydration, and ongoing losses through the diarrhoea. Ongoing losses are difficult to estimate and may be large. Frequent monitoring of PCV, total protein, electrolytes and lactate are recommended to guide fluid therapy.

Treatment to address endotoxaemia is addressed elsewhere (see Section 7).

Protein loss is a common feature of acute colitis and can be significant and cause decreasing colloid oncotic pressure. Therefore, in the face of hypoproteinaemia, fluid therapy can easily lead to formation of oedema. Even though hydration is a vital treatment for colitis, it is also important to avoid overhydration and not to prolong use of fluid therapy longer than needed to minimize formation of oedema. Colloids, ideally plasma (up to 20 ml/kg) can be required. The cost of plasma for adult horses is substantial. Synthetic colloids are also available, with Hetastarch (10 ml/kg/day) the most widely used, although Pentastarch and Tetrastarch have also been administered to horses with colitis, hypoproteinaemia and low colloid oncotic pressure. Evidence for their use is weak, but in a retrospective study evaluating the use of Hetastarch, a smaller proportion of cases (47%) receiving Hetastarch survived than cases treated with plasma (80% survival), even though they had similar disease severity on admission (164). There has been concern about adverse effects associated with treatment with synthetic colloids, but none were recorded in the 23 horses that received Hetastarch alone in this study. Further studies are needed to evaluate the benefits of these products. At this time, in colitis cases with severe hypoproteinaemia, when plasma is not available or cost-prohibitive, synthetic colloids can be considered to improve colloidal oncotic pressure. Administration by constant rate infusion is recommended when using synthetic colloids to increase colloidal oncotic pressure (165).

Non-steroidal anti-inflammatory drugs are integral to address endotoxaemia, SIRS and pain. Flunixin meglumine remains the most used NSAID at either the so-called 'anti-endotoxic dose' (0.25 mg/kg IV q 8 h), which has no anti-inflammatory effects, or at a higher dose (0.5 – 1.1 mg/kg IV q 12 h) (See Section 7 for more information on managing endotoxaemia). The authors recommended higher doses of flunixin meglumine for combatting inflammation and pain in addition to endotoxaemia. However, NSAIDs should be avoided in cases with right dorsal colitis. If pain cannot be managed with NSAIDS (or without NSAIDs, in right dorsal colitis), use of other analgesic medications is recommended (opioids, alpha2 agonists, lidocaine constant rate infusion). In cyathostominiasis cases, steroid therapy (prednisolone or dexamethasone) can be indicated, instead of NSAIDs, to reduce the intestinal inflammation (158).

In general, antimicrobials are not indicated in cases of colitis. Antimicrobial use results in intestinal dysbiosis, which may prolong recovery and shedding of pathogens in colitis cases. In addition, there is no evidence of a more rapid recovery in cases of salmonellosis after antimicrobial therapy. Translocation of bacteria across the damaged intestinal mucosa has been demonstrated, but there is no evidence that antimicrobial therapy improves the prognosis. Historically, clinicians have treated horses with broad-spectrum prophylactic antimicrobials when neutropaenia was severe. However, there are many clinicians managing colitis cases with severe neutropaenia without antimicrobial therapy with no adverse effects. If secondary infections develop, then antimicrobial therapy should be targeted to these infections.

It is appropriate to avoid potentially nephrotoxic drugs as much as possible until onset of fluid therapy or until creatinine normalises.

Cryotherapy for all four feet may reduce the incidence of laminitis. Ideally, cryotherapy should be applied for the duration of the developmental phase of laminitis, so horses exhibiting endotoxaemia should be treated from the first clinical examination (see Section 7). There is an excellent review by van Eps, (166) of mechanism and recommendations for cryotherapy.

Re-instauration of a healthy flora, by administration of probiotics, is often suggested, but evidence for this is lacking (167). Faecal microbiota transplantation (administration of faecal liquid from a healthy horse to a sick horse) can be performed and has been shown to be safe. Significant advantages to patients are yet to be demonstrated (168) and optimal methods and timing of this treatment remain unclear, however this treatment is common in horses. Donors should be healthy, have not been

exposed to antimicrobials in the past 6 months, and free from potential gastrointestinal pathogens, such as *Salmonella* spp. and gastrointestinal parasites. Ideally donors should be from the same farm and housed under the same conditions as the recipient. Recipients should have antimicrobial therapy discontinued prior to transplant and be pretreated with a protein pump inhibitor (omeprazole). Faeces are removed from the rectum of the donor horse and mixed with warm water or isotonic saline then the mixture blended and strained. A 2-3 L volume is administered by nasogastric tube for an average 450 kg horse. Free choice long stem early cut hay should be offered as soon as practical following faecal microbiota transplantation. The procedure should be repeated daily until there is improvement in faecal consistency, or for up to 3 days. A fresh transplant should be prepared daily (169).

General feeding guidelines for horses with colitis are:

1. Withhold food if the horse is in severe shock, as the reduced perfusion of the gastro-intestinal tract and potential ileus limit the capacity to tolerate food.
2. Do not force an inappetant horse to eat; this is a sign that the gastro-intestinal tract is probably not ready to tolerate food.
3. If there is a substantial period of inappetence, intravenous glucose and/or amino acids can be administered to provide calories.
4. There is no evidence to guide refeeding, and refeeding strategies vary – some authors advocate the use of fractioned feeding when the appetite returns (small portions multiple times per day), and high fibre but low bulk foods (grass, chaff, lucerne cubes, beet pulp, psyllium, avoiding significant amounts of hay, no straw), whereas others offer free access to lucerne hay throughout the course of disease with a view to providing nutrition to enterocytes to promote healing.

Disease specific treatments:

Antimicrobial-associated diarrhoea: Antimicrobial therapy should be discontinued.

Clostridial diarrhoea: Metronidazole is indicated (15 mg/kg PO q 8 h or 25 mg/kg PO q 12 h) for 3 days. Resolution of diarrhoea is often rapid following metronidazole therapy. Resistance has not been documented in Australia. Treatment should be reserved for cases where clostridial infection has been documented with concurrent toxin gene detection. Because the action of the metronidazole is required within the gastrointestinal tract, oral metronidazole treatment is recommended. The intravenous and rectal routes have not been evaluated and transport into the gastrointestinal tract is unknown.

Cyathostominosis: The preferred treatment is with moxidectin (0.4 mg/kg PO). Fenbendazole (10 mg/kg PO q 24 h for 5 days) can also be used, but there is increasing resistance of strongyles to fenbendazole. Prednisolone at 1 mg/kg PO q 24 h for 24-48 h is recommended in clinically affected horses prior to and during administration of anthelmintics to control inflammation in the colon.

Right dorsal colitis: There are four principles of treatment: 1, avoid further NSAID use; 2, minimise stress; 3, dietary modification; and 4, targeted medication. Large volume fibre should be eliminated from the diet to remove bulk from the colon and favour healing. Pelleted feed alone, or with small quantities of green grass, should be fed for 3-6 months. Oil can be used to increase calories in the diet, if necessary, and corn oil has been demonstrated to increase gastric PGE2 and promote mucosal healing. Misoprostol is a synthetic PGE1 analogue that can be administered at doses of 2-5 µg/kg every 6-12 h, but should be handled with caution, as exposure can cause abortion in people. Sucralfate and psyllium husks have also been used, but the efficacy of these treatments is unknown.

Sand enteropathy: Combination therapy with psyllium and $MgSO_4$ (Epsom salts) (both at 1 g/kg) via nasogastric tube once daily for multiple days is the preferred method of treatment. Further, the

collective findings of published research suggest that administering psyllium in feed as a preventative has no advantage over removing access to sand (170).

Antimicrobials used

- In non-infectious cases, antimicrobial therapy is not indicated and may exacerbate diarrhoea in the adult horse.
- For *Salmonella* spp:
    - Antimicrobial therapy is not indicated
- For *Clostridioides difficile* with presence of genes for pathogenic toxins:
    - Oral metronidazole (15 mg/kg PO q 8 h or 25 mg/kg PO q 12 h)
- For cyathostominosis:
    - Prednisolone at 1 mg/kg PO q 24 h for 24-48 h prior to and during deworming treatment
    - First line: moxidectin (0.4 mg/kg PO) once
    - Second line: fenbendazole (10 mg/kg PO q 24 h for 5 days)

Prognosis

The prognosis is guarded. Referral to a hospital that can provide 24 h intensive care is recommended, as retrospective studies have reported mortality rates of between 19 and 42%.

Serial blood lactate measurement can be used to guide the prognosis. In retrospective studies, non-survivors had the highest lactate concentrations (mean of 5.35 mmol/L) at admission and after 72 h (mean of 2.35 mmol/L), compared to survivors (means of 1.75 mmol/L at admission and 0.75 mmol/L after 72 h) (171). Another study found 4-8 h lactate concentration, 24 h lactate concentration and the percentage reduction in lactate concentration (≥ 30% at 4-8 h and ≥ 50% at 24 h) were significantly associated with survival. No clear “cut-off value” for non-survival has been elucidated, emphasising the importance of serial measurements and examination of trends in lactate concentration, and full assessment of all clinical aspects of the patient, rather than any one value in assessing the prognosis.

The prognosis for right dorsal colitis and larval cyathostominosis may be worse than for other aetiologies, with mortality rates of approximately 60% reported. Antimicrobial-associated diarrhoea has been shown in multiple studies to have a significantly higher mortality than other causes of diarrhoea.

Further reading

Durie I, van Galen G. Can the use of antimicrobials in adult equine patients with acute colitis be justified in the era of antimicrobial stewardship? Equine veterinary education. 2023;35(2):103-12.

Crabtree NE, Epstein KL. Current Concepts in Fluid Therapy in Horses. Frontiers in veterinary science. 2021;8:648774-.

Flood J, Byrne D, Bauquier J, Agne GF, Wise JC, Medina-Torres CE, et al. Right dorsal colitis in horses: A multicenter retrospective study of 35 cases. Journal of veterinary internal medicine. 2023;37(6):2535-43.

Chapter 2: Chronic diarrhoea

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Often difficult to identify the specific cause.
2. Assessment for dehydration, electrolyte abnormalities and renal function is important.
3. Chronic diarrhoea may be difficult to treat and time may be required for normalisation of the gut flora.

Chronic diarrhoea can be due to sand enteropathy, diet, dental disease, parasitism (cyathostomin infestation), chronic salmonellosis, alimentary lymphoma, or inflammatory bowel disease, but commonly has no identifiable cause (172), although it may be associated with gastrointestinal dysbiosis, leading to increased water loss in the faeces.

Sand causes enteropathy by physical irritation to the mucosa of the colon resulting in colitis which can be present as acute or recurrent colitis, diarrhoea, and/or unexplained weight loss. For more information see Chapter 1 in this section, part vii: Sand-irritation diarrhoea.

Cyathostomins are a group of small strongyle parasites of which the larvae and not the adults are pathogenic. For more information on see Chapter 1 in this section, part iv. Parasite-associated diarrhoea (cyathostomins).

Alimentary lymphosarcoma is an uncommon disease, but infiltration of neoplastic lymphocytes into the colon can disrupt colonic function.

Inflammatory bowel disease is a broad diagnosis that describes several specific diseases - granulomatous enteritis, lymphocytic-plasmacytic enterocolitis and eosinophilic enterocolitis - and is due to infiltration of inflammatory cells into the mucosa.

Alimentary lymphosarcoma and chronic inflammatory bowel disease usually also cause weight loss and a protein-losing enteropathy.

Chronic salmonellosis is covered in Chapter 8 of this section.

Diagnostics

History and clinical examination findings are critical. Diet, treatment history, including with drugs used to treat or prevent parasites or other infectious agents, are all important, as is assessment for dental diseases.

Faecal PCR and/or culture are indicated to rule out salmonellosis. Serial samples are required (see Chapter 8 in this section).

Haematology and serum biochemistry are important to assess hydration, electrolyte losses and renal function. Fibrinogen and serum amyloid A concentrations will help to assess the degree of inflammation present. Hypoalbuminaemia due to a protein-losing enteropathy is common.

The presence of sand can be diagnosed with abdominal radiographs, and suspension of the faeces in water, to observe sedimentation of the sand, is also a crude method of diagnosis.

When malabsorption is suspected, a glucose absorption test is also valuable, simple to perform and doesn't require specialised equipment. In healthy horses, the plasma glucose level should rise to higher than 85% over the baseline between 60 and 120 min after the oral administration of glucose (1 g/kg as a 20% solution) (173). If the peak is between 15% and 85%, this is classified as partial

malabsorption and is not specific for small intestinal disease. Total malabsorption occurs when the peak is less 15% higher than baseline and, in this case, diffuse, small intestinal disease is highly likely.

A faecal egg count is important but cyathostomin infestations may not be patent, so a negative faecal egg count does not rule out this differential diagnosis.

Abdominal ultrasound may identify thickened small or large intestine which, if diffuse, may increase the suspicion of an infiltrative disease. Enlarged lymph nodes are suggestive of lymphosarcoma. Abdominocentesis is generally normal, but neoplastic cells may be present in some cases of lymphosarcoma.

Alimentary lymphosarcoma and inflammatory bowel disease require histopathological examination of affected intestinal tissue collected by laparoscopy or laparotomy for definitive diagnosis. Sometimes a rectal mucosal biopsy may provide these diagnoses.

Treatment

Several studies have compared the efficacy of different treatments for sand enteropathy. Collectively they support the use of combination therapy with psyllium and $MgSO_4$ (Epsom salts) (both at 1 g/kg) by nasogastric tube once daily as the preferred method of treatment. Further, the collective findings of published research suggest that administering psyllium in feed as a preventative has no advantage over simply removing access to sand (170).

Cyathostomins can be treated with fenbendazole (10 mg/kg PO q 24 h for 5 days) or moxidectin (0.4 mg/kg PO). Prednisolone at 1 mg/kg PO q 24 h for 24-48 h is recommended in clinically affected horses prior to administration of anthelmintics to control inflammation in the colon (158).

Chronic shedding of *Salmonella* spp. generally requires time and normalisation of the gut flora. Faecal microbiota transplantation (faecal transfaunation) may be useful for these cases, and in inflammatory bowel diseases, although more research is needed before efficacy can be established. For the most current recommendations, see 'Overarching treatments' in Chapter 1 of this section.

Biosponge (di-tri-octahedral smectite) has also been used successfully in treatment of chronic diarrhoea in some horses, at a dose of 97.5 g PO q 12 h.

Chronic inflammatory bowel disease is usually treated with a long and tapering course of corticosteroids, with parenteral therapy considered initially due to the presence of malabsorption (dexamethasone at 0.1 mg/kg IV or IM q 24 h for 5 days, reducing the dose by 50% every 5-7 days or switching to prednisolone at 1 mg/kg PO q 24 h after the first 5 days, and reducing the dose by 50% every 5-7 days). Other immunosuppressive drugs have been used for refractory cases, including azathioprine (3 mg/kg PO q 24 h)(174).

Antimicrobials used

- Antimicrobial therapy is not indicated and may delay recovery due to ongoing dysbiosis.

Prognosis

Resolution of diarrhoea can take a long time due to the need to re-establish a normal gut flora following treatment of the primary cause. Intestinal lymphosarcoma has a poor prognosis and inflammatory bowel disease has a guarded prognosis.

Further reading

Vitale V. Inflammatory bowel diseases in horses: What do we know? Equine veterinary education. 2022;34(9):493-500.

Chapter 3: Cholangiohepatitis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Fever, colic, and jaundice are the classical triad of clinical signs.
2. Liver biopsy is strongly recommended to guide treatment and prognosis.
3. Ascending infection from the gastrointestinal tract is the probable origin.

Cholangiohepatitis and cholelithiasis are among the most commonly encountered liver diseases in horses. The inflammation probably originates in the gastrointestinal tract and ascends the biliary tree, but it appears rare that inflammation does not extend into at least the periportal region. Neutrophils predominate, which distinguishes the disease from other non-suppurative inflammatory hepatopathies (chronic active hepatitis).

Retrospective studies have identified Gram-negative and anaerobic bacteria as the most common organisms isolated from the liver tissue of affected horses. *E. coli*, *Actinobacillus equuli*, *Streptococcus* spp., *Klebsiella* spp., *Enterococcus* spp., *Clostridium* spp. and *Bacteroides* spp. have all been implicated (175). However, in the author's experience, culture is only successful in around 50% of cases and empirical treatment is often required. Ponies were overrepresented in a United Kingdom case-control study (176), but this could be geographically specific and may not reflect the Australian demographics. In the author's experience in Australia, horses are as commonly diagnosed as ponies, but biases in hospital populations may influence this. No risk factors have been identified.

Diagnostics

The classical clinical presentation is the triad of fever, colic, and jaundice. The severity of the colic varies with the degree of biliary obstruction. Complete biliary obstruction is associated with intractable abdominal pain, but, in most cases, outflow is reduced, but possible, and the colic is mild to moderate and responsive to NSAIDs.

Haematology and serum biochemistry generally reveal leukocytosis due to a mature neutrophilia, hyperfibrinogenaemia and elevation in both hepatocellular (aspartate aminotransferase [AST], sorbitol dehydrogenase [SDH]) and hepatobiliary enzymes (alkaline phosphatase [ALP], gamma-glutamyl transferase [GGT]). Hepatobiliary enzymes are typically increased more than hepatocellular enzymes. Bile acids are also elevated.

Ultrasonic examination of the liver is useful, but visualisation of the liver may be difficult in older horses, as the liver is subject to age-related atrophy. Hepatomegaly can be present in the acute phase. The main advantage of ultrasound is to guide liver biopsy. The liver can generally be imaged on the right side between the 7th and 16th intercostal spaces (ICS), and less reliably on the left (6-9th ICS) or in the ventral cranial abdomen. Fibrosis is generally quite advanced before there are changes in echogenicity on ultrasound, but dilated bile ducts are pathognomonic for biliary obstruction, and the most common reason for biliary obstruction is suppurative cholangiohepatitis. Small, calcified calculi are often found, including in normal horses, and appear as an acoustic shadow distally. Finding a high frequency of these ultrasonographic lesions is consistent with cholangiohepatitis.

A presumptive diagnosis can be made from clinical signs, haematology and serum biochemical analysis, but liver biopsy is very important for several reasons. Firstly, histopathology provides information on the degree of fibrosis, which is valuable in confirming the diagnosis and formulating a prognosis. Secondly, biopsy material should be cultured to guide antimicrobial selection and maximise

the efficacy of treatment. Coagulation capacity should be assessed prior to liver biopsy, as severe liver disease can impair coagulation.

Treatment

Antimicrobial therapy is critical for effective therapy. Antimicrobial selection is frequently empirical, as culture of hepatic biopsies is, frustratingly, often unsuccessful. The trimethoprim-sulphonamide combination has adequate spectrum against common pathogens, distributes well to the liver and can be administered orally, making it a good candidate for empirical treatment. Penicillin and gentamicin combinations and fluoroquinolones have also been used successfully.

Treatment duration is typically extended, with treatment recommended to continue until hepatic enzymes return to normal ranges (the median duration in one case series was 51 days (177)). Serum biochemistry should be repeated fortnightly. Early discontinuation can result in recurrence of disease, although recurrence can also occur following “appropriate” durations of therapy.

Antimicrobials used

- Trimethoprim-sulphonamide at 30 mg/kg PO q 12 h until hepatobiliary enzymes return to reference ranges
- Targeted therapy is based on susceptibility testing if culture is successful
- In cases that fail to respond to trimethoprim-sulphonamide treatment, enrofloxacin at 7.5 mg/kg PO q 24 h is generally the best second line treatment, as many horses will not tolerate long durations of treatment with penicillin and gentamicin.

Prognosis

Recurrence of disease occurs in some horses and subsequent bouts may increase hepatic fibrosis. The greater the degree of periportal and bridging fibrosis, the worse the prognosis.

Chapter 4: Duodenitis/proximal jejunitis (anterior enteritis)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Acute onset of fever, tachycardia, abdominal pain, ileus and gastric reflux.
2. Decompression with indwelling naso-gastric tube important aspect of diagnosis and treatment.
3. Peritoneal fluid usually has increased total protein with normal nucleated cell count.

Duodenitis/proximal jejunitis is an inflammatory disease that causes gastric and intestinal stasis, resulting in fluid accumulation and distension of the proximal part of the gastrointestinal tract. Lesions are usually confined to the proximal half of the small intestine, including all the duodenum and a variable amount of the jejunum, but in severe cases 90% of the small intestine can be involved. Duodenitis/proximal jejunitis is characterised by acute onset of fever, tachycardia, abdominal pain, ileus and the presence of reflux on placement of a nasogastric tube. The severity of pain varies from mild to severe, which manifests in some horses as inappetence, depression and a tendency to recumbency. Clinical signs of endotoxaemia, such as injected mucous membranes, a slow capillary refill time, dehydration, fever and tachycardia are common.

Numerous aetiological agents have been proposed, including clostridial species, mycotoxins and *Salmonella* spp., but the evidence is weak for all of them. Diet appears to play a role in some horses.

The major differential diagnosis is small intestinal obstruction, but these horses should not be febrile initially and their pain usually becomes more severe and does not completely resolve with gastric decompression, unless the affected viscus ruptures. However, differentiating duodenitis/proximal jejunitis from small intestinal obstructions can be a challenging.

Diagnostics

Clinical examination will reveal colic, fever and the presence of large volumes of gastric reflux. Fever may only be present in 25-30% of cases. Mild to moderate colic that resolves following gastric decompression is a hallmark of the disease, with signs of severe colic less common. The colour of the reflux is usually yellow-green to red-brown, and it usually has a fetid smell.

Abdominal ultrasonographical examination reveals a thickened and distended small intestine with no motility (ileus), which can also be palpated on rectal examination.

Abdominocentesis generally reveals peritoneal fluid with an elevated protein (> 35 g/L) and a normal total nucleated cell count (178).

Haematology is not distinctly different from horses with small intestinal strangulating lesions. Serum biochemistry often reveals increased liver enzymes and total bilirubin as a result of compression and occlusion of the bile duct or ascension of disease to the liver via the bile duct.

Treatment

Therapy is aimed at relieving gastric and intestinal distension, addressing dehydration and electrolyte abnormalities, alleviating pain and promoting gastrointestinal motility.

Regular decompression of the stomach by enabling reflux through an indwelling stomach tube, sometimes as often as every 2 h, is important to reduce pain and ileus and prevent gastric rupture.

Intravenous fluid therapy is required to treat the dehydration from fluid and electrolyte loss through gastric reflux and the inability to drink. Serial monitoring is required to adjust fluid therapy to compensate for ongoing losses through reflux.

Prokinetic therapy is commonly used to combat ileus, with drugs such as bethanechol, phenothiazine, metoclopramide, cisapride and lidocaine all reported, but there is only weak evidence to support its use. A lidocaine infusion (loading dose of 1.3 mg/kg, followed by a constant rate of infusion of 0.05 mg/kg/min), is often used as a prokinetic drug and for pain relief because of its anti-inflammatory properties. Adequate pain relief is critical in combating ileus.

Antimicrobial therapy is controversial. Some advocate for coverage of clostridial species. Penicillin alone or metronidazole are common, but oral metronidazole is ineffective because of the ileus, so penicillin is probably a better choice. Benzyl penicillin IV is a better choice than procaine penicillin IM because of the poor muscle perfusion caused by dehydration and endotoxaemia early in disease. Rectal administration of metronidazole is possible in a refluxing horse, but results in lower bioavailability compared to oral administration so doses of 20mg/kg bid should be used (179).

Treatment of endotoxaemia is covered elsewhere (see Section 7).

Cryotherapy for all four feet is indicated to reduce the risk of laminitis secondary to acute enteritis. Ideally, cryotherapy should be applied for the duration of the developmental phase of laminitis, so horses exhibiting signs of endotoxaemia should be treated when first seen. Continuous application is likely to yield the best results and should be continued until resolution of the primary disease, with some experts continuing for another 24-48 h after resolution of systemic inflammation. Immersion of the limb from the upper metacarpus and metatarsus distally in an ice and water mixture effectively achieves cooling to less than 10℃, although constant ice replenishment is labour intensive. Commercially available wader-style devices can be modified as an alternative. Although the degree to which the limb must be cooled to prevent laminitis has not been established, current recommendations are for a hoof temperature of 10ºC, although there may be some benefit from even mild cooling (166).

Antimicrobials used

- Benzyl penicillin (22,000 IU/kg IV q 6 h) for 3 days

Prognosis

Generally, the prognosis is guarded, depending on the length of time that gastric reflux persists. Laminitis has been reported to occur as a sequela in 30% of cases.

Survival rates of 25-94% have been reported. Case series have been small, so a wide range in survival rates is not surprising.

An anion gap of >15 mEq/L has been associated with 6 fold higher odds of mortality (178).

Further reading

Arroyo LG, Gomez DE, Martins C. Equine duodenitis-proximal jejunitis: A review. Can Vet J. 2018;59(5):510-7.

Freeman B. Tutorial article: Duodentitis-proximal jejunitis. Equine Vet Education. 2000;12:322-32.

Chapter 5: Equine Proliferative Enteropathy

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Disease results in severe hypoproteinaemia due to severe hypoalbuminaemia
2. Farms often have cases annually, possibly due to wildlife reservoirs
3. Diagnostic testing using both qPCR and serology is recommended

Equine proliferative enteropathy (EPE) is caused by *Lawsonia intracellularis*, an obligate intracellular anaerobic Gram-negative bacterium that mainly infects intestinal crypt cells. This causes proliferation of intestinal crypt cells, resulting in a severe protein-losing enteropathy due to thickened walls of the small intestine and, rarely, the large intestine. Lesions are most commonly seen in the ileum, near the ileo-caecal junction. Inflammation is not characteristic feature but can occur late in the progression of the disease.

The disease occurs worldwide. Affected horses are usually between 4 and 7 months of age. Transmission is faecal-oral. Research suggests that 1 g of faeces from an infected horse would be sufficient to deliver an infective dose to a foal, explaining the exposure rates of up to 100% on affected properties. Foals shed the pathogen for 10-27 days. The bacteria can survive in the environment for at least 1-2 weeks at 5-15°C (180).

L. intracellularis infects many animal species, including pigs, rabbits, foxes, deer and non-human primates. Rodents appear to be a suitable reservoir host. Properties that have previously housed pigs were initially thought to have been associated with outbreaks in horses, but most cases cannot be linked to exposure to pig faeces and the genomics of pig and equine isolates differ greatly. Year-to-year variation in occurrence on a farm can be expected due to changes in climatic conditions.

Diagnostics

Common clinical signs include peripheral oedema (ventrum, penile sheath, throat latch and distal limbs), fever, weight loss, diarrhoea, lethargy and colic. Early clinical signs can be vague and include mild depression, reduced appetite and fever. Diarrhoea can vary from 'cow pat' to watery, while some foals have normal faeces. Haematology and serum biochemistry reveal severe hypoproteinaemia due to hypoalbuminaemia. All other blood and serum abnormalities are non-specific and variable. Thickened small intestinal walls can be visualised by transabdominal ultrasonographic examination in many cases. Normal small intestinal wall thickness is less than 3 mm.

Two tests are available for ante-mortem diagnosis. Quantitative real-time polymerase chain reaction assays (qPCR) for pathogen detection in faeces and serological testing (i.e. ELISA). Both tests are recommended, as they have high analytical specificity, but variable sensitivity. In an outbreak in Germany, 21/40 foals tested positive by qPCR, whereas 40/40 were positive by serology (181). Negative PCR results can be expected if the faecal samples are collected from foals that have been treated with antimicrobials or are late in the course of disease. Negative serological tests can be expected in the early stage of the disease. Different PCR and serological assays can also yield variable results.

Clinical signs, in conjunction with hypoproteinaemia in foals on farms with a history of EPE is often sufficient to make a diagnosis. Following diagnosis of a horse on a farm with multiple weanlings, testing of herd mates is strongly recommended. Measurement of total plasma protein using refractometry is an inexpensive and easy way of monitoring at-risk horses. Animals with total plasma protein less than 50 g/L should be subjected to further testing.

Treatment

Early treatment is critical to avoid advanced disease that results in marked weight loss and critically low serum protein and the need for intensive therapy.

Antimicrobial therapy with oxytetracycline or doxycycline is most common. Early cases can be treated with oral doxycycline (for 7-10 days), but advanced disease should be treated with intravenous oxytetracycline in case gastrointestinal absorption is reduced.

Supportive care is critical in foals with advanced disease, with plasma transfusions, IV fluids and parenteral or partial parenteral nutrition most frequently necessary. Plasma transfusions often result in frustratingly small increases in total plasma protein, even when administered in large volumes (6-8 L). Hydroxyethyl starches (up to 10 ml/kg/day) can be administered, but high doses are associated with coagulopathy and total protein does not increase, so monitoring is difficult unless colloidal oncotic pressure (COP) can be measured.

Total plasma protein can remain low for long periods following clinical recovery.

Antimicrobials used

- Early disease: Doxycycline 10 mg/kg PO q 12 h for 7-10 days
- Late disease: Oxytetracycline 6.6 mg/kg IV q 12 h for 7 days followed by doxycycline 10 mg/kg PO q 12 h for 7 days

Prognosis

The prognosis is excellent with early treatment. Spontaneous recovery has not been reported, so treatment is essential. Overall, 93% of treated foals have been reported to fully recover, although mortality in severely affected cases can be as high as 30%.

Further reading

Pusterla N, Gebhart CJ. Equine proliferative enteropathy - a review of recent developments. Equine veterinary journal. 2013;45(4):403-9.

Chapter 6: Oesophagitis, Equine Squamous Gastric Disease (ESGD) and Equine Glandular Gastric Disease (EGGD) (Gastric Ulceration)

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Oesophageal ulceration occurs secondary to choke or gastric acid reflux because of delayed gastric emptying.
2. Squamous mucosal lesions (ESCG) occur secondary to intermittent feeding and increased concentrations of HCl.
3. Glandular lesions (EGGD) occur secondary to NSAID therapy and stressors in the environment.

Oesophagitis most commonly develops secondary to choke, when food material lodges in the oesophagus or when acidic gastric contents reflux into the distal oesophagus. Oesophageal ulceration occurs when gastric emptying is delayed because of pyloric obstruction.

Equine Squamous Gastric Disease (ESGD) occurs in the squamous mucosa, predominantly along the *margo plicatus*. Primary ESGD occurs in an otherwise healthy gastrointestinal tract and is the most common form of this disease. Secondary ESGD is due to delayed gastric outflow, as a sequela of other diseases, such as pyloric stenosis, severe EGGD or inflammatory bowel disease (IBD).

Horses evolved as grazing animals and secrete hydrochloric acid (HCl) continuously in the stomach, so, if they are stabled and only fed intermittently, acid concentrations increase in the stomach, damaging the cranial squamous mucosa. Fibre is critical to the pathogenesis and likely acts in two protective ways: firstly, by increasing the saliva produced by chewing, which has a buffering effect on stomach acid; and secondly, through formation of 'roughage balls' in the stomach to limit acid splashing. Fibre size is therefore an important factor, with long fibre length particularly important. Crib-biting and other stereotypical behaviours are also associated with ESGD.

The caudal glandular part of the stomach secretes mucus and bicarbonate, providing protection from the normal acidic environment. Ulceration in this area, Equine Glandular Gastric Disease (EGGD), is less well understood, but NSAID therapy blocking prostaglandin production, gastritis or an altered microbiota may be involved. Training and environmental stress are also thought to play a part in glandular ulceration, but diet has not been implicated.

ESGD is very common, with prevalences of 80 - 90% in horses in training and 30-60% in horses not in training and in wild populations. The prevalence of EGGD is more variable, with rates of between 15 and 65% reported.

Helicobacter pylori has not been cultured from the stomach of horses and is not thought to be involved in the pathogenesis of gastric ulcers in horses (182).

Diagnostics

Reported clinical signs vary and are often non-specific. They include colic, weight loss or poor body condition, poor coat condition, reduced appetite, diarrhoea, bruxism, a Flehmen response, behavioral changes and poor performance.

Gastroscopy using a 3 m endoscope, after 12 h of fasting, is the only reliable ante-mortem method of definitely diagnosing gastric ulceration (183). The oesophagus is best visualised when withdrawing the scope from the stomach, when the oesophagus is dilated between peristaltic waves. Mucosal biopsies are of limited value in detecting underlying disease compared to full thickness biopsies. For EGGD, assessment of the clinical relevance of ulceration should not be based on the endoscopic

appearance alone. Instead, the relevance of a lesion should be assessed in the light of clinical signs and the response to treatment. Faecal occult blood testing is unreliable.

ESGD can be graded based on its visual appearance on endoscopy. Grading allows lesions to be monitored.

- Grade 0: epithelium intact, no appearance of hyperkeratosis
- Grade 1: mucosa intact, areas of hyperkeratosis
- Grade 2: small, single or multifocal lesions
- Grade 3: large single or extensive superficial lesions
- Grade 4: extensive lesions with areas of deep lesions

For EGGD, the recommendation at this time remains not to assign a grade to these lesions, but rather describe the lesions by anatomical location, distribution, severity and appearance (183).

Treatment

Proton-pump inhibitors are currently the best acid suppressive therapy available and there is sufficient evidence for their use for ESGD. Growing evidence also supports the use of acid-suppression for EGGD, along with mucosal protectants.

Enteric coated omeprazole is recommended (1-2 mg/kg PO q 24 h). Administration should be in the morning approximately 30 min prior to feeding after fasting overnight. The long-acting injectable formulation of omeprazole appears to be more successful for treating EGGD when administered at 5-day intervals, although it was not registered in Australia at the time of writing these guidelines and local injections site reactions can occur. Treatment is generally for 3 weeks for ESGD and 3-4 weeks for EGGD.

Sucralfate (12 mg/kg PO q 12 h) is recommended in combination with omeprazole for EGGD (183), although doses of up to 20-30 mg/kg q 6-8 h are commonly used. Sucralfate should be administered at least 30 min after omeprazole.

Misoprostol has also been proposed as a treatment for EGGD, but further evidence is needed before a recommendation can be made.

Management changes are very important for ESGD. *Ad libitum* roughage, or at least 2% of bodyweight per day of good quality roughage, should be consumed. Afternoon exercising may also reduce acid exposure and limiting exercise to 40 minutes per day may be beneficial. For EGGD, duration of exercise is less important, but numbers of days of exercise have been associated with disease, so it is recommended that horses get 2 or, ideally, 3 full days rest per week (184). In addition, reducing stress may help in reducing EGGD, although evidence is lacking.

Oesophageal inflammation due to choke is treated by removing the food obstruction. Feeding a soft diet usually results in resolution of oesophageal inflammation. Sucralfate may be useful in coating ulceration.

Antimicrobials used

- Antimicrobial therapy is not indicated, as *Helicobacter pylori* has not been identified as a cause of gastric ulceration in horses.

Prognosis

The prognosis is good for oesophageal inflammation once the obstruction is resolved.

Healing rates for ESGD are good with oral omeprazole monotherapy (67-100%), but less successful for EGGD (14-25%).

Chapter 7: Septic peritonitis (excluding gastrointestinal rupture)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Primary and secondary cases of peritonitis occur and prognosis and treatment varies between the groups.
2. Primary peritonitis has been associated with *Actinobacillus* spp. but other pathogens can also be cultured.

Peritonitis can be primary or secondary. Secondary peritonitis can occur following traumatic injuries, abdominal surgery, parturition (rupture of the uterus or bladder), or rupture of the gastrointestinal tract.

Clinical signs include pyrexia, colic, inappetence and a dull demeanour, and, in chronic cases, weight loss.

In cases of secondary peritonitis, the principal decision is whether surgical or medical therapy is most appropriate. Horses with any of the following clinical findings are more likely to survive to discharge without surgery: absence of colic signs, normal rectal temperature or fever responsive to therapy, normal intestinal borborygmi or intestinal borborygmi that return after therapy, normal faecal production, normal rectal palpation, no gastrointestinal reflux or yellow/orange peritoneal fluid. Horses with colic, fever unresponsive to therapy, absent intestinal borborygmi following therapy, abnormal faeces, abnormal rectal palpation, gastrointestinal reflux or red/brown peritoneal fluid should be considered for exploratory laparotomy.

In cases of uterine rupture following parturition, in the only recent study there was no difference between medical and surgical therapy. Medical treatment may be a reasonable alternative to surgical treatment for uterine tears, although the severity of a tear that can resolve with medical treatment is unknown, and medical therapy can be as expensive as surgical treatment. Tears in this study were most likely to occur in the right horn (185). This is relevant, as there is a recent case series describing laparoscopic repair (186), which may be a useful alternative to ventral midline laparotomy.

In cases without an identified cause, primary or idiopathic peritonitis is diagnosed. Primary peritonitis has been associated with *Actinobacillus equuli*, which is associated with better outcomes. In a study in Sweden, in 21% of cases of primary peritonitis, peritoneal fluid cultures yielded *Actinobacillus* spp. (*A. equuli, A. suis, A. suis*-like) (187). Other species isolated included β-haemolytic streptococci, *Bacteroides* spp. and *E. coli*, and other bacterial species.

Diagnostics

Diagnosis is generally based on evaluation of peritoneal fluid, with elevated nucleated cell counts (> 10,000 cells/μL) indicative of peritoneal inflammation. Abdominal ultrasonographic examination may reveal increased peritoneal fluid and may be useful for identifying pockets of fluid to sample when effusion is minimal.

Peritoneal blood glucose of 0 mmol/L and peritoneal lactate (> blood lactate) can be indicative. Some use a difference between blood and peritoneal glucose of >2.8 mmol/L as a marker, but the accuracy of this marker is low (188).

Culture and susceptibility testing should be pursued in all cases. Haematology can reveal a lymphocytosis and a mature neutrophilia or leukopaenia, especially in cases with endotoxaemia.

All cases should have extensive evaluation for an underlying cause. A history of NSAID use should increase suspicion of right dorsal colitis. Parasitism should also be considered (*Parascaris equorum* or encysted larval cyathostominosis in particular, although *Strongylus vulgaris* could also be considered in regions other than Australia).

Treatment

Antimicrobial therapy is indicated in all cases. In primary peritonitis, penicillin monotherapy is likely to be sufficient, but broad-spectrum therapy is indicated pending culture results, and particularly in cases where there is clinical evidence of endotoxaemia. Antimicrobial therapy can be de-escalated when culture results are available.

Flunixin meglumine is generally administered for anti-pyretic, pain relieving and anti-endotoxic properties. IV fluid therapy is often required.

Antimicrobials used

- Initial therapy – procaine penicillin at 22,000 IU/kg IM q 12 h or benzyl penicillin at 12-16 mg/kg IV q 6 h
  AND gentamicin at 6.6 mg/kg IV q 24 h
  +/- metronidazole at 25 mg/kg PO q 12 h
- Ongoing therapy should be based on culture and susceptibility testing
- The duration of therapy might be as short as 5 days in uncomplicated primary peritonitis, but up to 30 days has been described

Prognosis

Cases of secondary peritonitis have a survival rate of between 40-86%. Cases of primary or idiopathic peritonitis have survival rates of between 57 and 94%.

Further reading

Southwood LL, Russell G. The use of clinical findings in the identification of equine peritonitis cases that respond favorably to medical therapy. Journal of Veterinary Emergency and Critical Care. 2007;17(4):382-90.

Chapter 8: Salmonellosis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Salmonella shedding is more common in horses presented for colic.
2. Fever, leukopaenia, and an elevated blood lactate should prompt testing for Salmonellosis.
3. Large veterinary hospitals should routinely screen horses with gastrointestinal disease for Salmonellosis.

Salmonella enterica can cause severe diarrhoea in the adult horse and is one of the most commonly identified agents associated with nosocomial outbreaks in veterinary hospitals, resulting in morbidity and mortality in patients, and zoonotic infections in personnel. Different serotypes have been identified in Australia, including *Salmonella* Typhimurium*, Salmonella* Montevideo*, Salmonella* Welikade (189) and *Salmonella* Bovismorbificans*,* with *Salmonella* Muenster being found more recently (unpublished research). Transmission is faecal-oral, typically through ingestion of contaminated material, with contamination of pastures by intermittently shedding, sub-clinically infected horses (estimated to be approximately 1% of the equine population). Salmonellae can persist in the environment for years, can withstand freezing temperatures and drying, and can replicate at a wide range of temperatures (7-45 ℃).

Salmonella infection can result in a range of disease from asymptomatic shedding to diarrhoea and septicaemia (mainly in foals). Horses with colic however, seem to have an increased risk of acquiring and shedding salmonellae, with a prevalence of 3.5% detected in a recent study of horses presenting with colic to a veterinary teaching hospital (190). Older studies have reported shedding rates of 9-20%. In a 2023 study (190), admission during summer months, fever, leukopaenia, and an elevated blood lactate were more likely to be found in horses shedding salmonellae.

Horses treated with antimicrobials can also develop acute diarrhoea and become culture positive for *Salmonella* spp. (see Chapter 1 part i: Antimicrobial-associated diarrhoea in this section).

Salmonella spp. also pose a biosecurity risk within equine facilities. Horses can be shedding *Salmonella* spp. on admission to hospitals (~7%) or acquire salmonellae while hospitalised. Clinically normal horses can shed salmonellae, with shedding more common during concurrent illness, especially if there is antimicrobial usage or the primary disease is gastrointestinal. Stress due to transportation, changes in herd dynamics and changes in diet also predispose to shedding. Shedding can be intermittent.

Salmonella spp. are among the aetiological agents associated with sepsis in foals (see Section 8).

Salmonellosis is potentially zoonotic, with young children and immunosuppressed people at highest risk.

Diagnostics

Faecal PCR is often used as a screening test, but Salmonella culture is required to confirm infection and for serotyping.

Salmonellae are shed intermittently in low numbers, necessitating repeated sample collection. There are no reference protocols for detecting Salmonella shedding but the most common is 3-5 samples collected at 12-24 h intervals and cultured using enrichment media. Salmonella culture should be requested specifically, along with serotyping and susceptibility testing.

Samples can be pooled using the following protocol: 5 samples (10 g each) collected at 8-24 h intervals and stored at 4 °C and submitted for culture as 1 sample (50 g total) (191).

PCR assays are also available for the detection of *Salmonella* spp. but enrichment culture is still required, so results are still delayed by 1-2 days (compared to 2-5 days for culture). PCR assays are extremely sensitive and can detect non-viable organisms and degraded DNA, so a positive test may not indicate an infectious risk in clinically normal animals or in environmental samples. However, in animals with colitis, a positive PCR result is probably a reliable indicator of salmonellosis.

Treatment

Therapy should be the same as for any acute colitis (see Chapter 1 in this section). Antimicrobial drugs are not indicated and adult horses that have been exposed to antimicrobials are more likely to shed salmonellae than adult horses without exposure to antimicrobials.

Biosecurity Guidelines

Quarantine horses that have 2 of the 3 classical signs of colitis (fever, diarrhoea, and leukopaenia). If isolation facilities are not available, establish barrier precautions at the current location.

Isolate horses after significant colic episodes and colic surgery. Ideally hospital facilities should be organised into zones, so that low risk cases (i.e. day patients and outpatients) do not come into contact with high-risk patients (colic cases and other critically ill patients).

Stalls from high-risk and known positive cases should have all organic material removed and disposed of in a manner than reduces the risk of re-exposure. Disinfection should follow. Pressure washers and hoses should be avoided as they can aerosolize salmonellae.

Affected horses should be isolated from unaffected animals on the farm for 30 days and until 5 consecutive negative faecal cultures are obtained. If housed in a paddock, manure should be removed and appropriately disposed of to reduce contamination. Caretakers should wear personal protective equipment.

Protocols for disinfection and environmental screening are outside the scope of these guidelines, but excellent recommendations have been developed by the AAEP (https://aaep.org/document/general-biosecurity-guidelines).

Antimicrobials used

- Antimicrobial therapy is not indicated for colitis caused by *Salmonella* spp.

Prognosis

The prognosis is guarded, similar to that of undifferentiated colitis (see Chapter 1 for details). Early identification and appropriate treatment may reduce complications and improve the prognosis.

Shedding has not been associated with increased long-term risk of mortality or colic. Salmonella-positive horses should be isolated with barrier precautions until proven to be negative in, ideally, five consecutive faecal cultures. The duration of shedding is highly variable, from days to > 1 month.

Further reading

Burgess BA. Salmonella in Horses. Vet Clin North Am Equine Pract. 2023;39(1):25-35.

Burgess BA, Bauknecht K, Slovis NM, Morley PS. Factors associated with equine shedding of multi-drug-resistant Salmonella enterica and its impact on health outcomes. Equine veterinary journal. 2018;50(5):616-23.

Chapter 9: Tyzzer's Disease

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Sudden death is a common presentation.
2. The rapid progression of disease makes successful treatment extremely difficult.

The disease is characterised by acute or peracute, rapidly progressive, necrotic hepatitis that typically results in death within 2-48 h. Foals at 1 to 6 weeks of age are the predominant age group affected, both sporadically and as outbreaks.

The causative agent is *Clostridium piliforme*, a spore-forming soil and manure-borne Gram-negative obligate intracellular bacterium. The pathogenesis is poorly understood, but oral exposure though ingestion of spore-containing faeces from carrier horses is presumed. Oral administration of faeces from experimentally infected horses to foals results in clinical disease.

Diagnostics

Reported clinical signs are non-specific and include lethargy, loss of the suckle reflux, dehydration, fever, icterus, diarrhoea and seizures, followed rapidly by recumbency, weakness, coma and death.

Clinical pathology generally reveals severe metabolic acidosis, hypoglycaemia, and marked hepatocellular injury.

A definitive diagnosis of Tyzzer's disease is based on histological demonstration of the organisms in hepatocytes surrounding necrotic foci in the liver or in sections of the intestine stained with silver. Infection can also be diagnosed by PCR of the faeces or affected tissues, and serology using an indirect immunofluorescence assay or a multiplexed fluorometric immunoassay.

Treatment

Intensive care is required if treatment is to be attempted. IV fluid therapy should be instituted for shock, and to correct acid-base abnormalities and electrolyte derangements. Plasma and total or partial parenteral nutrition are also often provided.

Antimicrobials with efficacy against *Clostridium* spp. should be administered intravenously. Benzyl penicillin (12-16 mg/kg IV q 6 h) or ampicillin (30 mg/kg IV q 8 h) are appropriate empirical choices. Metronidazole should be avoided, as neurological signs can be exacerbated in horses with liver disease when they are administered metronidazole.

Antimicrobials used (include recommended dose rates/duration)

- Benzyl penicillin at 22-44,000 IU/kg (12-24 mg/kg) IV q 4-6 h OR ampicillin at 30 mg/kg IV q 8 h for 5-8 days

Prognosis

This disease is generally fatal in foals. There is only one published report of successful treatment of a confirmed case.

Further reading

Borchers A, Magdesian KG, Halland S, Pusterla N, Wilson WD. Successful Treatment and Polymerase Chain Reaction (PCR) Confirmation of Tyzzer's Disease in a Foal and Clinical and Pathologic

Characteristics of 6 Additional Foals (1986-2005). Journal of veterinary internal medicine. 2006;20(5):1212-8.

García JA, Navarro MA, Fresneda K, Uzal FA. Clostridium piliforme infection (Tyzzer disease) in horses: retrospective study of 25 cases and literature review. Journal of veterinary diagnostic investigation. 2022;34(3):421-8.

Reference List

1. Fielding CL, Higgins JK, Higgins JC, McIntosh S, Scott E, Giannitti F, et al. Disease Associated with Equine Coronavirus Infection and High Case Fatality Rate. Journal of veterinary internal medicine. 2015;29(1):307-10.
2. Horner S, Agne GF, Byrne DP, Bain ME, Lynch BM, Gow WR, et al. Case series report: Equine coronavirus in Australia. Australian Veterinary Journal. 2025;103(1-2):56-62.
3. Gomez D, Toribio R, Caddey B, Costa M, Vijan S, Dembek K. Longitudinal effects of oral administration of antimicrobial drugs on fecal microbiota of horses. Journal of veterinary internal medicine. 2023;37(6):2562-72.
4. Gohari IM, Arroyo L, Macinnes JI, Timoney JF, Parreira VR, Prescott JF. Characterization of Clostridium perfringens in the feces of adult horses and foals with acute enterocolitis. Canadian journal of veterinary research. 2014;78(1):1-7.
5. Hain-Saunders NMR, Knight DR, Bruce M, Byrne D, Riley TV. Genomic Analysis of Clostridioides difficile Recovered from Horses in Western Australia. Microorganisms. 2023;11(7).
6. Walshe N, Mulcahy G, Crispie F, Cabrera-Rubio R, Cotter P, Jahns H, et al. Outbreak of acute larval cyathostominosis – A "perfect storm" of inflammation and dysbiosis. Equine veterinary journal. 2021;53(4):727-39.
7. Goer JR, Harris PA, editors. How to minimize gastrointestinal disease associated with carboyhdrate nutrition in horses. AAEP Annual Convention; 2007; Orlando: American Association of Equine Practitioners.
8. van Galen G, Saegerman C, Hyldahl Laursen S, Jacobsen S, Andersson Munk M, Sjöström H, et al. Colonic Health in Hospitalized Horses Treated with Non-Steroidal Anti-Inflammatory Drugs – A Preliminary Study. Journal of equine veterinary science. 2021;101:103451-.
9. Karcher LF, Dill SG, Anderson WI, King JM. Right dorsal colitis. J Vet Intern Med. 1990;4(5):247-53.
10. Davis JL. Nonsteroidal anti-inflammatory drug associated right dorsal colitis in the horse. Equine veterinary education. 2017;29(2):104-13.
11. Lightbody KL, Austin A, Lambert PA, von Samson-Himmelstjerna G, Jürgenschellert L, Krücken J, et al. Validation of a serum ELISA test for cyathostomin infection in equines. International journal for parasitology. 2024;54(1):23-32.
12. Kopper JJ, Kogan CJ, Cook VL, Schott nHC. Outcome of horses with enterocolitis receiving oncotic fluid support with either plasma or hetastarch. Canadian veterinary journal. 2019;60(11):1207-12.
13. van Galen G, Hallowell G. Hydroxyethyl starches in equine medicine. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2019;29(4):349-59.
14. van Eps AW. Therapeutic Hypothermia (Cryotherapy) to Prevent and Treat Acute Laminitis. The Veterinary clinics of North America Equine practice. 2010;26(1):125-33.
15. Schoster A, Weese JS, Guardabassi L. Probiotic Use in Horses - What is the Evidence for Their Clinical Efficacy? Journal of veterinary internal medicine. 2014;28(6):1640-52.
16. Quattrini C, Bozorgmanesh R, Egli P, Magdesian KG. Fecal microbiota transplant for treatment of diarrhoea in adult hospitalized horses—111 cases (2013–2018). Open veterinary journal (Tripoli, Libya). 2023;13(9):1135-40.

17. Mullen KR, Yasuda K, Divers TJ, Weese JS. Equine faecal microbiota transplant: Current knowledge, proposed guidelines and future directions. Equine veterinary education. 2018;30(3):151-60.

18. Niinistö K, Sykes BW. Diagnosis and management of sand enteropathy in the horse. Equine veterinary education. 2022;34(11):600-6.

19. Tennent-Brown BS, Wilkins PA, Lindborg S, Russell G, Boston RC. Sequential plasma lactate concentrations as prognostic indicators in adult equine emergencies. J Vet Intern Med. 2010;24(1):198-205.

20. Love S, Mair TS, Hillyer MH. Chronic diarrhoea in adult horses: a review of 51 referred cases. Vet Rec. 1992;130(11):217-9.

21. Murphy D, Reid SWJ, Love S. The effect of age and diet on the oral glucose tolerance test in ponies. Equine Veterinary Journal. 1997;29(6):467-70.

22. Divers TJ. Azathioprine - a useful treatment for immune-mediated disorders in the horse? Equine Veterinary Education. 2010;22(10):501-2.

23. Divers TJ, Barton MH. Chapter 13 - Disorders of the Liver. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine (Fourth Edition): W.B. Saunders; 2018. p. 843-87.

24. Smith MRW, Stevens KB, Durham AE, Marr CM. Equine hepatic disease: the effect of patient- and case-specific variables on risk and prognosis. Equine veterinary journal. 2003;35(6):549-52.

25. Peek SF, Divers TJ. Medical treatment of cholangiohepatitis and cholelithiasis in mature horses: 9 cases (1991-1998). Equine veterinary journal. 2000;32(4):301-6.

26. Seahorn TL, Cornick JL, Cohen ND. Prognostic indicators for horses with duodenitis-proximal jejunitis. 75 horses (1985-1989). J Vet Intern Med. 1992;6(6):307-11.

27. Steinman A, Gips M, Lavy E, Sinay I, Soback S. Pharmacokinetics of metronidazole in horses after intravenous, rectal and oral administration. Journal of veterinary pharmacology and therapeutics. 2000;23(6):353-7.

28. Collins A, Love RJ, Pozo J, Smith SH, McOrist S. Studies on the ex vivo survival of Lawsonia intracellularis. Swine Health and Production. 2000;8(5):211-5.

29. Dohrmann J, Hildebrand F, Straub J, Wadephul R, Pusterla N, Freise F, et al. Equine Proliferative Enteropathy in Weanling Foals on A German Breeding Farm: Clinical Course, Treatment and Long-Term Outcome. Journal of equine veterinary science. 2022;111:103873.

30. Sykes BW, Bowen M, Habershon-Butcher JL, Green M, Hallowell GD. Management factors and clinical implications of glandular and squamous gastric disease in horses. Journal of veterinary internal medicine. 2019;33(1):233-40.

31. Sykes BW, Hewetson M, Hepburn RJ, Luthersson N, Tamzali Y. European College of Equine Internal Medicine Consensus Statement-Equine Gastric Ulcer Syndrome in Adult Horses. Journal of veterinary internal medicine. 2015;29(5):1288-99.

32. Vokes J, Lovett A, Sykes B. Equine Gastric Ulcer Syndrome: An Update on Current Knowledge. Animals (Basel). 2023;13(7):1261.

33. Javsicas LH, GiguÈRe S, Freeman DE, Rodgerson DH, Slovis NM. Comparison of Surgical and Medical Treatment of 49 Postpartum Mares with Presumptive or Confirmed Uterine Tears. Veterinary surgery. 2010;39(2):254-60.

34. Diekstall M, Rohde C, Rijkenhuizen ABM. Post-partum uterine rupture: Standing repair in three mares using a laparoscopic technique. Equine veterinary education. 2020;32(6):319-24.

35. Odelros E, Kendall A, Hedberg-Alm Y, Pringle J. Idiopathic peritonitis in horses: A retrospective study of 130 cases in Sweden (2002-2017). Acta veterinaria scandinavica. 2019;61(1):18-.

36. Alonso JdM, Esper CS, Pantoja JCF, Rosa GdS, Giampietro RR, dos Santos B, et al. Accuracy of differences in blood and peritoneal glucose to differentiate between septic and non-septic peritonitis in horses. Research in veterinary science. 2020;132:237-42.

37. McTernan SP, Heller J, Clulow JR, Gannon L, Huang R, Tidd N, et al. The prevalence, serotypes and antibiograms of Salmonella isolates on Thoroughbred stud farms in New South Wales and Victoria. Australian Veterinary Journal. 2025;n/a(n/a).

38. Kilcoyne I, Magdesian KG, Guerra M, Dechant JE, Spier SJ, Kass PH. Prevalence of and risk factors associated with Salmonella shedding among equids presented to a veterinary teaching hospital for colic (2013–2018). Equine veterinary journal. 2023;55(3):446-55.

39. Goni JI, Hendrix K, Kritchevsky J. Recovery of Salmonella bacterial isolates from pooled fecal samples from horses. Journal of veterinary internal medicine. 2023;37(1):323-7.

Section 7 – Endotoxaemia

Contents

Chapter 1: Endotoxaemia

Author: Laura Hardefeldt, Jenni Bauquier, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Endotoxaemia results from many conditions in adults and foals.
2. Clinical and haematological signs reflect disease severity.
3. Can be fatal if severe or untreated.

Endotoxaemia refers to a syndrome of acute, systemic activation of the innate immune system in response to bacteria or bacterial toxins, also referred to as the systemic inflammatory response syndrome (SIRS), or sepsis when it occurs in response to bacterial infection. It is a common cause of morbidity, mortality and economic loss in horses. Endotoxaemia is commonly associated with disorders such as strangulating intestinal lesions, pleuropneumonia, peritonitis, enterocolitis, retained foetal membranes and foal sepsis.

Lipopolysaccharide (LPS) is a component of the outer cell membrane of Gram-negative bacteria. Other bacterial cell wall components, such as lipoteichoic acid (from Gram-positive bacteria) and peptidoglycan, can also be involved. When present in the circulation, bacterial toxins interact with toll-like receptors to stimulate release of cytokines that cause further release of inflammatory mediators, including prostaglandins, histamine, serotonin, kinins and others. Massive systemic inflammation results, which in turn is responsible for cardiovascular depression and arterial hypoxaemia. This leads to decreased tissue perfusion and peripheral hypoxia, and, in severe or untreated cases, multiple organ dysfunction (including laminitis) and death. Coagulation is also upregulated, often leading to thrombus formation, or development of microthrombi (more commonly in foals).

Endotoxaemia can also lead to an alteration in vascular tone and permeability, which might contribute to development of detectable oedema, particularly in septic foals receiving intravenous fluid therapy. In adults, oedema often results from the protein loss that mainly occurs secondarily to vascular leakage at the site of the primary disease (for example in colitis).

Diagnostics

Clinical signs of endotoxaemia include fever, hypothermia or normothermia, dull mentation, congested mucous membranes, injected sclera, tachycardia, and tachypnoea (although sometimes the respiratory rate is normal or reduced), and, sometimes, muscle fasciculations.

Blood lactate concentration is often increased, reflecting mainly hypovolaemia and reduced perfusion. White blood cell concentrations are initially reduced (leukopaenia, due primarily to neutropaenia) but often rebound after systemic inflammation has resolved, to a transient neutrophilic leukocytosis. Lymphopaenia and haemoconcentration (increased PCV) are also present. Platelet counts can be reduced, and PT and APTT prolonged, if coagulation has been upregulated, resulting in consumption of platelets and coagulation factors. Effects on haematological function reflect the severity of the disease. Pre-renal azotaemia, with or without renal azotaemia, is often present.

The blood glucose concentration is often low in foals.

Treatment

Many treatments have been used and examined to counteract the adverse effects of endotoxin on horses. Few have evidence supporting their efficacy. This section discusses proven treatment strategies, but is not exhaustive – there are several reviews in the literature (e.g. Kelmer, 2009 (192)). Overarching treatment goals have been aimed at:

1. Counteracting the inflammatory cascade induced by endotoxin.
2. Elimination of the source of endotoxin.
3. Blocking interactions between endotoxin and the immune system.

Counteracting the inflammatory cascade is the mainstay of therapy, as almost all cases have activation of the inflammatory cascade on presentation. The main aim of treatment is to provide supportive therapy - treating cardiovascular shock with fluid therapy, preventing laminitis, and suppressing inflammation. Prevention of laminitis is not included here, but there are several reviews published (e.g. Belkap & Durham, 2017(193)).

Fluid therapy is the mainstay, non-specific, supportive therapeutic strategy to combat cardiovascular shock. All endotoxaemic patients are at least moderately, if not severely, hypovolaemic, and thus the use of balanced crystalloid solutions (i.e. Hartmann's solution) is essential. Hypertonic saline (7% NaCl at 2-4 mL/kg) is a useful therapy to rapidly expand blood volume in adults, especially in the field, and especially in cases where drinking is not contraindicated. Even if drinking is contraindicated, isotonic IV fluid therapy can often be delayed following hypertonic saline administration, while the horse is transported to a hospital provided the trip is not too long. Hypertonic saline is usually unsuitable in foals because of its impact on electrolyte balance and acid-base abnormalities, but it is also less necessary in foals, as bolus isotonic fluids can be rapidly administered to achieve the same outcome. Commercially available plasma (2-8 L per horse) is also commonly administered to endotoxaemic patients. Hyperimmune plasma is typically used as there is some evidence of survival benefit in septic foals. While theoretically beneficial, evidence of efficacy in endotoxaemic adult horses is lacking and the cost is substantial. Synthetic colloids (such as Hetastarch) have also been administered to endotoxaemic horses with hypoproteinaemia and low colloid oncotic pressure, although evidence to support their use is lacking and they have fallen out of favour in other species because of the risk of complications.

Flunixin meglumine is a potent NSAID and the most common anti-inflammatory and antiendotoxic treatment administered other than fluid therapy. Flunixin inhibits the COX breakdown of arachidonic acid to prostaglandins, which are important mediators in the inflammatory pathway of endotoxaemia and lead to clinical features such as vasodilation and cardiovascular shock. Low doses of flunixin (0.25 mg/kg IV q 8 h) have been shown to be effective in experimental models and have been used clinically to avoid the gastrointestinal and nephrotoxic side-effects of higher doses. However, these lower doses usually do not prevent the clinical signs associated with endotoxaemia, such as colic, fever and dull mentation. In the authors' experience, doses of 0.5 mg/kg IV q 12 h are effective for anti-inflammatory effects and combating clinical signs and are less likely to be associated with adverse effects, but this may be variable depending on the underlying cause and the severity of disease.

Most cases with endotoxaemia require antimicrobials to address the primary disease or for surgical prophylaxis. Cases associated with colitis and anterior enteritis are the exception where most do not require antimicrobial therapy. The choice of antimicrobials should be made carefully, as, theoretically, rapid killing of Gram-negative bacteria may result in release of more endotoxin and exacerbation of clinical signs. Aminoglycosides cause minimal release of LPS (194) so gentamicin is a good choice in many patients, if renal function is normal.

Dimethyl sulfoxide (DMSO) is an oxygen free-radical scavenger and anti-inflammatory agent that is widely used for treating endotoxaemia. However, evidence to support its use is lacking and there are substantial occupational health and safety risks in humans, so its use is not recommended. Where it is used, low doses (20 mg/kg IV) should be used, as higher doses have been associated with gastrointestinal mucosal damage and haemolysis.

Pentoxifylline has been widely used as an adjunctive therapy for equine endotoxaemia based on experimental evidence of inhibition of inflammatory cytokine and tissue factor activity. However, absorption following oral administration is poor and erratic, and an intravenous formulation is not commercially available. In addition, responses after exposure to endotoxin have been less promising than administration before endotoxin exposure. Clinical trials are needed before its use can be recommended.

Low doses of corticosteroids have been shown to be beneficial in experimental endotoxaemia in horses and foals, but their use is controversial in clinical cases. Physiological doses of corticosteroids may provide benefit in some cases where there is dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis and inadequate cortisol release in response to illness – a syndrome called critical illness-related corticosteroid insufficiency (CIRCI). Hypotensive animals that are unresponsive to fluid therapy and vasopressors may have CIRCI and might benefit from corticosteroid administration, but in cases with hypotension that do respond to fluid therapy or vasopressors, corticosteroids are probably contraindicated. Hydrocortisone doses of 1.3 mg/kg/day IV divided and administered every 4 hours have been recommended for use in foals. For adults, the dose is 0.16-0.3 mg/kg IV q 4 h (195). A dose of 0.3 mg/kg did not have an impact on clinical signs or proinflammatory cytokine production, but did appear to protect against LPS-induced neutrophil depletion in an experimental model of endotoxaemia (196). As for many other adjunctive therapies, clinical trials are lacking and are needed before this therapy can be recommended.

Elimination of the source of endotoxin involves treatment of the primary disease – strangulating intestinal lesions should be treated surgically without delay. Similarly, antimicrobial therapy should be implemented promptly where the primary disease is likely to be bacterial infection (for example, retained foetal membranes, foal sepsis or pleuropneumonia) but preferably following collection of samples for culture and susceptibility testing, if possible.

Blocking or eliminating endotoxin before it interacts with the horse's immune system can be achieved by neutralising LPS with plasma rich in anti-LPS antibodies (hyperimmune plasma) (Equiplas E) or, potentially, polymyxin B. In a clinical trial of septic foals, foals treated with anti-LPS enriched plasma were more likely to survive than foals treated with regular plasma (197). However, other studies have only shown a small difference, and some have found no difference at all. A randomised controlled clinical trial is needed, but difficult to perform.

Polymyxin B has been shown to be effective in reducing the clinical signs associated with endotoxaemia in experimental scenarios, but it is nephrotoxic and the reduced perfusion and dehydration present in clinical cases means it is often contraindicated. In this author's experience there is no benefit to the administration of polymyxin B in clinical cases. In addition, the availability of this drug in Australia is variable.

Antimicrobials used

- Treat the primary disease, no antimicrobials are specifically recommended for endotoxaemia

Reference List

1. Kelmer G. Update on Treatments for Endotoxemia. The Veterinary clinics of North America Equine practice. 2009;25(2):259-70.

2. Belknap JK, Durham AE, Belknap JK, Geor RJ. Overview of Laminitis Prevention. Hoboken, NJ, USA: John Wiley & Sons, Inc; 2017. p. 421-6.

3. Kusser WC, Ishiguro EE. Effects of aminoglycosides and spectinomycin on the synthesis and release of lipopolysaccharide by Escherichia coli. Antimicrobial Agents and Chemotherapy. 1988;32(8):1247-50.

4. Hart KA, Barton MH. Adrenocortical Insufficiency in Horses and Foals. The Veterinary clinics of North America Equine practice. 2011;27(1):19-34.

5. Anderson MJ, Ibrahim AS, Cooper BR, Woolcock AD, Moore GE, Taylor SD. Effects of administration of ascorbic acid and low-dose hydrocortisone after infusion of sublethal doses of lipopolysaccharide to horses. Journal of veterinary internal medicine. 2020;34(6):2710-8.

6. Peek SF, Semrad S, McGuirk SM, Riseberg A, Slack JA, Marques F, et al. Prognostic value of clinicopathologic variables obtained at admission and effect of antiendotoxin plasma on survival in septic and critically ill foals. J Vet Intern Med. 2006;20(3):569-74.

Section 8 – Neonates

Contents

Chapter 1: Gastrointestinal tract/diarrhoea in foals

Authors: Rosemary Cuming, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Diarrhoea is common in foals of all ages and can range from self-limiting to severe.
2. Antimicrobial therapy is only indicated in selected cases.

Diarrhoea is a frequent presenting complaint in both neonatal and older foals. Disease can vary from mild and self-limiting to life-threatening if significant intestinal wall damage and secondary septicaemia/systemic inflammatory response syndrome (SIRS) are present. Clinical signs may include lethargy, weakness, inappetence, tachycardia, tachypnoea, fever or hypothermia, signs of dehydration (e.g. sunken eyes and cool extremities), colic and/or gastrointestinal intestinal reflux, in addition to diarrhoea. Establishing a definitive diagnosis is often challenging because there are numerous potential aetiologies (Table 8.1) and because of the limitations of available diagnostic tests.

Non-infectious aetiologies include 'foal heat' diarrhoea, mechanical irritation (e.g. from consuming sand or bedding), nutritional factors (e.g. dietary change), lactose intolerance, antimicrobial administration and hypoxic gastrointestinal tract damage.

Infectious aetiologies include neonatal sepsis, Group A or B equine rotaviruses, equine coronavirus (ECoV), *Salmonella spp., Clostridium perfringens, Clostridioides difficile* (re-classified from *'Clostridium difficile* in 2016), *Lawsonia intracellularis* (Section 6), *Rhodococcus equi* (Section 4) and *Cryptosporidium* spp.

Equine rotaviruses are the most common cause of infectious diarrhoea in foals, with around 25% of cases of foal diarrhoea attributed to rotaviruses worldwide and in Australia. While a positive rotavirus PCR assay result is associated with diarrhoea, the pathogen can also be found in around 5% of healthy age-matched foals (Bailey, 2017). Foals can be affected from the first week of life to 4 - 5 months of age, but most cases are diagnosed between 1 and 6 weeks of age. Infection results in small intestinal mucosal villus sloughing and compensatory crypt hyperplasia, and causes malabsorption, lactose intolerance and hypersecretion. Rotaviral diarrhoea has a high morbidity, but the clinical disease is often self-limiting. However, severe dehydration can lead to mortalities. Rotaviruses are highly

contagious, and peak disease prevalence in Australia correlates with periods of increasing horse movement and density on farms (October), so biosecurity is an important consideration.

Equine coronavirus (ECoV) has been associated with outbreaks of fever and diarrhoea in adult horses in the USA and Japan. In Australia (198) and the USA (199), ECoV has been detected in similar proportions of foals with and without gastrointestinal disease. Therefore, the significance of ECoV in the pathogenesis of diarrhoea in foals is unclear. There have been case reports of ECoV in foals with severe disease, but these foals had other complicating factors, such as combined immunodeficiency syndrome or concurrent infections with other pathogens, such as cryptosporidia and coccidia. The prevalence of ECoV in hospitalised foals with diarrhoea is very low (~1%), suggesting that any disease caused by ECoV is probably mild.

Salmonellosis is a known cause of diarrhoea in horses of all ages and can occur as isolated cases or in outbreaks. Salmonellosis can be severe and rapidly fatal and is potentially zoonotic. This is discussed in greater detail in Section 6.

C. difficile is a ubiquitous organism, but disruption of the normal protective enteric flora, for example by antimicrobials, leads to overgrowth of *C. difficile* and production of toxins, which are required for disease to occur. Diagnosis of disease caused by *C. difficile* is, therefore, not merely dependant on detection of the organism, but also determination of its toxigenicity. Isolation of *C. difficile* is slow and requires selective media and anaerobic conditions, which are not available in all diagnostic laboratories. The role of ***Clostridium perfringens*** remains unclear. It can be isolated from over 50% of foals with diarrhoea and many normal foals. Necrotising enteritis is a severe, acute form of foal diarrhoea associated with infection with clostridial species and characterised by marked intestinal inflammation and necrosis. For a discussion of necrotising enteritis see Section 6.

Infection with ***Cryptosporidium parvum*** is associated with sporadic disease and outbreaks of diarrhoea in foals aged 4 to 21 days. The parasite invades ileal microvilli, producing mild to profuse diarrhoea that lasts one to 21 days, although chronic, intermittent diarrhoea can occur in older animals. Diagnosis requires the identification of large numbers of oocysts in faecal smears using acid-fast staining. Care must be taken as *C. parvum* infection is zoonotic.

Table 8.1. Common causes of diarrhoea in foals by age.

Age range	Potential causes
Less than 2 weeks	Neonatal maladjustment syndrome Necrotising enterocolitis Foal heat Rotavirus *Clostridioides difficile* *Cryptosporidium parvum* Salmonellosis
2 weeks – 2 months	Rotavirus *Clostridioides difficile* *Cryptosporidium parvum* Salmonellosis Mechanical irritation (sand)
Over 2 months	Cyathostomiasis *Lawsonia intracellularis* *Clostridioides difficile* *Cryptosporidium parvum* Salmonellosis Mechanical irritation (sand) Nutritional change

Diagnostics

Faecal testing for infectious agents should be conducted. Identification of clostridial species or *E. coli* by faecal culture should be interpreted with caution, as these bacteria are a normal part of the microbiome of foals. PCR assays or ELISAs can be used to identify the toxin genes or toxins of pathogenic *C. perfringens* and *C. difficile*, although quantitative PCR assays are more useful. Serial faecal culture or PCR assays (3 - 5 samples collected a minimum of 12 hours apart) can be used to identify *Salmonella* spp. Faecal PCR assays can also be used to detect the presence of equine rotaviruses, ECoVs, *R. equi* or *L. intracellularis*. Microscopic examination of faecal smears can be used to detect *Cryptosporidium* spp. oocytes. In neonatal foals, blood culture should also be performed, as up to 50% of foals < 30 days of age with diarrhoea are bacteraemic.

Haematology and serum biochemical parameters may be within reference intervals in mild disease. Dehydration may be accompanied by elevations in packed cell volume and lactate concentration, and/or pre-renal azotaemia. Intestinal inflammation may result in leukopaenia or leukocytosis, with an immature neutropaenia reflective of SIRS. Concentrations of acute phase proteins (fibrinogen and serum amyloid A) are often elevated, but may be within normal limits, depending on the severity and stage of disease. Serum biochemistry may reveal hypoproteinaemia associated with intestinal losses of protein and/or consumption of immunoglobulins due to SIRS/sepsis and/or electrolyte abnormalities secondary to losses in diarrhoeic faeces and reduced milk consumption. Typical electrolyte abnormalities reported include hyponatraemia, hypokalaemia, hypobicarbonateaemia and hypo- or hyperchloraemia.

Findings from percutaneous abdominal ultrasonography may be normal or include thickening of the small and/or large intestinal walls, gas opacities within the small intestinal walls, swirling liquid ingesta within the small and/or large intestinal lumen and/or reduced intestinal motility. Gastrointestinal sand accumulation can be identified on abdominal radiographs. Nasogastric intubation may result in return of gastric reflux.

Treatment

In mild cases, where the foal is able to maintain their own hydration through nursing, disease may be self-limiting. Foal heat diarrhoea does not require any treatment. Intestinal protectants/adsorbents (e.g. sucralfate, proton pump inhibitors, di-octahedral smectite, bismuth subsalicylate) may be useful in some cases.

In more severe cases, correction of dehydration and electrolyte and acid-base disturbances through provision of enteral or intravenous fluids and electrolyte supplements is essential. Additional therapies that may be instituted when indicated include restricted feeding, total parenteral nutrition, intravenous plasma, analgesic medications (e.g. butorphanol, buprenorphine, flunixin meglumine), psyllium (to promote expulsion of ingested sand), lactase, faecal microbiota transplantation and/or blood pressure support (e.g. dobutamine, noradrenaline or vasopressin continuous rate infusions).

Strict biosecurity is essential to minimise environmental contamination and reduce the risk of transmission to other neonates and treating personnel in cases where diarrhoea is caused by contagious agents. Antimicrobial therapy should be instituted as outlined below.

Vaccination of mares may be useful in controlling rotavirus outbreaks on farms (see Section 16).

Antimicrobials used

- Prophylactic antimicrobial therapy: broad-spectrum antimicrobials should be administered to foals less than 30 days old presenting with diarrhoea that is not self-limiting (i.e. resolves in 3-4 days and is not associated with other clinical signs of illness) due to the high risk of translocation

of bacteria across the compromised intestinal wall and the subsequent potential for sepsis and/or localisation of bacterial infection at distant sites (e.g. joints). In older foals, broad-spectrum antimicrobials should only be administered on a case-by-case basis, and only if there is a high risk of sepsis and after considering the potential for adverse effects, such as dysbiosis and promotion of antimicrobial resistance.

- Penicillin (benzyl penicillin 22,000 - 44,000 IU/kg (12 - 24 mg/kg) IV q 6 h or procaine penicillin 22,000 IU/kg (22 mg/kg) IM q 12 h) plus gentamicin (12 mg/kg IV q 36 h for foals <2 weeks of age, 6.6. mg/kg IV q24h for foals >2 weeks of age)*
- OR trimethoprim/sulphadiazine (24 mg/kg IV, IM or PO q 12 h)
- OR ceftiofur sodium (5 mg/kg IV or IM q 12 h)**.
- There is no evidence for treatment duration, but 5-7 days is commonly used, based on time to resolution of diarrhoea and improvement in haematological and serum biochemical parameters.

*While one dose of gentamicin is unlikely to induce irreparable kidney injury, continued gentamicin therapy should proceed only if there is evidence that creatinine concentrations are reducing in response to fluid therapy.
** Ceftiofur should only be used as a last resort and should only be used based on blood culture and antimicrobial susceptibility testing.

- Targeted antimicrobial therapy:
    - Clostridial enteritis: metronidazole (10 mg/kg PO or IV q 12 h up to 2 weeks of age; there is no information available on use in older foals but 15 - 20 mg/kg q 8 h is commonly used) for 3 days. (See Section 6 for treatment of necrotising enteritis secondary to clostridial infection.)
    - Salmonellosis: antimicrobials are not indicated.
    - *R. equi* enteritis: azithromycin 10 mg/kg PO q 24 h OR clarithromycin (7.5 mg/kg PO q 12 h) PLUS rifampicin (5 mg/kg PO q 12 h), initially for 2 weeks, is recommended.
    - Lawsonia treatment is found in Section 6.

Prognosis

Prognosis varies from excellent to grave, depending on the aetiology, severity of intestinal pathology, and response to treatment.

Further reading

Lester G, Sanchez C, Smith R, Axon J, Byrne D. Chapter 17: Manifestations and Management of Disease in Neonatal Foals. In: Smith BP, Pusterla N, editors. Large Animal Internal Medicine. 6 ed. Missouri: Elsevier; 2020. p. 262-306.e7.

Oliver-Espinosa O. Foal Diarrhoea: Established and Postulated Causes, Prevention, Diagnostics, and Treatments. The Veterinary clinics of North America Equine practice. 2018;34(1):55-68.

Hollis AR, Wilkins PA, Palmer JE, Boston RC. Bacteremia in Equine Neonatal Diarrhoea: A Retrospective Study (1990-2007). Journal of veterinary internal medicine. 2008;22(5):1203-9.

Burton AJ, Giguère S, Warner L, Alhamhoom Y, Arnold RD. Effect of age on the pharmacokinetics of a single daily dose of gentamicin sulfate in healthy foals. Equine veterinary journal. 2013;45(4):507-11.

Swain EA, Magdesian KG, Kass PH, Edman JE, Knych HK. Pharmacokinetics of metronidazole in foals: influence of age within the neonatal period. Journal of veterinary pharmacology and therapeutics. 2015;38(3):227-34.

Chapter 2: Necrotising enterocolitis of neonatal foals

Authors: Rosemary Cuming, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Severe illness of neonates that requires prompt diagnosis and treatment
2. Empirical treatment for clostridial infection should be instituted whilst awaiting test results

Severe, acute onset disease of neonates characterised by marked intestinal inflammation and necrosis, and subsequent production of profuse yellow to brown diarrhoea, which may contain frank blood and/or mucosal shreds. Foals typically present with lethargy, dehydration, inappetence and colic, but may present moribund if very severely affected. These signs may precede or be concurrent with the onset of diarrhoea. Haemorrhagic gastric reflux may also develop as the disease progresses. The underlying aetiology may be Neonatal Maladjustment Syndrome or prematurity, with resultant gastrointestinal tract hypoperfusion and secondary bacterial invasion of the devitalised intestinal mucosa, or infection with *Clostridium perfringens* or *Clostridioides (Clostridium) difficile*. Foals may ingest clostridia from their environment (contaminated by asymptomatic shedders or sick herd mates) during their first few days of life. Clostridia grow rapidly within the intestinal lumen and produce an array of toxins, which may be protected from destruction by the presence of trypsin inhibitors in colostrum in young neonates. Clostridial toxins attach to the intestinal villi and cause necrosis and haemorrhage within the mucosa and submucosa, resulting in diarrhoea. Bacteraemia and systemic inflammatory response syndrome (SIRS)/sepsis frequently develop in these patients because of their compromised gut barrier.

Diagnostics

Percutaneous abdominal ultrasonography may identify thickening of the small intestinal walls, gas opacities within the small intestinal walls, swirling liquid ingesta within the small and/or large intestinal lumen and/or reduced intestinal motility. Nasogastric intubation may result in return of gastric reflux if ileus is present.

Haematology typically reveals leukopaenia, due to a neutropaenia (however the white blood cell count may be normal), with toxic changes present in the neutrophils. Anaemia may be present if there has been significant blood loss into the intestinal lumen. Blood lactate concentrations are typically elevated, but may be normal in milder cases. Serum biochemistry may reveal hypoproteinaemia associated with loss of protein into the intestine and/or consumption of immunoglobulins due to SIRS/sepsis, azotaemia that is pre-renal in origin and secondary to dehydration or indicative of kidney insufficiency related to underlying Neonatal Maladjustment Syndrome or sepsis, and/or electrolyte abnormalities secondary to losses in diarrhoeic faeces and reduced milk consumption.

Blood culture should be performed to guide antimicrobial therapy. Faecal PCR assays or ELISAs should be performed to detect toxin genes or toxins of *C. perfringens* and *C. difficile*. Samples should be submitted for faecal PCR assays, culture and examination of stained smears to rule out alternative differential diagnoses for neonatal foal diarrhoea (e.g. salmonellas, rotaviruses, *Cryptosporidium parvum*).

Treatment

Antimicrobial therapy should be instituted as outlined below. Correction of dehydration and electrolyte and acid-base disturbances through provision of intravenous fluids (+/- intravenous or oral electrolytes) is essential. Additional therapies that may be instituted include restricted feeding, total parenteral nutrition, intravenous plasma, analgesic medications (e.g. butorphanol, buprenorphine,

flunixin meglumine, lignocaine by continuous rate infusion), gastric protectants and anti-diarrhoeal agents (e.g. sucralfate, proton pump inhibitors, di-octahedral smectite).

In foals with significant SIRS/sepsis, blood pressure support (e.g. dobutamine, noradrenaline or vasopressin continuous rate infusions) may also be indicated. Strict biosecurity is essential to minimise environmental contamination and reduce the risk of reinfection and transmission to other neonates.

Antimicrobials used

- Metronidazole: 10 mg/kg PO or IV q 12 h* for 3 days
- Additional injectable broad-spectrum antimicrobial coverage is recommended because of the likelihood of bacteraemia because of the loss of intestinal wall integrity.
    - Penicillin (benzyl penicillin 22,000-44,000 IU/kg IV q 6 h OR procaine penicillin 22 000 IU/kg IM q 12 h) PLUS gentamicin (12 mg/kg IV q 36 h)**
    - OR trimethoprim/sulphadiazine (30 mg/kg IV or IM q 12 h)
    - OR ceftiofur sodium (5 mg/kg IV or IM q 12 h)***

    There is no evidence to support a recommendation for the duration of treatment, but 5 - 7 days is commonly used.

* Different dose rates used for neonatal foals < 2 weeks of age than for adult horses.
** Aminoglycoside therapy should only be initiated after confirming that the foal has adequate kidney function and ensuring the foal is hydrated.
*** Ceftiofur should only be used as a last resort and only if indicated by blood culture and antimicrobial susceptibility testing.

Prognosis

The prognosis is very poor for foals with necrotising enteritis associated with Neonatal Maladjustment Syndrome or prematurity, with rapid deterioration and death common. The prognosis is fair for foals with clostridial enteritis, with survival rates of 81% to 88% reported. Foals that survive their initial illness are at risk of delayed complications (e.g. septic arthritis, chronic diarrhoea and failure to thrive).

Further reading

Jones S. Chapter 32: Diseases of the alimentary tract. In: Smith BP, editor. Large Animal Internal Medicine. 5 ed. Missouri: Elsevier; 2015. p. 638-842.

Morresey P. Chapter 181: Colic in foals. In: Sprayberry KA, Robinson NE, editors. Current Therapy in Equine Medicine. 7 ed. Missouri: Elsevier Saunders; 2015. p. 758-65.

Mehdizadeh Gohari I, Unterer S, Whitehead AE, Prescott JF. NetF-producing Clostridium perfringens and its associated diseases in dogs and foals. Journal of veterinary diagnostic investigation. 2020;32(2):230-8.

Frederick J, Giguere S, Sanchez LC. Infectious agents detected in the feces of diarrheic foals: A retrospective study of 233 cases (2003-2008). Journal of veterinary internal medicine. 2009;23(6):1254-60.

Burton AJ, Giguère S, Warner L, Alhamhoom Y, Arnold RD. Effect of age on the pharmacokinetics of a single daily dose of gentamicin sulfate in healthy foals. Equine veterinary journal. 2013;45(4):507-11.

Swain EA, Magdesian KG, Kass PH, Edman JE, Knych HK. Pharmacokinetics of metronidazole in foals: influence of age within the neonatal period. Journal of veterinary pharmacology and therapeutics. 2015;38(3):227-34.

Chapter 3: Neonatal sepsis

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Key issues

1. Sepsis is a common, potentially life-threatening disease in neonatal foals.
2. A wide variety of both Gram-positive and Gram-negative organisms can cause sepsis.
3. Antimicrobial resistance is increasing in pathogens responsible for sepsis, so culture and susceptibility testing of appropriately collected blood, and other samples, is strongly recommended.
4. Rapid institution of antimicrobial therapy has been associated with improved outcomes (when the causative organism is susceptible to the antimicrobial used).

Sepsis is a major cause of morbidity and mortality in equine neonates, particularly in those under 7 days of age. Predisposing factors in the development of sepsis in neonatal foals include failure of transfer of passive immunity and exposure to pathogens, either *in utero* (e.g. if the mare has placentitis) or post-partum, through the umbilicus, wounds, or the respiratory, urogenital or gastrointestinal tracts. The latter is thought to be the most common route of infection, with translocation of bacteria across the neonatal gastrointestinal wall into the systemic circulation. The clinical manifestation of sepsis is largely attributable to a dysregulated host response to infection, rather than the infectious organism itself. The pathophysiology of sepsis involves a complex interplay between components of multiple inflammatory, coagulation and endocrine pathways, and has been reviewed extensively elsewhere (see further reading). The malignant global activation of pro-inflammatory pathways (systemic inflammatory response syndrome; SIRS), which occurs following the initial appropriate immune response to the presence of the bacterial invader, may be mild and the infection may be easily resolved with antimicrobial therapy in some foals, resulting in fairly minor clinical disease, but in many cases the SIRS response is marked and may be followed by shock, progressive dysfunction of the cardiovascular, renal, respiratory, hepatic, gastrointestinal and/or neurological systems (multiple organ dysfunction syndrome; MODS) and/or development of coagulopathies (including disseminated intravascular coagulopathy; DIC).

Clinical signs of sepsis can be variable and non-specific, so sepsis should be included as a differential diagnosis for any neonatal foal presenting with clinical illness. Clinical signs that may be observed include lethargy, reduced interest in nursing, depressed mentation, recumbency, increases or decreases in heart rate, respiratory rate or body temperature, abnormal mucous membrane colour, hyperaemic coronary bands, petechiation of the mucous membranes or skin of the pinnae, uveitis, a weak peripheral pulse strength and cool extremities. Signs of localised infection may also be present (e.g. joint effusion, respiratory distress, diarrhoea or umbilical abscessation). Normal vital signs of foals of varying ages are shown in Table 8.2.

Table 8.2. Normal vital signs of neonatal foals.

Age	Temperature (°C)	Heart rate (/min)	Respiratory rate (/min)	Behaviour
0 - 1 min	37.5	70 - 80	70	Breaks amnion by limb/head movement

Age	Temperature (°C)	Heart rate (/min)	Respiratory rate (/min)	Behaviour
2 - 30 min	37 - 39	120 - 140	50	Cord ruptures, shivering, sternal, sucking movements, attempts to stand
1—12 h	37 - 39	140 - 150	40	Standing (within 1 h), nursing (within 2 h), passes meconium and urine
12 - 18 h	37 - 39	110 - 120	35	
24 – 48 h	37 - 39	90 - 100	30	
48 – 72 h	37 - 39	60 - 80	20	

Multiple retrospective analyses of blood culture results from hospitalised neonatal foals have been published over the past 30 years, but Australian data is limited. A wide variety of bacteria have been implicated in neonatal sepsis, including *E. coli*, *Klebsiella pneumoniae*, *Actinobacillus* spp., *Streptococcus* spp., *Enterococcus* spp. and *Staphylococcus* spp. Gram-negative sepsis has consistently predominated, with *E. coli* the most common bacteria isolated. However, in recent years, a trend towards increasing Gram-positive sepsis, particularly associated with *Enterococcus* spp., has been reported in North America. Hypothesised explanations for this trend include increasing use in horses of antimicrobial drugs with a strong Gram-negative spectrum, emerging antimicrobial resistance in Gram-positive pathogens and increased ease of culture of Gram-positive compared to Gram-negative bacteria in septic patients ante-mortem (i.e. in blood culture, as opposed to culture of tissues).

In a recent analysis of blood culture results from 1,621 neonatal foals admitted to a neonatal intensive care unit in the Hunter Valley, NSW, between 2005 and 2022 (200), *E. coli* was the species most frequently isolated, but Gram-positive organisms constituted an overall majority of isolates (30 bacterial species isolated: 55.5% Gram-positive aerobes, 42.6% Gram-negative aerobes, 1.7% anaerobes). As in North America, an increase in prevalence of *Enteroccoccus* spp. was observed compared to neonatal blood culture results obtained from foals in the same unit between 1999 and 2004. *Enterococcus/*Group D *Streptococcus* spp. were the most frequently isolated group of Gram-positive organisms, followed by non-Group D *Streptococcus* spp. and *Staphylococcus* spp. *E. coli* was the most common Gram-negative species isolated, followed by *Enterobacter* spp. Mixed infections (2-3 organisms) were detected in 5.2% of foals.

Diagnostics

Definitive ante-mortem diagnosis of sepsis is difficult because of the broad spectrum of clinical presentations and the limitations of current microbial testing methods. Blood culture is the current diagnostic gold standard, but this technique has limitations, including a protracted time to results, a low chance of isolating some pathogens, and only fair sensitivity. Repeated blood cultures (at 12-24 h intervals) may improve the sensitivity, but antimicrobial therapy should not be delayed while repeating cultures.

Foal sepsis scores, which summate subjective clinical criteria and objective clinicopathological data (e.g. temperature, heart rate, neutrophil count, blood glucose concentration) have been developed

with the intention of providing the practitioner with a rapid ancillary aid to diagnosing septic patients, but they have only moderate sensitivity and specificity.

Despite its limitations, culture and antimicrobial susceptibility testing should be conducted on a blood sample collected using aseptic technique from any foal suspected of sepsis (preferably on admission, prior to administration of antimicrobials, then repeated if there has been a failure to respond to therapy). Culture and antimicrobial susceptibility testing should also be performed on samples from suspected sites of localised infection that are identified during the course of treatment (e.g. synovial fluid, urine). This provides information about causative organisms and their antimicrobial susceptibility patterns on a population level, and guides therapy in individual patients (including any need to switch from an empirical treatment choice to a better targeted option).

Several clinicopathological abnormalities are associated with neonatal sepsis. Haematology may reveal leukocytosis or leukopaenia (due to neutropaenia and/or lymphopaenia), an increased proportion of band neutrophils and toxic changes in the neutrophils. Serum biochemistry frequently reveals hypoglycaemia, secondary to reduced milk/colostrum intake and utilisation of glucose by tissues and alterations in hormonal control of glucose regulation, and/or hypoglobulinaemia, because of reduced colostrum intake or increased immunoglobulin consumption, and/or transient azotaemia secondary to placental insufficiency (spurious hypercreatinaemia) or hypoperfusion (prerenal azotaemia). If MODs is present, persistent azotaemia (renal azotaemia), electrolyte abnormalities and/or elevations in liver enzymes might be observed. Elevations in concentrations of acute phase proteins (fibrinogen and serum amyloid A) are present in many septic foals, but normal concentrations do not rule out sepsis. Low IgG concentrations (< 8 g/L) are common because of insufficient colostrum intake, poor colostrum quality and/or increased immunoglobulin consumption. Arterial blood gas testing often reveals metabolic, respiratory or mixed acidosis, with hyperlactataemia frequently reported. Laboratory findings may be unremarkable in foals with mild sepsis.

Ultrasonography is a very useful diagnostic method in septic foals and may identify evidence of localised infection or organ dysfunction within the thoracic or abdominal cavities or in joints/physes. Serial physical examinations and laboratory evaluations should be performed to identify trends over time, which can help confirm evidence of sepsis and assist in evaluation of the response to therapy.

Treatment

Treatment is aimed at eliminating the infectious organism and restoring homeostasis through aggressive supportive care.

Early initiation of antimicrobial therapy has been shown to improve outcomes in neonatal sepsis. Intravenous antimicrobial therapy is preferable, as poor perfusion and organ compromise may limit absorption of orally and intramuscularly administered medications.

Initial hypovolaemia should be corrected by administering intravenous boluses of a balanced electrolyte solution, such Plasmalyte A or Hartmann's Solution. If peripheral perfusion does not improve, then additional haemodynamic support, by continuous rate infusion of inotropes or vasopressors, might be required. Maintenance intravenous fluids are indicated in foals that are unable to maintain their hydration through milk consumption alone. Foals that are unable to nurse effectively, and that have a functional gastrointestinal tract, may benefit from feeding with mare's milk or mare milk replacer via an indwelling nasogastric tube. Foals that cannot tolerate enteral nutrition (e.g. with poor perfusion, hypothermia, absent borborygmi or faecal passage, ultrasound evidence of gastrointestinal tract abnormalities) require provision of energy through addition of glucose to their maintenance fluids and/or additional nutrients via total parenteral nutrition. Insulin therapy should be instituted if persistent hyperglycaemia develops. Guidelines on developing fluid and pharmacological

plans for managing septic foals is outside the scope of these guidelines, but there are several excellent texts available (201, 202, 203).

Patients that have respiratory tract compromise or that are spending extended periods of time recumbent should be provided with intranasal oxygen supplementation. In cases with hypoventilation administration of respiratory stimulants or mechanical ventilation may be required.

Fresh frozen plasma can provide multiple benefits, including colloidal support and provision of immunoglobulins, platelets and coagulation factors. A 1-2 litre volume is commonly administered, but this may need to be repeated.

Anti-inflammatory therapy is occasionally provided (non-steroidal anti-inflammatory drugs [NSAIDS] or low dose hydrocortisone) but should be used with caution in neonates due to the risk of gastrointestinal and renal injury. Physiological doses of corticosteroids may provide benefit in some cases where there is dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis and inadequate cortisol release in response to illness – a syndrome referred to as critical illness-related corticosteroid insufficiency (CIRCI). Hypotensive animals that are unresponsive to fluid therapy and vasopressors may have CIRCI and may benefit from corticosteroid administration, but in cases with hypotension that do respond to fluid therapy or vasopressors, corticosteroids are probably contraindicated.

In some septic foals, NSAIDs may be beneficial (e.g. if pain or fever is a clinical sign), but in many critically ill foals, a compensatory anti-inflammatory response (CARS) may predominate over SIRS and NSAIDs may be detrimental in these cases.

Recumbent foals additionally require attentive nursing care to reduce the risk of decubital ulcers.

Antimicrobials used

Empirical broad-spectrum antibiotic therapy should be instituted whilst awaiting results of blood culture, based on regional information about common causes of sepsis in foals and their antibiograms. Published first-line recommendations for neonatal sepsis include:

- Penicillin (benzyl penicillin 22,000-44,000 IU/kg [12-24 mg/kg] IV q 6 h OR procaine penicillin 22,000 IU/kg [22 mg/kg] IM q 12 h) PLUS gentamicin (12 mg/kg IV q 36 h), if renal function is normal
- Ceftiofur (5 mg/kg IV or IM q12h) if the foal has renal insufficiency*
- Trimethoprim/sulphadiazine (24 mg/kg IV or IM q 12 h) monotherapy ONLY if there are financial constraints and susceptibility to this antimicrobial remains high in your local region
- Local antimicrobial therapy (e.g. nebulisation or intra-articular injection) is indicated in cases of localised infection (see Section 12 for intra-synovial and intravenous regional perfusion, and section 4 for pneumonia)
- Importantly, in the recent Hunter Valley study no one single antimicrobial could be classed as an effective empirical choice using the criterion of > 70% sensitivity across all isolates tested; high susceptibility to the combination of penicillin and gentamicin had been retained (200). Published information is lacking in other regions of Australia.

Use of several antibiotics of high importance, including fourth generation cephalosporins, amikacin and marbofloxacin, has been reported in treatment of neonatal sepsis, but these should only be used in individual animals in exceptional circumstances and only based on culture and susceptibility results.

*Renal insufficiency can be suspected when there is persistent azotaemia despite appropriate intravenous fluid therapy. Azotaemia that responds quickly to appropriate intravenous fluid therapy and hyposthenuric urine is indicative of normal renal function in foals.

Prognosis

The prognosis is guarded to fair, depending on disease severity. Outcomes have improved over the past 20 years with advances in veterinary medicine, but mortality rates remain high (20 – 50%).

Further reading

Wong DM, Wilkins PA. Equine Neonatal Medicine. New Jersey: John Wiley & Sons, Inc; 2024.

Mckenzie HC. Chapter 20: Disorders of foals. In: Reed S, Bayley W, Sellon D, editors. Equine Internal Medicine. 4 ed. Michigan: Elsevier; 2018. p. 1365-459.

Dunkel B, Corley KTT. Pathophysiology, diagnosis and treatment of neonatal sepsis. Equine veterinary education. 2015;27(2):92-8.

Eaton S. Neonatal sepsis – Pathology and clinical signs. Equine veterinary education. 2023;35(9):498-503.

Theelen MJP, Wilson WD, Edman JM, Magdesian KG, Kass PH. Temporal trends in in vitro antimicrobial susceptibility patterns of bacteria isolated from foals with sepsis: 1979-2010. Equine veterinary journal. 2014;46(2):161-8.

Theelen MJP, Wilson WD, Byrne BA, Edman JM, Kass PH, Magdesian KG. Initial antimicrobial treatment of foals with sepsis: Do our choices make a difference? The veterinary journal (1997). 2019;243:74-6.

Floyd EF, Easton-Jones CA, Theelen MJP. Systemic antimicrobial therapy in foals. Equine veterinary education. 2022;34(1):49-56.

Wong DM, Ruby RE, Dembek KA, Barr BS, Reuss SM, Magdesian KG, et al. Evaluation of updated sepsis scoring systems and systemic inflammatory response syndrome criteria and their association with sepsis in equine neonates. Journal of veterinary internal medicine. 2018;32(3):1185-93.

Flood JA, Collins NM, Russell CM, Cuming RS, Carrick JB, Cudmore LA. Blood culture isolates and antimicrobial sensitivities from 1621 critically ill neonatal foals (2005–2022). Australian veterinary journal. 2025;103(4):163-70.

Bookbinder LC, Mani R, Carr EA. Antibiograms of field and hospital acquired equine neonatal bacterial fluid cultures in the Midwestern United States: 149 samples (2007-2018). Journal of veterinary internal medicine. 2023;37(3):1193-200.

Chapter 4: Patent Urachus

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Key issues

1. A common condition in foals.
2. Can be uncomplicated or a consequence of underlying disease, with omphalophlebitis the most important underlying cause.

The urachus normally closes soon after birth. Trauma to the cord may result in failure of initial closure. Clamping, cutting or tying the umbilical cord may predispose to a patent urachus. A patent urachus may also develop up to 1 month of age, as a result of urachal infection or recumbency caused by other disease processes (sepsis, Neonatal Maladjustment Syndrome).

Diagnostics

Urine voided from the umbilical stump as a few drops to a full stream is consistent with the diagnosis.

Further diagnostics are required to investigate for underlying causes, particularly omphalophlebitis, as undiagnosed infection can result in sepsis or septic arthritis. Infection resulting in a patent urachus is relatively common. Ultrasonography and haematology are useful when making a diagnosis (see omphalophlebitis).

Treatment

Surgical resection is rarely necessary. Where infection is not present, most cases resolve with supportive care only. Cautery with silver nitrate or iodine-based solutions should be avoided, as the additional irritation predisposes to infection. Gentle cleaning with diluted chlorhexidine solutions and drying until closure occurs is sufficient in most cases. Application of insect repellent solutions or creams designed for equine use on the skin around the umbilicus is recommended to prevent maggot infestation of the umbilical stump.

Antimicrobials used

- None, unless omphalophlebitis is present or the foal is systemically compromised (see the section above on Sepsis, Chapter 3 in this Section.)

Prognosis

Excellent. Most cases close spontaneously over several days.

Chapter 5. Bacterial pneumonia in foals

Authors: Laura Hardefeldt, Rosemary Cuming, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Pneumonia is a common disease in neonatal foals and older foals
2. In primary pneumonia, *S. zooepidemicus* and *R. equi* occur with equal frequency

Background/nature of infection/organisms involved

Bacterial pneumonia is usually secondary to sepsis or aspiration either of meconium contaminated foetal fluids during birth or milk during nursing. In neonatal foals, pathogens associated with sepsis are most frequently implicated (chapter 3, section 8). In older foals, *Rhodococcus equi* and *Streptococcus zooepidemicus* are the most frequent pathogens. *R. equi* is discussed elsewhere (chapter 4, section 4). Bacterial infection in older foals may follow viral infection (EHV 1 or 4) or other stressful events that may impact on pulmonary defence mechanisms.

Diagnostics

Clinical signs include fever, tachypnoea, dyspnoea and purulent nasal discharge. Respiratory distress can occur if pneumonia is severe or there is secondary acute respiratory distress syndrome (ARDS). Coughing is not a reliable clinical sign. Auscultation and percussion should be undertaken, however, abnormalities can be surprisingly mild in some foals with significant disease.

Haematology generally shows alterations to leukocytes (leukocytosis or leukopaenia) with left shift in acute cases and hyperfibrinogenaemia in more chronic cases. Serum amyloid A concentrations are elevated in many pneumonia foals, however a significant proportion of foals with pneumonia will have a normal serum amyloid A concentration.

Transtracheal aspirate should be submitted for cytology and culture. Isolates generally fall into two categories; those common to neonatal sepsis and primary disease. In the latter, *S. zooepidemicus* and *R. equi* occur with equal frequency and can only be differentiated by tracheal fluid cytology and culture.

Radiography and thoracic ultrasound are useful for making a diagnosis and assessing the extent of disease. Aspiration pneumonia and *S. zooepidemicus* pneumonia are generally restricted to the cranioventral lung fields whereas haematogenous spread secondary to sepsis tends to be generalised throughout the lung.

Treatment

Initial antimicrobial therapy should be broad-spectrum (penicillin and gentamicin or trimethoprim sulphonamide). Antimicrobial therapy can then be adapted based on culture and susceptibility.

Aerosolisation of antimicrobials can allow direct delivery to the site of infection, which may overcome some of the theoretical limitations of systemically administered drugs in the treatment of purulent infections of the LRT. Achievement of high and prolonged drug concentrations within the airways while maintaining low serum concentrations has been clearly demonstrated with various antibiotics (gentamicin and marbofloxacin) when aerosolised delivery has been compared with systemic (intravenous) administration (12, 13). Clear benefit of aerosolised medication in horses has yet to be demonstrated and a randomised clinical trial is needed.

Aerosol particle sizes between 1 and 5 µm are thought to be ideal for therapy using ultrasonic or jet nebulizers. The Flexineb Equine Nebulizer is best suited. Aminoglycosides are the most reported

aerosolised antimicrobial agents because they remain bioactive when aerosolised, and are poorly absorbed across epithelial surfaces, thus remaining within the pulmonary tree where they exert concentration-dependent effects (14).

Table 1. Recommendations for inhaled antimicrobials in foals

Antimicrobial	Spectrum	Delivery method	Volume	Dosage
Gentamicin	Primarily aerobic Gram-negatives, some *Staphylococcus* and *Rhodococcus equi* species	Ultrasonic nebuliser	Dilute to 50 mg/mg (from 100 mg/ml) using sterile water or saline	2 mg/kg q24 h
Ceftiofur	Aerobic Gram-positives and negatives	Nebulised with Flexineb	Dilute to 25 mg/ml using sterile water	2.2 mg/kg q24 h (or 1.1 mg/kg q12 h)

Seven days of once-a-day administration of gentamicin through inhalation at 1000 mg (20 ml of 50 mg/ml) per day per adult horse did not result in side effects. There was also no evidence of inflammation in BALF (14). The primary disadvantage of gentamicin and other aminoglycosides is that they poorly penetrate abscessed pulmonary tissue.

Use of inhaled cephalosporins may maximise clinical efficacy in the treatment of infections of the respiratory tract, whilst minimizing the risk of antimicrobial resistance. Cefquinome has been evaluated but is not available in Australia. Ceftiofur is a third-generation cephalosporin. The recommended concentration to nebulise is 25 mg/ml but the concentration of 50mg/ml has been reported without complications in one study (15).

Marbofloxacin concentrations in bronchoalveolar fluid following nebulization (300 mg/horse) higher than those following systemic administration but did not reach MIC values for most bacterial pathogens, so this drug is not recommended (16).

Antimicrobials used

- Empiric therapy: Penicillin (procaine penicillin 22,000 IU/kg IM q12h or benzyl penicillin 12-16 mg/kg IV q6h) and gentamicin (6.6 mg/kg IV q24h for animals aged >2 weeks, 11mg/kg IV q36h for foals < 2weeks old) for 5-14 days (depending on severity)
- OR trimethoprim sulphonamide 30 mg/kg PO q12h for 5-14 days (depending on severity)
- Directed therapy should be based on culture and susceptibility testing.

Chapter 6: Omphalophlebitis (Umbilical remnant infection)

Authors: Laura Hardefeldt, Rosemary Cuming, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Most likely results from ascending infection soon after birth.
2. Beta-haemolytic streptococci and coliforms are most commonly isolated.
3. Swelling and purulent discharge are not always present.

The internal umbilical remnants include the urachus, two umbilical arteries and the umbilical vein. The urachus courses from the external umbilicus to the apex of the bladder. The umbilical arteries extend along both left and right sides of the bladder and the umbilical vein courses from the external umbilicus to the liver. One or more of these structures can become infected, most likely from ascending infection soon after birth or haematogenous spread in foals with sepsis.

Overzealous dipping of the umbilicus (particularly with iodine, but also with chlorhexidine) in neonates can predispose to infection.

Beta-haemolytic streptococci and coliforms are most commonly isolated. *Staphylococcus aureus*, *Klebsiella* spp. and anaerobes can also be involved, and multiple pathogens are commonly isolated.

Diagnostics

Purulent discharge from the umbilical stump, umbilical swelling, a patent urachus, septic arthritis and fever of unknown origin are common presenting complaints.

Haematology and ultrasonography are useful diagnostic tools. Haematology generally reveals a leukocytosis with mature neutrophilia, although leukopaenia or no abnormalities are sometimes detected. Ultrasonographic examination of the internal umbilical remnants reveals enlargement and/or anechoic to hyperechoic fluid within the lumen of the remnants, or thickening of the umbilical vein or artery walls. The normal ultrasonographic measurements of these structures have been described for foals from 24 h to 6 weeks (204).

Samples for culture are not readily obtained unless there is purulent discharge from the external umbilicus or distant infection (i.e. septic arthritis).

Treatment

Most resolve with medical therapy. Oral or parenteral broad-spectrum antimicrobial therapy is indicated – trimethoprim/sulphadiazine or penicillin PLUS gentamicin. While gas shadows are commonly seen by ultrasonography, a foul-smelling purulent discharge should increase suspicion of anaerobic infection and metronidazole should be added to the treatment regimen. Treatment should continue until ultrasonographic abnormalities resolve – generally 2-4 weeks.

In regions where trimethoprim/sulphadiazine resistance is common, such as the Hunter Valley, alternative oral treatment options include amoxicillin-clavulanate and doxycycline. Amoxicillin-clavulanate can be used in foals up to 4 months of age but should not be used in older horses as this combination is associated with severe antimicrobial-associated diarrhoea in older foals. Although rare, when doxycycline is used, foals should be monitored for distal limb laxity and therapy discontinued if this side-effect develops.

Surgical resection can also be considered, but post-operative complications are common (205). However, duration of antimicrobial therapy after surgery is generally shorter, and fewer ultrasonographic examinations are required, so surgical management is often cheaper.

If an abscess is located in the umbilical stump, drainage can be established via a stab incision.

Antimicrobials used

Foals < 2 weeks of age:

- Trimethoprim/sulphadiazine at 24 mg/kg PO q 12 h
- OR penicillin at 22,000 IU/kg IM q 12 h PLUS gentamicin at 12 mg/kg IV q 36 h
- OR amoxicillin-clavulanate at 30 mg/kg PO q 8 h
- If anaerobes are suspected, add metronidazole at 10 mg/kg PO or IV q 12 h

  Duration of therapy of 2-4 weeks is common (until ultrasonographic abnormalities resolve)

Foals > 2 weeks of age:

- Trimethoprim/sulphadiazine at 30 mg/kg PO q 12 h
- OR penicillin at 22,000 IU/kg IM q 12 h PLUS gentamicin at 6.6 mg/kg IV q 24 h
- OR doxycycline at 10 mg/kg PO q 12 h
- OR amoxicillin-clavulanate at 30 mg/kg PO q 8 h (only in foals < 4 months of age)
- If anaerobes are suspected add metronidazole (no information is available on its use in older foals, but 15-20 mg/kg PO or IV q 8 h is commonly used)

  Duration of therapy of 2-4 weeks is common (until ultrasonographic abnormalities resolve)

Prognosis

Good to excellent. Repeated ultrasonographic examinations should be used to assess the response to treatment.

Further reading

Rampacci E, Passamonti F, Bottinelli M, Stefanetti V, Cercone M, Nannarone S, et al. Umbilical infections in foals: microbiological investigation and management. Veterinary record. 2017;180(22):543-543.

McCoy et al., 2019. Normal regression of the internal umbilical remnant structures in standardbred foals. EVJ. https://beva.onlinelibrary.wiley.com/doi/epdf/10.1111/evj.13267?saml_referrer

Chapter 7: Uroperitoneum

Authors: Laura Hardefeldt, Rosemary Cuming, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Uroperitoneum can be a primary condition of otherwise 'healthy' foals or develop secondarily in foals undergoing treatment of other illnesses (e.g. neonatal maladjustment syndrome, sepsis).
2. Correction of fluid deficits, partial correction of electrolyte abnormalities and reduction in abdominal distension prior to surgery decreases the risk of potentially fatal anaesthetic complications (e.g. significant cardiac arrhythmias).
3. Localised infection of the urinary tract/umbilical remnants or concurrent sepsis is common, so broad-spectrum antimicrobial therapy should be administered to all foals with uroperitoneum.

Uroperitoneum (urine leakage into the peritoneal space) has a reported incidence in foals of 0.2-2.5%. Most patients present during their first week of life, but this condition can be seen in foals up to 6 weeks of age. Bladder rupture is the most common cause of uroperitoneum in foals, followed by urachal leakage, with ureteral and urethral defects rarely reported. Proposed mechanisms include periparturient trauma, congenital defects, external trauma, focal necrotic cystitis and urachal infection. Presenting signs include stranguria, oliguria, lethargy, inappetence, abdominal distension and/or scrotal/subcutaneous urine accumulation and, in some advanced cases, significant cardiac and/or respiratory compromise. The presence of sepsis and/or localised infection has been reported in up to 63% of foals presenting with uroperitoneum. *E. coli* have frequently been implicated as causative agents, with *Enterococcus* spp. and *Clostridium* spp. also cultured from the peritoneal fluid or urinary tract tissues of cases (206, 207, 208). Pathogens associated with sepsis in foals are numerous and based on author's clinical experience of culturing varying samples in uroperitoneum cases, it is possible to identify a much broader range of Gram-positive and Gram-negative bacteria than those listed above.

Diagnostics

Laboratory findings vary, depending on the duration of uroperitoneum and the presence or absence of sepsis or other concurrent conditions. Typical abnormalities result from reabsorption of water and electrolytes across the peritoneal membrane and include hyponatraemia, hypochloraemia, hyperkalaemia and azotaemia. These may not be present early in disease or in foals already receiving fluid therapy at the time of urinary tract rupture.

Blood gas assays may reveal metabolic acidosis and hypoxia. Failure of transfer of passive immunity (IgG < 8 g/L) is frequently reported. Abdominocentesis yields a clear yellow fluid. A peritoneal fluid:serum creatinine ratio of 2:1 is diagnostic for uroperitoneum. Peritoneal fluid cytology and culture should be performed to detect evidence of peritonitis or concurrent gastrointestinal tract compromise. Culture of blood, peritoneal fluid and tissue samples collected at surgery, and subsequent antimicrobial susceptibility testing, should be performed to guide antimicrobial therapy.

Percutaneous ultrasonography reveals increased (typically substantially increased) amounts of anechoic free fluid within the abdominal cavity and/or scrotum, and/or subcutaneous fluid accumulation along the ventrum. Bladder wall and urachal defects can sometimes be visualised ultrasonographically. Advanced imaging (e.g. computed tomography, contrast radiology or urethral endoscopy) is indicated to investigate suspected ureteral or urethral abnormalities.

Electrocardiographic (ECG) findings may be normal or may include an array of abnormalities related to hyperkalaemia, including bradycardia, increased QRS or P-wave duration, shortened QT interval, prolonged P-R interval, 3rd degree atrioventricular block, ventricular premature complexes or ventricular fibrillation.

Treatment

Treatment consists of initial medical stabilisation followed by surgical closure of the defect, supportive post-operative care, and broad-spectrum antimicrobial therapy.

Azotaemia and electrolyte abnormalities are unlikely to resolve until leakage of urine into the peritoneal cavity has ceased, but surgery should be delayed until electrolyte abnormalities have been partially corrected (serum potassium reduced to < 6 mmol/L) and normovolaemia has been restored by intravenous fluid therapy alone, or in combination with slow peritoneal drainage (via a teat cannula, peritoneal dialysis catheter or intravenous catheter) and/or urinary catheterisation in foals where abdominal distension is resulting in respiratory or circulatory compromise, or hyperkalaemia is marked.

Administration of 0.45-0.9% saline containing up to 5% glucose IV and withholding milk is typically sufficient to achieve these goals, but in cases with marked hyperkalaemia and ECG abnormalities additional therapies may be required (e.g. insulin, calcium gluconate or sodium bicarbonate continuous rate infusions). Hyponatraemia must be corrected slowly.

Non-surgical management with an indwelling urinary catheter has been successfully reported in a handful of cases.

Antimicrobials used

Foals < 2 weeks of age:

- Either:
    - Benzyl penicillin at 22,000-44,000 IU/kg [12-24 mg/kg] IV q 6 h OR procaine penicillin at 22,000 IU/kg [22 mg/kg] IM q 12 h
      PLUS gentamicin at 12 mg/kg IV q 36 h
    - OR trimethoprim/suphadiazine at 24 mg/kg IV or IM q 12 h
    - OR ceftiofur sodium** at 5 mg/kg IV or IM q 12 h.
- PLUS, if there is evidence of infection with anaerobes, metronidazole at 10 mg/kg PO or IV q 12 h.

Foals > 2 weeks of age:

- Either:
    - Benzyl penicillin at 22,000-44,000 IU/kg [12-24 mg/kg] IV q 6 h OR procaine penicillin at 22,000 IU/kg [22 mg/kg] IM q 12 h)
      PLUS gentamicin at 8.8 mg/kg IV q 24 h **if 2-4 weeks old** or at 6.6 mg/kg IV q 24 h if **>4 weeks old)**
    - OR trimethoprim/sulphadiazine at 24 mg/kg IV or IM q 12 h
    - OR ceftiofur sodium** at 5 mg/kg IV or IM q 12 h
- PLUS, if there is evidence of infection with anaerobes, metronidazole (there is no information about dose rates in older foals, but 15-20 mg/kg PO or IV q 8 h is commonly used).

Duration of treatment in all ages of foals:

- There is no evidence for a specific duration for treatment, but 3 days in patients with no evidence of infection, or 5 - 7 days if evidence of infection is present, are common initial

courses. The patient should then be reevaluated and antimicrobials therapy extended if indicated by laboratory or clinical examination findings.

- Azotaemia is purely post-renal in many foals with uroperitoneum, so aminoglycosides can probably be used safely, but aminoglycoside therapy should only be initiated after confirming adequate kidney function and ensuring that the foal is hydrated, given the frequency of concurrent illness in these foals.
- ** Ceftiofur should only be used as a last resort and only if indicated by blood culture and antimicrobial susceptibility testing results because of the importance of third generation cephalosporins in human medicine.

Prognosis

The prognosis is good for foals with uncomplicated uroperitoneum caused by bladder rupture but is poorer if the defect is located elsewhere. Several complications can be seen in these patients, including sepsis, pneumonia, peritonitis, acute respiratory distress syndrome, incisional complications, abdominal adhesions and recurrence of urinary tract rupture. In these cases, the prognosis is associated with concurrent illness.

Further reading

Barrell EA, Burton AJ. Chapter 34: Diseases of the renal system. In: Smith BP, Pusterla N, editors. Large Animal Internal Medicine. 6 ed. Missouri: Elsevier; 2019. p. 956-1005.

Wilkins PA, Dunkel B. Chapter 12.2: Rupture of the urinary bladder. In: Paradis MR, editor. Equine Neonatal Medicine: A Case-Based Approach. Pennsylvania: Elsevier Saunders; 2006. p. 237-45.

Adams R, Koterba AM, Cudd TC, Baker WA. Exploratory celiotomy for suspected urinary tract disruption in neonatal foals: a review of 18 cases. Equine veterinary journal. 1988;20(1):13-7.

Reference List

1. Bailey K. Investigation of the infectious causes of diarrhoea in Australian thoroughbred foals: University of Melbourne; 2017.
2. Slovis NM, Elam J, Estrada M, Leutenegger CM. Infectious agents associated with diarrhoea in neonatal foals in central Kentucky: A comprehensive molecular study. Equine veterinary journal. 2014;46(3):311-6.
3. Flood JA, Collins NM, Russell CM, Cuming RS, Carrick JB, Cudmore LA. Blood culture isolates and antimicrobial sensitivities from 1621 critically ill neonatal foals (2005–2022). Australian veterinary journal. 2025;103(4):163-70.
4. Wong DM, Wilkins PA. Equine Neonatal Medicine. New Jersey: John Wiley & Sons, Inc; 2024.
5. Mckenzie HC. Chapter 20: Disorders of foals. In: Reed S, Bayley W, Sellon D, editors. Equine Internal Medicine. 4 ed. Michigan: Elsevier; 2018. p. 1365-459.
6. Dunkel B, Corley KTT. Pathophysiology, diagnosis and treatment of neonatal sepsis. Equine veterinary education. 2015;27(2):92-8.
7. McCoy AM, Lopp CT, Kooy S, Migliorisi AC, Austin SM, Wilkins PA. Normal regression of the internal umbilical remnant structures in Standardbred foals. Equine veterinary journal. 2020;52(6):876-83.
8. Reig Codina L, Werre SR, Brown JA. Short-term outcome and risk factors for post-operative complications following umbilical resection in 82 foals (2004–2016). Equine veterinary journal. 2019;51(3):323-8.

9. Dunkel B, Palmer JE, Olson KN, Boston RC, Wilkins PA. Uroperitoneum in 32 foals: Influence of intravenous fluid therapy, infection, and sepsis. Journal of veterinary internal medicine. 2005;19(6):889-93.

10. Kablack KA, Embertson RM, Bernard WV, Bramlage LR, Hance S, Reimer JM, et al. Uroperitoneum in the hospitalised equine neonate: retrospective study of 31 cases, 1988-1997. Equine veterinary journal. 2000;32(6):505-8.

11. Hyman SS, Wilkins PA, Palmer JE, Schaer TP, Piero FD. Clostridium perfringens Urachitis and Uroperitoneum in 2 Neonatal Foals. Oxford, UK: Blackwell Publishing Ltd; 2002. Report No.: 0891-6640.

12. McKenzie HC, 3rd, Murray MJ. Concentrations of gentamicin in serum and bronchial lavage fluid after intravenous and aerosol administration of gentamicin to horses. *Am J Vet Res* 2000; **61**(10): 1185–1190.
13. Art T, de Moffarts B, Bedoret D, et al. Pulmonary function and antimicrobial concentration after marbofloxacin inhalation in horses. *Vet Rec* 2007; **161**(10): 348–350.
14. McKenzie HC, Murray MJ. Concentrations of gentamicin in serum and bronchial lavage fluid after once-daily aerosol administration to horses for seven days. *American J Vet Res* 2004; **65**(2): 173–178.
15. Fultz et al., 2015. Pulmonary pharmacokinetics of desfuroylceftiofur acetamide after nebulisation or intramuscular administration of ceftiofur sodium to weanling foals EVJ, 47(4);473-477
16. Carretero et al., 2002. Pharmacokinetics of marbofloxacin in mature horses after single intravenous and intramuscular administration EVJ, 34(4); 360-365

Section 9 - Urinary system

Contents

Chapter 1: Urinary tract infection

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Urinary tract infection is rarely the primary cause of disease.
2. Urinary tract infection is rare in idiopathic haemorrhagic cystitis and is variably reported in cases of sabulous cystitis and urolithiasis.
3. Antimicrobial susceptibility results may not reflect the *in vivo* response to therapy because of the high concentrations of antimicrobials that can be achieved in urine.

Equine urinary tract infection (UTI) is uncommon and rarely occurs as a primary event. When UTIs do occur in horses, they are most commonly after a mechanical or functional impairment of normal urine flow. The bacteria most frequently isolated in recent global case reports include *E. coli, Staphylococcus spp., Streptococcus spp. and Enterococcus spp. (209, 210, 211). However, it is worth noting that most cultures from published case series of sabulous (sandy) cystitis, urolithiasis and idiopathic haemorrhagic cystitis do not yield growth. In addition, these organisms have been detected in cultures of normal equine urine (212). This finding suggests that weakened host defences allow virulent strains of normal flora to contribute opportunistically to ascending UTI in the horse and supports the proposal that, as in other animal species, asymptomatic bacteriuria should not be treated.*

Diagnostics

In cases of suspected UTI, a definitive diagnosis and isolation of causative organisms by culture, with antimicrobial susceptibility testing, should be pursued. To minimise contamination of urine, samples should be collected by catheterization, following cleansing of the distal penis or perivulvar region with chlorhexidine-based soap. The first 20 ml of urine should be discarded and the next 20 ml collected for analysis. Causative organisms are not predictable and multi-drug resistance is becoming increasingly common, particularly in cases of sabulous cystitis where chronicity is a feature. Culture of more than 20,000 CFU of bacteria/mL of urine should be used as a cut-off for a diagnosis of UTI for free-catch samples (Table 9.1) (212). *In vitro* resistance may not reflect *in vivo* efficacy for common antimicrobials (such as penicillins, cephalosporins and potentiated sulphonamides), as high concentrations are achieved in the urine because of glomerular filtration and active tubular secretion. In such cases, the clinical response to therapy should be interpreted alongside susceptibility testing results.

Table 9.1. Bacteriuria in male and female horses

Empty Cell	Clinically relevant (CFU/mL)	Suspicious (CFU/mL)	Contamination (CFU/mL)
Midstream voided urine	> 40,000	20,000 - 40,000	< 20,000
Catheterized urine	> 1,000	500 - 1,000	< 500

Abbreviation: CFU/mL, colony-forming units of bacteria per millilitre of urine.
Data from MacLeay JM, Kohn CW. Results of quantitative cultures of urine by free catch and catheterization from healthy horses. J Vet Intern Med 1998;12:76–8 (212).

Cystoscopy is a useful tool when identifying conditions that contribute to the development of UTIs. A flexible endoscope with a minimum length of 100 cm and an outside diameter of less than 12 mm is appropriate for visualization of the bladder in adult horses of either gender (213).

Treatment

Because UTI is most often secondary in horses, it is critical to diagnose and treat the primary problem before, or concomitant with, antimicrobial therapy.

The trimethoprim/sulphadiazine combination is an excellent choice for treatment of UTIs in horses because of its broad antibacterial spectrum, low cost, and ease of administration.

Penicillins are also a good choice because of the high concentrations excreted into the urine. Procaine penicillin G or benzyl penicillin may be combined with aminoglycosides to enhance activity against Gram-negative urinary tract pathogens.

The recommended duration of therapy is based on those for other animal species.

Antimicrobials used

- Trimethoprim/sulphadiazine at 30mg/kg PO q 12 h for 3-5 days
- Procaine penicillin G at 22,000 IU/kg IM q 12 h for 3-5 days
- Procaine penicillin G at 22,000 IU/kg IM q 12 h and gentamicin at 6.6 mg/kg IV q 24 h for 3-5 days

Prognosis

Guarded and dependent on primary disease.

Reference List

1. Rendle DI, Durham AE, Lloyd D, Summerhays GES, Hughes KJ. Long-term management of sabulous cystitis in five horses. Veterinary record. 2008;162(24):783-7.
2. Zakia LS, Gomez DE, Kenney DG, Arroyo LG. Sabulous cystitis in the horse: 13 cases (2013-2020). Canadian veterinary journal. 2021;62(7):743-50.
3. Laverty S, Pascoe JR, Ling GV, Lavoie JP, Ruby AL. Urolithiasis in 68 horses. Vet Surg. 1992;21(1):56-62.
4. MacLeay JM, Kohn CW. Results of quantitative cultures of urine by free catch and catheterization from healthy adult horses. Journal of veterinary internal medicine. 1998;12(2):76-8.
5. Sprayberry KA. Cystoscopy. In: Slovis NM, editor. Atlas of equine endoscopy. St Louis (MO): Mosby; 2004. p. 169-82.

Section 10 – Foot Disorders

Contents

Chapter 1: Hoof abscess

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Non-weight bearing lameness with an increased digital pulse.
2. Hoof testers will help in localisation of the area on the sole to pare for drainage.
3. Mixed bacterial infection with anaerobes.

Hoof abscesses occur more frequently following wet weather, when the sole of the hoof tends to be softer and more easily penetrated by foreign objects. Infection generally ascends from the solar corium (white line) and results in abscess formation. The accumulation of purulent exudate results in acute pain and non-weight bearing lameness in the affected leg. Mixed bacterial infection, including anaerobes, usually occurs due to inoculation of organisms from the environment into a relatively anaerobic area. Abscesses can drain through either the sole or coronary band.

Diagnostics

Non-weight bearing lameness in one leg with an increased digital pulse. Pain is detected with hoof testers over the location of the abscess. Often there is a discoloured area of sole that can be pared with a hoof knife to allow drainage of the abscess.

If there are recurrent episodes of hoof abscessation in the same leg, radiographs are indicated to rule out infectious osteitis of the pedal bone (see chapter 2). Pars pituitary intermedius dysfunction (PPID) is another differential diagnosis in these cases and ACTH testing can assist in making a diagnosis, as long as seasonal and geographical reference ranges are used.

Treatment

Drainage is key to resolution of the abscess. If the site to drain is not initially obvious, then bathing the hoof in hot water and poulticing it will aid in abscess localisation and establishing drainage.

Tetanus prophylaxis is required if the horse is not currently vaccinated for tetanus.

Antimicrobials used

- Antimicrobial therapy is not indicated for treating hoof abscesses unless there is bony involvement (see septic pedal osteitis).

Prognosis

Excellent with rapid improvement following drainage of the abscess.

Chapter 2: Septic pedal osteitis

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Identification of site of solar penetration and structures involved is important.
2. Mixed bacterial infection, including anaerobes, from environmental contamination is common.
3. Penetration of the navicular bursa and distal interphalangeal joint significantly worsens the prognosis.

Septic pedal osteitis can be a sequela of penetrating wounds, subsolar abscesses and laminitis, where penetration of infection to the depth of the pedal bone can result in bone infection and formation of a sequestrum. Affected horses normally have a history of chronic lameness and drainage of purulent material from the hoof that does not resolve. Mixed bacterial infection, including anaerobes, is common due to inoculation from the environment into a relatively anaerobic area.

Diagnostics

Detailed examination of the sole of the hoof for the site of penetration and purulent discharge is required. Radiographs of the hoof reveal decreased bone density, demineralisation and irregularity of bone margins at the level of the infected bone (214). Injection of contrast medium into the site of penetration may help to assess which structures are involved. It may take 7 days or longer for infection and sequestrum formation to result in radiographically detectable bone lysis. Examination of the hoof using computed tomography can be useful in difficult cases, to identify lytic areas of bone and small areas of sequestrum formation that are not evident on radiographs. Penetration of the navicular bursa and distal interphalangeal joint significantly worsens the prognosis.

Treatment

Treatment requires a combination of surgical debridement of the infected bone and surrounding tissues, in addition to systemic and local antimicrobial therapy. Surgical debridement can be performed in the standing horse with appropriate sedation, regional anaesthesia, and the application of a tourniquet to control haemorrhage (215). The infected tissues are debrided, and the bone curetted and these samples should be submitted for culture and antimicrobial susceptibility testing. The defect is then lavaged and metronidazole is frequently used as a topical antimicrobial (214) before sterile bandaging. Systemic antimicrobials are continued until a healthy bed of granulation tissue has covered the pedal bone. Regional limb perfusions (see Section 12) are also frequently used. A treatment plate can be applied to protect the hoof and allow easy access for cleaning and flushing. Support for the opposite weight bearing foot by housing on sand, or use of soft-ride boots for frog support, is recommended to minimise the likelihood of support limb laminitis. Tetanus prophylaxis is required if the patient is not currently vaccinated for tetanus.

Antimicrobials used

- Procaine penicillin G (22 000 IU/kg IM q 12 h), gentamicin (6.6 mg/kg IV q 24 h) and metronidazole (25 mg/k PO q 8 h) until there is a healthy bed of granulation tissue following debridement.
- Intravenous regional limb perfusions may be used (see Section 12)

Prognosis

Septic pedal osteitis has a fair to good prognosis after surgical treatment, but there is a poorer prognosis without surgical debridement. The prognosis is guarded if the distal interphalangeal joint or navicular bursa are involved.

Chapter 3: Street nail

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Identification of the site of solar penetration and the structures involved is critical.
2. Mixed bacterial infection, including anaerobes, is typical and results from environmental contamination.
3. Penetration of navicular bursa significantly worsens the prognosis.

Street nail is a term describing a penetrating injury to the sole of the hoof. The site of penetration determines the severity of the injury, with an injury in the middle third of the frog most likely to result in penetration of the navicular bursa, which complicates treatment and significantly worsens the prognosis. Penetration to the depth of the pedal bone can also result in infectious osteitis and formation of a sequestrum. Horses quickly develop non-weight bearing lameness due to infection in the pedal bone and/or navicular bursa. Mixed bacterial infection, including anaerobes, is common due to inoculation from environment bacteria into a relatively anaerobic area. Historically, the procedure to establish drainage of the navicular bursa has been referred to as the 'street nail procedure' (216).

Diagnostics

If the foreign penetrating body has been removed, detailed examination of the sole of the hoof should be performed to identify the site of penetration. Hoof testers are helpful to identify the site, as it will be painful on sole pressure. Radiographs are required to assess for pedal bone fracture. Injection of contrast medium into the site of penetration may help to assess which structures are involved. Infection and sequestrum formation can also be assessed with radiographs, but it may take 7 days or longer for bone lysis to occur and become detectable radiographically.

Treatment

The area of the puncture should be opened and drained and the foot cleaned and poulticed. When penetration to the pedal bone is suspected, radiographs can be taken with contrast medium injected into the site of penetration.

If the penetrating object has penetrated the pedal bone or navicular bursa, surgery to curette the pedal bone and potentially flush the navicular bursa is required. A treatment plate can be applied to protect the hoof and allow easy access for cleaning and flushing.

Regional limb perfusion can also be used (see Section 12). Support for the opposite weight bearing foot by housing on sand, or the use of soft-ride boots for frog support, helps to minimise the likelihood of support-limb laminitis. Tetanus prophylaxis is required if the horse is not currently vaccinated for tetanus.

Antimicrobials used

- Procaine penicillin G (22 000 IU/kg IM q 12 h), gentamicin (6.6 mg/kg IV q 24 h) and metronidazole (25 mg/k PO q 8 h) for a minimum of three days, but longer treatment may be required if infection involves the pedal bone or navicular bursa.
- Intravenous regional limb perfusions may be used (see Section 12)

Prognosis

Guarded if the penetrating injury involves the navicular bursa. Infections of the pedal bone can also have a poor prognosis without surgical debridement.

Reference List

1. Cauvin ERJ, Munroe GA. Septic osteitis of the distal phalanx: findings and surgical treatment in 18 cases. Equine veterinary journal. 1998;30(6):512-9.
2. Cillán-García E. Can septic pedal osteitis be managed in the standing patient? Equine veterinary education. 2015;27(5):277-.
3. Dyson SJ, Ross MW. Diagnosis and management of lameness in the horse. Second edition. ed. St. Louis, Mo: Elsevier/Saunders; 2011.

Section 11 - Musculoskeletal

Contents

Chapter 1: Clostridial myonecrosis (clostridial myositis/cellulitis, malignant oedema)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Clinical progression is rapid, so prompt identification of clinical cases is essential.
2. Soft tissue swelling, along with signs of systemic disease, following IM injection should raise suspicion of clostridial myonecrosis.

Clostridial myonecrosis is a syndrome of severe necrotizing soft tissue infection associated with *Clostridium* spp. It typically presents as peracute emphysematous soft tissue swelling in the region of an injection or wound within hours of the inciting cause. Intramuscular injection of several common drugs, including flunixin meglumine, ivermectin, omeprazole, antihistamines, phenylbutazone, dipyrone, vitamin B complex and synthetic prostaglandins, has been implicated. Disease following injection of flunixin meglumine appears over-represented and the association with wounds seems less common. Central to the aetiology is the inoculation of the organisms and the creation of anerobic foci in which the organisms can proliferate, sometimes facilitated by irritant medications. *Clostridium perfringens* and *C. septicum* are the species that have most often been reported as causative organisms, but other *Clostridium* species have also been implicated. Rapid identification of cases is critical, as prompt treatment can improve survival rates. Horses can develop clinical signs and die within 48 - 72 h.

Diagnostics

Horses are generally febrile and have moderate to severe depression and inappetence. They are generally stiff and reluctant to move. Severe toxaemia and cardiovascular collapse can occur soon after clinical signs develop, with diffuse intravascular coagulation and acute renal failure as consequences.

Soft tissue swelling, with palpable subcutaneous emphysema, is very common, especially when disease affects the cervical region, and this generally leads to a presumptive diagnosis. When the disease affects the gluteal region, subcutaneous emphysema may be a less reliable clinical sign. The overlying skin may initially feel hot, but quickly becomes cold, tough and insensitive due to the underlying necrosis. Aspiration of fluid from the affected region, or upon myotomy/fasciotomy, reveals large parallel-sided, Gram-positive rods. Ultrasonography can be useful to identify gas shadows within deeper soft tissues and pockets of necrotic tissue to target for fasciotomy.

All horses that develop soft-tissue swellings acutely after IM, SC or inadvertent perivascular administration of drugs and have systemic signs of illness should be assessed by examining a Gram-stained smear of an aspirate from the affected area. Release of exotoxins by the bacteria causes muscle necrosis and destruction of white blood cells. Absorption of the exotoxins into the circulation causes widespread damage to the endothelium, liver and muscles, leading quickly to death.

Treatment

An aggressive approach to therapy is prudent when clostridial myonecrosis is suspected or confirmed. Medical and surgical therapy should be pursued.

Medical:

1. Antimicrobials – high doses of crystalline penicillin (benzyl penicillin) at 12,000-48,000 IU/kg IV q 4-6 h. Other beta-lactams may be used, but clinical experience suggests that high-dose crystalline penicillin is superior. Aggressive antimicrobial therapy in the first 2-3 days of therapy may improve survival rates. Therapy beyond 10 days is probably unnecessary.
2. Anti-inflammatory and analgesic medication – flunixin meglumine or phenylbutazone at standard dose rates. Opioids are probably necessary for adequate analgesia.
3. Supportive adjunctive care – plasma transfusion may be indicated, especially in cases where coagulation is delayed and prior to surgical interventions. Treatment of shock with corticosteroids has been employed in some case reports, but the efficacy of this therapy is unknown. Fluid therapy with isotonic fluids is required in most cases.

Surgical:

Fenestration of the emphysematous area is indicated to improve oxygenation, reduce swelling and facilitate debridement of necrotic tissue. This is typically performed standing with only light systemic sedation. Due to the extensive necrosis, only light local analgesia is needed. Multiple vertical incisions, approximately 2.5 cm apart, should be made through the muscles in the affected area. Exposed tissues can be irrigated and many different solutions have been advocated (hydrogen peroxide, chlorhexidine, crystalline penicillin), but there is no evidence that any one agent is more beneficial. Daily hydrotherapy should follow to keep the area clean and facilitate granulation. Owners should be warned of the significant soft tissue and skin sloughing that will probably occur over the medium to long term.

Antimicrobials used

- Crystalline penicillin (benzyl penicillin at 12,000-48,000 IU/kg IV q 4-6 h) for 3-5 days, after which more typical doses of penicillin are probably adequate. Total antimicrobial duration ~10 days.

Prognosis

In a series of 37 cases, 27 horses (73%) survived to discharge, with a median duration of hospitalisation of 12 days, although treatment was necessary following discharge in all cases. There has been speculation that survival rates may differ depending on the *Clostridium* species involved, but there is insufficient evidence to make such distinctions.

Further reading

Peek SF, Semrad SD, & Perkins, GA. "Clostridial myonecrosis in horses (37 cases 1985–2000)." Equine veterinary journal 35.1 (2003): 86-92 (217).

Chapter 2: Immune-mediated myositis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. A rare, but severe, rapidly progressing syndrome of muscle atrophy.
2. Predominately affects Quarter horses and related breeds.

Immune mediated myositis is a rare, but severe, disease that typically causes rapid and severe symmetrical wasting of the topline muscles, often following exposure to, or vaccination against, *Streptococcus equi* subspecies *equi* (strangles). The disease appears to predominately affect Quarter horses and related breeds and has been associated with a specific genetic variant in these breeds. Atrophy may progress to involve 50% of the horse's muscle mass within 1 week and may lead to generalised weakness. The reason specific muscle groups are affected is unclear.

Muscle loss is caused by inflammatory destruction of fast-twitch muscle fibres.

Diagnostics

Haematological abnormalities are generally minor, with relatively mild increases in CK and AST, given the severity of disease.

Although clinical signs are suggestive, a muscle biopsy is required to confirm the diagnosis.

Treatment

Horses with concurrent evidence of strangles should be treated with antimicrobials (penicillin) and it is prudent to avoid IM injections. Administration of corticosteroids seems to immediately improve clinical signs and prevent further progression of muscle atrophy. Dexamethasone is generally administered (0.1 mg/kg IV for 3 days) and then the dose tapered over 1 month. Some recommend switching to prednisolone (not prednisone) for oral administration (1 mg/kg) following the initial 3 days of therapy.

Antimicrobials used

- None, unless there is concurrent infection with *S. equi* ss *equi*. In these cases, benzyl penicillin (22,000 IU/kg IV q 6 h) is preferred, as IM injections should be avoided.

Prognosis

Full muscle mass can be regained within weeks to months, but recurrence of atrophic episodes is common (~40% of horses). Euthanasia because of severe muscle loss and poor quality of life is common.

Further reading

Durward-Akhurst, SA & Valberg, S. 2017. Immune mediated muscle diseases of the horse. https://doi.org/10.1177/0300985816688755 (218).

Chapter 3: Septic synovial structures

Authors: Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Early detection of a septic synovial structure and prompt treatment are crucial to a successful outcome.
2. Collection of synovial fluid for cytology and culture and sensitivity testing is very important and ideally should be performed prior to initiation of antimicrobial therapy.
3. Lavage of synovial structures is associated with better outcomes.

Synovial structures can become infected by direct inoculation following a wound, by iatrogenic introduction with intra-synovial injections or by haematogenous spread. Although haematogenous spread is more common in foals, it can occur in adult horses. Early diagnosis and aggressive treatment with lavage and appropriate antimicrobial therapy is critically important, as chronic disease is associated with higher mortality. The most common bacterial isolates from wounds are *Enterobacter* spp., *Staphylococcus* spp., *Streptococcus* spp. and *Pseudomonas* spp., but infections are often mixed and can involve anaerobic bacteria. Iatrogenic infections are often caused by *Staphylococcus* spp.. Studies of the efficacy of addition of prophylactic antimicrobials (such as amikacin) to intra-articular medications (such as corticosteroids) have not demonstrated a reduction in joint sepsis, so this prophylactic use is not recommended. Aseptic joint preparation and adequate injection technique are sufficient to prevent sepsis (219). Polysulphated glycosaminoglycans (PSGAGs) are the only exception to this, with the current recommendation being to use concurrent intra-articular antimicrobials to reduce the risk of infection (220).

Although the use of intra-articular antimicrobials for treatment of joint sepsis is widespread, there are important clinical knowledge gaps about the appropriate intra-articular doses to use, the potential for contribution to the development of antimicrobial resistance with overuse, and whether there are long-term adverse side effects of the cytotoxicity of local antimicrobial treatment for cartilage. The intra-articular administration of amikacin can induce dose-dependent increases in cartilage degradation products and biomarkers of inflammation. It is thought that concurrent administration of other medications, such as hyaluronic acid, may mitigate antimicrobial-induced cytotoxicity (221).

Intravenous regional limb perfusions (IVRLP) are used to treat distal limb infections by isolating the limb from the systemic circulation with a tourniquet and infusing a high concentration of an antimicrobial intravenously. The antimicrobial diffuses passively into all tissues throughout the isolated region until the tourniquet is removed, after approximately 20 min. Ceftiofur sodium administered at a dose of 2 g diluted in 60 mL of sterile saline as an IVRLP maintained regional plasma concentrations above MIC (1 µg/mL) for 12 h, and subcutaneous tissue concentrations above MIC for 24 h, but bone concentrations were only above MIC until immediately after tourniquet removal (222). Inflamed joints have been shown to have increased concentrations of amikacin after IVRLP, when a 5 mg/kg dose (one-third of the systemic dose) was diluted in 60 mL of sterile saline, and the concentrations reached the recommended Cmax-to-MIC ratio of 8 (MIC of 16 µg/mL) in most inflamed joints, but not in normal joints (223). There are many published reports describing variations in this technique, including the dose used, the dose volume and the concentration of perfusate, the dosing interval, the type, method and duration of tourniquet application (with or without an Esmarch bandage) and whether the technique is performed standing or under general anaesthesia, so the optimal method for performing IVRLP has not been established and the apparent clinical benefits of the technique are often difficult to confirm and quantify (224). For detailed recommendations on intra-synovial and intravenous regional perfusion, see the next section (Section 12).

Diagnostics

Horses with septic synovial structures are generally febrile and non-weight-bearing lame in the affected leg, with effusion into the infected synovial structure. Synovial fluid analysis reveals an elevated nucleated cell count (> 2.5 x 10^9/L), with a neutrophilia (> 80%) and an elevated protein concentration (> 25 g/L). Synovial fluid should be submitted for culture and susceptibility testing.

Treatment

1. Needle lavage of the affected joint can be done standing, or via arthroscopy under general anaesthesia.
2. Arthroscopy allows visualisation of the joint and may enable determination of a more accurate prognosis, and enables debridement of infected tissue.
3. Broad spectrum antimicrobial therapy is indicated until culture results are available.
4. Intra-articular administration and regional limb perfusions have been used to deliver increased concentrations of antimicrobials to synovial structures. Concentration-dependant antimicrobial drugs (aminoglycosides) are the best choice, as high concentration-to-MIC ratios can be achieved, which enhances bacterial killing, and these drugs are also amenable to once daily administration due to the presence of a post-antibiotic effect.

Antimicrobials used

- Procaine penicillin (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h) until resolution of lameness.
- Intra-articular administration (gentamicin at 150 -500 mg; amikacin at 250 -1000 mg) q 24 h until resolution of lameness.
- Intravenous regional limb perfusion (gentamicin at 500 – 1000 mg; amikacin at 500 – 2000 mg) q 24 h until resolution of lameness.

Prognosis

Fair to good with early detection and prompt treatment of infection. In recent studies 84% and 90% survived to discharge (mean duration of antimicrobial therapy is 12 days), but only 54% and 65% returned to function (225, 226).

Reference List

1. Peek SF, Semrad SD, Perkins GA. Clostridial myonecrosis in horses (37 cases 1985-2000). Equine veterinary journal. 2003;35(1):86-92.
2. Durward-Akhurst SA, Valberg SJ. Immune-Mediated Muscle Diseases of the Horse. Vet Pathol. Los Angeles, CA: SAGE Publications; 2018. p. 68-75.
3. Gillespie CC, Adams SB, Moore GE. Methods and Variables Associated with the Risk of Septic Arthritis Following Intra-Articular Injections in Horses: A Survey of Veterinarians. Veterinary surgery. 2016;45(8):1071-6.
4. Smith LCR, Wylie CE, Palmer L, Ramzan PHL. Synovial sepsis is rare following intrasynovial medication in equine ambulatory practice. Equine veterinary journal. 2019;51(5):595-9.
5. Pezzanite LM, Hendrickson DA, Dow S, Stoneback J, Chow L, Krause D, et al. Intra-articular administration of antibiotics in horses: Justifications, risks, reconsideration of use and outcomes. Equine veterinary journal. 2022;54(1):24-38.
6. Cox KS, Nelson BB, Wittenburg L, Gold JR. Plasma, subcutaneous tissue and bone concentrations of ceftiofur sodium after regional limb perfusion in horses. Equine veterinary journal. 2017;49(3):341-4.

7. Beccar-Varela AM, Epstein KL, White CL. Effect of Experimentally Induced Synovitis on Amikacin Concentrations after Intravenous Regional Limb Perfusion. Veterinary surgery. 2011;40(7):891-7.

8. Biasutti SA, Cox E, Jeffcott LB, Dart AJ. A review of regional limb perfusion for distal limb infections in the horse. Equine veterinary education. 2021;33(5):263-77.

9. Crosby DE, Labens R, Hughes KJ, Nielsen S, Hilbert BJ. Factors Associated With Survival and Return to Function Following Synovial Infections in Horses. Frontiers in veterinary science. 2019;6:367-.

10. Walmsley EA, Anderson GA, Muurlink MA, Whitton RC. Retrospective investigation of prognostic indicators for adult horses with infection of a synovial structure. Australian veterinary journal. 2011;89(6):226-31.

Section 12 - Intra-synovial and regional antimicrobial therapy

Contents

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Antimicrobials should only be used for prophylaxis when administering intra-articular polysulphated glycosaminoglycan injections and not when injecting joints with other medications to treat osteoarthritis.
2. Repeated intra-synovial (IS) injections can be performed easily on most horses and should be considered in cases of synovial sepsis.
3. IVRP achieves high concentrations of antimicrobials in the distal limb of the horse and is extremely useful for treatment of cellulitis, soft-tissue infection, or when IS injections are not possible due to the risk of contamination (e.g. if a wound is present over the injection site).
4. A wide rubber tourniquet helps in achieving higher concentrations of antimicrobial at the target sites. Local anaesthetic blocks may prevent movement while the tourniquet is in place.
5. Local anaesthetic should not be combined with antimicrobials in the perfusate.

Intra-synovial (IS) injection of antimicrobials has been widely used by equine veterinarians, prophylactically when injecting joints with osteoarthritis and therapeutically to treat septic synovial structures. This route has been popular as it avoids common issues when administering systemic antimicrobials to horses – side effects such as diarrhoea, poor penetration into joints and the high cost of some treatments. However, there are also negative impacts, including deleterious effects on local tissues, expense to the owner and potential contributions to antimicrobial resistance. In addition, as this form of treatment is off-label, the safety and efficacy of many medications are unknown.

Intra-articular antimicrobial use for prophylaxis has been reported by almost half of equine veterinarians, especially when injecting corticosteroids (227), though the risk of septic arthritis following joint injections is exceedingly low (< 0.1%), even in ambulatory practice (221). There is some evidence that intra-articular injection of polysulphated glycosaminoglycans is associated with an increased risk of septic arthritis and, given the consequences of these infections, prophylactic antimicrobial use is indicated in these cases. Because of the infrequent use of this medication, strong evidence for the quantitative risk is lacking, but in the author's opinion, and that of many specialist surgeons, polysulphated glycosaminoglycans should be delivered with prophylactic antimicrobials. There is no evidence in the literature that intra-articular administration of polyacrylamide hydrogel is associated with a similar increased risk of sepsis.

Local antimicrobial therapy by multiple routes (intra-articular, IS, intraosseous, intravenous regional limb perfusion [IVRP]) has been reported in the treatment of **septic arthritis** in horses, with the goal of achieving high local concentrations. IS injection has the advantage of achieving very high concentrations immediately following administration. Gentamicin reached higher peak concentrations in synovial fluid administered intra-articularly than when delivered by IVRP, but the concentrations did not differ in serum or bone (228). Continuous IS antimicrobial therapy has also been reported but requires considerable nursing care and is largely limited to use in hospital situations. Continuous therapy is not necessary if antimicrobials exhibiting concentration-dependent activity are selected.

Intravenous Regional Limb Perfusion (IVRP) can be performed in the standing, sedated horse following proper tourniquet application proximal to the site of infection. This technique has been shown to be effective in achieving a maximum concentration (Cmax) of an aminoglycoside that is greater than 10 times above the minimum inhibitory concentration (MIC) for the bacteria of interest in tissues and synovial fluid distal to the tourniquet (229). A meta-analysis of treatment by IVRLP found that wide rubber tourniquets (vs pneumatic tourniquets) and concurrent use of local anaesthetic, perineurally or within the perfusate, increased the likelihood of achieving Cmax:MIC >10 (230). The concurrent use of local anaesthetics is presumed to decrease tourniquet-induced pain, thereby limiting horse movement and improving the efficacy of tourniquets. However, a recent study has demonstrated an antagonistic effect on antimicrobial efficacy against multiple Gram-negative bacteria when combining local anaesthesia (lignocaine, bupivacaine or mepivacaine) and antimicrobials (gentamicin, amikacin). Caution should be used when combining aminoglycosides with local anaesthetics during IVRP (231).

In a meta-analysis of IVRP techniques, higher volumes of perfusate achieved a higher Cmax than lower volumes. Larger volumes probably achieve higher intravascular pressures, facilitating diffusion of the antimicrobial into peripheral tissues. However, IVRP is often repeated in clinical cases and there is a greater potential for complications with high perfusate volumes (i.e. vasculitis). Selecting the lowest perfusate volume that reliably achieves an efficacious Cmax:MIC would be clinically beneficial. From the meta-analysis, low, medium and high-volume perfusions achieved Cmax:MIC ≥ 10 for sensitive bacteria, while only high-volume perfusions achieved Cmax:MIC ≥ 10 for resistant bacteria. Therefore, clinicians are encouraged to consider the bacterial susceptibility when selecting their IVRP technique (230).

Treatment

Osteoarthritis:

Antimicrobials should only be used for prophylaxis when administering intra-articular injections of polysulphated glycosaminoglycan and not when injecting joints with other medications to treat osteoarthritis

Septic arthritis:

In cases of septic arthritis, selection of an antimicrobial for IS therapy should, ideally, be based on culture and susceptibility testing of the organism involved, when available. In lieu of a positive culture, or while waiting for culture and susceptibility results, it is not recommended to delay local or systemic antimicrobial therapy. Antimicrobial selection should be guided by the following factors. Firstly, the cytological appearance of the bacteria on examination of a Gram stain, secondly, on reports in the literature of the most common isolates found after iatrogenic or traumatic introduction of bacteria into the joint, and finally on the pharmacokinetics and safety profile of the antimicrobials. Aminoglycosides are preferred because of their concentration dependent activity (see Table 12.1 for dose recommendations). Amikacin should only be used when there is demonstrated resistance to gentamicin. Because very high concentrations are achieved in synovial structures, gentamicin may still be effective even though the organism responsible may be classified as resistant in susceptibility tests, as susceptibility cut-offs are based on concentrations that can be achieved in serum after systemic administration. Ceftiofur has also been used in IS therapy. Cephalosporins are time-dependent antimicrobials - high concentrations are of limited value and there is no post-antibiotic effect, so frequent dosing is required. Ceftiofur is suitable for continuous infusions.

The Cmax of gentamicin in synovial fluid was significantly higher (800 times) with intra-articular administration than with regional perfusion and remained six times higher 24 hours after treatment (228). Compared to systemic administration, injection of 150 mg of gentamicin has been shown to yield 1000-fold higher concentrations in synovial fluid, and concentrations remain above the MIC for many equine pathogens for more than 24 h (232).

While the incidence of complications following intra-articular injection is low, synovitis and cellulitis of the surrounding tissues and iatrogenic septic arthritis are all possible sequelae.

Although direct IS injection achieves high concentrations of antimicrobials, investigations have demonstrated dose-dependent deleterious effects of antimicrobials on cartilage *in vitro*, with chondrotoxicity noted even at low doses of amikacin, carbapenems, ceftiofur sodium and ampicillin (221). Amikacin has been shown to be significantly more chondrotoxic than other antimicrobial drugs. Dose-dependent increases in synovial fluid inflammatory markers, including TNF-α and IL-1β, have been seen following intra-articular administration of amikacin *in vivo*, at doses as low as 32.5 mg/joint. This inflammation can make it difficult to interpret the response to therapy when treating septic arthritis, particularly when repeated IS injections are administered. Inflammatory markers, such as total protein concentration and total nucleated cell counts should be expected to be elevated in horses after IS administration of amikacin and therefore should not be used to assess the response to therapy.

In the light of these findings, titration of the intra-articular dose to the lowest effective concentration is probably prudent. *In vivo* assessment of synovial fluid has demonstrated concentrations exceeding 100 × MIC for most common bacterial pathogens involved in septic arthritis after administration of amikacin at doses as low as 31.25 mg/joint (221).

IVRP is extremely useful in cases where there is cellulitis or evidence of soft-tissue infection, or when IS injections are not possible due to a risk of contamination (e.g. if a wound is present over the injection site). Ceftiofur has also been evaluated for IVRP. A dose of 2 g (in 100 ml into the cephalic vein) has been recommended, but this should be repeated every 8-12 h (233).

Table 12.1. Recommendations for IVRP doses and techniques in horses.

Drug	Dose	Perfusate volume	Duration of torniquet use*
Gentamicin	1/3 systemic dose (2.2 mg/kg)	Higher volumes associated with higher concentrations, but low and high volumes all achieved adequate concentrations. Common: 10 ml for palmar digital vein. Larger veins – 20 – 60 mL common. Higher perfusate volumes should be considered for resistant bacterial pathogens.	30 min (where possible) Shorter durations may be sufficient but maximum concentrations not achieved until 30 min
Amikacin (HIGH IMPORTANCE ANTIMICROBIAL – SHOULD ONLY BE USED WHEN THERE IS DOCUMENTED RESISTANCE TO GENTAMICIN)	1/3 systemic dose (3 - 5 mg/kg)		
Ceftiofur (HIGH IMPORTANCE ANTIMICROBIAL – SHOULD ONLY BE USED WHEN THERE IS DOCUMENTED RESISTANCE TO GENTAMICIN)	2 g (for a 500 kg horse) Must be repeated every 8-12 h	100 mL into cephalic vein, no information on other veins	20 min

*A wide rubber torniquet is recommended and perineural analgesia performed prior to tourniquet placement.

Antimicrobials used

- Intra-synovial: Gentamicin at 150 mg (higher doses may be required for resistant bacteria, but higher doses associated with chondrotoxicity)
- Intra-synovial: Amikacin at 30-250 mg (induces dose-dependent synovial inflammation and high doses are associated with chondrotoxicity)
- IVRP: 1/3 of systemic dose of gentamicin or amikacin.

Further reading

Hyde RM, Lynch TM, Clark CK, Slone DE, Hughes FE. The influence of perfusate volume on antimicrobial concentration in synovial fluid following intravenous regional limb perfusion in the standing horse. Can Vet J. 2013 Apr;54(4):363-7. PMID: 24082163; PMCID: PMC3595939. (234)

Reference List

1. Ferris DJ, Frisbie DD, McIlwraith CW, Kawcak CE. Current joint therapy usage in equine practice: A survey of veterinarians 2009. Equine veterinary journal. 2011;43(5):530-5.
2. Pezzanite LM, Hendrickson DA, Dow S, Stoneback J, Chow L, Krause D, et al. Intra-articular administration of antibiotics in horses: Justifications, risks, reconsideration of use and outcomes. Equine veterinary journal. 2022;54(1):24-38.
3. Werner LA, Hardy J, Bertone AL. Bone gentamicin concentration after intra-articular injection or regional intravenous perfusion in the horse. Veterinary surgery. 2003;32(6):559-65.
4. Freeland RB, Morello SL, DeLombaert M, Rajamanickam V. Influence of intravenous regional limb perfusion with amikacin sulfate on Staphylococcus aureus bioburden in distal limb wounds in horses. Veterinary surgery. 2017;46(5):663-74.
5. Redding LE, Elzer EJ, Ortved KF. Effects of regional limb perfusion technique on concentrations of antibiotic achieved at the target site: A meta-analysis. PloS one. 2022;17(4):e0265971.
6. Adler DMT, Nielsen AT, Olsen C, Verwilghen D, Damborg P, Olsen RH. Local anesthetics and antibiotics display synergistic and antagonistic drug interactions against pathogens causing septic arthritis in horses. American journal of veterinary research. 2025:1-8.
7. Lloyd KC, Stover SM, Pascoe JR, Baggot JD, Kurpershoek C, Hietala S. Plasma and synovial fluid concentrations of gentamicin in horses after intra-articular administration of buffered and unbuffered gentamicin. Am J Vet Res. 1988;49(5):644-9.
8. Bonilla AG, Causeret L, Torrent-Crosa A. Pharmacokinetics of ceftiofur in the metacarpophalangeal joint after standing intravenous regional limb perfusion in horses. Canadian veterinary journal. 2021;62(9):975-81.
9. Hyde RM, Lynch TM, Clark CK, Slone DE, Hughes FE. The influence of perfusate volume on antimicrobial concentration in synovial fluid following intravenous regional limb perfusion in the standing horse. Canadian veterinary journal. 2013;54(4):363-7.

Section 13 – Ophthalmology

Contents

Chapter 1: Corneal ulceration

Authors: Benjamin Reynolds, Cameron Whittaker, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Antimicrobial and antifungal resistance are emerging.
2. Vision-threatening and globe-threatening disease of horses.
3. Empirical therapy should be based on cytology until culture and susceptibility results are available.

Corneal ulceration is the result of damage or destruction of parts of the corneal epithelium. This can be initiated by any trauma, exposure injury, a disorder of the cilia, inherited corneal dystrophy, corneal degeneration or calcific band keratopathy. The laterally projecting globes of horses make them particularly susceptible to traumatic ocular injuries. As corneal disease advances, via keratomalacia induced by bacterial, fungal or local host enzymatic destruction, corneal ulceration can involve the corneal stroma, Descemet's membrane, or may result in a full-thickness corneal perforation. The ocular surface of the horse is constantly exposed to pathogenic bacteria and fungi. *Pseudomonas* spp., *Streptococcus* spp. and *Staphylococcus* spp. are the most common bacterial pathogens involved, while *Aspergillus* spp. and *Fusarium* spp. predominate in cases of fungal keratitis. There may be regional variation in the most common microbial pathogens involved (235, 236), and there are multiple reports of emerging antimicrobial and anti-fungal resistance in ocular pathogens in Australia and other parts of the world (235, 237, 238).

Diagnostics

A thorough ophthalmic examination performed in a dark stall, with sedation and auriculopalpebral nerve blockade, is necessary to identify a corneal ulcer and assess potential predisposing factors. Fluorescein staining and examination with cobalt-blue light is useful to highlight exposed corneal stroma. A very deep defect down to Descemet's membrane (a descemetocoele) will not fluoresce. An inability to completely blink may result in an exposure ulcer and therefore the ability to completely blink should be assessed. The adnexa should be inspected for possible distichiasis or ectopic cilia. The surrounding cornea should be assessed for other possible inciting causes and signs of chronicity, such as corneal vascularisation, fibrosis or pigmentation. Initially, corneal/conjunctival swabs should be collected from the affected areas and then immersed in Stuart's transport medium and submitted for bacterial and fungal culture and susceptibility testing. After collection of a swab for culture, samples should be collected for cytological examination using a Kimura platinum spatula, a cytobrush or the back of a scalpel blade, using a topical anaesthetic specifically formulated for ocular administration, such as proxymetacaine hydrochloride at 5 mg/ml or oxybuprocaine hydrochloride at 0.4%. Fungal hyphae and yeasts have a predilection for Descemet's membrane but, while detection of them by cytology is confirmatory, failure to observe them by cytological examination does not establish that fungi are not involved. Bacterial, fungal or mixed bacterial and fungal infections can occur in corneal ulcers.

Treatment

Note: use of a sub-palpebral lavage system will greatly enhance the reliability of drug delivery to the cornea.

No infectious agent observed by cytology:

Broad-spectrum antimicrobial to prevent bacterial colonisation.

1. Topical chloramphenicol
2. Topical chloramphenicol/polymyxin-B combination, or
3. Topical neomycin-polymyxin B-bacitracin triple combination.

Apply q 8 h for ointments, q 6 h for drops. Use of prophylactic antifungals is not necessary and promotes resistance.

Cocci observed by cytology:

Topical chloramphenicol – q 8 h for ointments, q 6 h for drops.

Rods observed by cytology:

Topical polymyxin B, neomycin, gentamicin – q 8 h for ointments, q 6 h for drops.
Ofloxacin or ciprofloxacin are also frequently used but should be reserved for cases where resistance is detected to lower importance agents.

Fungi observed by cytology:

See guidelines for fungal keratitis

If keratomalacia is observed, use serum eye drops every 2 - 4 h or compounded eye drops containing 3% EDTA every 2 - 4 h (poorly tolerated on corneal ulcers). Serum eye drops are prepared by collecting 6 plain clot vacutainer tubes of blood. They should ideally be incubated at 37 °C for 10-15 min to allow the clot to retract and enhance the yield of serum, then centrifuged at 3, 600 x g for 10 min. The serum should then be pipetted or poured off the top and refrigerated. It can be used for 5 days if stored at 4 °C.

Atropine should be used in all patients with ulcers, to effect (as observed by mydriasis), for cycloplegia and stabilization of the blood-aqueous humour barrier. The purported association of its use with colic and ileus is dubious (239). Ideally, horses should be housed in a darkened environment if atropine is administered.

Treatment with flunixin at 1.1 mg/kg IV q 12 h, to effect for up to 5 days, or, less ideally, phenylbutazone at 2.2 - 4.4 mg/kg PO q 12-24 h to effect, should be instituted to provide analgesia and reduce the risk of reflex iridocyclitis.

When culture and susceptibility test results are available, and a clinical response to therapy is not apparent, then altering therapy based on the test results is appropriate.

If progression occurs despite appropriate therapy, then globe-sparing surgery is indicated. This may necessitate referral to a veterinary ophthalmologist.

Table 13.1. Antimicrobials used (Corneal ulceration)

Topical Antimicrobial	Use
Chloramphenicol (10 mg/g)	Gram positives, such as *Staphylococcus* and *Streptococcus* spp.
Polymyxin B (5000 – 10000 IU/g)	*Pseudomonas aeruginosa*, but significant resistance reported in Australia (235)
Neomycin (3.5 mg/g)	*Pseudomonas aeruginosa,* but significant resistance reported in Australia (235)
Zinc bacitracin (500 IU/g)	Gram positives, such as *Staphylococcus* and *Streptococcus* spp.
Gentamicin (0.3%)	Predominately Gram negatives, also *Staphylococcus* spp.
Ofloxacin/ciprofloxacin (0.3%)	Gram positives (such as *Staphylococcus* and *Streptococcus* spp.) and Gram negatives (such as *Pseudomonas aeruginosa*).

Prognosis

Fair with appropriate management. Despite appropriate management, bacterial colonisation can initiate keratomalacia, which can necessitate rapid surgical intervention. Corneal ulceration is a major cause of vision loss and globe loss in horses.

Further reading

Williams LB & Pinard CL (2013). Corneal ulcers in horses. Compendium: Continuing Education for Veterinarians. 35(1):E4. (240)

Brooks, D. E. and C. E. Plummer (2022). Diseases of the Equine Cornea. Equine Ophthalmology. B. C. Gilger. Hoboken, NJ, John Wiley & Sons: 253-440.(241)

Chapter 2: Fungal keratitis

Authors: Benjamin Reynolds, Cameron Whittaker, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Antifungal resistance is emerging.
2. Vision-threatening and globe-threatening disease of horses.

Fungal keratitis can range from non-ulcerative disease, to rapidly progressive keratomalacia involving all layers of the cornea, to stromal abscessation. The ocular surface of the horse is constantly exposed to pathogenic fungi, so any alteration of host innate defense mechanisms can result in fungal colonisation of the cornea. This colonisation of the cornea has been associated with topical steroid use. The most common species involved include filamentous fungi, such as *Aspergillus, Fusarium* and *Penicillium* spp., or yeasts, such as *Candida albicans*. There are probably regional differences in the fungal species most commonly involved and there are multiple reports of emerging resistance to anti-fungal agents from around the world (238, 242).

Ulcerative fungal keratitis is a very serious clinical condition and is a leading cause of blindness and globe loss in horses. However, with swift medical, and often surgical, intervention, the globe can be preserved in up to 80% of eyes (243). Fungal keratitis can be slow to resolve medically, with a median healing time of 17 days (range, 12 – 87 days) for *Fusarium* spp. and 31 days (range, 22 - 63 days) for *Aspergillus* spp. (238).

Diagnostics

See Section 13, Chapter 1.

Treatment

<u>Note: use of a sub-palpebral lavage system will greatly enhance the reliability of drug delivery to the cornea.</u>

If fungal hyphae or yeasts are observed on cytology:

1. Topical voriconazole at 10 mg/mL q 2-4 h - excellent corneal penetration, and historically low resistance in filamentous fungi
2. Topical 1% itraconazole in 30% DMSO q 2-4 h

Topical fluconazole (0.3% solution) has been used q 2-4 h, but it has a more limited spectrum of activity than the other azoles (especially against yeasts).

Silver sulfadiazine (Flamazine) can be used topically q 8-12 h if treatment via subpalpebral lavage is not possible.

If keratomalacia is observed, use serum eye drops every 2 - 4 h or compounded eye drops containing 3% EDTA every 2 - 4 h (poorly tolerated on corneal ulcers). (See Section 13, Chapter 1 for serum eyedrop production and storage).

Atropine and non-steroidal anti-inflammatory use is as recommended for bacterial corneal ulcers (Section 13. Chapter 1.)

When culture and susceptibility results are available and a clinical response to therapy is not apparent, then altering therapy based on the test results is appropriate. Continue treatment until resolution of the keratitis.

If progression occurs, despite appropriate therapy, then globe-sparing surgery is indicated. This may necessitate referral to a veterinary ophthalmologist.

Table 13.2. Antimicrobials used (Fungal keratitis)

Antimicrobial	Use
Voriconazole at 1%	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts
Itraconazole at 1% in 30% DMSO	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts
Ketoconazole at 1%	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts.
Miconazole at 1%	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts.
Fluconazole at 0.3%	Yeasts and filamentous fungi but less efficacious than other azoles
Silver sulfadiazine at 1% in an ointment	Good historical efficacy against filamentous fungi and yeasts.

Prognosis

With swift and appropriate medical and/or surgical management, vision sparing has been achieved in up to 80% of cases. However, up to 64% of cases require some type of surgical intervention (243).

Further reading

Galera PD & Brooks DE (2012). Optimal management of equine keratomycosis. Veterinary Medicine: Research and Reports. 3: 7-17.(244)

Chapter 3: Stromal abscess

Authors: Benjamin Reynolds, Cameron Whittaker, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Antimicrobial and antifungal resistance is emerging.
2. Drug delivery is challenging because of the intact corneal epithelium.
3. Early and aggressive medical therapy, using both antibacterial and antifungal agents with good corneal penetration, is indicated.
4. Progression or a poor response to therapy is an indication for surgical intervention.

Stromal abscessation can occur at any depth of the corneal stroma, although it most commonly occurs in the mid to deep corneal stroma. Abscesses form because of micropunctures of the corneal epithelium, with normal epithelial sliding and migration covering the inoculated bacteria and/or fungi, resulting in an abscessed area (245). Environmental factors, such as high wind speed, low temperatures and atmospheric pollutants that disrupt the protective tear film, may contribute to the pathogenesis (246). Horses with stromal abscesses often present with blepharospasm and, initially, a small focal white to yellow opacity in the stroma. An intense iridocyclitis (anterior uveitis) is also often observed.

Covering of the initial epithelial defect with a layer of migrating epithelium can retard the antimicrobial properties of tears and also inhibit access of high concentrations of topical medications to the affected region. Stromal abscesses often require prolonged and aggressive medical and surgical therapy. Deep stromal abscesses are more likely to require surgical intervention than superficial stromal abscesses. Recurrence of abscessation is possible.

Diagnostics

A thorough ophthalmic examination should be performed in a dark stall, with sedation and an auriculopalpebral nerve blockade. There should be a careful assessment for iridocyclitis. Fluorescein staining and examination with cobalt-blue light is typically negative, and cytology and culture are often unrewarding.

Treatment

<u>Note: use of a sub-palpebral lavage system will greatly enhance the reliability of drug delivery to the cornea.</u>

1. Topical chloramphenicol q 4-6 h, topical ofloxacin q 4-6 h and voriconazole q 4-6 h.
2. Epithelial debridement under local anaesthesia above the region of abscessation will enhance drug penetration.
3. Intra-lesional injection of 5% voriconazole under local anaesthesia using a 27 gauge needle enables good local drug deposition (247).

Atropine and non-steroidal anti-inflammatory use is as recommended for bacterial corneal ulcers (Section 13. Chapter 1.)

Signs of improvement include neovascularisation extending throughout the abscessed area, a change in abscess colour to grey-tinged tissue, and control of reflex anterior uveitis.

If progression occurs or appropriate medical therapy does not result in improvement after a week, then surgery is indicated. This may necessitate referral to a veterinary ophthalmologist.

Table 13.3 Antimicrobials used (Stromal abscess)

Antimicrobial	Use
Chloramphenicol (10 mg/g)	Excellent corneal penetration. Useful against Gram positives, such as *Staphylococcus* and *Streptococcus* spp.
Ofloxacin (0.3%)/ciprofloxacin (0.3%)	Excellent corneal penetration. Broad spectrum, useful against Gram positives (such as *Staphylococcus* and *Streptococcus* spp.) and Gram negatives (such as *Pseudomonas aeruginosa*).
Voriconazole at 1%:	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts.
Itraconazole at 1% in 30% DMSO	Good corneal penetration, good historical efficacy against filamentous fungi and yeasts.

Prognosis

Good for superficial stromal abscesses and fair for deep stromal abscesses. Despite appropriate management, the deep corneal stroma is a difficult location to achieve good drug delivery and extensive corneal vascularisation is needed to achieve complete resolution. Deep stromal abscesses often require surgical intervention.

Further reading

Henriksen MDL, Andersen PH, Plummer CE, Mangan B, Brooks DE (2012). Equine corneal stromal abscesses: An evolution in the understanding of pathogenesis and treatment during the past 30 years. Equine Veterinary Education. June:315-323.(248)

Chapter 4: Anterior uveitis

Authors: Benjamin Reynolds, Cameron Whittaker, Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Rarely due to bacterial causes, so topical antimicrobials are never indicated, and systemic antimicrobials are rarely indicated.
2. Initial aggressive anti-inflammatory therapy is needed.
3. If uveitis becomes recurrent, the prognosis for vision is guarded.

Equine anterior uveitis is an inflammatory disorder of the equine uveal tract. It can be acute, recurrent or chronic. Uveitis is quite common, occurring in up to 1% of Australian Thoroughbreds (249). The causes of uveitis are often not identified. In cases of uveitis in which a specific cause is identified, the aetiological agent is most often non-infectious, but infectious agents can be involved. A lack of response to symptomatic therapy may necessitate further investigations for infectious causes.

The clinical signs are all due to ocular pain and compromise of the blood-aqueous humour barrier, and include blepharospasm, epiphora, diffuse corneal oedema, aqueous flare, hypopyon and miosis. A particular syndrome of recurrent episodes of uveitis separated by quiescent periods, called equine recurrent uveitis (ERU), is the leading cause of permanent blindness in horses worldwide. Up to 60% of horses diagnosed with ERU do not return to their previous role or perform at a reduced level (250). The development of ERU is complex and multifactorial, but it is probably initiated by a bout of uveitis that alters immune self-recognition via epitope spreading, resulting in autoantigens in various tissues within the uveal tract.

Diagnostics

A thorough ophthalmic examination should be performed in a dark stall, with sedation and auriculopalpebral nerve blockade, to diagnose anterior uveitis. The hallmark of active uveitis is aqueous flare, and it may be coupled with corneal oedema, miosis, hypopyon, hyphaema or the presence of fibrin in the anterior chamber. Chronic uveitis may result in posterior synechiae, cataracts, atrophy of the *corpora nigra*, rubeiosis iridis and retinal detachment. In young animals, primary disease, such as septicaemia and infection with *Rhodococcus equi* should be considered. If active uveitis does not respond to therapy, then potential infectious causes, such as leptospirosis in endemic areas, should be investigated. Warm, wet environmental conditions support the survival of leptospires in the environment for longer periods, increasing the opportunities for exposure. Paired serum samples can be submitted for serology.

Treatment

Reduce discomfort with cycloplegics (atropine at 1%), given topically until mydriasis occurs, then continue as needed. The purported association of its use with colic and ileus is dubious (239). Ideally, horses should be housed in a darkened environment if atropine is administered.

Reduce inflammation - topical steroids, such as prednisolone acetate at 1% or dexamethasone HCl at 0.1%, are the most effective, but may potentiate keratomycosis. Topical non-steroidal anti-inflammatory drugs (NSAIDs), such as 0.1% diclofenac sodium, can be used, but these are less effective and can also potentiate keratomycosis. These should be dosed by need, up to 6 times daily, and the frequency of treatment reduced as clinical signs improve. Flunixin meglumine is a potent anti-inflammatory for the eye and can be delivered via intravenous or oral routes. Intravenous administration at 1.1 mg/kg q 12 h is the preferred route. Oral administration of flunixin meglumine

is far less effective. Other NSAIDs, such as phenylbutazone, are much less effective in treating the signs of uveitis in horses.

In cases of ERU when inflammation cannot be controlled medically, immune modulation may be warranted. This involves surgical implantation of cyclosporine-impregnated implants into the suprachoroidal space to provide a constant local supply of drug to the uveal tract. This procedure warrants referral to a veterinary ophthalmologist.

Antimicrobials used

Antimicrobials are not used to treat primary non-infectious uveitis, but they are indicated in uveitis that occurs secondary to a specific infectious cause.

1. *Rhodococcus equi in foals:*
   (See Section 4, Chapter 4)

2. Leptospirosis:
   Oxytetracycline at 6.6 mg/kg IV q 12 h for 5 days

   OR doxycycline at 10 mg/kg PO q 12 h for 5 days.

Prognosis

Acute uveitis has a good prognosis with appropriate management. Chronic and recurrent uveitis may have a poor prognosis for vision, with the sequelae of cataracts, retinal detachment and glaucoma occurring frequently.

Further reading

Charnock LN, Keys DA, McMullen RJ (2022). Clinical findings associated with blunt ocular trauma in horses: a retrospective analysis. Veterinary Ophthalmology.25(1):52-61. (251)

Habin DJ (1994). Equine traumatic uveitis. Equine Veterinary Education. 6(3):122-127. (252)

Allbaugh RA (2016). Equine recurrent uveitis: a review of clinical assessment and management. Equine Veterinary Education;29(5):279-288. (253)

Reference List

1. Deniaud M, Tee E. Susceptibility pattern of bacterial isolates in equine ulcerative keratitis: Implications for empirical treatment at a university teaching hospital in Sydney. Australian veterinary journal. 2023;101(3):115-20.
2. Reed Z, Thomasy SM, Good KL, Maggs DJ, Magdesian KG, Pusterla N, et al. Equine keratomycoses in California from 1987 to 2010 (47 cases). Equine veterinary journal. 2013;45(3):361-6.
3. Chalder RH, Knott T, Rushton JO, Nikolic-Pollard D. Changes in antimicrobial resistance patterns of ocular surface bacteria isolated from horses in the UK: An eight-year surveillance study (2012-2019). Veterinary ophthalmology. 2020;23(6):950-6.
4. Martinez PS, Whitley RD, Plummer CE, Richardson RL, Hamor RE, Wellehan JFX. In vitro antifungal susceptibility of Fusarium species and Aspergillus fumigatus cultured from eleven horses with fungal keratitis. Veterinary ophthalmology. 2022;25(5):376-84.
5. Wehrman RF, Gemensky-Metzler AJ, Zibura AE, Nyhart AB, Chandler HL. Objective evaluation of the systemic effects of topical application of 1% atropine sulfate ophthalmic solution in healthy horses. Journal of the American Veterinary Medical Association. 2017;251(11):1324-30.
6. Williams LB, Pinard CL. Corneal ulcers in horses. Compend Contin Educ Vet. 2013;35(1):E4.

7. Brooks DE, Plummer CE. Diseases of the Equine Cornea. In: Gilger BC, editor. Equine Ophthalmology. Hoboken, New Jersey: John Wiley & Sons; 2022. p. 253-440.

8. Hampson ECGM, Gibson JS, Barot M, Shapter FM, Greer RM. Identification of bacteria and fungi sampled from the conjunctival surface of normal horses in South-East Queensland, Australia. Veterinary ophthalmology. 2019;22(3):265-75.

9. Sherman AB, Clode AB, Gilger BC. Impact of fungal species cultured on outcome in horses with fungal keratitis. Veterinary ophthalmology. 2017;20(2):140-6.

10. Galera PD, Brooks DE. Optimal management of equine keratomycosis. Vet Med (Auckl). 2012;3:7-17.

11. Rebhun WC. Corneal stromal abscesses in the horse. J Am Vet Med Assoc. 1982;181(7):677-9.

12. Proietto LR, Plummer CE, Maxwell KM, Lamb KE, Brooks DE. A retrospective analysis of environmental risk factors for the diagnosis of deep stromal abscess in 390 horses in North Central Florida from 1991 to 2013. Veterinary ophthalmology. 2016;19(4):291-6.

13. Smith KM, Pucket JD, Gilmour MA. Treatment of six cases of equine corneal stromal abscessation with intracorneal injection of 5% voriconazole solution. Veterinary ophthalmology. 2014;17(1):179-85.

14. Henriksen MDL, Andersen PH, Plummer CE, Mangan B, Brooks DE. Equine corneal stromal abscesses: An evolution in the understanding of pathogenesis and treatment during the past 30 years. Equine veterinary education. 2013;25(6):315-23.

15. Hurn SD, Turner AG. Ophthalmic examination findings of Thoroughbred racehorses in Australia. Veterinary ophthalmology. 2006;9(2):95-100.

16. Gerding JC, Gilger BC. Prognosis and impact of equine recurrent uveitis. Equine veterinary journal. 2016;48(3):290-8.

17. Charnock LN, Keys DA, McMullen RJ. Clinical findings associated with blunt ocular trauma in horses: a retrospective analysis. Veterinary ophthalmology. 2022;25(1):52-61.

18. Habin DJ. Equine traumatic uveitis. Equine veterinary education. 1994;6(3):122-7.

19. Allbaugh RA. Equine recurrent uveitis: A review of clinical assessment and management. Equine veterinary education. 2016;29(5):279-88.

Section 14 – Dermatology

Contents

Chapter 1: Burns/Thermal Injuries

Author: Edwina Wilkes, Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

Key issues

1. Wound assessment can be difficult due to 'latent wounds'- heat is slow to dissipate from wounds and it can be difficult to accurately evaluate the amount of tissue damage on initial presentation (Figure 14.1). Tissue ischaemia can also continue for 24 - 48 h after the initial injury (254). Wound management is time intensive and costly and wound contracture and skin fragility (Figure 14.2) can occur.
2. Pain can be difficult to manage.
3. Pruritis can lead to self-trauma and may require appropriate control (e.g. reserpine for longer acting sedation, gabapentin to modulate sensitisation of neuronal pathways). Non-pharmacological treatment options include cooling, cross-ties, neck cradles and pressure garment therapy (e.g. Hidez® compression suit).
4. There is a significant increase in metabolic rate in patients with burn injuries and this will result in increased calorific expenditure and protein catabolism(254). Calorific and protein intakes must be adjusted to maintain bodyweight, which can include enteral and parenteral routes of administration.

Equine thermal injuries may result from barn fires, bushfires, grass fires, contact with hot solutions, electrocution or lightning strike, friction (e.g. rope burns), abrasions or chemicals. There are some important differences between the impact and types of injuries sustained during barn fires compared to bushfires. In grass fires and bushfires, burns are usually located on the extremities and ventral abdomen, whereas in barn fires, dorsal thermal injuries are more common (255). The literature on the management of equine thermal injuries is predominantly based on injuries sustained during barn fires, with little information available about the types of injuries sustained during bushfires (255, 256).

The most common pathogens causing secondary infections in burn wounds are *Staphylococcus aureus* and *Pseudomonas aeruginosa* (257).

Diagnostics

A thorough patient assessment is important prior to the instigation of treatment of thermal injuries, paying particular attention to cardiovascular function, pulmonary status, ocular lesions and the extent and severity of the burns (254).

The extent of the burn depends on the size of the area exposed, whereas the severity is determined by the maximum temperature the tissue attains and the duration of overheating (254). The percentage total body surface area affected usually correlates with mortality, whereas the depth determines morbidity (254).

There are several physical criteria used to evaluate burns, including erythema, oedema and pain, blister formation, eschar (slough produced by a thermal burn) formation, the presence of infection, body temperature and cardiovascular status (254). Erythema, oedema and pain indicate the presence of some viable tissue and are therefore favourable signs. However, pain is not a reliable indicator for determining burn depth. An accurate evaluation of the severity of a burn often cannot be made until there has been time for further tissue changes (254).

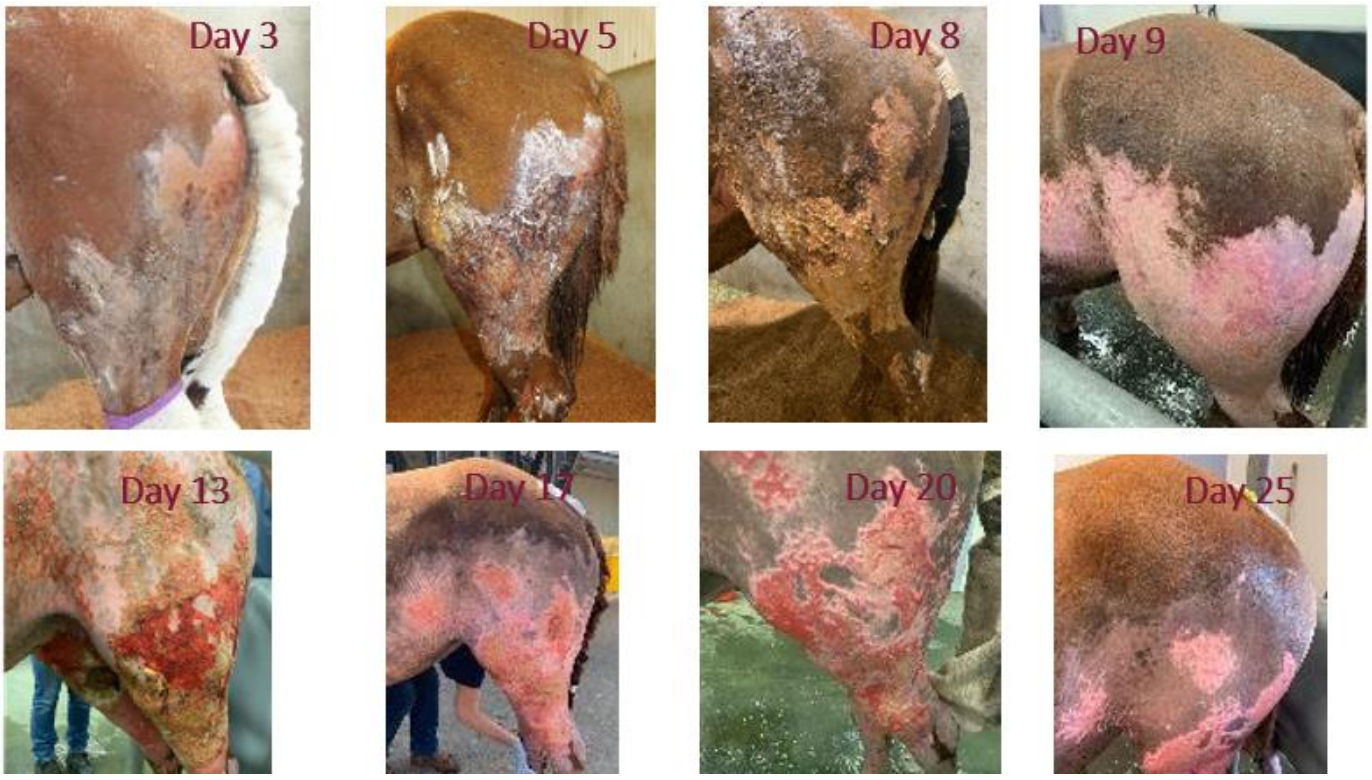

Figure 14.1 Progression of wounds following severe thermal injuries (3rd degree).

Burns are classified by the depth of injury, with first-degree burns involving the most superficial layers of epidermis. Second-degree burns may be superficial (basal layers remain relatively uninjured) or deep (all layers of the epidermis). Third-degree burns involve loss of the epidermal and dermal components and are accompanied by extensive fluid loss, lack of pain, and eschar formation. Fourth-degree burns involve all skin and underlying muscle, bone, ligaments, fat and fascia (254).

It is important to identify injury to major vessels of the lower limbs and the presence of eye, perineal and synovial structure involvement. Signs of ocular/corneal damage include blepharospasm and excessive lacrimation. The presence of a cough may indicate smoke inhalation, and this is often a predominant feature of thermal injuries sustained in barn fires due to exposure to a large accumulation of smoke in a confined/closed space.

Figure 14.2 Wound contracture after Grade 3 burns to the head of a 3 year old Quarterhorse filly at 19 days, 29 days and 2 months after the initial injury.

Horses may present with clinical signs consistent with a systemic response to thermal injuries, including tachycardia, fever and injected mucous membranes. Haematological and serum biochemical analysis is useful to assess the systemic response and to identify the presence of organ dysfunction, which may develop because of systemic inflammation, generalised hypoxia and/or severe cardiovascular and haemodynamic compromise. Abnormalities reported in horses with thermal injuries include a low total protein concentration and anaemia that can be marked and gradually progressive. This is initially caused by immediate red blood cell (RBC) destruction by heat and wound haemorrhage with subsequent RBC loss from intravascular and extravascular removal of damaged cells (254). Haemoglobinuria can also develop and platelet aggregation on damaged capillary endothelium can result in thrombocytopaenia (254).

Other diagnostic tests that can be considered in cases of thermal injury include a clotting profile, urinalysis, arterial blood gas analysis, thoracic radiography and bronchoalveolar lavage (BAL).

Treatment

Initial Stabilisation

Severe burns can lead to dramatic cardiovascular effects, often referred to as 'burn shock'. This resembles hypovolaemic shock (254). A combination of vascular responses ultimately results in an accumulation of fluid, protein and inflammatory cells in the wound. There is also fluid loss into the extravascular space, which leads to an acute reduction in blood volume. The extent of fluid loss is determined by the severity of the burns, and fluid losses will result in increased heat loss from evaporation and an increased metabolic rate (254).

Initial patient stabilisation involves fluid support for the acute haemodynamic alterations that can occur in these cases, as well as immediate cooling to halt the burn process (256). Fluid resuscitation is important in avoiding the sequelae of haemodynamic shock, including decreased gastrointestinal and renal perfusion.

Wound management

The local care of burns generally involves halting the burning process, cleansing and debridement, and application of topical ointments and/or dressings to support healing. The use of cold water (2 - 15°C) treatment as first aid for burns has the greatest volume of supporting evidence, compared to using

ice, which may lead to a thicker eschar and may worsen ischaemic necrosis (258). Mild natural soaps (e.g. Sunlight soap) are recommended for wound cleansing and to aid in softening and removal of dead skin. Other soaps and cleansers containing dilute chlorhexidine and/or betadine/iodine should be avoided as they may cause skin irritation.

Although bandaging is the standard of care in the management of burns in human patients, bandaging may not be well tolerated by horses. Pruritis is common during the wound healing process and continual scratching can cause bandages to slip. The use of single layer compression bandages is often much better tolerated and can also reduce distal limb oedema and the amount of exudation from wounds (see Case Study and Figure 14.3).

Pain management

With the severe tissue injury that occurs with thermal injuries, physiological pain can evolve to a state of pathological pain if not appropriately managed. Multimodal pain control is often considered most appropriate, as it has the advantage of additive or synergistic analgesic effects and also allows for the use of lower doses of individual analgesic agents to limit the adverse side effects. An example of agents that may be utilised in a multimodal pain management protocol for thermal injuries is summarised in table 14.1 below. See the case study in this chapter for a specific protocol used on a patient with a mixture of 1st, 2nd and 3rd degree burns to 30% of their body (Figure 14.3).

Table 14.1. Multimodal pain management protocol for thermal injuries*

Drug or drug class	Route	Dose	Comments
NSAIDS	Oral or IV	Specific to drug	
Lignocaine	CRI	Bolus of 1.3 mg/kg then 0.05 mg/kg/minute	Overdose may result in seizures or CNS excitation. May be used for several days.
Ketamine	CRI	0.4 - 1.2 mg/kg/h	Ataxia and sensitivity to sound possible at higher doses. May be used for days to weeks.
Opioid			
morphine	CRI	Loading dose of 0.3 mg/kg, then 0.05 mg/kg/h	Should give the loading dose with an alpha-2 agonist (eg. detomidine) to prevent excitement. May impact gastrointestinal motility.
OR			
butorphanol	CRI	Bolus of 17.8 µg/kg then 10-15 µg/kg/h	Tolerance may develop, usually used for 12-24h
Alpha-2 agonists	IV or IM	Specific to drug	
Paracetamol	PO	20 - 25 mg/kg q 12 h	
Gabapentin	PO	20 - 60 mg/kg q 12 h	Poor bioavailability so high dose required. Mixing crushed tablets with oil (e.g. corn oil) can make administration easier.

* Not all horses will need all medications in this list.

Antimicrobials used

The use of systemic antimicrobials is not warranted to protect against wound infection in horses with thermal injuries. They cannot penetrate the avascular eschar, where the risk of contamination is greatest (254). In addition, circulation to the burned area is often compromised, making it highly

unlikely that parenteral administration of antimicrobials can achieve therapeutic concentrations at the wound. Systemic antimicrobials do not favourably influence wound healing, fever or mortality and can also facilitate the emergence of resistant microorganisms.

The warm, moist site of a burn wound is an ideal environment for bacteria to multiply. Topical antimicrobials can prevent the conversion of superficial wound sepsis to full-thickness infection and possible systemic sepsis (254). Examples of topical antimicrobials used include:

- Silver sulfadiazine (SSD) as a 1% water-miscible cream. Treatment with SSD has led to significant reductions in the incidence of burn wound sepsis in humans (259).
- Honey (Manuka honey is a superior product to regular honey). Antibacterial properties (for example, methylglyoxal) and viscosity generate a barrier preventing cross-infection of wounds. The acidity of honey (usually pH < 4) is important in killing bacteria. Honey provides a moist healing environment, and prevents bacterial growth (259).

Prognosis

The prognosis depends on the systemic condition of the patient and the extent, depth and location of the thermal injuries. The proportion of the total body surface area affected usually correlates with mortality, while the depth of the burn determines the morbidity (254). If > 50% of the body surface is affected, euthanasia is recommended.

Minor first-degree and superficial second-degree burns are easily managed in the field, while extensive first- and second-degree burns, and third- and fourth-degree burns, are usually best managed by referral to an institution where the level of intensive care required is available. Long-term care is required to prevent continued trauma and the associated pruritis needs to be managed.

The prognosis will also depend on the development of secondary injuries and/or complications (e.g. laminitis, colic, colitis).

Case Study

<u>Yearling Quarter Horse Filly</u>

- Burn injuries sustained during bushfire 2 days prior to presentation.
- Presented with 1st, 2nd and 3rd degree burns to face, pectoral region, axilla, hindlimbs, perineum, udder and coronary bands.
- Approximately 30% total body surface is affected
- Hospitalised for ongoing wound and pain management
- IV fluid therapy with balanced crystalloids commenced on initial hospitalisation

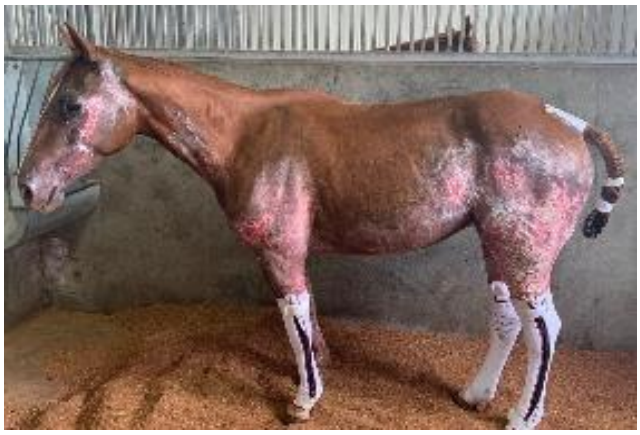

Figure 14.3. Silver impregnated compression wraps on distal limbs of yearling Quarterhorse filly with severe thermal injuries.

- Wound management twice daily – cold water hosing, gentle debridement using Sunlight® soap, application of Flamazine® (silver sulfadiazine) cream topically to affected areas.
    - Sedation (α2 agonist +/- opioid) often required due to pain and agitation during wound cleaning
    - Compression bandages applied to distal limbs (Figure 14.3)
- Pain management

    - NSAID – 2.2mg/kg phenylbutazone PO q12h
    - CRI – ketamine, morphine, lignocaine
    - Eventually placed indwelling epidural catheter due to ongoing challenges with wound management and associated pain and discomfort.
        - Administered morphine (0.15-0.2mg/kg) + detomidine 0.02-0.03mg/kg once daily prior to wound cleaning
        - Facilitated provision of analgesic effects with significantly decreased systemic adverse effects
- Hospitalised for 3 months
- Development of hypertrophic scars (common sequelae of deep 2nd-degree burns) on rump and hindlimbs
- Foaled a healthy filly foal 18 months after discharge from hospital

Further reading

- Wilkes EJA, Woolsey Herbert E. Chapter 85.1: Management of Burns in Horses. *In: Equine Emergencies. Treatment and Procedures, 5th Edition, 2023* Eds: Orsini, J, Grenager N. (260)(Fourth edition available now, updated fifth edition from January, 2026)

Chapter 2: Cellulitis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Primary cellulitis is a common condition in general practice and may respond well to empirical antimicrobial therapy, but recurrence or a poor response to treatment should prompt further diagnostic investigation.
2. Many of the pathogens involved have unpredictable susceptibility patterns, so culture and susceptibility testing are recommended to guide therapy, especially in cases with severe or recurrent disease.

The term cellulitis refers to diffuse infection of the subcutaneous tissues. In horses, cellulitis involving the limbs is typically acute in onset and characterized by substantial inflammation, swelling, heat and pain. Lameness is variable, but non-weight bearing (5/5) or substantial lameness at the walk (4/5) is common. Cellulitis can be primary or secondary, and the underlying cause is often unknown, although it can develop associated with soft tissue trauma and concomitant inoculation of bacteria. The common primary causes of secondary cellulitis include wounds, surgical incisions and intra-articular medication (261). Regardless of whether it is primary or secondary, cellulitis is a serious condition and can be frustrating for both veterinarians and owners when it is recurrent. In addition, severe complications, such as dermal necrosis, laminitis and vascular thrombosis, have been reported. Coagulase-positive *Staphylococcus* spp. (followed by *Streptococcus* spp. and *E. coli*) seem to be the bacteria most commonly isolated from cases of primary cellulitis and *Streptococcus* spp. (followed by coagulase-positive *Staphylococcus* spp. and *Pseudomonas* spp.) the bacteria most commonly isolated cases of secondary cellulitis in the UK (261), but no data are available from Australia.

Diagnostics

Diagnosis is usually based on clinical signs, but additional diagnostics may be useful. Ultrasonographic examination may be useful, especially to identify areas of fluid accumulation for sampling for further diagnostic investigation. Haematology generally reveals a leukocytosis (usually without a left shift) and hyperfibrinogenaemia. Given the common organisms have susceptibility patterns that are unpredictable (*Staphylococcus* spp., *Pseudomonas* spp.), culture of fluid collected from pockets in affected areas and susceptibility testing of bacterial isolates is recommended.

Treatment

NSAIDs (most commonly phenylbutazone) and systemic antimicrobials are the mainstay of treatment. Empirical therapy is generally with either penicillin and gentamicin or trimethoprim/sulphadiazine. In mild to moderate cases, oral, intravenous or intramuscular administration of antimicrobials is likely to be sufficient and the duration of therapy is typically five days. Three days may be adequate for mild cases. Resolution of clinical signs can be used as an indication that antimicrobial therapy can be discontinued.

In severe cases, intravenous regional limb perfusion (IVRP) should be considered (See Section 12). In extensive cases, IV access for IVRP may not be possible and should not be attempted through affected tissue as septic thrombophlebitis can result. IVRP with gentamicin is most appropriate and 1/3 of the systemic dose is recommended. (See the IVRP guideline in Section 12 for more details.) The perfusate volume does not seem to affect antimicrobial concentrations in the limb, but a pneumatic or wide rubber (12.5 cm) tourniquet should be used (262).

Ancillary treatment is also helpful. Cold water hosing, compression bandaging and light exercise (walking) can all help to reduce oedema and prevent dermal necrosis. In secondary cases, especially following intra-articular injection or intra-synovial surgery (arthroscopy or tenoscopy), septic synovitis should be considered.

Antimicrobials used

- Procaine penicillin at 22,000 IU/kg IM q 12 h and gentamicin at 6.6 mg/kg IV q 24 h for 3 - 5 days for mild to moderate cases. Severe cases may need longer (10 days is common).
- Trimethoprim/sulphadiazine at 30 mg/kg PO q 12 h for 3 - 5 days in mild to moderate cases.

Prognosis

In mild to moderate cases, the prognosis is good.

In severe cases, the prognosis is guarded. Cases that develop laminitis have a worse prognosis and horses with fever tend to be more severely affected (261).

Further reading

Braid, H.R. and Ireland, J.L. (2022), A cross-sectional survey of the diagnosis and treatment of distal limb cellulitis in horses by veterinary surgeons in the United Kingdom. Equine Vet Educ, 34: e234-e244. https://doi.org/10.1111/eve.13484 (263)

Chapter 3: Cutaneous habronemiasis (summer sores)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. The clinical appearance is similar to other common diseases (pythiosis, sarcoids).

Summer sores typically occur in pre-existing wounds, but can occur on the commissures of the lips, the medial canthus of the eye, the nasolacrimal ducts and the prepuce/urethra of stallions or geldings (muco-cutaneous habronemiasis). The onset is often characterised by the rapid development of papules or the failure of a wound to heal, and the development of exuberant granulation tissue. Ulceration, intermittent haemorrhage and a serosanguinous exudate are also common. Pruritis is variable. Small (1 mm diameter) granules may be seen within the affected tissue, which are necrotic, caseous-to-calcified foci surrounding nematode larvae. In contrast to the lesions seen in pythiosis, the granules do not branch.

The chest, fetlocks and the medial surface of the legs are the most commonly affected areas on the body. Lesions may heal, or recurrent lesions may evolve into non-healing granulomatous cancer-like masses that attract more flies leading to a super-infection. Wounds tend to disappear spontaneously in the cold months, but re-appear when the environmental temperature rises again months later.

The lesions are caused by the larvae of the nematodes *Habronema muscae* and *Draschia megastoma,* less commonly *Habronema microstoma*. The differential diagnoses include exuberant granulation tissue, squamous cell carcinoma, sarcoids and pythiosis.

Adult *Habronema muscae* are found in the stomach, causing minimal problems. The mature worms lay their eggs, which are passed in the manure. The eggs are consumed by stable fly larvae and are normally deposited near the mouth of the horse, where they are swallowed and develop in the stomach, completing their life cycle. However, when the larvae are deposited onto a wound they cannot develop further and migrate through the tissues, causing intense itching. The self-trauma caused by the itching contributes to the size of the lesion.

Diagnostics

Histological examination of affected tissue is generally diagnostic. The wounds are infiltrated with eosinophils, macrophages, lymphocytes and a few plasma cells. In peripheral areas, an abundance of vascular and fibro-connective tissue can be observed, with masses of eosinophils in areas of coagulative necrosis. Sections of nematodes can be also detected. However, the larvae tend to be few and may have been digested or be necrotic in more chronic lesions. Larvae live for < 1 month in cutaneous tissues, and larval death may cause even more necrosis and calcification than when alive. The diagnosis may be challenging when sarcoid and habronemiasis occur concurrently.

Treatment

Many treatment regimens have been described, and no “optimal” therapy can be recommended. The therapeutic strategy will depend on the chronicity, the size and location of the lesions, as well as financial considerations and practicality for clients, but typically includes local and systemic therapy. Surgical debulking intervention is indicated in large and more chronic wounds or when the medical treatment of summer sores is refractory, although other differential diagnoses should be considered in these cases.

Ivermectin (0.2 mg/kg PO) and moxidectin (0.4 - 0.5 mg/kg PO) are both very effective larvicides and have wide margins of safety. Two doses are given at a 21-day interval.

Systemic glucocorticoids have been found to be very effective as the sole systemic agent in equine habronemiasis and have also been used to reduce pruritis following antiparasitic therapy. Prednisolone (1 mg/kg PO every 24 h), dexamethasone (0.04 mg/kg PO), or intralesional triamcinolone (10 - 20 mg/lesion) results in a marked resolution of most lesions within 7 - 14 days. Topical steroids have also been used, along with many other different topical therapies, usually in combination, and, given that some summer sores regress spontaneously, it is difficult to infer the efficacy of any product.

Any topical treatment should be applied under a bandage to prevent the deposition of new larvae during the healing process. When bandaging is not possible, a fly repellent ointment should be applied.

Antimicrobials used

- None

Prognosis

Good for small to medium sized lesions. Guarded for extremely large or chronic lesions.

Further reading

Herd RP, Donham JC. Efficacy of Ivermectin against cutaneous Draschia and Habronema infection (summer sores) in horses. Am J Vet Res. (1981) 42:1953–5. (264)

Scott DW, Miller WH. Parasitic diseases. In: Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011. (265)

Chapter 4: Decubital ulcers (see also staphylococcal folliculitis and furunculosis)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning & Leanne Begg

Key issues

1. Result from poor fitting tack
2. Ulcers can be very slow to heal

Poorly fitting tack may cause friction and pressure sores that result in pain and skin injuries. Prolonged, continuous pressure — often relatively mild — leads to ischaemic necrosis. Ill-fitting bandages and casts, prolonged anaesthesia/surgical procedures, and prolonged recumbency can also lead to ulcers. Mixed bacterial infections of ulcers occur secondarily.

Diagnostics

The diagnosis is based on the history and physical examination.

Early signs include:

- Rubbed or chafed skin
- Swollen areas
- Hair that is rough-looking, ruffled, or missing
- Areas that are tender to the touch

If untreated, the injured area will progress to ulcers that tend to be deep and become secondarily infected and cause pain, most commonly on the withers. The ulcers tend to be very slow to heal. Scarring and leukotrichia after healing are common.

Treatment

The most important aspect of therapy is to identify and correct the cause. Routine wound care includes daily cleansing and drying agents, and topical antiseptics. Systemic antimicrobials are virtually useless. Surgical debridement, surgical excision or skin grafting may be necessary. Prevention is vastly superior to any kind of therapy.

Antimicrobials used

- Topical antiseptics, combined with drying of the skin

Prognosis

Good when primary cause is addressed, although recovery can be slow.

Further reading

Scott DW, Miller WH. Environmental Skin Disease. In: Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.(266)

Chapter 5: Dermatophilosis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. The cause is an opportunistic pathogen of the skin
2. Continued wetting of the skin must be prevented to control infection
3. Biting insects are another source of skin penetration that needs to be controlled

Dermatophilosis (rain scald) is one of the most common bacterial infections of equine skin worldwide and yet studies on its treatment are uncommon. It is caused by *Dermatophilus congolensis*, a Gram-positive, facultatively anaerobic, branching filamentous rod with a distinctive appearance. Infections cause a superficial pyoderma that can be acute or chronic.

D. congolensis is an opportunist pathogen of the skin of infected horses. Transmission is by direct contact with infected animals, contaminated environments (like shared blankets or grooming tools), and possibly via insects. Factors that suppress the host's immune system, such as concurrent disease and/or stress, may enable the organism to proliferate and produce clinical disease. However, lesions most commonly develop when the skin is exposed to chronic moisture, such as when wet horses are rugged.

Diagnostics

Clinical signs of dermatophilosis include a mildly painful, non-pruritic superficial pyoderma with regional or generalized papules and crusts that can resemble small paintbrushes when lifted. A yellow/green exudate is commonly present under the crusts in early lesions, which occur most commonly on the dorsum, face and neck. In very severely affected horses, and those with secondary bacterial infections, fever, depression, lethargy, and anorexia may be present and some may have a regional lymphadenopathy, but this is rare. Most diagnoses are made on clinical signs alone.

Dermatophilosis is diagnosed by demonstration of the distinctive branching filamentous rods in direct smears of the exudate, in histopathological sections, or in a preparation made from dried or fresh crusts. Cytological examination of samples of exudate or rehydrated crusts reveals the classical "railroad track appearance" of longitudinally arranged coccoid zoospores (figure 14.4). If performing a skin biopsy, it is important to submit a specimen with the crust attached to the skin or hairs. The organism is often found only in crusts, and, if needed, the crust can be submitted instead of a full biopsy specimen if the history, signalment and physical examination support a diagnosis of dermatophilosis, but this is rarely required to make a diagnosis.

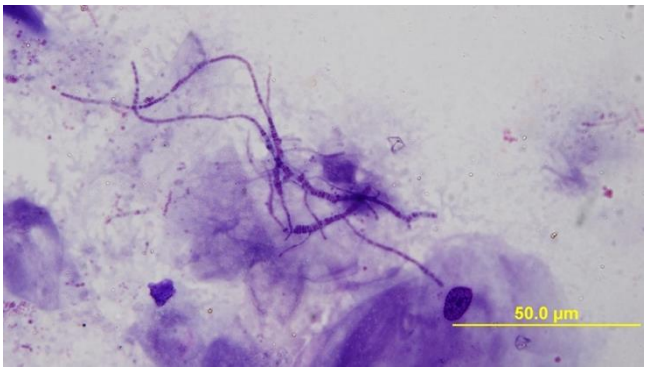

Figure 14.4. Classic 'railroad track' appearance of dermatophilosis on cytology. (Giemsa stain. Image courtesy of J. Norris.)

Treatment

Topical therapy is generally successful in horses with mild to moderate infections. The bacteria seek carbon dioxide and the layering and crusts created by the exudative host response provide a protective environment. Thus, removal of the crusts is essential for treatment. Crusts are gently soaked and removed while bathing with a mild antibacterial shampoo, such as one containing chlorhexidine. For some horses this is quite painful and may require sedation. Drying the skin is important. Severely affected animals may require systemic antimicrobial treatment to lift the crusts, such as administration of procaine penicillin at 22,000 IU/kg IM twice daily for 2-3 days. Trimethoprim/sulphadiazine (TMS) at 30 mg/kg orally twice daily for 2-3 days also may be effective.

Regardless of all other treatments, exposure to excessive moisture must be controlled.

Antimicrobials used

- Topical antiseptics and removal of the crusts combined with drying of the skin
- In severe cases, 2-3 days of therapy with procaine penicillin at 22,000 IU/kg IM twice a day
- In severe cases, TMS at 30 mg/kg PO twice a day for 2-3 days may also be effective

Prognosis

Good when skin moisture can be controlled.

Further reading

Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. Fourth Edition ed: Elsevier Inc; 2018. p. 1159-216.(267)

Pilsworth RC, Knottenbelt D. Dermatophilosis (rain scald). Equine veterinary education. 2007;19(4):212-4. (268)

Chapter 6: Staphylococcal folliculitis and furunculosis (acne, heat rash)

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Folliculitis is usually secondary and identifying the primary cause is critical for successful outcome

Cases most commonly start in spring and early summer, which is likely to be because of the coat shedding, clipping, heavy riding and work schedules, higher environmental temperatures and humidity, and increased insect population densities that occur during this time of year. However, there are many predisposing causes (e.g. hypersensitivities, ectoparasites, trauma), so lesions can occur at any time of year.

The sides of the neck, the saddle region, rump and shoulders are commonly affected. The superficial lesions of folliculitis are usually asymptomatic, while the deep lesions of furunculosis are often painful. Pruritis is not usually present. If triggering factors are not addressed, recurrences are common.

Diagnostics

The diagnosis is usually based on history and physical examination. Cytology, culture, and/or examination of biopsies can be used to confirm the diagnosis.

Frequently, the first sign is erect hairs over a 2 to 3 mm diameter papule that is more easily felt than seen. Small crusts may also be present. These lesions can regress spontaneously, but often enlarge progressively. Some lesions enlarge to 0.5 – 1 cm in diameter, develop a central ulcer that discharges a purulent or serosanguineous material, and then become encrusted.

Treatment

Treatment/elimination of underlying or associated disorders is critical to a successful outcome. Clip, clean and establish drainage. Treat topically. Cleaning of all tack, grooming equipment, blankets, and other equipment may be necessary.

Mild, superficial infections may resolve spontaneously, but most require therapy with topical cleansing, drying and antibacterial therapy. Topical applications of chlorhexidine, as a shampoo for widespread infections, daily for 5 - 7 days, is generally successful, especially if the scabs are removed effectively in the early stages. Mupirocin ointment may be useful for localised superficial or deep infections.

Severe furunculosis may require combined topical and systemic antibiotic therapy. Staphylococci have unpredictable susceptibility patterns, so empirical recommendations are difficult and therapy should be based on culture and susceptibility testing results. Trimethoprim/sulfadiazine is commonly used as first line therapy. Antimicrobial therapy is continued until clinical resolution of disease is seen.

Antimicrobials used

- Topical antiseptics combined with drying of the skin
- In severe furunculosis (widespread disease), systemic antimicrobials based on culture and susceptibility testing.

- Trimethoprim/sulphadiazine (30 mg/kg PO q 12 h) may be used in severe disease while awaiting culture and susceptibility testing results.
- Treat until clinical resolution of disease is seen

Prognosis

Good when the primary cause is addressed.

Further reading

Scott DW, Miller WH, Bacterial skin disease. In: Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011. (269)

Chapter 7: Pastern dermatitis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Persistent and recurrent disease is common, but it is associated with persistence of risk factors, not antimicrobial resistance.
2. Environmental management is critical –wetness and humidity should be avoided and skin hygiene improved.

Equine pastern dermatitis (EPD) is a term used to describe inflammatory cutaneous lesions on the lower legs of horses. There are numerous lay terms for these lesions, including “scratches,” “mud fever,” and “greasy heel.” In lighter breeds, mild to moderate disease is most common, while the severe form is most commonly seen in cob and draft-type horses. Although three forms have been described, the disease presents across a continuum, rather than categorically. The mildest form is characterised by alopecia, dry scales and crusts, without pain or pruritis. With increasing severity, lesions become exudative and form crusts and may extend beyond the pastern. In advanced and chronic cases, hyperkeratosis, lichenification and fissured skin, sometimes with hyperplasia, fibrosis and excessive granulation tissue, can involve large areas of the distal limb. Pain in these cases can be considerable and lameness is common. Lesions can be constantly present, appear acutely or recur after phases of remission (270). Risk factors include feathered limbs, unpigmented pasterns (in light horses, but not in heavy breed horses). Although no genes for susceptibility have been identified, a genetic link seems likely, particularly in heavy breed horses. Chronic wetting of the skin and unhygienic conditions also promote EPD. Infestation with *Chorioptes bovis* is the most frequently cited parasitic cause in draft and cob/pony breeds but is not reported as a cause in lighter breeds. Bacterial involvement is likely opportunistic. Most studies including bacterial culture have detected mixed flora or a range of bacterial species, with staphylococci and β-haemolytic streptococci isolated most commonly. Drug resistance appears uncommon.

Diagnostics

A complete history should include investigation of the signalment, onset and course of clinical signs, seasonality, signs of disease in companion horses, previous treatment and the outcome of these treatments. An assessment of housing and environmental management is also important to identify potential risk factors.

Crusts, scales, thickened skin, ulceration and pruritis are all common signs. There are several scoring systems for assessing lesions and these may be useful in cases where lesions are constantly present (271). However, none of the scoring systems have been validated outside of the institution where they were developed, and none have been uniformly adopted in Australia.

In feathered horses, clipping is critical for proper examination of the skin lesions. Sedation and soaking of crusts may be required before clipping is tolerated. In ongoing or recurrent cases, superficial swab or tissue samples should be collected for bacterial and fungal culture, and impression smears collected for cytological examination. Many aetiologies are possible and they all are clinically indistinguishable. If photosensitivity is suspected, a serum chemistry panel should be performed to investigate whether there is primary hepatic disease.

Treatment

Environmental management is key and includes avoiding wetness and humidity around the affected skin, improving pasture and stable hygiene, or cleaning and drying legs following turnout.

Feathers are an important predisposing factor, so they should be clipped to decrease moisture retention and allow for effective treatment, regular inspection and maintenance of hygiene.

Sedation may be required to facilitate initial treatment. There have not been any controlled trials of commonly used treatments. Topical preparations should include initial cleaning to remove crusts, and debridement and disinfection of the lesions. Povidone-iodine should probably be avoided as it can be irritating to the skin, so chlorhexidine is preferred. Common topical preparations include agents that promote wound healing (e.g. zinc oxide, honey, colloidal silver), astringents (e.g. benzoyl peroxide) or that have hypertonic properties (e.g. magnesium sulphate), as well as antiseptic or antimicrobial agents (e.g. chlorhexidine, neomycin) and corticosteroids (e.g. betamethasone, prednisolone or hydrocortisone).

Antimicrobials used

- No systemic therapy is indicated.
- Topical therapy, with an antiseptic as a minimum, is recommended.

Prognosis

Guarded. Persistent and recurrent disease is common.

Chapter 8: Pythiosis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. *P. insidiosum* is an aquatic oomycete requiring warm environmental temperatures to survive
2. Infections are thought to develop secondary to wound inoculation with the pathogen
3. Invasion of the dermis results in pyogranulomatous inflammation that rapidly progresses

Pythiosis (swamp cancer) is a deep, invasive and rapidly progressive subcutaneous oomycotic (fungal-like) infection. The disease predominantly occurs in tropical and subtropical regions and generally during the warmer and wetter months of the year, although climate change seems to be increasing the range of regions where pythiosis occurs. It is caused by the waterborne pathogen *Pythium insidiosum* and can affect the skin, subcutaneous tissue and occasionally the gastrointestinal tract. The organism thrives in swampy, aquatic environments and infects horses though wounds or breaks in the skin, or after prolonged contact with contaminated water. Deep or disseminated infection may invade bone, synovial structures, the lungs and the gastrointestinal tract.

The onset is insidious, with fast-growing lesions. Common areas affected include the distal limbs, the ventral abdomen and thorax, as well as the lips, nostrils, face, external genitalia, neck and trunk. Early lesions are usually single or multiple small foci of necrosis that progress rapidly to single and large nodular eroded to ulcerative granulomas. Formation of small hard coral-like masses, called “kunkers”, is a characteristic of the disease in horses. Moderate to severe pruritis that leads to self-mutilation is a hallmark of the disease. Oozing of serosanguinous discharge is typical. Tissue necrosis leads to malodorous lesions. Severe oedema of the affected limb is also common.

Infection is locally invasive and spreads to lymphatic vessels and nodes, and deeper tissues. Osseous involvement can occur when lesions are chronic. Metastasis to the lungs may also occur.

Diagnostics

Differential diagnoses include exuberant granulation tissue and cutaneous habronemiasis. The diagnosis of *pythiosis* can be made quickly by evaluation of the kunkers if they are sent to a laboratory specialising in the diagnosis of the disease. An initial diagnosis can be made grossly on lesion appearance, location, and/or the presence of kunkers. A definitive diagnosis can also be made by serology, examination of biopsies, culture, and cytological examination of exudates. Biopsies of early lesions reveal abundant microabscesses with eosinophils and a few neutrophils, lymphocytes, and macrophages. In chronic cases, an eosinophilic granuloma with giant cells is observed, with microabscesses and kunkers at the centre. *P. insidiosum* appears as sparsely septate hyphae 6 to 10 mm in diameter in sections or smears stained with periodic acid-Schiff or silver.

Treatment

Surgical excision has been the most commonly performed therapy, but recurrence is common (up to 30% of cases) and surgical excision is difficult on limbs. Iodides and amphotericin B have both been used systemically. There is no theoretical basis for the use of amphotericin B (the target of the drug is missing) and systemic therapy does not greatly improve the outcome. A therapeutic vaccine has been developed in the USA and has been found successful in acute and chronic cases. This vaccine is not currently available in Australia, but there may be some Australian companies

that can make autogenous pythiosis vaccines on request. The efficacy of these vaccines is unknown, but success has been reported anecdotally.

Lesions in horses are best treated with a combination of therapies, including radical surgical excision of the lesion and topical application of antifungal solutions. Systemic iodides (sodium iodide at 10-40 mg/kg per day as a 20% solution given slowly IV for 2 - 5 days, then oral potassium iodide at 20 - 40 mg/kg/day). Topical antifungals are generally used despite lack of theoretical benefit – amphotericin B or ketoconazole.

Antimicrobials used

- Sodium iodide at 10 - 40 mg/kg per day as a 20% solution given slowly IV for 2-5 days, then oral potassium iodide at 20 - 40 mg/kg per day.
- Topical amphotericin B or ketoconazole

Prognosis

The prognosis for horses with cutaneous pythiosis is guarded, even if it is recognised early and immediately and aggressively treated. Immunotherapy may improve the prognosis if it becomes available. If surgical excision cannot be achieved, the prognosis is worse. The fatality rate is 100% if lesions are left untreated and the success of treatment declines with the chronicity of the lesions (> 1 - 2 months in duration).

Further reading

Loreto ES, Tondolo JS, Zanette RA, Alves SH, Santurio JM. Update on pythiosis immunobiology and immunotherapy. World J Immunol 2014; 4(2): 88-97 .DOI: 10.5411/wji.v4.i2.88 (272)

Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine (Fourth Edition): W.B. Saunders; 2018. p. 1159-216.(273)

Chapter 9: Wounds

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. It is important to determine the site, depth and synovial structures involved in the wound.
2. If a synovial structure is potentially involved, flushing is required to confirm communication.
3. If communication is confirmed, then broad spectrum antimicrobial therapy is indicated until results of culture and susceptibility testing are known.

Wounds are common in horses. The site of the wound, its depth and the involvement of synovial structures are important to assess to determine what treatment is required. Simple wounds generally require only cleaning and bandaging to prevent infection, but deeper wounds may require suturing. Those potentially involving synovial structures should be assessed with distension of the joint or tendon sheath to determine whether communication occurs with the wound.

Diagnostics

Careful assessment of the wound, with cleaning to assess depth and any involvement of synovial structures. If significant blood loss is occurring, pressure bandaging is indicated to encourage clotting. If a synovial structure is potentially involved, the joint or tendon sheath should be sampled and synovial fluid collected for cytology, and culture and susceptibility testing. The synovial structure should then be distended with sterile fluid and communication with the wound assessed. If communication occurs, further flushing of the synovial structure is indicated. Suturing of the deeper areas of the wound may then be possible. Bandaging to keep the wound clean is also important.

Treatment

Simple wounds do not require antimicrobial therapy, even if they are superficially contaminated. Topical wound care, including regular removal of biofilms, necrotic tissue and exudates, along with bandaging, is generally sufficient. Many topical wound therapies have been evaluated, but there is insufficient evidence to recommend one over another. Topical antimicrobials are not indicated. Wounds involving the distal limb can be slow to heal. Exercise restriction and bandaging can help to reduce the formation of excessive granulation tissue.

Deeper wounds that involve synovial structures should be flushed. Antimicrobial therapy is indicated, pending results of culture and susceptibility testing (see Synovial sepsis guideline).

Tetanus prophylaxis is critically important.

Antimicrobials used

- None
- For wounds involving synovial structures, procaine penicillin G (22 000 IU/kg IM q 12 h) and gentamicin (6.6 mg/kg IV q 24 h)

Prognosis

Good with appropriate therapy, unless infection of synovial structures occurs. Wounds on the distal limbs can be slow to heal and are prone to formation of exuberant granulation tissue. Wounds on the head and body tend to heal quickly and with fewer complications.

Reference List

1. Hanson RR. Management of burn injuries in the horse. The Veterinary clinics of North America Equine practice. 2005;21(1):105-23.

2. Herbert EW. Findings and strategies for treating horses injured in open range fires. Equine veterinary education. 2018;30(4):177-86.

3. Marsh PS. Fire and Smoke Inhalation Injury in Horses. The Veterinary clinics of North America Equine practice. 2007;23(1):19-30.

4. Garcia JAG, Chavez AMG, Grados JDJO. Topical Antimicrobial Agents for the Prevention of Burn-Wound Infection. What Do International Guidelines Recommend? A Systematic Review. World journal of plastic surgery. 2022;11(3):3-12.

5. Cuttle L, Pearn J, McMillan JR, Kimble RM. A review of first aid treatments for burn injuries. BURNS. 2009;35(6):768-75.

6. Malik KI, Malik MAN, Aslam A. Honey compared with silver sulphadiazine in the treatment of superficial partial-thickness burns. International wound journal. 2010;7(5):413-7.

7. Wilkes EJA, Woolsey HE. Chapter 85.1: Management of Burns in Horses. In: Orsini J, Grenager N, editors. Equine Emergencies. Fifth ed. Philadelphia: Saunders Elsevier; 2026.

8. Adam EN, Southwood LL. Primary and secondary limb cellulitis in horses: 44 cases (2000-2006). Journal of the American Veterinary Medical Association. 2007;231(11):1696-703.

9. Levine DG, Epstein KL, Ahern BJ, Richardson DW. Efficacy of Three Tourniquet Types for Intravenous Antimicrobial Regional Limb Perfusion in Standing Horses: Tourniquet Types for Regional Limb Perfusion in Horses. Veterinary surgery. 2010;39(8):1021-4.

10. Braid HR, Ireland JL. A cross-sectional survey of the diagnosis and treatment of distal limb cellulitis in horses by veterinary surgeons in the United Kingdom. Equine veterinary education. 2021;34(6):e234-e44.

11. Herd RP, Donham JC. Efficacy of ivermectin against cutaneous Draschia and Habronema infection (summer sores) in horses. Am J Vet Res. 1981;42(11):1953-5.

12. Scott DW, Miller WH. Parasitic diseases. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.

13. Scott DW, Miller WH. Environmental Skin Disease. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.

14. Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. Fourth Edition ed: Elsevier Inc; 2018. p. 1159-216.

15. Pilsworth RC, Knottenbelt D. Dermatophilosis (rain scald). Equine veterinary education. 2007;19(4):212-4.

16. Scott DW, Miller WH. Bacterial skin disease. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.

17. Oesch S, Kaiser-Thom S, Vidondo B, Gerber V. Owner reported clinical signns and treatment decisions in equine pastern dermatitis. SAT ASMV. 2022;164(5):401-12.

18. Gerber V, Kaiser-Thom S, Oesch S. Equine pastern dermatitis: a narrative review on clinical presentation, diagnosis, risk factors, prevention, and therapeutic approaches. Journal of the American Veterinary Medical Association. 2023;261(S1):S58-S65.

19. Loreto ES, Tondolo JS, Zanette RA, Alves SH, Santurio JM. Update on pythiosis immunobiology and immunotherapuy. World Journal of Immunology. 2014;4(2):88-97.

20. Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine (Fourth Edition): W.B. Saunders; 2018. p. 1159-216.

Section 15 – Reproduction

Contents

Chapter 1: Clitoral pathogens

Authors: Jen Clulow*, Chelsea Burden*, Leanne Begg, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Laura Hardefeldt

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Key issues

1. Environmental pathogens vs venereal pathogens.
2. Increasing antimicrobial resistance due to selection pressure on these organisms.
3. Capsule typing of *Klebsiella pneumoniae* is important to identify pathogenic strains.

The equine clitoris has a unique microbiome (274), including several pathogens that have been implicated in reproductive disease. The three main pathogens implicated as transmissible venereal pathogens of the clitoris are *Taylorella equigenitalis*, the organism responsible for contagious equine metritis (CEM), *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

CEM is characterised by a thick muco-purulent vulvar discharge in the mare, while the stallion usually remains asymptomatic. The organism may reside in asymptomatic carriers in the urethra, urethral fossa and prepuce of the stallion or in the clitoral fossa or clitoral sinus of the mare (275). Venereal transmission occurs during natural mating, artificial insemination with semen from an affected carrier, or indirectly via contaminated equipment. CEM is a disease of international significance because of its highly contagious nature and its impact on fertility. As it is not present in Australia, the remainder of this section will focus on *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.*

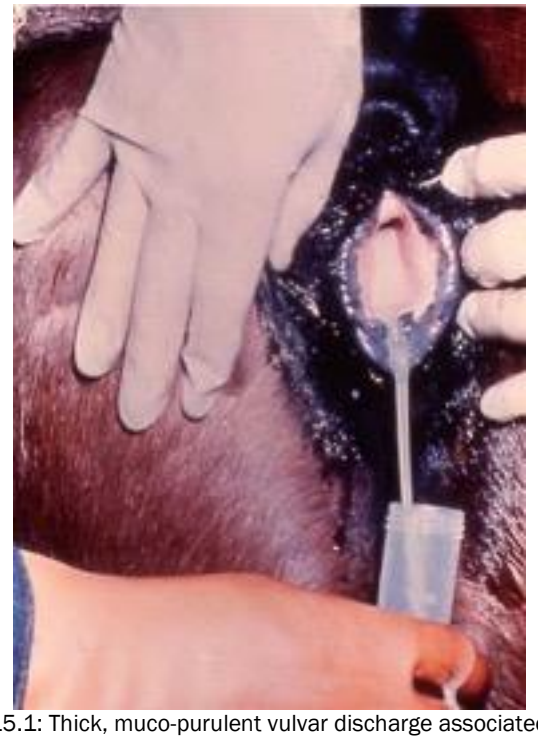

Figure 15.1: Thick, muco-purulent vulvar discharge associated with CEM caused by *Taylorella equigenitalis.* (Image courtesy of J. Norris.)

While *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* have long been considered pathogens of the equine reproductive tract, their role as a venereal pathogen has recently been questioned (276, 277). In many countries, including Australia, these organisms are included in routine pre-breeding microbiological assessments of the mare's reproductive tract. Results from endometrial cultures should be examined in association with cytology results and the clinical presentation (Please see Chapter 2 of this section for further details). Mares with clitoral cultures positive for *Pseudomonas aeruginosa* or *Klebsiella pneumoniae* are usually excluded from the breeding shed until a negative swab can be obtained. In many cases, these are multi-drug resistant (MDR) organisms that may require treatment with antimicrobials of high importance to eliminate them from the clitoris. Furthermore, once isolated, these organisms are rarely typed to determine their pathogenicity for the reproductive tract. In a recent study examining 117 isolates of *Klebsiella pneumoniae* from routine mare reproductive cultures in Australia, only five isolates had capsule types known to be associated with pathogenicity for the equine reproductive tract (Hardefeldt pers comm). Multi-drug resistance was present in 59% of isolates; 52% in isolates from clitoral swabs, 62.5% in isolates from uterine swabs and 83% in isolates from uterine lavages. Furthermore, as the breeding season progressed, the proportion of MDR isolates increased from 22% in August to 69% by November (Hardefeldt pers comm), presumably a result of increased selection pressure from antimicrobial treatment during the relatively brief breeding season. This increase in MDR is concerning, particularly without conclusive evidence identifying the organism as a venereally transmitted pathogen (276, 277).

In the absence of clinical endometritis, the requirement for routine culture and treatment of the equine clitoris in Australia should be re-evaluated. Furthermore, these organisms are environmental contaminants, highlighting the role of minimal contamination techniques in the breeding shed, as well as routine testing of water used to clean mares prior to service or insemination (277).

Diagnostics

A routine swab of the clitoris can be performed using a sterile collection swab in Amies medium. A swab of the clitoral fossa is performed by separating the labia to expose and evert the clitoris to visualise the clitoral fossa. The clitoris should not be cleaned prior to sample collection. Swabs should be kept refrigerated and submitted to the laboratory as soon as practically possible, ideally within 48 h of collection. Clitoral cultures to identify *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* can be performed on blood agar or MacConkey agar. Organism-specific media are also available. Isolates should be confirmed by biochemical typing and, in the case of *Klebsiella pneumoniae*, further differentiation should be performed to identify the capsule type.

If collecting a clitoral swab for *Taylorella equigenitalis,* which may be required for import/export purposes, the swab needs to be transported in Amies medium with charcoal and a swab of the clitoral sinuses needs to be performed using a narrow-tipped swab. It is important to note that this procedure can create discomfort in mares, so appropriate analgesia, sedation and restraint is advised.

Treatment

Treatment of the clitoris is difficult and controversial. Initial thorough cleaning of the clitoris is important to remove smegma and reduce bacterial loads. Cleaning with a chlorhexidine scrub is recommended with particular attention to the removal of smegma within the clitoral fossa and clitoral sinuses. This can be facilitated with the use of a 14 gauge catheter to flush the clitoral sinuses. The clitoris should then be flushed with sterile saline to remove detergent residues, as these will further irritate the tissues. The authors recommend treating with an appropriate antimicrobial (following culture and susceptibility testing) using an ophthalmic preparation of the drug. This helps to mitigate (but usually does not eliminate) the local tissue irritation and pain associated with treatment. If an ophthalmic preparation is not available or local tissue inflammation is severe, packing the clitoris with silver sulfadiazine is recommended. Treatment is usually performed for 3 - 5 days. Smegma should be removed daily prior to topical treatment. Transfaunation should be considered following the final antimicrobial treatment. The mare should be swabbed 1 - 2 weeks after treatment, thereby allowing the normal population of microflora to recolonise the area.

If the organism is MDR, then transfaunation can be attempted using clitoral smegma from a mare with a normal clitoral microflora. Clitorectomy has been advocated in the past with recalcitrant organisms. Considering the questionable implication of these organisms in venereal transmission, clitorectomy can no longer be a recommended as first-line therapy.

Antimicrobials used

- Gentamicin sulphate – ophthalmic preparation (ointment/gel), applied into the clitoral fossa daily for 5 days
- Silver sulfadiazine cream, applied into the clitoral fossa daily for 5 days

Prognosis

The prognosis for response to treatment is varied. Thorough cleaning is required prior to the application of antimicrobials for resolution of the bacterial overload. The prognosis is poor for mares with MDR organisms. However, these infections do tend to clear with time.

Mares found to have a heavy growth of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* in their clitoris may be considered immunocompromised, as this often occurs following prolonged exposure to antimicrobials or a period of stress. Therefore, addressing overall health and nutrition may help to re-establish a normal microflora.

Chapter 2: Endometritis

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Key issues

1. Equine endometritis is inflammation with or without infection of the endometrium. It is a major cause of subfertility in the mare.
2. Post breeding induced endometritis (PBIE) predisposes susceptible mares to infectious endometritis.
3. Mares may develop PBIE as they age and with increasing parity, due to breakdowns in their normal anatomical defence mechanisms.
4. If left untreated, infectious endometritis may progress to chronic degenerative endometritis or endometrosis. Treatment for infectious endometritis should be guided by cytology, culture and susceptibility testing.
5. Prophylactic intrauterine antimicrobials are not a recommended treatment regimen in the mare.

Endometritis is inflammation and/or infection of the uterine luminal surface, the uterine endometrium. Endometritis is a normal physiological process in the mare, enabling sperm, seminal plasma, bacteria and other debris that accumulates within the uterus during oestrus or breeding to be removed by a combination of both immunological and mechanical clearance mechanisms(278). Failure of this normal physiological process within the first 48 hours after breeding (279) is referred to as persistent breeding-induced endometritis or PBIE. Mares susceptible to PBIE have been identified as having a compromised immune system, in addition to weak mechanical defences, rendering them “susceptible” to uterine contamination and potential infection, which may lead to irreversible chronic degenerative changes in the uterus (Figure 15.1). Equine endometritis is one of the major causes of subfertility in the mare (280).

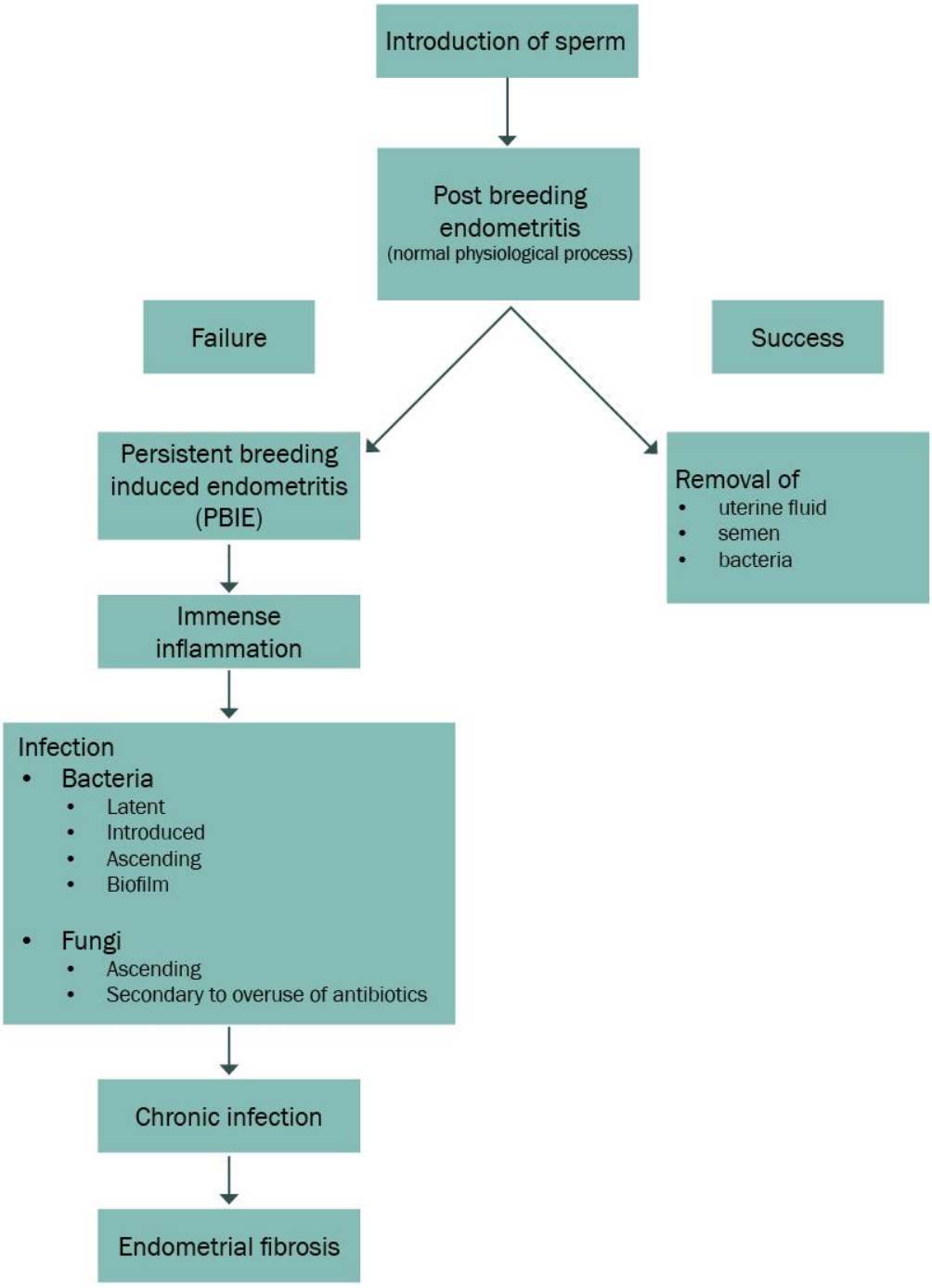

Figure 15.2. The aetiology of post breeding endometritis in the mare. Source: Morris LHA, McCue PM, Aurich C. Equine endometritis: a review of challenges and new approaches. *Reproduction (Cambridge, England)* 2020;160:R95-R110. (278)

Bacterial endometritis occurs when a mare fails to resolve the physiological endometritis and bacteria remain in the uterus and proliferate. The most common bacterial species isolated from the mare's uterus are *Streptococcus equi* subspecies *zooepidemicus* (*S. zooepidemicus*) and *E. coli* (281). However, a number of other species of bacteria and fungi have been isolated from the mare's uterus (Table 15.1).

Table 15.1. Common bacteria and fungi isolated from the uteri of mares suffering from endometritis.

	Microorganisms	Features
Bacteria	*Streptococcus equi* subspecies *zooepidemicus*	Gram positive, opportunistic bacteria, potentially venereally transmitted
	Escherichia coli	Gram negative, opportunistic, facultatively anaerobic
	Pseudomonas aeruginosa	Gram negative, aerobic, potentially venereally transmitted
	Klebsiella pneumoniae	Gram negative, opportunistic, facultatively anaerobic, potentially venereally transmitted
	Staphylococcus spp.	Gram positive, opportunistic, facultatively anaerobic
	Taylorella equigenitalis	Gram negative, venereal, microaerophilic, severe purulent endometritis. **Not currently present in Australia**. Notifiable disease.
	Enterobacter cloacae	Gram negative, opportunistic, facultatively anaerobic
	Proteus spp.	Gram negative, opportunistic, facultatively anaerobic
Fungi	*Candida* spp.	Yeast, causes 58-69% of fungal endometritis cases
	Aspergillus spp.	Mould with septate hyphae, causes 25-26% of fungal endometritis cases
	Mucor spp.	Mould with aseptate hyphae, causes 5-12% of fungal endometritis cases

(Adapted from Canisso IF, Segabinazzi LGTM, Fedorka CE. Persistent breeding-induced endometritis in mares — a multifaceted challenge: from clinical aspects to immunopathogenesis and pathobiology. *International Journal of Molecular Sciences* 2020;21:1432. (279))

Endometritis can be further complicated by the ability of many of these organisms to form a biofilm, with approximately 80% of isolates collected from the equine uterus capable of forming a biofilm (279). A biofilm is formed by the secretion of an exopolysaccharide matrix that allows microorganisms to evade the host's immune system by creating a physical barrier resistant to penetration by both immune cells and antimicrobials (282). This effectively protects bacteria from traditional intrauterine antimicrobial therapy and, in fact, has promoted antimicrobial resistance in these species (283). By evading the host immune system, these organisms may lie dormant within

the mare's uterus without any clinical or cytological evidence of inflammation, delaying diagnosis and treatment (284, 285, 286).

Failure to identify and treat infectious endometritis may result in chronic degenerative changes to the uterine endometrium and the formation of endometrosis (287). These pathological changes can be identified histologically as severe endometrial fibrosis and cystic dilation of uterine glands (287, 288), and eventually result in infertility.

Diagnostics

Persistent breeding induced endometritis

In the normal mare, the physiological endometritis following breeding is resolved within 48 h, with the successful clearance of debris, uterine fluid, seminal plasma and sperm. This presents a conundrum for the clinician, who ideally needs to identify mares that will have PBIE prior to breeding, so treatment can be initiated prior to closure of the cervix. The cervix increases in tone and effectively closes under the influence of rising progesterone post-ovulation. A history of fluid accumulation post-breeding is useful information, but there are also other diagnostic tests that can help to identify individuals with PBIE.

A careful reproductive tract examination of the broodmare, including a physical examination of the external reproductive tract and a trans-rectal ultrasonographic examination of the internal reproductive tract should be performed.

Mares susceptible to PBIE have compromised systemic and physical defence mechanisms. Often these mares will have poor external reproductive conformation, including breakdown of the three barriers to external contamination - vulvar conformation, the vestibulo-vaginal seal and the cervix (289). Age and parity results in acquired anatomical defects of the reproductive tract, with poor perineal and vulvar conformation, cervical incompetence and a pendulous uterus identified as significant structural issues in susceptible mares(278, 290). These anatomical defects can be identified during a reproductive tract examination of the broodmare. Surgical correction of the conformational defect should be addressed in these cases. A simple Caslick's vulvoplasty may be the first surgical line of defence, followed by perineal body repair, urethral extension or uteropexy to correct more severe defects and to prevent further disease of the reproductive tract. It is important to note that a uteropexy should not be considered a last resort technique in mares. Performing this surgery earlier in the mare's career may help to restore the normal position of the reproductive tract, thereby preventing both vaginitis and endometritis. Correction of these anatomical defects should improve the mare's resistance against PBIE and, in turn, improve fertility and reduce the incidence of infectious endometritis.

Evidence of inflammation within the uterus can be identified as inappropriate oedema for the stage of the oestrus cycle and the presence of fluid within the uterine lumen. A mare can be diagnosed as susceptible when > 2 cm of fluid can be detected by trans-rectal ultrasonography during oestrus or within 36 hours of breeding, demonstrating a failure of both mechanical and immunological clearance mechanisms (278). This may be exacerbated by the position of the uterus over the pelvic brim, resulting in a dependant or pendulous uterus. In cases where uterine fluid accumulation is identified prior to breeding, an endometrial culture is recommended.

Once a presumptive diagnosis of PBIE is made, a breeding management plan can be formulated.

Infectious endometritis

The significant difference between PBIE and infectious endometritis is the presence of a pathological organism within the uterine lumen. Often the conditions are not mutually exclusive, with untreated PBIE often progressing to infectious endometritis (278). Bacterial or fungal contamination of the uterus may occur at the time of mating, ascend from the external environment or via iatrogenic introduction. Infectious endometritis presents with similar clinical signs to PBIE, including intrauterine fluid accumulation and inappropriate uterine oedema for the stage of the oestrus cycle. A vulvar discharge may also be present and vaginoscopy may assist in determining the source of the discharge to differentiate between endometritis and vaginitis. Infectious endometritis caused by *Taylorella equigenitalis* is not currently present in Australia and thus will not be discussed in this section.

A definitive diagnosis of infectious endometritis can be made from an endometrial sample following culture and cytological examination. Endometrial samples for culture can be taken using a double guarded swab, low volume uterine lavage or uterine biopsy. Care should be taken to ensure that only the endometrium is sampled using any of these methods. Uterine sampling is inherently problematic as all sampling equipment passes through the potentially contaminated caudal reproductive tract. Therefore, careful cleaning and preparation of the vulva prior to vaginal entry is important to reduce false positives due to contamination and prevent iatrogenic infection. Whilst the double guarded swab technique is quick and easy to perform, low volume lavage has the advantage of sampling the entire surface of endometrium resulting in greater sensitivity (291, 292). The technique for performing a low volume uterine lavage for endometrial culture is described by Dr Michelle LeBlanc and a link can be found in the further reading section of this chapter (293). Uterine biopsy is not performed routinely for culture, but may be considered, particularly if the clinician suspects that there may be bacteria dormant within the crypts of the endometrium or biofilm-producing organisms (286).

Interpretation of results should be based on consideration of the findings of the breeding evaluation of the mare. If there is evidence of uterine fluid and excessive oedema in addition to a cloudy flush, positive culture and evidence of inflammation on cytology, then the treatment plan is usually straight forward. Culture and cytology should be performed together and interpreted based on the clinical presentation. When a uterine lavage has been performed to obtain the sample, characterisation of the efflux fluid and presence of debris can also help to rule out false positive culture results (293). Small number of single bacterial colonies are likely to be the result of contamination, especially in the absence of any additional supportive information. A confident diagnosis of bacterial endometritis can be made when there is evidence of inflammation (2-5 polymorphonuclear cells per microscope field at 400 x) and/or a pure bacterial culture (294). However, *E. coli* infections tend to suppress inflammation and organisms within a biofilm or in a latent state, such as *Streptococcus* spp., may not stimulate recruitment of immune cells into the uterine lumen. Activation of such organisms with a commercial growth medium, such as B-Activate (295), or disruption of the biofilm with a suitable biofilm disrupter (296, 297) may assist detection of these organisms and ensure adequate treatment to clear the infection. It is also important to note that the failure to culture bacteria when there is evidence of inflammation is not necessarily a false negative result. In these instances, care should be taken to look for clinical evidence of pneumovagina and urine pooling and consider the relevant breeding history of the mare.

Treatment

Treatment of endometritis focuses on the physical removal of fluid, bacteria and debris from the uterus, in addition to antimicrobial therapy when a positive culture result has been obtained. Targeted treatment of the uterus is preferred over systemic antimicrobial therapy, which does not specifically target just the problematic organisms, is more likely to promote antimicrobial

resistance, changes the microflora of the gastrointestinal tract and contributes to environmental contamination. Treating the uterus also allows the dose and duration of antimicrobial treatment to be reduced and refined. Systemic antimicrobial use should only be considered in cases of chronic endometritis or when infusion into the uterus is contraindicated.

The uterus is an easily accessible cavity allowing uterine lavage to be performed safely to reduce contamination and allow better penetration of antimicrobials. Uterine lavage and ecbolic (oxytocin) therapy are the mainstays of treatment of endometritis. Sterile saline or lactated Ringer's/Hartmann's solution are suitable for uterine lavage and should be followed by administration of oxytocin at 10-20 IU IM or IV to further promote uterine contractility. Following appropriate cleaning and preparation of the vulva, a gloved (sterile, where possible) hand is passed through the labia and into the vagina. A sterile Foley catheter is passed through the cervix and the cuff inflated cranial to the internal cervical os. Sterile fluid can then be instilled into the uterine lumen and syphoned back out. This step is repeated until the efflux is clear. In mares with a dependant uterus and fluid accumulation, this step may need to be repeated twice daily and oxytocin administered as frequently as every 2 h.

Post-breeding uterine lavage can be considered in mares with known PBIE and should be performed at 4 hours after breeding to allow sufficient time for spermatozoa involved in fertilisation to move through the utero-tubal papillae into the oviducts. The normal physiological immune response of the uterus occurs as soon as 30 minutes after breeding with a peak at around 4-6 h (298). Uterine lavage at this stage helps to mitigate the inflammatory response in mares with PBIE by physically removing the antigenic products of breeding and promoting uterine contractility. If uterine lavage is unable to be performed, oxytocin should be administered to these mares in this same time frame to promote uterine contractility and clearance. However, this clearance is far more effective when combined with uterine lavage.

Historically, intrauterine treatment of mares with prophylactic antimicrobials was encouraged to improve pregnancy rates in thoroughbred mares. However, more recent publications have contradicted this recommendation, demonstrating that prophylactic infusion of antimicrobials does not improve pregnancy rates in mares and, furthermore, can contribute to antimicrobial resistance (299, 300). Whilst there has been an increased reliance on post-breeding therapy, including the use of intrauterine antimicrobials, over the past 20 years, the incidence of pregnancy loss and live foaling rates have remained unchanged (301). If there is no evidence of a pathogen, based on cytology and culture, treatment using intrauterine antimicrobials cannot be recommended. Prophylactic therapy should therefore include uterine lavage and oxytocin, which have been shown to not only improve pregnancy rates (300), but also mitigate the effects of PBIE in susceptible mares.

Antimicrobials should only be considered when a pathogen has been cultured from the uterus. Often it may take several days to receive culture and susceptibility test results. During this time uterine lavage and treatment with oxytocin can be performed as pretreatment prior to antimicrobial administration. This effectively reduces the bacterial overgrowth, thereby reducing the reliance on antimicrobials to clear the infection. Furthermore, the presence of debris or excessive fluid in the uterus may inhibit the action of infused antimicrobials or excessively dilute them to subtherapeutic concentrations (302). A biofilm reducer may also be considered as part of the treatment regimen at this stage to eliminate any potential biofilms, thereby improving penetration of antimicrobials once the susceptibility test results are available.

Biofilm reducers or mucolytics have been recommended by several researchers and veterinarians. However, it is important to note that not all biofilm reducers are effective for all bacterial species (Table 15.2). Furthermore, occasionally the introduction of a biofilm reducer into the uterus may result in an inflammatory effect (e.g. H_2O_2), so care should be taken when selecting the timing of

infusion. In suspect cases of infectious endometritis without confirmatory culture results, infusion of a biofilm reducer or mucolytic may result in biofilm breakdown, releasing the pathogen and enabling it to be cultured.

Table 15.2. Compounds used to degrade biofilms.

Bacteria	Degradation of biofilm mass	Killing of bacteria within a biofilm
Esherichia coli	Tris-EDTA/Tricide Acetylcysteine H_2O_2 Dimethylsulphoxide (DMSO)	Acetylcysteine H_2O_2
Streptococcus zooepidemicus	Tris-EDTA/Tricide H_2O_2 Dimethylsulphoxide (DMSO) Hypochlorous acid	Tris-EDTA/Tricide H_2O_2 Dimethylsulphoxide (DMSO) Hypochlorous acid
Pseudomonas aeruginosa	Tris-EDTA/Tricide H_2O_2	Acetylcysteine
Klebsiella pneumonia		H_2O_2

(Adapted from: Ferris RA, McCue PM, Borlee GI, Loncar KD, Hennet ML, Borlee BR. In Vitro Efficacy of Nonantibiotic Treatments on Biofilm Disruption of Gram-Negative Pathogens and an In Vivo Model of Infectious Endometritis Utilizing Isolates from the Equine Uterus. J Clin Microbiol. 2016;54(3):631-9. (303))

Other mucolytics such as Ceragyn™ are not currently available in Australia but also show promising results for the removal of biofilm from pathogenic equine reproductive bacteria.

Several different antimicrobials have been infused into the uterus to eliminate bacteria or fungi causing endometritis. However, the dose rates of many of these antimicrobials have limited supporting data to establish an MIC for specific organisms. Intrauterine infusions should be administered following appropriate cleaning and preparation of the vulva and perineum. Clean equipment should be used to ensure that no further contamination occurs at the time of infusion that may compromise the effectiveness of the antimicrobial.

The volume of solution instilled into the uterus should be sufficient to achieve uniform distribution of the antimicrobial over the luminal surface without excessive losses from reflux. Therefore, volumes of 20-60 mL are usually recommended. Antimicrobials can be diluted in sterile saline, water for injection or, in some cases, 7.5% sodium bicarbonate to buffer and dilute to the infusion volume.

Fungal endometritis is difficult to treat, with recurrent infections common because of the anatomical defects that contribute to the problem. Organisms are often not detected because long incubation times are needed to culture them. In addition, getting a definitive speciation is also difficult. More commonly, fungi are detected by observation of them in cytological samples, further highlighting the importance of performing both cytological examination of samples and culture. Mares with fungal endometritis usually have a history of bacterial endometritis, with intrauterine

antibacterial therapy predisposing them to fungal infection (302). Effective treatment of intrauterine fungal infections requires a combination of uterine lavage, uterine disinfection and intrauterine antimicrobials (Table 15.3). The aim of uterine lavage and disinfection is to physically remove all fungal elements from the uterus and create a hostile environment to inhibit further growth. Antiseptic solutions that have been advocated for this purpose include 1% hydrogen peroxide solution, 2% acetic acid solution (vinegar), 0.1 - 0.2% povidone iodine solution and 20% dimethylsulphoxide solution (302, 304). These antiseptic solutions are diluted in 1 L of 0.9% saline solution to achieve the desired concentration and daily lavage is performed during oestrus (5 - 7 days). Following uterine antiseptic lavage, a repeat culture should be performed, as lavage is sufficient treatment in some cases. In recalcitrant fungal endometritis, further treatment using intrauterine antifungals is required. It is important that any anatomical defects are addressed surgically to prevent further infection. If immunocompromise of the individual is suspected, then investigation of endocrine disorders, such as pituitary pars intermedia dysfunction or equine metabolic syndrome, is warranted.

In addition to these therapies, treatment with immunomodulators has been investigated as an adjunctive therapeutic approach. Whilst non-steroidal anti-inflammatory drugs and glucocorticoids have been used successfully to reduce inflammation following breeding, there are some drawbacks to their administration, including impairment of the normal reproductive hormonal cascade. Bacterial extracts, such as *Mycobacterium phlei* cell wall extract (Settle), have been used to enhance the innate humoral immune response by decreasing pro-inflammatory cytokines and increasing anti-inflammatory cytokine production (279). Mares treated with this product had reduced immune cell infiltration into the uterus, mimicking the immune response of a resistant mare. This immune stimulant can be administered to the broodmare as part of the routine breeding management of the mare to normalise the immune response to breeding (305).

Antimicrobials used

Drug	*IU infusion dose*	*Comments*
Ampicillin	2 g	Soluble product, high dilution to prevent irritation
Ceftiofur sodium	1 g	*Reserved for resistant organisms, use only with culture and susceptibility results
Gentamicin sulphate	1 g	Buffered with equal volumes of 7.5% sodium bicarbonate or a large volume (60 mL) of sterile saline
Penicillin (procaine)	3 – 6 g	High dilution (60 mL) to prevent irritation
Enrofloxacin	250 mg	High dilution (60 mL) to prevent irritation *Caution: may cause severe, acute ulcerative endometritis and possible fibrosis. Ciprofloxacin (600 mg) may be used as an alternative when indicated by culture and susceptibility testing
Clotrimazole	400 – 700 mg	Intrauterine infusion q 24 h for 7 days, moulds and yeasts
Miconazole	500 - 700 mg	Intrauterine infusion q 24 h for 7 days, moulds and yeasts
Nystatin	0.5 - 2.5 x 10^6 IU	Intrauterine infusion q 24 h for 7 days, yeasts only
Amphotericin B	100 - 200 mg	Intrauterine infusion q 24 h for 7 days, moulds and yeasts
Fluconazole	100 mg	Intrauterine infusion q 24 h for 7 days, yeasts only

Prognosis

- Appropriate timing of breeding, management with uterine lavage and ecbolic therapy and administration of an immune modulator is usually successful in mitigating the inappropriate inflammatory response, creating a hospitable environment for the developing conceptus. Appropriate management is critical to a good prognosis.
- Bacterial endometritis can be successfully treated in most instances with a combination of sexual rest, uterine lavage, ecbolics and antimicrobials. Follow up endometrial culture is recommended prior to breeding these mares again following a treatment cycle. Management for the breeding cycle should anticipate PBIE and proactive treatment with uterine lavage and ecbolics post-breeding will yield the best fertility outcomes.
- Fungal endometritis is difficult to treat and often requires intensive and long intrauterine treatment regimens. The prognosis is fair if it is diagnosed early in the disease process but guarded to poor in chronic cases.
- Anatomical defects that are identified should be surgically repaired as soon as possible to provide the best reproductive outcomes for the mare and reduce reliance on antimicrobials in future breeding cycles.
- Chronic untreated bacterial endometritis may irreparably damage the endometrium. The prognosis for future fertility in guarded for mares with endometritis.

Further reading

LeBlanc MM. How to Perform and Interpret Findings From a Low-Volume Uterine Flush. *AAEP Proceedings* 2011;57:32-36.

Chapter 3: Mastitis

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Key issues

1. Most commonly caused by *Streptococcus equi* subspecies *zooepidemicus*, *Staphylococcus* spp., *Klebsiella* spp., *Actinobacillus* spp. and *E. coli.*
2. Treat with a combination of intramammary infusion and systemic antimicrobials.
3. Prognosis is generally good, with full return of function.

The incidence of mastitis in mares is relatively low. Mares with mastitis typically present with a warm, swollen and painful udder. Mammary enlargement can be unilateral or bilateral and affect one or both lobe(s) of each mammary gland. Some mares will develop a mild hindlimb lameness, ventral oedema, and become febrile, dull and anorexic (306, 307). Mastitis can occur at any age but is most commonly seen in lactating mares. A higher case prevalence has been reported through the summer months (307). It more commonly occurs during lactation when a foal fails to nurse normally, or in the weeks following weaning (308, 309). It can occur in mares that have not had a foal in multiple years, mares that have never been in foal, and even the newborn or younger filly (306, 307, 310). Infection probably results from entry of bacteria through the teat canal, although percutaneous or haematogenous spread to the mammary tissue is also possible (311).

The most common pathogens isolated from mares with clinical mastitis are *Streptococcus equi* subspecies *zooepidemicus*, *Staphylococcus* spp., *Klebsiella* spp., *Actinobacillus* spp. and *E. coli*. A range of other pathogens are less common causes. Fungal mastitis has been reported on rare occasions, along with verminous mastitis and toxic mastitis following exposure to avocado trees and fruit (311, 312).

General hygiene is the best way to prevent mastitis. Close monitoring of mares after weaning, cleaning of the udder and insect control are helpful. Frequent milking of mares that have a foal that is unable to nurse also helps prevent mastitis (313).

Diagnostics

After careful cleaning of the teats, secretions should be collected from each teat canal to identify which mammary lobe(s) are affected. This can be difficult in cases that are severely inflamed. The secretions may show abnormal discoloration or consistency, but the samples should be examined cytologically and submitted for culture and antimicrobial susceptibility testing. Cytology of milk from mares with clinical mastitis often reveals neutrophils and cellular debris, and bacteria are evident in a subset of cases.

Haematology and serum biochemistry may be useful in monitoring cases of clinical mastitis. Haematology is likely to reveal a leukocytosis and neutrophilia. Increased inflammatory markers have potential use diagnostically and to monitoring the success of therapy (311, 314).

Ultrasonographic examination is useful in differentiating mastitis from udder abscessation, neoplasia and trauma. Ventral oedema just cranial to the mammary gland is common in late gestation and should be considered as a differential diagnosis when mammary enlargement is reported in late pregnancy.

Treatment

Therapy includes treatment with systemic and local antimicrobials, and non-steroidal anti-inflammatory drugs, in combination with frequent milking or stripping of the affected gland, hot

packing and hydrotherapy (307, 313). In a review from North America, more than 75% of bacterial isolates were susceptible to trimethoprim-sulphadiazine (TMS), while less than 60% of isolates were susceptible to penicillin (307). Stripping the mammary gland is necessary to remove bacteria and necrotic debris from the affected gland. Hot packs and cold-hosing can help reduce oedema and promote drainage.

Antimicrobials used

The choice of antimicrobials should be based on culture and susceptibility testing results, but treatment is usually initiated prior to the availability of these results. Broad-spectrum antimicrobials should be selected initially and then adjusted based on the susceptibility test results.

In most cases, an intramammary preparation is infused once into the teat of the affected gland to initiate local treatment, along with systemic antibiotic therapy.

Numerous formulations of intramammary antibiotic infusions are available.

- Ampiclox Dry Cow (500 mg of cloxacillin, 250 mg of ampicillin). Clean and disinfect the teat, and then apply the intramammary preparation into the teat, being sure not to damage the teat orifice or canal. A single administration is sufficient.

Systemic antibiotic therapy is used in ongoing or advanced cases of clinical mastitis.

- Trimethoprim/sulphadiazine (TMS) at 30 mg/kg PO q 12 h for 5 - 7 days. Continue for 1 day after resolution of clinical signs.

  OR

- Penicillin (procaine or potassium) at 22,000 – 44,000 IU/kg IM q 12 h or IV q 6 h for 3 - 5 days, in combination with gentamicin at 6.6 mg/kg IV 24 h for 5 - 7 days.

Prognosis

Cases of acute, clinical mastitis often respond quickly to appropriate therapy. Recurrence is uncommon, and the mammary gland usually returns to a normal anatomy and function.

Chronic, severe or recurrent cases have been associated with fibrosis of the gland and a potential reduction in milk production. Surgical resection of the mammary gland has been described for cases refractory to medical treatment (315).

Further reading

Mastitis In: McKinnon AO SE, Vaala WE, et al, ed. *Equine Reproduction Second Edition*: Wiley-Blackwell, 2011;2738-2741.

Lactation In: McKinnon AO SE, Vaala WE, et al, ed. *Equine Reproduction Second Edition*: Wiley-Blackwell, 2011;2277-2290.

Chapter 4: Metritis

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Key issues

1. Medical emergency requiring intensive management.
2. Difficult to interpret culture results because of the inevitable contamination of the uterus during parturition and the multiple species involved.
3. Prognosis from good to guarded, depending on the degree of tissue damage, bacterial overgrowth and endotoxin production.

Equine metritis involves all layers of the uterus, including the endometrium, myometrium and the perimetrium. It is a complication of the early post-partum period, but can be seen up to 7 - 10 days after foaling. Predisposing factors include dystocia, retained foetal membranes, delayed uterine clearance and uterine atony. Occasionally, no predisposing factors are identified. It is important to note that it does not occur in the normal post-foaling mare (316). Equine metritis is a potentially life-threatening condition and requires appropriate and immediate treatment in the acute phase for a positive outcome.

There is considerable contamination of the uterine environment during parturition. In the absence of a fully functional defence system, bacterial (or fungal) overgrowth may occur. Damage to the uterine tissues allows systemic absorption of toxins from the uterine lumen, resulting in overwhelming endotoxaemia, septicaemia and/or the systemic inflammatory response syndrome (SIRS) (316).

Several bacterial species can cause equine metritis, but Gram-negative organisms are most commonly associated with overwhelming endotoxaemia. The species isolated from clinical cases include *E. coli, Klebsiella* spp*., Enterobacter* spp*., Streptococcus equi* subspecies *zooepidemicus,* other *Streptococcus* spp*., Enterococcus* spp. and *Staphylococcus* spp*.,* as well as other Gram-negative and Gram-positive organisms (317). A mixed bacterial population is most often detected (317), consistent with the contamination experienced during parturition. As a result, culture is often non-specific and empirical treatment, including broad spectrum antimicrobials, is recommended.

Diagnostics

Diagnosis of clinical metritis is usually made following a reproductive tract examination in the post-partum period. Clinical signs of equine metritis include:

- Dullness/inappetence
- Increased heart rate, respiratory rate and rectal temperature
- Tacky mucous membranes with or without poor perfusion
- Increased digital pulse
- Reddish-brown to purulent vulval discharge
- Occasionally abdominal discomfort or lameness

The severity of clinical signs may vary, with more severe signs indicative of a guarded prognosis. A reproductive tract examination of the mare should include vaginoscopic examination, manual palpation of the caudal reproductive tract and trans-rectal ultrasonographic examination to evaluate the uterine size, tone, wall thickness and the echogenicity of any uterine contents (318). In metritis cases, the following are common:

- Large fluid filled uterus with a fetid vulval discharge
- Thickened/roughened endometrial surface
- Increased uterine thickness due to inflammation of the tissues (> 2 cm using trans-rectal or trans-abdominal ultrasonography), but decreased uterine thickness has also been reported in cases where there is excessive fluid accumulation and delayed uterine clearance.
- +/- retained foetal membranes
- +/- trauma to the caudal reproductive tract

It is recommended that a trans-abdominal ultrasonographic examination is performed to rule out a uterine tear or other gastrointestinal complications, as these conditions may result in similar clinical signs in the post-partum period. Haematology is usually indicative of overwhelming systemic inflammation, with a pronounced neutropaenia, depending on the severity and disease progression (319). A double guarded uterine swab can be used to sample the uterine fluid for culture and sensitivity. However, empirical treatment is usually initiated, and clinical signs are often resolved prior to receiving the results from culture and susceptibility testing.

Treatment

Treatment for post-partum metritis aims to reduce bacterial overgrowth, reduce inflammation and treat the systemic sequelae. As there is an inevitable delay between the submission of swabs for culture and the availability of results, it is imperative that a mare with suspected metritis receives treatment immediately, as there is a high risk of life-threatening complications (such as laminitis) if treatment is delayed. Broad-spectrum antimicrobials and anti-inflammatories should be initiated as soon as practicable. More than 65% of the organisms isolated in one study were susceptible to the combination of procaine penicillin and gentamicin i (318). If an anaerobe is suspected, metronidazole may also be included in the treatment regimen. Early intervention in these cases is imperative for a good clinical outcome. Anti-inflammatories, such as flunixin meglumine, which also ameliorate the effects of endotoxin (see Section 7), are recommended in these cases. Whilst lower doses are often recommended for this purpose, it is also important to address the pain and inflammation associated with any additional trauma that may have occurred during parturition. Therefore, higher doses of 0.5 – 1.1 mg/kg IV q 12-24 h are recommended in the acute phase, prior to reducing the dose to 0.25 mg/kg IV q 8 h. Other treatments for endotoxaemia can be found in Section 7.

Physical removal of bacterial contamination from the uterus using large volume uterine lavage and ecbolic therapy is important to reduce bacterial overgrowth and promote uterine contractility. Uterine lavage can be performed using an isotonic saline solution made by dissolving 90 g of table salt in 10 L warmed clean water or a 0.05% povidone iodine solution. A large bore tube (stomach tube) is inserted through the vagina into the uterus and the lumen is gently filled and emptied using 2-3 L at a time to syphon out debris and fluid *in situ*. This procedure can be repeated as many times as it is tolerated by the mare or until the fluid efflux is clear. Uterine lavage should be performed initially once to twice daily, or more often if required to ensure a minimal nidus for further endotoxin absorption. There appear to be adverse negative effects of uterine lavage on the inflammatory profile of mares with metritis and it is the safest and fastest way to remove debris and toxic material from the uterine lumen (320). Use of ecbolic therapy - oxytocin at 10-20 IU IM or IV as frequently as q 2 h, in addition to uterine lavage, helps to further promote uterine contractility.

If there is evidence of an increased digital pulse or signs of laminitis, cryotherapy should be considered to mitigate the effects of endotoxaemia on the sensitive laminae. Other supportive care, such as IV fluid therapy, is often indicated in hospitalised cases. The systemically ill broodmare may also experience a significant decline in milk production. Promotion of lactation in

these mares can be supported by the administration of domperidone (1.1 mg/kg PO q 12 h) and regular milking or nursing by the neonate.

Antimicrobials used

- Procaine penicillin at 22,000 IU/kg (22 mg/kg) IM q 12 h until 24 h after the resolution of clinical signs
- AND gentamicin at 6.6 mg/kg IV q 24 h until 24 h after the resolution of clinical signs
- +/- metronidazole at 15 mg/kg q 8 h or 25 mg/kg q 12 h until 24 h after the resolution of clinical signs

Prognosis

The prognosis is good if treatment is initiated early in the disease process, prior to overwhelming SIRS and other disease sequelae such as endotoxemia and laminitis. Equine metritis is a life-threatening condition and should be high on the list of differential diagnoses for the unwell post-partum mare. Careful investigation and monitoring of mares with retained foetal membranes, delayed uterine clearance or after a dystocia may help to identify mares at risk and facilitate prompt initiation of treatment.

Chapter 5: Placentitis

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Key Issues

1. Clinical signs of placentitis are frequently absent and/or cases present in advanced stages of pathology.
2. Diagnostic tests are limited.
    a. Samples for culture and cytology can only be collected in cases of ascending placentitis with active discharge.
    b. Biomarkers are inconsistent and necessitate serial sample collection for interpretation and monitoring.
    c. Many potential diagnostic biomarker tests are not commercially available in Australia.
3. Ultrasonographic diagnosis of placentitis and foetal disease is useful, but can yield false positive results if performed inappropriately.

Equine placentitis is a common cause of pregnancy loss due to late term abortion in the mare. Placentitis is also frequently associated with the delivery of premature or weak foals that may require expensive intensive care if they are to survive (321).

Clinical signs of placentitis may include vulval discharge, premature mammary gland development and other impending signs of parturition (e.g., elongation of the vulva, relaxation of the muscles around the tail head) (322, 323, 324). Vulval discharge is highly variable and only associated with cases of ascending placentitis and can easily be missed without close and frequent monitoring. Premature mammary gland development is not a pathognomonic sign of placentitis, but rather a non-specific sign of impending pregnancy loss, which can be associated with a variety of other conditions, including twin pregnancy, umbilical cord torsion, poor perfusion and idiopathic/non-specific imminent abortion (324)(figure 1). Enlargement of the mammary gland may also be observed in mares suffering from placental hydrops, pre-pubic tendon rupture and in mares with normal pre-foaling ventral oedema (325). In mares with placentitis, premature mammary development might not be present until the placental inflammation/infection is well advanced.

Four different types of placentitis have been identified, based on their differing morphological lesions and pathogenesis: (1) ascending placentitis; (2) focal mucoid placentitis; (3) diffuse placentitis; and (4) multifocal placentitis (326). The pathogenesis of the different types of equine placentitis are poorly understood. In most cases, infection of the placenta results in placental inflammation and release of prostaglandins, which ultimately leads to abortion or delivery of a premature foal. Foetal infection may also occur, depending on the pathogen involved and the chronicity of the disease process.

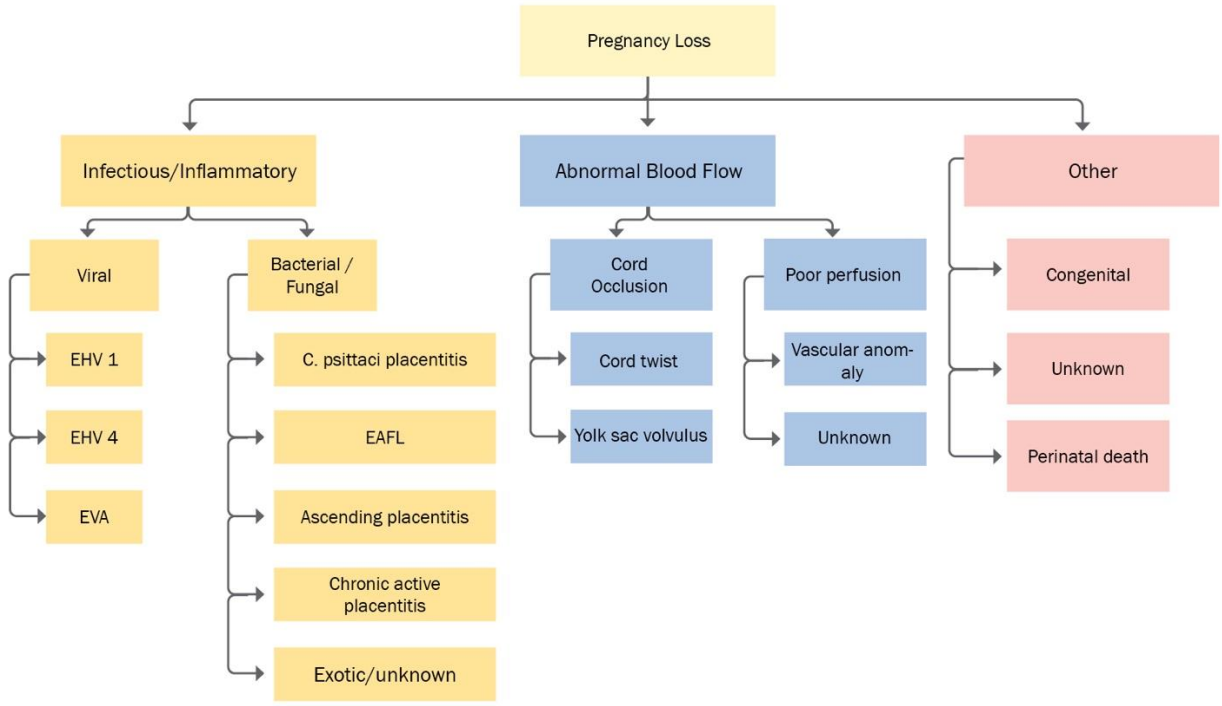

Figure 15.3: Common causes of equine pregnancy loss and their associated pathology. Reproduced from: Joan Carrick, Angela Begg, Melinda Stewert, Pat Shearer. AgriFutures Thoroughbred Program.

Several infectious agents are associated with placentitis (Figure 15.3). The primary causes of equine ascending placentitis are *Streptococcus equi* subspecies *zooepidemicus* and *E. coli*, with infection occurring as bacteria ascend through the caudal reproductive tract to the cervical pole region of the chorioallantois (327, 328). Other bacterial agents cultured from cases of placentitis include, *Streptococcus dysgalactiae* subspecies *equisimilis, Klebsiella pneumoniae, Pseudomonas aeruginosa* and nocardioform species. Fungi and viruses can also infect the placenta of mares. However, these pathogens typically cause abortion earlier in gestation (327). Fungi most commonly associated with equine placentitis include *Aspergillus* spp. and *Candida albicans* (328). Nocardioform placentitis, a focal mucoid placentitis, is associated with multiple Gram-positive filamentous bacteria. In Kentucky, the most common agents cultured were *Crossiella equi*, and *Amycolatopsis* spp. (329). Several cases of focal mucoid placentitis have been reported in Australia (330), but the causative agents may differ from those seen elsewhere. *Leptospira* spp. are notable causes of placentitis and funisitis in the mare, but no cases of placentitis or abortion attributable to leptospirosis have been reported in Australia (321). A notable cause of placentitis in Australia is Equine Amnionitis and Foetal Loss (EAFL), caused by ingestion of processionary caterpillars. The pathology alone is not specific for EAFL and diagnosis requires demonstration of a combination of pathological and bacteriological features found at necropsy (331). Recently, *Chlamydia psittaci* has been identified as an important cause of pregnancy loss, premature birth and neonatal loss in Australia and has also resulted in zoonotic disease after contact with infected horses or their tissues *(332, 333)*. While the pathogenesis is not completely understood, the *C. psittaci* responsible are thought to originate from carrier psittacine birds.

The infection/inflammatory response in placentitis contributes significantly to foetal stress and predisposes to premature parturition or abortion (321). Treatment of placentitis should be aimed at prolonging the presence of the foetus *in utero* long enough to allow precocious foetal maturation and improved foal survival rates. To achieve a live foal, a prompt diagnosis and effective treatment need to be initiated. Therapy is often necessary before clinical signs are observed to achieve a positive outcome.

Diagnostics

Diagnosis of placentitis is often based on a combination of clinical signs and ultrasonographic findings. Unfortunately, clinical signs are often only present in more advanced stages of placentitis. Ultrasonographic examination may be used for both diagnosis and to monitor mares at risk of pregnancy loss. Mares with high-risk pregnancies can be classified into 3 groups: 1) mares with a previous history of abnormal pregnancy, premature delivery or delivery of a septic foal; 2) mares showing clinical signs of an abnormal pregnancy – premature lactation, vulvar discharge, perineal relaxation; and 3) mares with a systemic illness that can affect the foetus, including colic, prolonged surgery, severe lameness, chronic laminitis or systemic infection (321). A complete physical examination should be performed on all mares presenting with clinical signs or for monitoring. Close inspection of the perineal region, the labia and the udder is critical. Any vulval discharge, premature perineal relaxation or precocious mammary development is significant and warrants further examination (322).

Transrectal ultrasonographic examination of the caudal placental pole is commonly used to diagnose ascending placentitis. The correct technique is critical to gain relevant diagnostic information. The clinician should position the transducer with a slight off-midline alignment, with the cervix and ventral aspect of the uterus and placenta at the caudal pole. A ventral branch of the uterine artery/cranial vaginal artery is imaged to ensure correct placement. Three measurements are usually taken of the combined thickness of uterus and placenta (CTUP) and the values can be compared with reported normal ranges (334) (Table 2). Increased CTUP and areas of placental separation are suggestive of ascending placentitis. Improper use of the technique can yield false positive results and should be considered when a clear image is not obtained. Foetal fluid consistency can also be assessed using transrectal ultrasonography. Increased echogenicity can be related to foetal movement but is also correlated with foetal stress.

Table 15.3. Upper limits for the combined thickness of the uterus and placenta (CTUP) by transrectal ultrasonography during late gestation

Day of gestation	Normal CTUP (mm)
151 - 270	< 7
271 - 300	< 8
301 - 330	< 10
331 +	< 12

(Adapted from Renaudin CD, Troedsson MHT, Gillis CL, King VL, Bodena A. Ultrasonographic evaluation of the equine placenta by transrectal and transabdominal approach in the normal pregnant mare. Theriogenology. 1997;47 2:559-73. (334).)

Transabdominal ultrasonographic examination of the foetus and placenta is used to assess and monitor foetal and placental health (335, 336). It is particularly useful for diagnosis of focal active, diffuse and multifocal placentitis, such as nocardioform placentitis, infection with *C. psittaci* and cases of EAFL. However, given that a limited area of the uterus is accurately visualized by transabdominal ultrasonography, the apparent absence of pathology does not exclude the possibility of disease. Areas of placental separation with a hyperechoic exudate between the

chorioallantois and the uterus are suggestive of nocardioform placentitis (326). The normal amnion appears as a thin membrane surrounding the foetus. Amnionitis can be indicated by a thickened and irregular amniotic membrane (324). Amnionitis, along with funisitis, occurs at the amniotic cord attachment in cases of EAFL and equine psittacosis *(332)*. Foetal heart rate monitoring and the ultrasonographic character of the foetal fluids can also be evaluated (335). A reduced or increased foetal heart rates (normal heart rate is 80 beats/min during late pregnancy) are associated with pathology and are predictive of a poor pregnancy outcome (324, 335). Increased echogenicity of the foetal fluids is often associated with advanced pathology and may also increase with foetal stress and expulsion of meconium, which results in solid particles floating in the amniotic fluid. It is important to note that, in late gestation, increased echogenicity of the amniotic fluid, compared to earlier stages of gestation, is normal.

Cytology and culture of swabs obtained from the external cervical os in pregnant mares can be useful in diagnosis of cases of ascending placentitis when the cervix is open and discharge is present (323). If there is a vaginal discharge, some of the purulent material can be collected aseptically from the caudal vagina without significantly disrupting the vestibular sphincter seal (321). Samples can be collected using a double-guarded cytobrush or swab via vaginoscopy or manually with a sterile rectal sleeve. The presence of inflammatory cells, bacteria, yeasts and/or fungal hyphae will aid the diagnosis of ascending placentitis. A definitive diagnosis of placentitis cannot be made until the foetal membranes are examined for pathology and microbiological investigations are performed after parturition (328). Evaluation of the foetal membranes is a valuable diagnostic tool for cases of known and unknown placentitis related to abortion or neonatal illness (Pozor, 2016). Following abortion, a diagnostic work-up is recommended to determine the cause of foetal loss. Swabs should be collected from the affected membranes for culture and PCR testing for abortogenic agents (e.g., equine herpesviruses types 1 and 4). In addition, foetal tissues (liver, spleen, kidney, heart, and lungs) and foetal body fluids (thoracic and abdominal fluids) can be used for diagnostic testing (337). Because some of the causative agents are contagious (e.g. equine herpesvirus 1) and/or zoonotic (e.g. *C. psittaci*), appropriate biosecurity measures should be considered when collecting samples.

Several diagnostic biomarkers can be used to monitor placentitis in the mare. Currently, these markers lack the specificity and sensitivity necessary to accurately diagnosis placentitis, but several are helpful in assessing disease progression and response to treatment. In combination with transrectal and transabdominal ultrasonography, the endocrinological markers, progestagins (338, 339), oestrogens (339) and relaxin (340), and the inflammatory biomarker serum amyloid A (341, 342), along with alpha-fetoprotein (343), could be used as additional diagnostic tools. These tests generally require regular monitoring to assess foeto-placental health in late gestation (326). In cases with placentitis, there is frequently an abnormally elevated maternal concentration of progesterone. This is probably a result of dysregulation of progestagen synthesis in the abnormal placenta. Clinical signs of placentitis and low maternal progesterone are indicative of a very poor prognosis for foetal survival. Low oestrogen concentrations in mid pregnancy can indicate severe foetal compromise and imminent abortion. After 280 days of gestation, interpretation of maternal oestrogen concentrations is limited and not well correlated with foetal survival (321). Because the placenta is the sole source of relaxin, plasma concentrations could be used as a biomarker of placental function, but plasma concentrations vary greatly between breeds. Currently, the lack of a commercially available test impedes the clinical use of relaxin assays in mares (321, 340). Alpha-fetoprotein is present in the foetal fluids of mares during late gestation (343), but it remains to be determined whether this protein is a useful marker for spontaneous cases of equine placentitis.

As stated above, placentitis frequently has no associated clinical signs. A preventative monitoring program has been suggested for high-risk mares (321). In one study, mares with a history of abortion or birth of weak premature/dysmature or septic foals were selected for monthly transrectal and transabdominal ultrasonographic examination. The incidence of ultrasonographic

abnormalities in these mares was over 70%. The clinicians were able to initiate treatment based on the ultrasonographic findings. The monitoring program and treatment resulted in a foaling rate of > 90 %, with only 5% of the foals born requiring intensive veterinary care (321).

Treatment

Current treatment protocols for mares with placentitis are ill defined and largely empirical. Many treatment strategies aim to combat infection, reduce inflammation and control myometrial activity (344, 345). Therapeutic options include antimicrobials, anti-inflammatories, and progestins (323, 324). Tocolytic therapy has also been suggested, but has minimal clinical efficacy (327).

Although some antimicrobials can cross the placental barrier, foetal fluid concentrations are consistently low. This results in suppression of the growth of bacteria, rather than their elimination. The priority should be to prescribe antimicrobials that cross the placental barrier at doses that maintain sufficient concentrations (MIC) for a duration of time (326). Antimicrobials that have been shown to cross the placenta include trimethoprim/sulphadiazine (346), penicillin and gentamicin (347). The duration of antimicrobial therapy required once a diagnosis of placentitis is made is debated. Anecdotally, short-term antimicrobial treatment (10 – 15 d) has been advocated to be an effective in treating placentitis and avoiding the selection of resistance associated with prolonged antimicrobial therapy (324). Experimental models of induced placentitis do not support the effectiveness of short-term antimicrobial therapy. Mares with experimentally induced ascending placentitis did not carry foals to term when treatment was discontinued after 2 weeks. However, an apparent increase in survival rates was observed when mares were kept on antimicrobials for a prolonged period of time (345). These mares remained culture positive after parturition, suggesting that antimicrobials administered to mares with experimentally induced placentitis may suppress the growth of bacteria, but may not completely eliminate them.

Administration of antimicrobials for 5 - 10 days periodically throughout pregnancy should be avoided. Pulse administration of antimicrobials is often performed in some parts of the world, even in the absence of a diagnosis of placentitis. The idea of such practices would be that this would treat subclinical/undiagnosed placental infection. This practice should be discouraged because of the lack of proven efficacy, and also because it favours selection of antimicrobial resistance that may become a major threat to the health of horses and humans.

Non-steroidal anti-inflammatory drugs should be administered to mares with evidence of placentitis. Flunixin meglumine is very effective in inhibiting prostaglandin synthesis in response to many different inflammatory stimuli, particularly bacterial toxins. Administration of flunixin meglumine (1.1 mg/kg IV q 12 h) is recommend as an initial treatment (345). Once the infection and inflammatory response is adequately controlled, the dose can be reduced or the drug changed (321). Phenylbutazone (2.2 mg/kg PO q 12 h) or firocoxib (0.1 mg/kg, PO, q 24 h) can be administered as an alternative or following cessation of treatment with flunixin meglumine. Firocoxib has the advantage of being a Cox-2 inhibitor, with reduced risks of the side-effects typical of NSAID therapy, and it can be administered long term with limited risk (348).

There is significant synthesis of cytokines by the placenta in response to infection. Pentoxifylline (8.5 mg/kg PO q 8 h) is effective in reducing endotoxin-induced cytokine synthesis. While there are conflicting reports, it may improve oxygenation of the placenta by improving blood flow (321, 345, 349).

The use of altrenogest in high-risk pregnancies is widespread, but its use is controversial because mares with clinical placentitis already have elevated concentrations of progesterone metabolites (338). Most mares with placentitis receive multimodal therapy, including antimicrobials, anti-inflammatories and anti-cytokine drugs, making it difficult to assess the sole impact of altrenogest administration. However, as administration may be very important in maintaining myometrial quiescence, many clinicians continue to administer altrenogest as part of the treatment protocol.

It is recommended that, in addition to antimicrobial and anti-inflammatory drugs, altrenogest (44 mg PO q 12 h) is given for an initial 14 days. If there is an adequate response, the dose is reduced to 44 mg q 24 h and maintained until 330 days of gestation. If there is no response, the dose is increased to 88 mg PO q 12 h for 14 days and the efficacy of the therapy then reevaluated (321).

Clenbuterol has been used to inhibit uterine contractility. However, the dose required in the mare to reduce uterine contractility can result in significant adverse side effects, including major alterations in cardiac and skeletal muscle function, so its use is not recommended (350).

Intranasal oxygen (to improve foetal oxygenation), vitamin E (antioxidant) and low dose aspirin (to improve placental oxygenation (351)) have all been administered to high-risk mares. Oestrogen supplementation has been advocated to treat mares with placentitis, as well as treatment with dexamethasone (323), but there are no data available to indicate the success of these treatments.

Repeat ultrasonographic assessment is useful to assess the response to treatment and guide ongoing therapy. The thickening of the placenta, its degree of folding and roughening, and the cloudiness of the fluid will all improve significantly with successfully treatment. Mares with a high-risk pregnancy that fail to have any improvement in these ultrasonographic parameters generally have a worse outcome than mares in which improvement is seen.

Antimicrobials used

For ascending bacterial placentitis:

- Benzyl penicillin G at 22,000 IU/kg (12 mg/kg) IV q 6 h or procaine penicillin at 22,000 IU/kg (22 mg/kg) IM q 12 h
- AND gentamicin at 6.6 m/kg IV q 24 h

  *Penicillin and gentamicin should be used in combination to achieve broad-spectrum therapy unless culture and antimicrobial sensitivity testing has been performed.
- Trimethoprim/sulphadiazine at 30 mg/kg PO q 12 h

The duration of treatment required to control bacterial proliferation is unknown. Studies show that mares with experimentally induced placentitis remain culture positive at the time of foaling despite ongoing therapy (345).

Treatment protocols should be tailored to the individual animal, with treatment duration based on disease progression. Frequent ultrasonographic examination and monitoring are necessary and recommended.

Ascending infection is associated with mares with poor vulval conformation. It remains best practice to perform a Caslick's procedure or some other surgical correction, such as perineal body repair or uteropexy, in mares with poor conformation.

For diffuse placentitis (EAFL, *Chlamydia psittaci*)

EAFL is largely associated with abortion without clinical signs and non-specific findings on ultrasonographic examination. To date there are no reports supporting antimicrobial treatment. *Chlamydia psittaci* placentitis is a post-partum diagnosis. Ultrasonographic changes and/or abortion of other mares in proximity may suggest infection (333). Control of chlamydial infections relies on the use of macrolides, fluoroquinolones or tetracyclines (352). There are no evidence-based reports supporting antimicrobial treatment. Empirical antimicrobial therapy using tetracyclines is suggested when ultrasonographic findings are consistent with potential *C. psittaci* infection (Carrick personnel communication). Premonitory signs are very rare, and are only seen in 5% of cases (337).

- Doxycycline at 10mg/kg PO q 12 h or oxytetracycline at 6.6 mg/kg IV q 12-24 h

For focal mucoid placentitis (nocardioform placentitis)

To date there are no evidence-based reports supporting antimicrobial treatment of nocardioform placentitis in mares. Therapeutic management of the disease using traditional treatment modalities has had minimal beneficial effect on the foaling outcome. Prophylactic therapy did not decrease the incidence of disease (353).

Prognosis

Early identification and treatment of mares with placentitis has a fair prognosis for foal viability.

It is important to recognise that mares diagnosed with ascending placentitis are at high risk of "red bag delivery" due to thickening and separation of the chorioallantois from the uterus at the cervical pole. These mares should be closely monitored, with foaling attended.

Foals born from mares affected with any form of placentitis are likely to have complications. Neonatal septicaemia is likely if the foal has been exposed to the causative pathogen *in utero* and the foal may require intensive medical care following delivery.

The mare may also require further treatment after delivery. Even when there has been extended treatment during pregnancy, it is likely that the pathogen remains in the reproductive tract and this increases the risk of metritis and endometritis.

Further reading

Canisso Igor, Ball Barry A., Squires Edward L., Troedsson Mats H.T. Comprehensive Review on Equine Placentitis. *AAEP Proceedings* 2015; 61: 490-509.

Pozor M. Equine placenta – A clinician's perspective. Part 2: Abnormalities. *Equine Veterinary Education* 2016;28:396-404.

Equine Veterinarians Australia. Keeping yourself safe - Foetal & placental post mortem techniques. How to video: https://www.ava.com.au/about-us/ava-groups/equine/resources/videos/

Angela Begg, Joan Carrick, Pat Shearer, Melinda Stewart. Visual Atlas of the Gross Pathology of Equine Reproductive Loss, First Edition. February 2022. https://agrifutures.com.au/product/visual-atlas-of-the-gross-pathology-of-equine-reproductive-loss/

Angela Begg, Melinda Stewart, Joan Carrick, Pat Shearer and Victoria Brookes. Visual Atlas of the Histopathology of Equine Reproductive Loss, First Edition. February 2022. https://agrifutures.com.au/product/visual-atlas-of-the-histopathology-of-equine-reproductive-loss/

Chapter 6: Pyometra

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Key Issues

1. Often associated with previous foaling trauma or anatomical defects of the caudal reproductive tract.
2. Clinical signs of pyometra in the mare are not always obvious and are rarely associated with systemic illness.
3. Treatment is focused around drainage of uterine fluid contents (lavage, surgical corrections) prior to antimicrobial therapy.

Pyometra is defined as the accumulation of inflammatory, mucopurulent material within the uterus with or without the presence of an active corpus luteum and is relatively uncommon in the mare (354). While the cause can be multifactorial, the accumulation of fluid and debris is generally associated with failure of the uterus to physiologically drain, in combination with poor perineal conformation (355). Drainage may be limited or completely impaired by the presence of cervical and/or vaginal adhesions, stenosis, or other irregularities of the cervical canal. Pyometra can also be considered a chronic inflammatory condition, developing from ongoing clinical endometritis (356). The tissue inflammation and associated fluid can be sterile or infectious.

Multiple organisms are associated with pyometra in the mare. The organisms most commonly isolated include *Streptococcus equi* subspecies *zooepidemicus, E. coli, Actinomyces* spp., *Pasteurella* spp., *Pseudomonas* spp., *Propionibacterium* spp. and *Candidia* spp.(355). *Streptococcus dysgalactiae* subspecies *equisimilis* and *Serratia* spp. have been isolated in cases associated with urine contamination (357).

A reproductive examination is warranted to differentiate pyometra from pregnancy, mucometra, hydrometra, pneumometra or haemorrhage prior to initiation of further diagnostic investigation and treatment.

Diagnostics

In some cases, clinical signs of pyometra are completely absent. Other mares may present for examination because of vulval discharge, weight loss, abdominal distension, reduced performance, fever or colic (355).

Diagnosis is based on a complete reproductive examination, including transrectal palpation and ultrasonographic examination, a digital vaginal examination and a vaginoscopic examination. When possible, samples of any fluid exudate can be collected for cytological examination and culture and susceptibility testing. Hysteroscopy is another useful diagnostic aid in cases of atypical pyometra (358). An endometrial biopsy can also be considered for culture and to determine the prognosis for future fertility when considering treatment options.

In cases of pyometra, the uterus is often enlarged and atonic on palpation, with echogenic fluid detectable by transrectal ultrasonography. Some cases may have evidence of more solidified exudate (355, 358). In a case that occurred following dystocia, vaginal endoscopy and transrectal ultrasonography revealed a blind-ended vaginal cavity and distended uterus (359). In another case, masses evident on ultrasonography were identified as purulent concretions by hysteroscopy (358). Cytological examination enables confirmation of inflammation and aids in detection of the presence of bacteria, yeasts or fungi. In a case study, cytological examination also revealed numerous calcium carbonate crystals in the sample. This case of pyometra was associated with

urine pooling and persistent contamination of the uterine environment (357). Culture and antimicrobial susceptibility testing are used to determine whether infection is present and to direct antimicrobial treatment, if necessary.

Treatment

Conservative therapy consists of draining and flushing the uterus, in combination with systemic anti-inflammatory and antimicrobial treatment (based on culture and susceptibility testing). If possible, a sample of the uterine exudate should be collected for cytology, culture and antimicrobial susceptibility testing. Many pyometra cases will improve after uterine fluid is siphoned and repeated lavage with large volumes of saline or 0.05% povidone-iodine solution (360). Depending on the case, this may initially require manual breakdown of adhesions or scar tissue in the vaginal and/or cervical canal (355) if drainage is compromised. Topical application of anti-inflammatory ointments may help to prevent further formation of adhesions.

If a corpus luteum is present, prostaglandin F2α (250 µg of cloprostenol IM or 2.5-10 mg of dinoprost tromethamine IM) should be administered to induce luteolysis and cervical relaxation. Oxytocin (10-20 IU IM or IV) is often used concurrently to promote uterine contractility. Misoprostol, a synthetic prostaglandin E_1 analogue, can also be administered to promote cervical relaxation in cases where manual dilation is necessary to perform diagnostic testing and lavage (361). Hysteroscopy can be a useful therapeutic tool to assist lavage in clearing inspissated debris and concretions (358). The use of a permanent cervical stent for long-term drainage in cases of pyometra has been described (362). As many affected mares have conformational or anatomical abnormalities impairing uterine clearance, stent placement is often not a curative therapy. In many cases the stent was displaced, or removal was required, and pyometra was re-occurred after the stent was removed.

Complete recovery can be achieved in cases of pyometra (363), but is unlikely due to the anatomical limitations of affected mares. Correction of the primary cause is often necessary and may include an episiotomy or perineal body reconstruction for mares with abnormal perineal conformation, a urethral extension for mares with evidence of urine pooling, or surgical breakdown of advanced adhesions found in the reproductive tract.

Surgery is often necessary as a salvage procedure to resolve cases of pyometra. Cervical wedge resection is beneficial when cervical stenosis or adhesions of the os cervix limit uterine drainage. The uterus is lavaged prior to surgery and a full-thickness wedge-shaped cervical defect is created (364). This procedure results in a permanent opening that allows drainage and the mare is then managed medically as described above. Another surgical intervention used in cases of complete vaginal adhesion or unresolved pyometra is hysterectomy. Under general anaesthesia, the exudate is aspirated from the uterus and the uterus is removed. This procedure is not commonly practiced because of the risk of post-operative peritonitis and the difficulty of surgical access to the uterus in a mature horse (354, 365).

Antimicrobials used

Antimicrobial therapy is only warranted in cases of infectious (bacterial) pyometra. Treatment should be selected based on culture and susceptibility testing results. Whilst awaiting culture and susceptibility testing results, clinicians can implement uterine lavage and ecbolic treatment to improve the efficiency of antimicrobial therapy once an appropriate selection is possible. Systemic therapy is often used rather than intrauterine antimicrobial infusion because of the need to rid the uterine environment of fluid and the requirement for ongoing uterine lavage.

Prognosis

The prognosis for future fertility in mares with pyometra is poor. While it limits breeding capacity, adequate treatment can result in a good outcome for general health and performance.

Chapter 7: Retained Foetal Membranes (RFM)

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Key Issues

1. Medical emergency requiring prompt management and often associated with metritis.
    a. Removal of all remnants of the retained foetal membranes is critical in treatment with even small segments of retained villi lead to complications necessitating further medical management.
2. Importance of a complete examination of the foetal membranes at the time of parturition as a routine and diagnostic management tool.
3. Method of foetal membrane removal is controversial but should be performed in a controlled manner to avoid adverse effects such as bleeding, discomfort or uterine prolapse.

Retained foetal membranes (RFM) are one of the more common complications in the post-partum mare. Management of retained foetal membranes in the mare requires prompt veterinary intervention, as a delay in treatment leads to an increased risk of potentially fatal sequelae, including toxic metritis and laminitis. Acute metritis can develop, with autolysis of the retained allantochorion or microvilli within the endometrial crypts providing a nidus for infection. The environment becomes ideal for bacterial invasion and replication, leading to inflammation and intrauterine fluid accumulation. Toxins from the bacteria may be absorbed systemically, leading to endotoxaemia, septicaemia and subsequent laminitis (366).

In the mare, the foetal membranes (the foetal portion of the placenta) include the allantochorion, amnion and umbilical cord. These membranes are normally passed during the third stage of parturition, occasionally accompanied by signs of transient abdominal discomfort because of ongoing uterine contractions. Retained foetal membranes occur when there is complete or partial failure of the chorioallantois to separate from the endometrium (366). The equine placenta is diffuse, microcotyledonary and epitheliochorial. Microcotyledons with vascular chorionic villi interdigitate with endometrial crypts to allow increased surface area for nutrient exchange (367). Following parturition, the umbilical cord ruptures, leading to collapse of the umbilical vasculature and smaller vessels throughout the foetal membranes, allowing shrinkage and detachment of the microvilli from the endometrial crypts. Endogenous oxytocin release stimulates rhythmic contractions of the uterine myometrium to expel the free foetal membranes from the uterus (368). In the normal mare, the horns of the allantochorion invaginate as they are released and pass through the ruptured cervical star. This is facilitated by the dependent weight of the membranes (amnion and umbilical cord remnants) hanging externally from the vulva. The membranes are expelled intact, with the allantoic surface outermost.

Foetal membranes are normally expelled within the first three hours post-partum, and membranes retained longer than this are considered ‘retained foetal membranes’ (367, 369). The overall incidence of retained foetal membranes is low in light breeds (2 - 11%) but can be much higher in heavy draught breeds, with the highest prevalence reported in Friesian mares (up to 54%) (370, 371, 372). Although mares may retain foetal membranes following a normal gestation and foaling, several risk factors are associated with a higher incidence of retained foetal membranes, including mare age, breed, a history of retained foetal membranes in a previous pregnancy, and peripartum complications, such as Caesarean delivery, abortion, dystocia, placentitis, prolonged gestation and hydropic conditions (366, 367, 369, 370).

Diagnostics

Reaching a diagnosis that a mare has retained foetal membranes may be obvious, as portions of the membranes may protrude externally from the vulva. However, mares may present with concerns of incomplete membrane expulsion or unknown expulsion in the case of an unattended foaling. In many cases, a portion of the allantochorion (i.e. the tip of the non-gravid horn) can be retained and this may not be noticed if the foetal membranes have not been closely examined. Some mares with partial retention of the allantochorion can present 24 to 48 hours post-partum with clinical signs of metritis and/or endotoxaemia, including a fetid vulval discharge, dullness, pyrexia, injected mucous membranes, tachycardia and an increased digital pulse, which is associated with the onset of laminitis (366).

If the membranes have already passed or are expelled following presentation, they should be examined thoroughly to determine whether they are complete and whether there is evidence of pathology. The chorioallantois can be laid out in the shape of an F when it is intact, with the ruptured cervical star at the base and each horn forming the arms. The umbilicus should be located at the base of the gravid horn, with any remnants of the amnion attached. Occasionally the membranes may have been damaged, leading to tearing within the chorioallantois. Often the damaged portions can be pieced together by following the vascular patterns (373, 374). Evidence of incomplete foetal membranes or uncertainty about whether they are complete necessitates further examination of the reproductive tract of the mare.

Further diagnostic procedures are valuable in the diagnosis of retained foetal membranes and metritis. Transrectal palpation of the uterus can be used to determine the degree of uterine tone and involution. Both are reduced with metritis or retained foetal membranes. Transrectal ultrasonography can be used to determine the degree of fluid accumulation and echogenicity within the uterus and may reveal tags of retained chorioallantois. Following cleansing of the perineal area, a transvaginal digital examination can help characterize the nature of fluid within the vaginal cavity and the uterine lumen. Retained membranes can be located and their degree of attachment evaluated. When endotoxaemia is suspected, blood samples should be collected for haematology and plasma biochemical analysis.

Culture of the uterine environment, discharge or uterine effluent is not performed routinely in mares with retained foetal membranes because of the significant level of contamination of the reproductive tract. In cases of ongoing metritis or secondary endometritis, endometrial culture and cytological examination may help determine the need for ongoing antimicrobial therapy.

Treatment

The objective when managing retained foetal membranes is to attain complete expulsion or removal of the foetal membranes, while avoiding trauma to the entire reproductive tract, minimizing excessive force that could lead to uterine horn eversion/uterine prolapse and preventing metritis and endotoxaemia, which can have fatal consequences. There does not appear to be any agreement on or evidence of a ‘best’ method of treatment for retained foetal membranes nor the timing of when removal should be attempted (375). The method selected for removal of retained foetal membranes is dependent on effectiveness, safety, cost, convenience and the experience of the veterinarian.

The most common method to aid in foetal membrane removal is administration of oxytocin in the early post-partum period. For healthy mares presented within 12 h of routine foaling, conservative therapy with oxytocin may be all that is necessary. Mares are highly sensitive to the effects of oxytocin in the immediate post-partum period – 10 IU given intravenously or intramuscularly may be all that is necessary for membrane expulsion. The portion of the membranes external to the vulva (if there are any any) should be tied in a knot above the hock to ensure they provide constant traction without being trampled or pulled on by the mare. Repeat doses of oxytocin can be

considered every two hours for the first 6 h after foaling or until placental expulsion has occurred. Higher doses of oxytocin can result in myometrial spasm and cramping, or signs of colic. Oxytocin can also be administered as a constant rate intravenous infusion (50 - 60 IU oxytocin in 1 L of saline administered slowly over 30 - 60 min) (372) to reduce spasm and signs of colic. In some cases, especially Friesian mares with lower serum calcium levels post-partum, the addition of calcium-magnesium borogluconate (200 ml of a 23% solution) can aid in membrane expulsion (366, 376). Uterine lavage is often combined with oxytocin administration to hasten membrane expulsion.

When the membranes are intact and firmly attached, the chorioallantois can be distended with dilute betadine solution or 0.9% saline (Burns technique), which often will stimulate release of microcotyledons from the endometrium(377). This technique is atraumatic and does not result in any contamination of the uterus when the membranes are intact, without any autolysis. The uterine distension may need to be maintained for up to 30 minutes before membranes are passed, but expulsion often occurs within minutes of distension.

Large volume uterine lavage can be performed to promote separation of the chorioallantois from the endometrial surface. This can be used when the membranes are no longer intact but the fluid runs between the chorion and the endometrial surface (378). Uterine lavage is further indicated when the membranes have been retained for a length of time, which would predispose the mare to metritis. Large volume lavage is used to remove intrauterine accumulations of fluid, inflammatory products, debris and bacteria. Two to 3 litres of warm saline, lactated Ringer's solution or 0.05% povidone-iodine are infused into the uterine lumen (360). With the hand forming a cage around the tip of the tube, the efflux is removed without aspiration of the endometrium or any retained foetal membrane tags that may remain. The lavage is repeated until the effluent is clear or light pink in colour. In cases of retained foetal membranes following a Caesarean section, uterine lavage should be performed with caution, as excessive fluid distension of the uterus could cause leakage along the suture line (368).

Manual removal of foetal membranes is commonly used, but opinions vary about its use. Techniques that have been described for manual foetal membrane removal include grasping the externalized free portion of the membranes and applying controlled traction (369, 379), placing a hand between the endometrium and chorion to separate the attached membranes in a controlled motion (380), twisting of the allantochorionic membrane into a tight cord (381), and placing a wooden ring between the chorion and endometrium and advancing the ring to separate the membranes from the endometrium (369). The degree of membrane attachment, as well as duration of membrane retention, can affect the outcome of manual membrane removal, whichever procedure is used. Potential risks of manual membrane removal are a result of excessive traction, leading to retention of the microvilli, tearing and retention of foetal membrane tags, haemorrhage and uterine horn eversion/uterine prolapse. Factors related to the mare (normal vs high risk pregnancy) and the veterinarian (experience, access to the mare) also influence the decision to attempt manual membrane removal.

Another technique, using catheterisation of an exposed umbilical vessel to infuse water, causing distension of membrane vasculature and detachment of the chorioallantois from the endometrium, has been described (382). This procedure leads to stretching of the umbilical vessels, interstitial distension, and subsequent detachment of the microvilli. The result is a rapid but gentle separation of the foetal membranes from the endometrium. The procedure is atraumatic and effective when performed on intact membranes retained for less than 12 h.

Exercise is important to aid in uterine clearance and involution, thus reducing the risk of development of metritis. Paddock turn-out is ideal. Hand-walking with frequent uterine lavage and oxytocin therapy can be used when stall confinement is necessary.

Tetanus prophylaxis should be administered if the vaccination status of the mare is unknown. Treatment for endotoxaemia is discussed elsewhere (Section 7).

A survey of equine veterinarians (54% of whom were reproduction specialists) found that the vast variety of treatments for retained foetal membranes reported reflected a lack of specific treatment guidelines and management recommendations. Large volume lavage was the most common treatment used by more than half of the survey respondents. Prophylactic antimicrobials were administered by 42%, with a variety of types, frequency and routes of administration reported (383). The efficacy of antimicrobial use is unknown and intrauterine administration of antimicrobials and antiseptics has been reported to irritate the endometrium and decrease the phagocytic activity of uterine neutrophils (384).

Antimicrobials used

Prophylactic, broad-spectrum systemic antimicrobial therapy should be initiated in mares with suspect metritis or when foetal membranes have been retained for longer than 12 h post-partum. In uncomplicated cases, systemic antimicrobials are continued until uterine lavage is no longer necessary or uterine involution is evident. Intrauterine antimicrobials are not recommended in the immediate post-partum period, with clearing the uterus of fluid and debris using lavage and oxytocin being the preferred option.

- Penicillin (procaine or potassium) at 22,000–44,000 IU/kg IM q 12 h or IV q 6 h for 3 - 5 days, in combination with gentamicin at 6.6 mg/kg IV q 24 h until the membranes are expelled, or longer in cases of metritis.

Or

- Trimethoprim/sulphadiazine (TMS) at 30 mg/kg PO q 12 h until the membranes are expelled, or longer in cases of metritis.

Prognosis

The prognosis for survival and future fertility is good in mares that do not develop metritis or endotoxaemia, when resolution of retained foetal membranes is effective and efficient (379, 385). Endometrial culture and cytological examination are recommended on the subsequent breeding cycle to determine if the uterine environment is suitable for breeding. A uterine biopsy maybe useful to evaluate fibrosis if membrane retention has occurred previously. Additionally, mares that have suffered a difficult foaling or dystocia should have a digital cervical evaluation in dioestrus to rule-out cervical abnormalities related to trauma.

The prognosis varies from guarded to moderate in mares that develop metritis, endotoxaemia and subsequent laminitis. The prognosis is further determined by the severity of the metritis, sepsis and endotoxin-induced laminitis, a prolonged disease process and the response to therapy.

Further reading

Threlfall W. Retained Fetal Membranes In: McKinnon AO SE, Valla WE, Varner DD, ed. *Equine Reproduction*: Blackwell Publishing LTD, 2011;2520-2529.

Chapter 8: Seminal vesiculitis

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Key issues

1. Reduced fertility due to pyospermia and bacterial contamination of the ejaculate.
2. Potential for venereal transmission of bacteria to the mare.
3. Difficult to treat the target organ effectively with antimicrobials.

Seminal vesiculitis is an uncommon condition in the stallion. However, its presence is often a source of frustration for clinicians because of the invasive and persistent nature of the disease and its potential for disruption of fertility (386). Seminal vesiculitis may be caused by several bacterial species and can be contracted via a range of routes, including both ascending and descending infection from the urinary and reproductive tracts (387). It occurs when pathogenic bacteria colonise the seminal vesicles, resulting in the accumulation of inflammatory products within the gland that are expelled during ejaculation (388). Diagnosis of the disease is usually achieved by cytological examination of semen samples, as affected stallions can appear clinically normal. Treatment of seminal vesiculitis in the stallion can often be unrewarding, as achieving adequate therapeutic concentrations of antimicrobial drugs within the seminal vesicles is difficult.

Diagnostics

Clinical signs are usually absent in stallions with seminal vesiculitis. However, variable numbers of white blood cells and bacteria within the stallion's ejaculate are usually characteristic of the disease. Grossly, the ejaculate may appear discoloured and flocculant, but, in some cases, no gross changes may be apparent. Swabs can be collected from the prepuce, urethral fossa, semen, and the urethra pre- and post-ejaculation to determine the source of infection. A heavy pure growth of bacteria from the post-ejaculatory urethra and semen is strongly suggestive of infection in the seminal vesicles.

To differentiate seminal vasculitis from other diseases of the urogenital tract, a semen sample can be fractionated to isolate the pre-ejaculatory fluid from the sperm-rich fraction and the gel fraction expelled at the completion of ejaculation. As the seminal vesicles contribute a significant portion of the gel fraction in the stallion's ejaculate, more white blood cells are likely to be detected in the gel fraction than the other fractions. The gel fraction can be filtered from a normal collection obtained with a artificial vagina using a commercial semen filter. Simple smears can be prepared on a slide and stained with Diff-Quik to examine white blood cell morphology and to compare the sperm-rich and gel fractions.

A definitive diagnosis can be achieved using uroscopy to catheterise the seminal colliculi, allowing direct sampling of the seminal vesicles, with or without trans-rectal massage. Transrectal ultrasonographic examination may help to confirm the diagnosis, with the affected vesicles appearing enlarged, with variable echogenicity. However, this procedure is often unrewarding (389).

Culture of the organism is imperative to allow formulation of a treatment plan. The species most commonly cultured from the seminal vesicles of stallions include *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (388, 389, 390). In addition to compromising the fertility of semen from the affected stallion, venereal transmission of these bacteria may result in bacterial endometritis in susceptible mares.

Treatment

Treatment of seminal vesiculitis is often unrewarding. Even after treatment with both systemic and local application of antimicrobials, there is a high recurrence rate. Treatment of acute seminal vesiculitis appears to be more successful (388).

Endoscopic catheterisation of the seminal colliculus is the most effective method to achieve direct delivery of antimicrobials to the site of infection. This method also allows targeted treatment with mucolytics and gland lavage to physically remove biofilms and inflammatory products. Whilst this treatment method is an intensive "in hospital" method of antimicrobial delivery, it is the most effective treatment method for achieving resolution of the infection. A combination of systemic and direct therapy is recommended, as this disease often reoccurs.

Systemic therapy is often the most practical way to tackle seminal vesiculitis in the stallion. However, it is important that the antimicrobial selected has good penetration into the reproductive tract, in addition to antibacterial efficacy against the targeted organism. Lipophilic (fat soluble) drugs should be selected to achieve good penetration into these tissues. Treatment duration may vary between individuals. However, it is likely that 2-4 weeks of therapy will be required before there is an appreciable reduction in contamination of semen with bacteria and white blood cells. The response to treatment can be monitored with routine culture and susceptibility testing of the semen/seminal plasma. Resolution is only effective if the antimicrobial selected can achieve adequate penetration into the seminal vesicles and reach therapeutic concentrations (388). Microorganisms capable of forming biofilms complicate therapy and a combination targeted approach is usually more effective.

If the stallion needs to continue his breeding duties whilst being treated for this condition, careful management of the ejaculate may prevent venereal transmission. The most effective post-ejaculatory treatment of semen is the use of gradient or colloid centrifugation. In addition to the removal of seminal plasma and the selection of a "good" population of spermatozoa (391), colloid centrifugation also removes bacteria and viral particles from semen (392, 393). Reducing or even eliminating the bacterial load of the semen sample may allow control of bacterial contamination without the excessive use of antimicrobials. Mixing an affected ejaculate with a commercial semen extender containing appropriate antimicrobials may also provide effective treatment of an ejaculate prior to insemination.

Seminal vesiculectomy is rarely performed in the stallion. However, there are some reports of chemical cauterisation of the seminal vesicles, which may be effective in cases of chronic and persistent seminal vesciulitis in a breeding stallion (388).

Antimicrobials used

- Systemic: therapy should be initiated following culture and susceptibility testing. Antimicrobials that can reach effective therapeutic concentrations in the seminal vesicles include trimethoprim/sulphadiazine at 30 mg/kg PO q 12 h or enrofloxacin at 5 mg/kg PO q 24 h. The duration of treatment is determined by monitoring for negative cultures and resolution of pyospermia, but a minimum of 2-4 weeks is usually required.
- Intraluminal: several antimicrobials have been instilled into the seminal vesicles, including procaine penicillin (2,400,000 IU q 48 h for 2 treatments) (389), amikacin (1 g q 24 h for 10 days) (394), ceftiofur (1 g q 24 h for 10 days) (394) and ciprofloxacin (200 mg q 24 h for 10 days) (394).
- Combination therapy is considered the most effective treatment, and can include catheterisation of the seminal colliculus, lavage of the vesicle contents, instillation of a mucolytic (acetylcysteine), and administration of an antimicrobial to which the target organism is susceptible for 5 - 10 days. Systemic therapy may also be administered after a period of intensive local treatment.

Prognosis

Because the efficacy of antimicrobial therapy is poor and the recurrence rate in stallions is high, the prognosis for affected breeding stallions is guarded. Unless routine semen evaluation is being performed, the condition is rarely identified early, which would enable more effective treatment and elimination of the disease. Treatment of the stallion may result in transient resolution of bacterial shedding and pyospermia, which may improve fertility transiently to enable breeding or semen cryopreservation prior to castration. However, there is a high chance of re-infection after treatment. In chronically affected stallions refractory to treatment, semen collection and colloid centrifugation is the recommended method for preparation of semen for insemination.

Reference List

1. Herzog FE. The effect of Lactobacillus containing gel on the clitoral microbiome of the mare: Louisiana State University; 2024.
2. Timoney PJ. Contagious equine metritis. Comparative Immunology, Microbiology and Infectious Diseases. 1996;19(3):199-204.
3. Scholtz M, Guthrie AJ, Newton R, Schulman ML. Review of Pseudomonas aeruginosa and Klebsiella pneumoniae as venereal pathogens in horses. Equine Veterinary Journal. 2024;n/a(n/a):1-11.
4. Storme J, Brookes VJ, Gunn A. Is there evidence demonstrating venereal transmission of clitoral Pseudomonas aeruginosa in horses? Veterinary record. 2023;192(11):444-6.
5. Morris LHA, McCue PM, Aurich C. Equine endometritis: a review of challenges and new approaches. Reproduction (Cambridge, England). 2020;160(5):R95-R110.
6. Canisso IF, Segabinazzi LGTM, Fedorka CE. Persistent Breeding-Induced Endometritis in Mares—A Multifaceted Challenge: From Clinical Aspects to Immunopathogenesis and Pathobiology. International Journal of Molecular Sciences. 2020;21(4):1432.
7. Troedsson MHT. Uterine clearance and resistance to persistent endometritis in the mare. Theriogenology. 1999;52(3):461-71.
8. Frontoso R, De Carlo E, Pasolini MP, van der Meulen K, Pagnini U, Iovane G, et al. Retrospective study of bacterial isolates and their antimicrobial susceptibilities in equine uteri during fertility problems. Research in Veterinary Science. 2008;84(1):1-6.
9. Ferris RA. Current understanding of bacterial biofilms and latent infections: A clinical perspective. Rev Bras Reprod Anim. 2017;41:74-80.
10. Donlan RM, Costerton JW. Biofilms: Survival Mechanisms of Clinically Relevant Microorganisms. Clinical Microbiology Reviews. 2002;15(2):167-93.
11. Davis HA, Stanton MB, Thungrat K, Boothe DM. Uterine bacterial isolates from mares and their resistance to antimicrobials: 8,296 cases (2003–2008). Journal of the American Veterinary Medical Association. 2013;242(7):977-83.
12. Olsen I. Biofilm-specific antibiotic tolerance and resistance. European Journal of Clinical Microbiology & Infectious Diseases. 2015;34(5):877-86.
13. Petersen MR, Rosenbrock A, Osborne M, Bojesen AM. High Prevalence of Subclinical Endometritis in Problem Mares– Effect of Activation and Treatment on Fertility. Journal of Equine Veterinary Science. 2018;66:117.
14. Hoffmann C, Ellenberger C, Mattos RC, Aupperle H, Dhein S, Stief B, et al. The equine endometrosis: new insights into the pathogenesis. Anim Reprod Sci. 2009;111(2-4):261-78.
15. Snider TA, Sepoy C, Holyoak GR. Equine endometrial biopsy reviewed: Observation, interpretation, and application of histopathologic data. Theriogenology. 2011;75(9):1567-81.
16. Pascoe RR. CHAPTER 23 - Vulvar Conformation. In: Samper JC, Pycock JF, McKinnon AO, editors. Current Therapy in Equine Reproduction. Saint Louis: W.B. Saunders; 2007. p. 140-5.

17. Scoggin CF. Not just a number: effect of age on fertility, pregnancy and offspring vigour in thoroughbred brood-mares. Reprod Fertil Dev. 2015;27(6):872-9.

18. Katila T. Evaluation of diagnostic methods in equine endometritis. Reproductive Biology. 2016;16:189-96.

19. Heil BA, van Heule M, Thompson SK, Kearns TA, Oberhaus EL, King G, et al. Effect of Sampling Method on Detection of the Equine Uterine Microbiome during Estrus. Veterinary Sciences. 2023;10(11):644.

20. LeBlanc MM. How to Perform and Interpret Findings From a Low-Volume Uterine Flush. AAEP Proceedings. 2011;57:32-6.

21. Riddle WT, LeBlanc MM, Stromberg AJ. Relationships between uterine culture, cytology and pregnancy rates in a Thoroughbred practice. Theriogenology. 2007;68(3):395-402.

22. Petersen MR, Skive B, Christoffersen M, Lu K, Nielsen JM, Troedsson MHT, et al. Activation of persistent Streptococcus equi subspecies zooepidemicus in mares with subclinical endometritis. Veterinary Microbiology. 2015;179(1):119-25.

23. LeBlanc M. Advances in the Diagnosis and Treatment of Chronic Infectious and Post–Mating-Induced Endometritis in the Mare. Reproduction in Domestic Animals. 2010;45(s2):21-7.

24. Ferris RA, Wittstock SM, McCue PM, Borlee BR. Evaluation of biofilms in gram-negative bacteria isolated from the equine uterus. Journal of Equine Veterinary Science. 2014;34(1):121.

25. Katila T. Onset and Duration of Uterine Inflammatory Response of Mares after Insemination with Fresh Semen. Biology of Reproduction. 2018;52(monograph_series1):515-7.

26. Scoggin CF, Burden CA, Schnobrich MR, Bradecamp EA. A single post-mating infusion of penicillin does not improve pregnancy rates in maiden Thoroughbred broodmares. Clinical Theriogenology. 2017;9(1):53-8.

27. Karam KM, Alebady AS, Alhilfi HO, Al-Delemi DH. Comparative study utilizing different post-breeding treatment regimens in cyclic Arabian mares. Vet World. 2021;14(11):2863-8.

28. Rose BV, Firth M, Morris B, Roach JM, Wathes DC, Verheyen KLP, et al. Descriptive study of current therapeutic practices, clinical reproductive findings and incidence of pregnancy loss in intensively managed thoroughbred mares. Animal reproduction science. 2018;188:74-84.

29. LeBlanc MM. The current status of antibiotic use in equine reproduction. Equine Veterinary Education. 2009;21(3):156-67.

30. Ferris RA, McCue PM, Borlee GI, Loncar KD, Hennet ML, Borlee BR. In Vitro Efficacy of Nonantibiotic Treatments on Biofilm Disruption of Gram-Negative Pathogens and an In Vivo Model of Infectious Endometritis Utilizing Isolates from the Equine Uterus. J Clin Microbiol. 2016;54(3):631-9.

31. Dascanio JJ, Schweizer C, Ley WB. Equine fungal endometritis. Equine Veterinary Education. 2001;13(6):324-9.

32. Rogan D, Fumuso E, Rodríguez E, Wade J, Sánchez Bruni SF. Use of a Mycobacterial Cell Wall Extract (MCWE) in Susceptible Mares to Clear Experimentally Induced Endometritis With Streptococcus zooepidemicus. Journal of Equine Veterinary Science. 2007;27(3):112-7.

33. Perkins N, Threlfall W. Mastitis in the mare. Equine Veterinary Education. 2010;5:192-5.

34. McCUE PM, WILSON WD. Equine mastitis - a review of 28 cases. Equine Veterinary Journal. 1989;21(5):351-3.

35. McCue P, Sitters, S. Lactation. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2277-90.

36. Ginther O. How ultrasound technologies have expanded and revolutionized research in reproduction in large animals. Theriogenology. 2014;81(1):112-25.

37. Pugh DG, Magnusson RA, Modransky PD, Darnton KR. A case of mastitis in a young filly. Journal of Equine Veterinary Science. 1985;5(3):132-4.

38. Gee Erica K. MPM. Mastitis. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2738-41.

39. McKenzie RA, Brown OP. Avocado (Persea americana) poisoning of horses. Aust Vet J. 1991;68(2):77-8.

40. Canisso IF, Podico G, Ellerbrock RE. Diagnosis and treatment of mastitis in mares. Equine Veterinary Education. 2021;33(6):320-6.

41. Trela M, Domańska D, Witkowska-Piłaszewicz O. Diagnostic Use of Serum Amyloid A in Dairy Cattle. Agriculture. 2022;12(4):459.

42. Schiemann V, Bartmann C. Mastectomia in the horse- Indication and surgical procedure. Pferdeheilkunde. 2004;20:506-10.

43. Blanchard TL, Elmore RG, Kinden DA, Berg JN, Mollett TA, Garcia MC. Effect of intrauterine infusion of Escherichia coli endotoxin in postpartum pony mares. Am J Vet Res. 1985;46(10):2157-62.

44. Ferrer MS, Palomares R. Aerobic uterine isolates and antimicrobial susceptibility in mares with post-partum metritis. Equine Veterinary Journal. 2018;50(2):202-7.

45. Ferrer MS, Pozor MA. How to Manage the Post-Partum Mare with Metritis—Lessons Learned from a Retrospective Bacteriological Study. Proceedings of the American Association of Equine Practitioners. 2018;64:236-9.

46. Crabtree J. Peripartum problems in mares 2. Postpartum problems. In Practice. 2012;34(8):462-71.

47. Tukia E, Wagner B, Vainio K, Mönki J, Kareskoski M. The Effect of Uterine Lavage on Soluble CD14, Chemokine Ligand 2, and Interleukin 10 Levels in Mares With Postpartum Metritis. Journal of Equine Veterinary Science. 2021;98:103365.

48. Carrick J, editor Assessment and Treatment of Placentitis College Science Week Scientific Meeting, Equine Chapter Proceedings; 2007; Gold Coast.

49. Carrick JB, Perkins N, Zalucki MP. Causes of abortion in Australia (2005-2012) – proportion of cases due to Equine Amnionitis and Foetal Loss (EAFL). Journal of Equine Veterinary Science. 2014;34:212-4.

50. LeBlanc MM. Ascending placentitis in the mare: an update. Reprod Domest Anim. 2010;45 Suppl 2:28-34.

51. Troedsson MH MM. Placentitis. In: McKinnon AO SE, Vaala WE, Varner DD, editor. Equine Reproduction, 2nd ed. 2. Hoboken NJ2011. p. 2359–67.

52. R. L. Abnormalities of pregnancy. In: McKinnon AO SE, Vaala WE, Varner DD, editor. eds Equine Reproduction, Vol 2 2nd ed. Hoboken NJ: Wiley-Blackwell; 2011. p. 2441–53.

53. Troedsson M, Miller L. Equine placentitis. Pferdeheilkunde. 2016;32:49-53.

54. Macpherson ML. Treatment strategies for mares with placentitis. Theriogenology. 2005;64(3):528-34.

55. Hong CB, Donahue JM, Giles RC, Jr., Petrites-Murphy MB, Poonacha KB, Roberts AW, et al. Etiology and pathology of equine placentitis. J Vet Diagn Invest. 1993;5(1):56-63.

56. Erol E, Sells SF, Williams NM, Kennedy L, Locke SJ, Labeda DP, et al. An investigation of a recent outbreak of nocardioform placentitis caused abortions in horses. Vet Microbiol. 2012;158(3-4):425-30.

57. El-Sheikh Ali H, Ball B, Carleigh, Fedorka C, Scoggin K, Schnobrich M, et al. Nocardioform Placentitis: A Continuing Question. 2021.

58. Todhunter K, Perkins N, Wylie R, Chicken C, Blishen A, Racklyeft D, et al. Equine amnionitis and fetal loss: The case definition for an unrecognised cause of abortion in mares. Australian Veterinary Journal. 2009;87(1-2):35-8.

59. Begg AP, Carrick J, Chicken C, Blishen A, Todhunter K, Eamens K, et al. Fetoplacental pathology of equine abortion, premature birth, and neonatal loss due to Chlamydia psittaci. Vet Pathol. 2022;59(6):983-96.

60. El-Hage C, Legione A, Devlin J, Hughes K, Jenkins C, Gilkerson J. Equine Psittacosis and the Emergence of Chlamydia psittaci as an Equine Abortigenic Pathogen in Southeastern Australia: A Retrospective Data Analysis. Animals (Basel). 2023;13(15).

61. Renaudin CD, Troedsson MHT, Gillis CL, King VL, Bodena A. Ultrasonographic evaluation of the equine placenta by transrectal and transabdominal approach in the normal pregnant mare. Theriogenology. 1997;47 2:559-73.

62. Reef V, Vaala W, Worth L, Sertich P, Spencer P. Ultrasonographic assessment of fetal well-being during late gestation: Development of an equine biophysical profile. Equine Veterinary Journal. 2010;28:200-8.

63. Bucca S, Fogarty U, Collins A, Small V. Assessment of feto-placental well-being in the mare from mid-gestation to term: Transrectal and transabdominal ultrasonographic features. Theriogenology. 2005;64(3):542-57.

64. Begg A CJ, Shearer P, Stewart M VISUAL ATLAS OF THE GROSS PATHOLOGY OF EQUINE REPRODUCTIVE LOSS, First Edition 2022 [Available from: https://agrifutures.com.au/product/visual-atlas-of-the-gross-pathology-of-equine-reproductive-loss/

65. Ousey JC, Houghton E, Grainger L, Rossdale PD, Fowden AL. Progestagen profiles during the last trimester of gestation in Thoroughbred mares with normal or compromised pregnancies. Theriogenology. 2005;63(7):1844-56.

66. Santschi EM, LeBlanc MM, Weston PG. Progestagen, oestrone sulphate and cortisol concentrations in pregnant mares during medical and surgical disease. J Reprod Fertil Suppl. 1991;44:627-34.

67. Ryan PL, Christiansen DL, Hopper RM, Bagnell CA, Vaala WE, Leblanc MM. Evaluation of systemic relaxin blood profiles in horses as a means of assessing placental function in high-risk pregnancies and responsiveness to therapeutic strategies. Ann N Y Acad Sci. 2009;1160:169-78.

68. Canisso IF, Ball BA, Cray C, Williams NM, Scoggin KE, Davolli GM, et al. Serum amyloid A and haptoglobin concentrations are increased in plasma of mares with ascending placentitis in the absence of changes in peripheral leukocyte counts or fibrinogen concentration. Am J Reprod Immunol. 2014;72(4):376-85.

69. Coutinho da Silva MA, Canisso IF, MacPherson ML, Johnson AE, Divers TJ. Serum amyloid A concentration in healthy periparturient mares and mares with ascending placentitis. Equine Vet J. 2013;45(5):619-24.

70. Canisso IF, Ball BA, Scoggin KE, Squires EL, Williams NM, Troedsson MH. Alpha-fetoprotein is present in the fetal fluids and is increased in plasma of mares with experimentally induced ascending placentitis. Anim Reprod Sci. 2015;154:48-55.

71. LeBlanc MM, Giguère S, Lester GD, Brauer K, Paccamonti DL. Relationship between infection, inflammation and premature parturition in mares with experimentally induced placentitis. Equine Vet J Suppl. 2012(41):8-14.

72. Bailey CS, Macpherson ML, Pozor MA, Troedsson MH, Benson S, Giguere S, et al. Treatment efficacy of trimethoprim sulfamethoxazole, pentoxifylline and altrenogest in experimentally induced equine placentitis. Theriogenology. 2010;74(3):402-12.

73. Rebello SA, Macpherson ML, Murchie TA, LeBlanc MM, Vickroy TW. Placental transfer of trimethoprim sulfamethoxazole and pentoxifylline in pony mares. Animal Reproduction Science. 2006;94(1-4):432-3.

74. Murchie TA, Macpherson ML, LeBlanc MM, Luznar S, Vickroy TW. Continuous monitoring of penicillin G and gentamicin in allantoic fluid of pregnant pony mares by in vivo microdialysis. Equine Vet J. 2006;38(6):520-5.

75. Macpherson ML, Giguère S, Pozor MA, Burden CA, Berghaus LJ, Berghaus RD, et al. Evidence for anti-inflammatory effects of firocoxib administered to mares with experimentally induced placentitis. Am J Reprod Immunol. 2021;86(1):e13396.

76. Bailey CS, Sper RB, Schewmaker JL, Buchanan CN, Beachler TM, Pozor MA, et al. Uterine artery blood flow remains unchanged in pregnant mares in response to short-term administration of pentoxifylline. Theriogenology. 2012;77(2):430-6.

77. Palmer E, Chavatte-Palmer P, Duchamp G, Levy I. Lack of effect of clenbuterol for delaying parturition in late pregnant mares2002. 797-9 p.

78. Sielhorst J, Roggel-Buecker U, Neudeck KC, Kahler A, Rohn K, Luettgenau J, et al. Effect of Acetylsalicylic Acid on Uterine Blood Flow, Gestation Length, Foal Birth Weight and Placental Weight in Pregnant Thoroughbred Mares - A Clinical Pilot Study. J Equine Vet Sci. 2022;118:104107.

79. Bommana S, Polkinghorne A. Mini Review: Antimicrobial Control of Chlamydial Infections in Animals: Current Practices and Issues. Front Microbiol. 2019;10:113.

80. Fedorka CE, Scoggin KE, Ruby RE, Erol E, Ball BA. Clinical, pathologic, and epidemiologic features of nocardioform placentitis in the mare. Theriogenology. 2021;171:155-61.

81. Santschi EM, Adams SB, Robertson JT, DeBowes RM, Mitten LA, Sojka JE. Ovariohysterectomy in six mares. Vet Surg. 1995;24(2):165-71.

82. Lu KG. Pyometra. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2652-4.

83. LeBlanc M, Causey R. Clinical and Subclinical Endometritis in the Mare: Both Threats to Fertility. Reproduction in Domestic Animals. 2009;44(s3):10-22.

84. Naguib M, Rais B, Adzahan N, Armiladiana M, Adamu L. Equine Pyometra: A Case Report. IOSR Journal of Agriculture and Veterinary Science (IOSR-JAVS) IMPACT FACTOR 1485. 2013;2:2319-72.

85. Köhne M, Tönissen A, Unruh C, Pruß D, Sieme H. Occurrence of Intrauterine Purulent Concrements in a Maiden Mare—A Case Report. Journal of Equine Veterinary Science. 2020;95:103278.

86. Cozens ER. Pyometra and complete vaginal adhesion in a miniature horse. Can Vet J. 2009;50(9):971-2.

87. Brinsko S, Act D. How to Perform Uterine Lavage: Indications and Practical Techniques. Proc Am Assoc Equine Pract. 2001;47.

88. McNaughten J, Pozor M, Macpherson M, Kelleman A, Woodward E, Troedsson M. Effects of topical application of misoprostol on cervical relaxation in mares. Reprod Domest Anim. 2014;49(6):1057-62.

89. Krohn J, Ennen S, Hospes R, Nieth J, Wehrend A. Use of a cervical stent for long-term treatment of pyometra in the mare: A report of three cases. Reprod Domest Anim. 2019;54(8):1155-9.

90. Sharma S, Thapak S. Chronic pyometra in a thoroughbred mare. Veterinary Practitioner. 2010;11:116-7.

91. Arnold CE, Brinsko SP, Varner DD. Cervical wedge resection for treatment of pyometra secondary to transluminal cervical adhesions in six mares. J Am Vet Med Assoc. 2015;246(12):1354-7.

92. Prestes NC, et al. . Total Hysterectomy as Treatment for Recurrent Chronic Pyometra in Mares With Total Cervical AdhesioneCase Report. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2018;63:61-4.

93. P OB. Retained Fetal Membranes In: Sprayberry KAR, N.E., editor. Robertson's Current Therapy In Equine Medicine 7th Edition: WB Saunders Co LTD; 2015. p. 713-6.

94. Asbury AC LM. The fetal membranes. In: McKinnon AO VJ, editor. Equine Reproduction. 1st Edition. Philadelphia: Lea & Febiger; 1992. p. 510-6.

95. Canisso I, Rodriguez J, Sanz M, Silva M. A Clinical Approach to the Diagnosis and Treatment of Retained Fetal Membranes with an Emphasis Placed on the Critically Ill Mare. Journal of Equine Veterinary Science. 2013;33.

96. Threlfall W. Retained Fetal Membranes. In: McKinnon AO SE, Valla WE, Varner DD, editor. Equine Reproduction. 2nd Edition: Blackwell Publishing LTD; 2011. p. 2520-9.

97. Provencher R, Threlfall WR, Murdick PW, Wearly WK. Retained fetal membranes in the mare: A retrospective study. Can Vet J. 1988;29(11):903-10.

98. Sevinga M, Barkema HW, Stryhn H, Hesselink JW. Retained placenta in Friesian mares: incidence, and potential risk factors with special emphasis on gestational length. Theriogenology. 2004;61(5):851-9.

99. Vandeplassche M, Spincemaille J, Bouters R. Aetiology, pathogenesis and treatment of retained placenta in the mare. Equine Vet J. 1971;3(4):144-7.

100. Pozor M. Equine placenta – A clinician's perspective. Part 1: Normal placenta – Physiology and evaluation. Equine Veterinary Education. 2015;28(6):327-34.

101. Pozor M. Equine placenta - A clinician's perspective. Part 2: Abnormalities. Equine Veterinary Education. 2016;28(7):396-404.

102. Brinsko SP. Common procedures in broodmare practice: what is the evidence? Vet Clin North Am Equine Pract. 2007;23(2):385-402.

103. Sevinga M, Barkema HW, Hesselink JW. Serum calcium and magnesium concentrations and the use of a calcium-magnesium-borogluconate solution in the treatment of Friesian mares with retained placenta. Theriogenology. 2002;57(2):941-7.

104. Burns SJ JN, Martin JE, et al, editor Management of retained placenta in mares. Am Assoc Equine Pract; 1977.

105. Samper JC PT, editor How to deal with dystocia and retained placenta in the field. Proceedings of the 58th annual convention of the AAEP; 2012; Anaheim CA.

106. Cuervo-Arango J, Newcombe J. The Effect of Manual Removal of Placenta Immediately after Foaling on Subsequent Fertility Parameters in the Mare. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2009;29:771-4.

107. Burden CA, Meijer M, Pozor MA, Macpherson ML. Fetal Membrane Removal in the Mare: Proactive Versus Reactive Approaches. Vet Clin North Am Equine Pract. 2019;35(2):289-98.

108. Rapacz-Leonard A, Paździor-Czapula K, Raś A, Tadeusz R, Janowski T. Retained Fetal Membranes in Heavy Draft Mares Associated with Histological Abnormalities. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2012;32.

109. Meijer MAJ, Macpherson ML, Dijkman R, editors. How to use umbilical vessel water infusion to treat retained fetal membranes in mares2015.

110. Warnakulasooriya DN, Marth CD, McLeod JA, Hanlon DW, Krekeler N. Treatment of Retained Fetal Membranes in the Mare-A Practitioner Survey. Front Vet Sci. 2018;5:128.

111. Frazer G. Post partum complications in the mare. Part 2: Fetal membrane retention and conditions of the gastrointestinal tract, bladder and vagina. Equine Veterinary Education. 2010;15:91-100.

112. Sevinga M, Hesselink JW, Barkema HW. Reproductive performance of Friesian mares after retained placenta and manual removal of the placenta. Theriogenology. 2002;57(2):923-30.

113. Malaluang P, Åkerholm T, Nyman G, Lindahl J, Hansson I, Morrell JM. Bacteria in the healthy equine vagina during the estrous cycle. Theriogenology. 2024;213:11-8.

114. LeBlanc MM. Common Peripartum Problems in the Mare. Journal of Equine Veterinary Science. 2008;28(11):709-15.

115. Papa FO, Melo CM, Monteiro GA, Papa PM, Guasti PN, Maziero RRD, et al. Equine Perineal and Vulvar Conformation Correction Using a Modification of Pouret's Technique. Journal of Equine Veterinary Science. 2014;34(3):459-64.

116. Newcombe JR. CHAPTER 2 - The Follicle: Practical Aspects of Follicle Control. In: Samper JC, Pycock JF, McKinnon AO, editors. Current Therapy in Equine Reproduction. Saint Louis: W.B. Saunders; 2007. p. 14-21.

117. Varner DD, Blanchard TL, Brinsko SP, Love CC, Taylor TS, Johnson L. Techniques for evaluating selected reproductive disorders of stallions. Animal reproduction science. 2000;60:493-509.

118. Hull BL, Vogel SR. Seminal Vesiculitis. Veterinary Clinics of North America: Food Animal Practice. 2008;24(2):267-72.

119. Scheeren VFC, Sancler-Silva YFR, El-Sheikh Ali H, Kastelic JP, Alvarenga MA, Papa FO. Update on Seminal Vesiculitis in Stallions. Journal of equine veterinary science. 2020;94:103234-.

120. Fennell LC, McKinnon AO, Savage CJ. Cryopreservation of semen from a stallion with seminal vesiculitis. Equine Veterinary Education. 2010;22(5):215-9.

121. Samper JC, Tibary A. Disease transmission in horses. Theriogenology. 2006;66(3):551-9.

122. Morrell JM, Rodriguez-Martinez H. Practical Applications of Sperm Selection Techniques as a Tool for Improving Reproductive Efficiency. Veterinary medicine international. 2010;2011:1-9.

123. Morrell JM, Geraghty RM. Effective removal of equine arteritis virus from stallion semen. Equine Veterinary Journal. 2006;38(3):224-9.

124. Morrell JM, Klein C, Lundeheim N, Erol E, Troedsson MHT. Removal of bacteria from stallion semen by colloid centrifugation. Animal reproduction science. 2014;145(1-2):47-53.

125. Sancler-Silva YFR, Monteiro GA, Ramires-Neto C, Freitas-Dell'aqua CP, Crespilho AM, Franco MMJ, et al. Does semen quality change after local treatment of seminal vesiculitis in stallions? Theriogenology. 2020;144:139-45.

Chapter 9: Vaginitis

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Key issues

1. Post-partum vaginitis associated with damage to the tissues during a dystocia may result in necrotic vaginitis, which may be life threatening or compromise future breeding.
2. Pneumo-vagina and associated urine pooling may be able to be prevented surgically.

There is a normal population of microflora in the vaginal mucosa in healthy mares (395). However, breaches in the defence mechanisms that protect the caudal reproductive tract in the mare may result in inflammation or infection of these tissues. There are two physical barriers, the vulval and the vestibulo-vaginal seal, in addition to the humoral mucosal immune defence system, which protects the vagina against these attacks (289). The vaginal mucosa is most vulnerable in the post-foaling mare, when inflammation of the caudal reproductive tract is a normal part of the puerperal period. Other predisposing factors may include dystocia, poor perineal/vulval conformation, insertion of an intravaginal device, or contagious equine metritis (CEM), resulting from the transmission of *Taylorella equigenitalis*, a disease currently exotic to Australia.

Post-foaling vaginitis may occur following the delivery of a large foal or a dystocia, which can cause vaginal contusions, haematomas or lacerations. Whilst the caudal reproductive tract of the mare usually has a rapid healing response in the puerperal period, extensive damage to the vaginal mucosa during delivery may result in abscess formation, necrotic vaginitis and subsequent stricture formation (396). Poor perineal and vulval conformation may result in aspiration of air and subsequent contamination of the reproductive tract. The resulting vaginitis may progress through the cervix, resulting in an endometritis, which may, in turn, affect the future fertility of the mare (397). These conformational changes are usually acquired following foaling trauma or age-related changes resulting in poor muscular tone of the perineal body and labia. Intravaginal devices, such as off-label use of progesterone releasing devices can initiate a localised vaginitis, which usually resolves within 24 h of removal (398). However, cases of severe necrotising vaginitis and perivaginal abscessation have been reported following insertion of CIDR-B devices into the mare, so these devices should be used with care (Clulow, pers comm).

The most common endemic pathogens associated with vaginitis are β-haemolytic streptococci or *E. coli* (396). In cases of severe contamination and necrotic vaginitis, other organisms, such as clostridia or Gram-negative anaerobes may also be involved.

Diagnostics

Diagnosis of vaginitis can be achieved via manual palpation and vaginoscopy using a vaginal speculum or video endoscope. A sample of the vaginal mucosa for culture can be obtained through a speculum using a double-guarded swab technique, taking care not to swab the vestibule. In the immediate post-partum period care should be taken to wear appropriate personal protective equipment, especially in areas where infection of horses with *Chlamydia psittaci* is endemic.

Vaginoscopy or manual palpation of the vagina should be performed as part of the routine post-partum examination of the mare. Identification of damaged tissues or excessive bruising/haematomas may prompt the clinician to closely monitor the area or initiate treatment to prevent necrotic vaginitis. Use of video endoscopy is useful to monitor progress and the response to treatment.

Treatment

Post-foaling vaginitis

Treatment of the vaginal mucosa can be effectively performed topically in most circumstances. If vaginal lacerations/bruising is noted in the post-partum examination, a topical broad spectrum antibacterial/anti-inflammatory cream can be applied to the area to promote healing and prevent formation of adhesions. Treatment should continue daily until the area appears to be healing appropriately – usually 3-5 days of treatment is sufficient. A vaginoscopic examination should be performed around 10 days post-partum to ensure there has been no adhesion formation.

Pneumo-vagina-associated vaginitis

Correction of the conformational defect should be addressed in these cases. A simple Caslick's operation may be the first surgical line of defence, followed by perineal body repair, urethral extension or uteropexy to correct the conformation and prevent further disease of the reproductive tract. If a profound vaginitis is present, culture and sensitivity testing should be performed to direct therapy.

Antimicrobials used

- Broad spectrum topical creams/ointments (e.g. Neocort®, Prednoderm®) applied to the area daily for 5-10 days
- In cases of severe vaginal trauma, broad spectrum antimicrobial therapy is recommended, with penicillin at 22,000 IU/kg (22 mg/kg) IM q 12 h and gentamicin at 6.6mg/kg IV q 24 h for 3-5 days or until clinical resolution is seen.

Prognosis

Post-partum vaginitis

Early identification of the severity of any severe vaginal trauma and appropriate treatment will help to improve prognosis. Severe vaginal trauma may lead to the formation of perivaginal haematomas or peritonitis, which can be life threatening. Careful examination of these mares in the post-partum period may help to identify lesions early and prevent overwhelming sepsis. Superficial vaginal lacerations usually heal within the first 3 days post-partum. However, more severe lacerations may require therapy for a longer duration to prevent formation of adhesions. A vaginoscopic examination can be performed 10 days post-partum and again at 30 days post-partum to ensure that vaginal adhesion formation has not occurred, and to enable adhesions to be broken down and treated.

Pneumovagina-associated vaginitis

The prognosis in these mares relies on the correction of the conformational defect. Whilst the vaginitis may be treated directly in these cases, the recurrence rate is high unless the inciting cause is addressed. A Caslick's operation may be sufficient to prevent aspiration of air and debris through the vulva and into the vagina. If the perineal body is weak, the mare is experiencing urine pooling or she has a pendulous uterus, further surgical intervention may be required. Repairing the structural integrity of the caudal reproductive tract by perineal body repair, urethral extension and uteropexy should prevent further episodes of pneumovagina-associated vaginitis. A uteropexy should not be considered a last resort technique in mares. Performing this surgery earlier in the mare's career may help to restore the normal position of the reproductive tract, thereby preventing both vaginitis and endometritis. This in turn may help to prolong the mare's reproductive life without ongoing reliance on antimicrobial treatment.

Section 16 – Immunisation

Contents

Chapter 1: Immunisation

Authors: Laura Hardefeldt, Gaby van Galen, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Vaccination can reduce the severity and frequency of disease, which is critical in improving welfare and reducing antimicrobial use.

The agents of disease against which vaccines are currently available for horses in Australia include *Clostridium tetani* (tetanus), *Streptococcus equi* subspecies *equi* (strangles), Hendra virus, equine herpesviruses 1 and 4, *Salmonella* spp. and rotaviruses.

Tetanus (*Clostridium tetani*)

Preventative vaccination.

Tetanus is caused by the anaerobic bacterium *Clostridium tetani*. The spores are found in soil, dust and animal faeces and survive in the environment for long periods, as they are highly resistant to heat and desiccation. Tetanus spores are introduced into the subcutaneous tissues or muscles by any penetrating wound, injections, surgical procedures, foot abscesses or erupting teeth. The key element is that the trauma causes tissue damage and results in anaerobic conditions suitable for germination of the spores and vegetative growth of *C. tetani*. The feet of horses are less well supplied with blood and are thus favoured places for instilled tetanus spores to germinate. *C. tetani* then produces a neurotoxin that results in spastic paralysis of the skeletal muscles, resulting in rigidity and spasm. The incubation period varies and is dependent on the time taken for germination and growth of the organism in the damaged tissue and for the ascent of the neurotoxin (tetanospasmin) from the wound to the central nervous system via the axons of motor and sensory fibres. Once clinical signs commence, the progression of disease is rapid. Tetanus has a high case-fatality rate in horses, which are the species most sensitive to the effects of tetanospasmin. Prophylactic vaccination with a toxoid vaccine, which induces production of antibody against tetanospasmin, is extremely effective. Protective responses are usually attained within 2 weeks of the second dose of the vaccine.

Post-exposure anti-toxin.

Administration of 1500 IU of tetanus antitoxin provides immediate protection and lasts for 2-3 weeks, with higher doses believed to provide longer lasting protection. Although rare, there is an association between administration of tetanus antitoxin and Theiler's disease (serum sickness, serum hepatitis) in horses, so vaccination should be advocated rather than relying on administration of antitoxin. Tetanus antitoxin administration can be combined with tetanus toxoid vaccination so long as injections are given at different sites (such as opposite sides of the neck).

Strangles (*Streptococcus equi* subspecies *equi*)

Detailed information about Strangles can be found elsewhere (Section 3, Chapter 6). Vaccination with currently available vaccines may reduce the severity of clinical signs but does not prevent disease.

Hendra Virus

Hendra virus is a highly pathogenic zoonotic virus causing disease with high mortality rates in people (57%) and horses (80%). Hendra virus first emerged in Australia in 1994 and is a notifiable disease in all states and territories of Australia. Horses generally have severe respiratory and/or neurological signs, but there are no pathognomonic clinical signs. The natural hosts of Hendra virus are the black flying fox, the grey headed flying fox, the spectacled flying fox and the little red flying fox. Horses are an amplifying host. Direct or indirect contact with flying fox urine is thought to be the main route of transmission from bats to horses. Infected horses can transmit the virus to other horses and humans via aerosols. Most outbreaks occur in the autumn and winter months and the disease has previously only been detected in Queensland and northeast NSW, but positive cases have now been found as far south as Newcastle. The natural range of bat species implicated as reservoirs of Hendra Virus is wide and climate change may result in disease in other parts of the country over time. The vaccine is protective while antibody titres remain above 64.

Equine Herpesviruses 1 and 4

Detailed information about Equine Herpesviruses 1 and 4 can be found elsewhere (Section 3). Vaccination reduces the clinical signs of respiratory disease caused by both EHV 1 and 4. The vaccine is also used as an aid in the control of abortion caused by EHV 1.

Salmonella Typhimurium

Detailed information about salmonellosis can be found in Section 6. A commercial vaccine is available to aid in the control of disease caused by *Salmonella* Typhimurium. The vaccine is only recommended for mares and foals and should not be administered to horses in training or to stallions. Research has shown that vaccination of mares results in increased *Salmonella*-specific antibody delivery to foals, but the impact of vaccination varies between farms and there is no information on the effect it has on clinical disease (399).

Rotaviruses

Detailed information about rotaviruses can be found in Sections 6 and 8. Vaccination of pregnant mares boosts colostral antibodies and may enhance protection of foals by increasing lactogenic immunity. Results from field vaccination studies have been equivocal, with some studies reporting a reduction in the incidence and severity of diarrhoea and the shedding of virus in faeces (400, 401), while another study found no significant reduction in the incidence of diarrhoea (402). However, as foals from vaccinated mares in all of these studies were still affected by rotavirus diarrhoea, at best these vaccines can only be considered partially protective.

Treatment

Figure 16.1 to 16.5 demonstrate the recommended vaccination protocols for foals, breeding mares, and adult horses in Australia, including recommendations for tetanus prophylaxis for wounds or surgery in foals and adult horses.

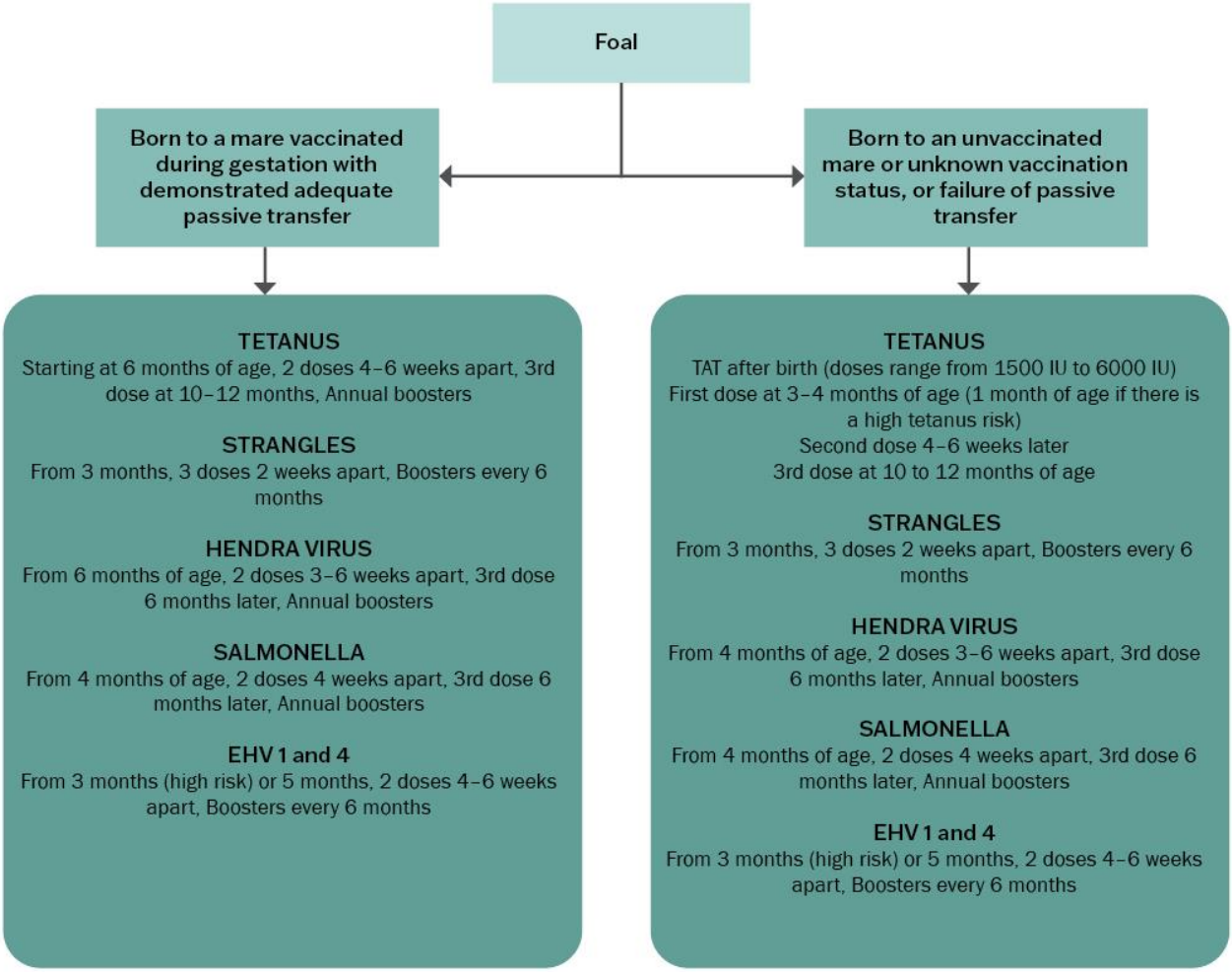

Figure 16.1. Immunisation protocol for foals.

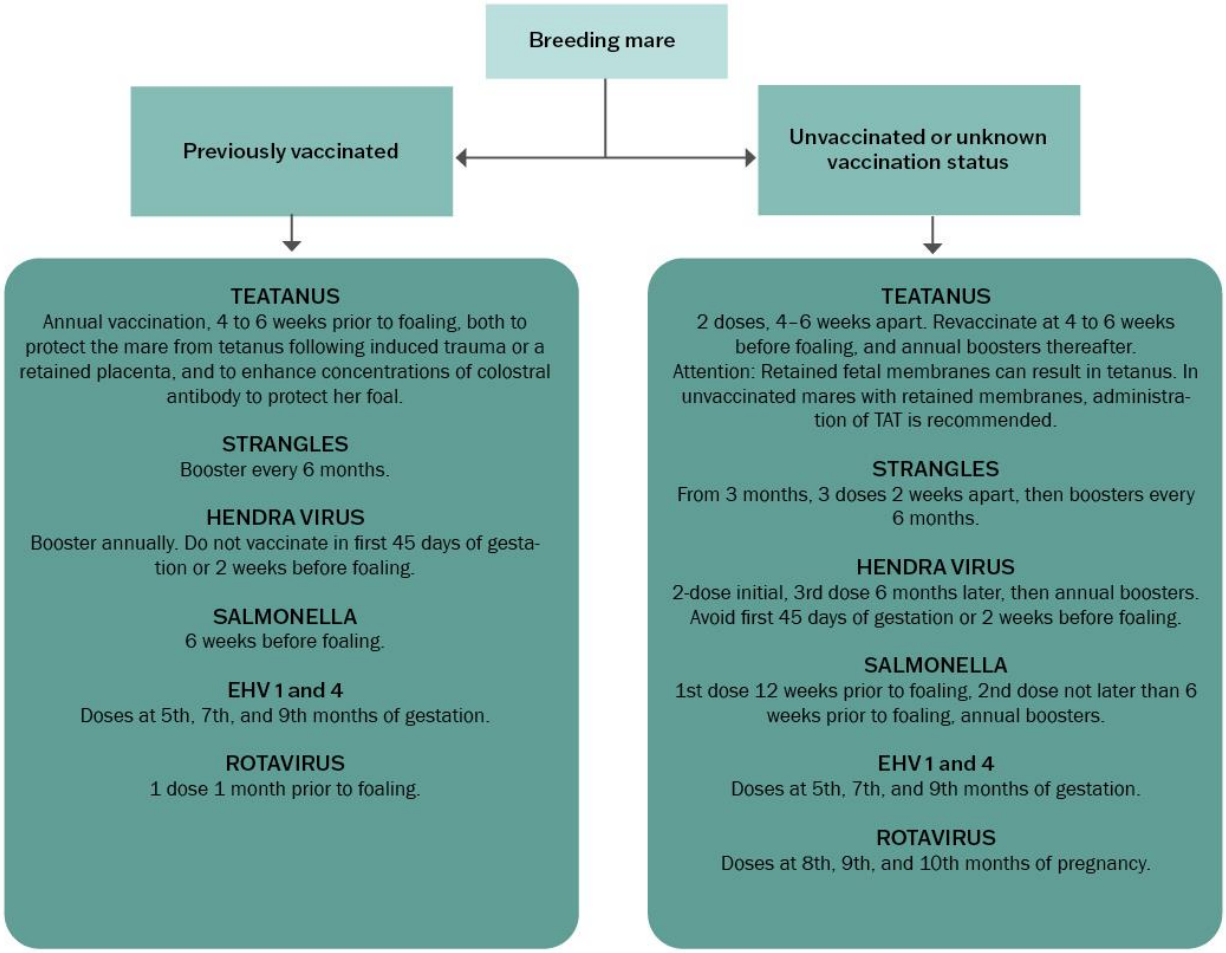

Figure 16.2. Immunisation protocol for breeding mare.

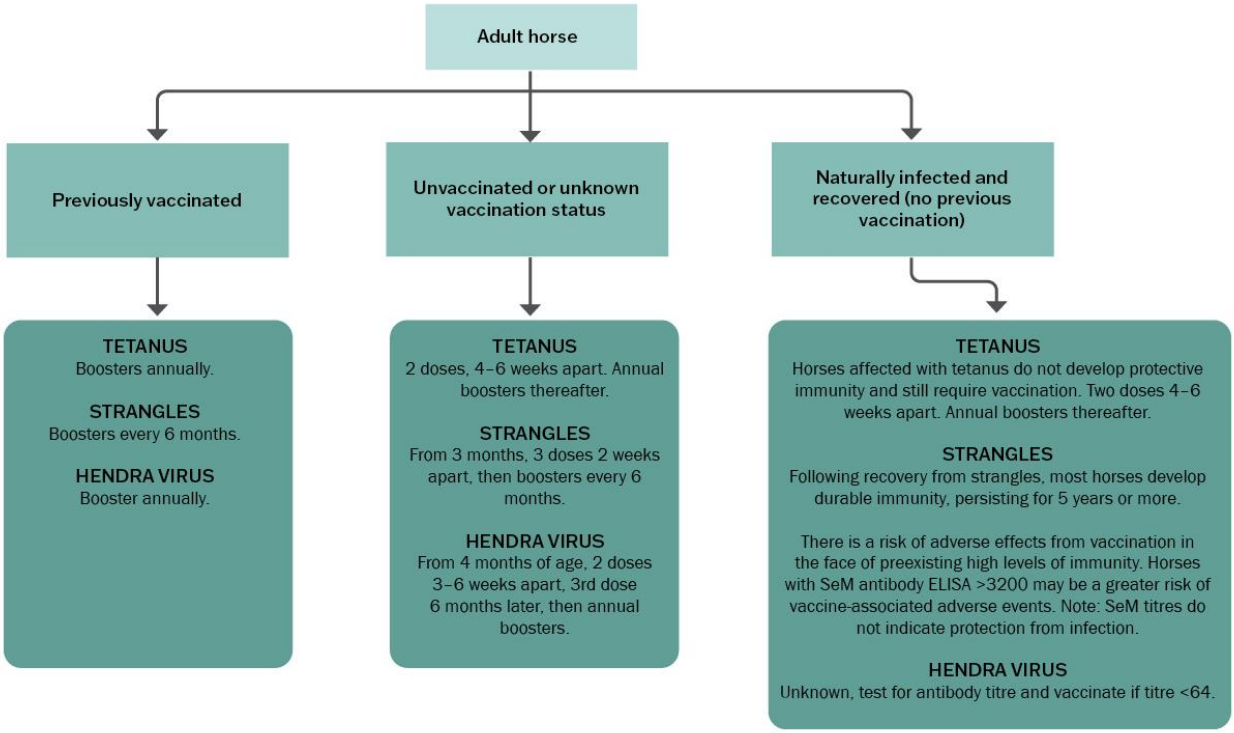

Figure 16.3. Vaccination protocol for adult horses.

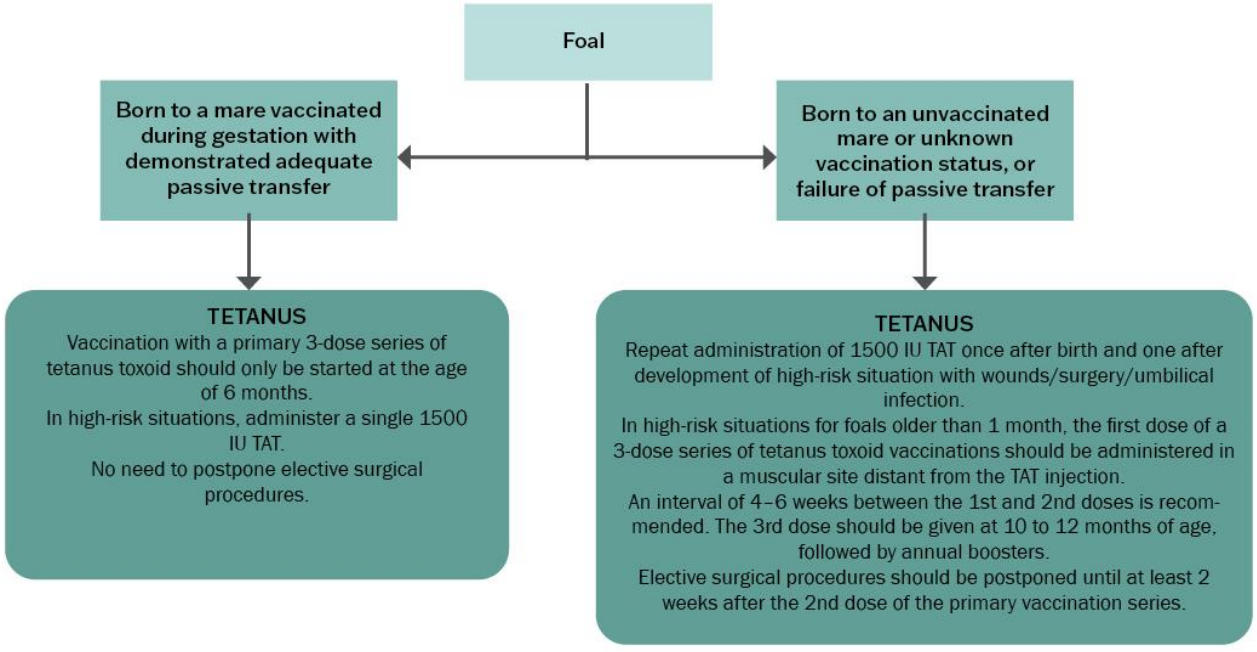

Figure 16.4. Tetanus prophylaxis for wounds or surgery in the foal.

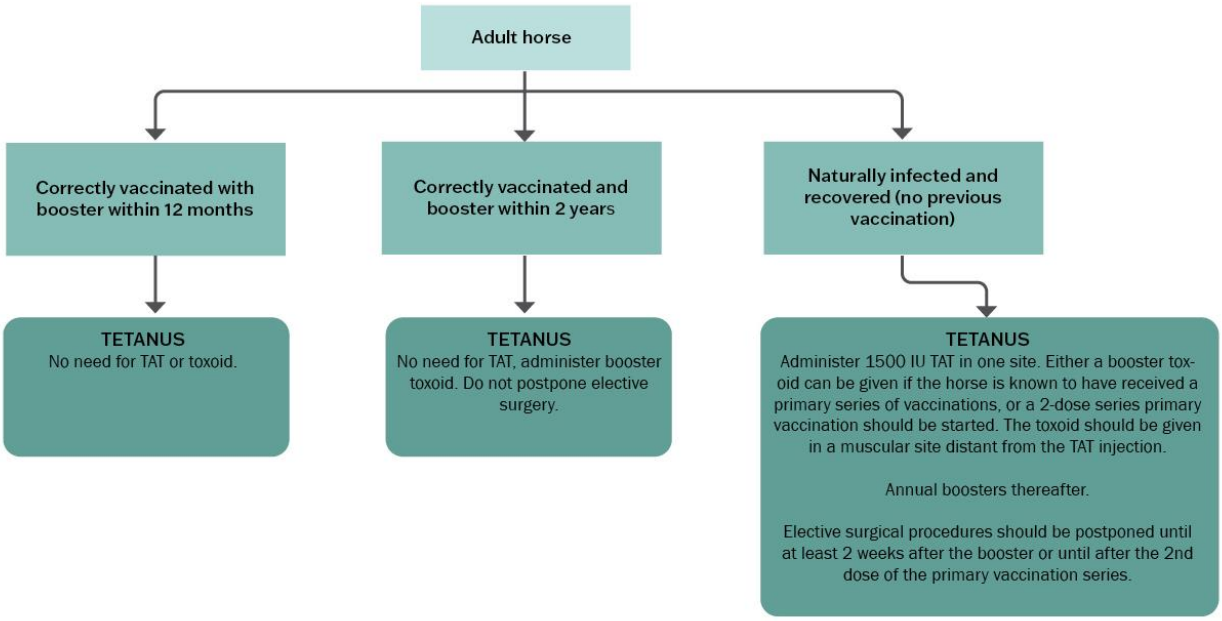

Figure 16.5. Tetanus prophylaxis for wounds or surgery in the adult horse.

Further reading

Wang X, Wise JC, Stewart AJ. Hendra Virus: An Update on Diagnosis, Vaccination, and Biosecurity Protocols for Horses. The Veterinary clinics of North America Equine practice. 2023;39(1):89-98.

Ramsauer AS, Badenhorst M, Cavalleri JMV. Equine parvovirus hepatitis. Equine veterinary journal. 2021;53(5):886-94.

Fortier C, El-Hage C, Hue E, Sutton G, Marcillaud-Pitel C, Jeffers K, et al. Hepatitis viruses: prevalence of equine parvovirus-hepatitis virus and equine hepacivirus in France and Australia. Equine Veterinary Journal. 2021;53(S56):68-.

Reference List

1. Bailey CS, Fallon L, Wang W, Borst L, Timoney J. Serum and Colostral Antibody Responses of Pregnant Mares to Salmonella Bacterins and Colostral Antibody Transfer to Their Foals. Journal of equine veterinary science. 2012;32(9):575-8.
2. Barrandeguy M, Parreño V, Lagos Mármol M, Pont Lezica F, Rivas C, Valle C, et al. Prevention of rotavirus diarrhoea in foals by parenteral vaccination of the mares: field trial. Dev Biol Stand. 1998;92:253-7.
3. Imagawa H, Kato T, Tsunemitsu H, Tanaka H, Sato S, Higuchi T. Field Study of Inactivated Equine Rotavirus Vaccine. Journal of Equine Science. 2005;16(2):35-44.
4. Powell DG, Dwyer RM, Traub-Dargatz JL, Fulker RH, Whalen JW, Srinivasappa J, et al. Field study of the safety, immunogenicity, and efficacy of an inactivated equine rotavirus vaccine. Journal of the American Veterinary Medical Association. 1997;211(2):193-8.

Section 17 – Other

Contents

Chapter 1: Bacterial meningitis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. High case fatality rate.
2. Many potential underlying causes, which will determine the likely pathogens.

Meningitis is inflammation of the meninges of the brain and spinal cord. The aetiology may be infectious or non-infectious. In horses, meningitis typically has an infectious aetiology. Organisms can invade the central nervous system (CNS) via traumatic injury, ascending infection, haematogenous spread (particularly in septic foals) or iatrogenic routes. Ascending infections can originate from the eyes, oral cavity, nasal passages, sinuses or osteomyelitis of the cranial bones or vertebrae. Inflammation of the meninges may lead to increased permeability of the blood-brain barrier, vasculitis, and central nervous system oedema.

Bacterial meningitis and meningoencephalitis are uncommon diseases of horses. They generally have high case fatality rates. Horses are particularly difficult to treat because of their large size and the challenge and hazards associated with nursing care.

Diagnostics

Neurological deficits are common, with changes to mentation, ataxia, recumbency or other gait abnormalities seen in most cases. Cranial nerve deficits are also very commonly detected, with head tilt (cranial nerve VIII), nystagmus (cranial nerve VIII) and strabismus (multiple cranial nerves) most common, followed by an absent menace response (cranial nerve VII), absence of pupillary light response (cranial nerve II and/or III) and facial nerve paralysis (cranial nerve VII).

Fever, tachycardia and tachypnoea may or may not be present. Haematological analysis commonly reveals changes in leukocytes (either leukocytosis or leukopaenia). Cerebrospinal fluid (CSF) sample collection, from the site closest to the lesion (usually the atlanto-occipital cistern), is essential for making a diagnosis and CSF is generally grossly abnormal, with a cloudy or serosanguinous appearance most common. Cytology of CSF reveals moderate to marked suppurative inflammation. Intra or extracellular bacteria are only seen in a third of cases. Culture should be pursued, but is frequently unsuccessful, even in cases where bacteria are seen on cytology. Many different pathogens have been isolated from cases, reflecting the wide range of predisposing causes.

Imaging should be undertaken in cases of suspected trauma. Computed tomography (CT) or magnetic resonance imaging may be necessary to detect fractures but are not widely available.

Treatment

Intravenous fluid support, anti-inflammatory drugs, sedatives and intensive nursing care are of critical importance.

Broad spectrum antimicrobials are indicated and, although the blood-brain barrier is probably disrupted, antimicrobials that penetrate the blood-brain barrier should be prioritised. Trimethoprim/sulphadiazine or oxytetracycline are good empirical choices. Penicillin, gentamicin and ceftiofur have poor penetration.

Antimicrobials used

- Trimethoprim/sulphadiazine at 30 mg/kg IV q 12 h
- OR oxytetracycline at 6.6 mg/kg IV q 12 h
- Benzyl penicillin at 12-16 mg/kg IV q 6 h and gentamicin at 6.6 mg/kg IV q 24 h can be used but blood-brain-barrier penetration is poor.

There is no information available to guide the duration of treatment because of the poor clinical outcomes in most cases.

Prognosis

Poor to grave, even with aggressive treatment. There are few clinical reports of successful treatment.

Further reading

Toth B, Aleman M, Nogradi N, Madigan JE. Meningitis and meningoencephalomyelitis in horses: 28 cases (1985-2010). Journal of the American Veterinary Medical Association. 2012;240(5):580-7. (403)

Viu J, Monreal L, Jose-Cunilleras E, Cesarini C, AÑOr S, Armengou L. Clinical findings in 10 foals with bacterial meningoencephalitis. Equine veterinary journal. 2012;44(s41):100-4. (404)

Bach FS, Bodo G, Kuemmerle JM, Bienert-Zeit A, Hainisch EK, Simhofer H. Bacterial Meningitis After Sinus Surgery in Five Adult Horses. Veterinary surgery. 2014;43(6):697-703. (129)

Chapter 2: Otitis media, otitis interna and temporohyoid osteoarthropathy

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. Definitive diagnosis of otitis media/interna is difficult, and temporohyoid osteoarthropathy is generally diagnosed with a presumption of otitis media/interna.
2. Thickening of the proximal stylohyoid bone can be visualised within the guttural pouch.

Otitis media refers to inflammation of the middle ear or tympanic cavity, which contains the three small ossicles. Otitis interna results in inflammation of the inner ear and bony labyrinth, where the cochlear (auditory) and vestibular nerves are located. The pathogenesis is unknown, but haematogenous spread of bacteria, ascending infection from the respiratory tract, extension of otitis externa or extension of guttural pouch infection may be responsible for disease.

Lesions in the area of the petrous part of the temporal bone, tympanic bulla and hyoid apparatus can result in clinical signs of otitis media/interna in horses.

Inflammation may result in osseous proliferation and thickening of the temporohyoid joint, resulting in fusion – known as temporohyoid osteoarthropathy (THO). It is unknown whether THO is a primary osteoarthropathy or occurs secondary to inner ear infection. Many, including these authors, do not believe that otitis media/interna is a frequent underlying pathology in THO.

Diagnostics

Clinical signs of otitis media/interna result in deficits attributable to the facial and vestibulocochlear nerves (cranial nerves VII and VIII) and can include a head tilt, nystagmus, falling, circling, ataxia (worsened with blindfolding), muzzle deviation, decreased lacrimation, ear paresis, corneal ulceration, loss of the blink reflex and depression. The head tilt is towards the side of the lesion and animals tend to circle towards the lesion or lie on the side of the lesion.

Diagnosis is made based on clinical signs, radiographic findings, endoscopic examination of the guttural pouch, computed tomography and the results of tympanocentesis. Haematology is generally unremarkable, and horses are rarely febrile.

Radiographs reveal enlargement of the proximal portion of the stylohyoid bone and sclerosis of the petrous part of the temporal bone. Endoscopic examination may be more sensitive than radiography, as enlargement of the proximal stylohyoid bone can be observed.

Tympanocentesis is technically difficult because of the long ear canal of the horse. General anaesthesia is required and may be difficult to justify in an ataxic horse. Without tympanocentesis, only a diagnosis of THO can be made. However, this procedure is not undertaken in most cases and thus in a diagnosis of THO otitis media/interna is often presumed to be the primary disease.

Although clinical signs are generally unilateral, bilateral disease is common.

Treatment

Surgical management of temporohyoid osteoarthropathy has been shown to improve survival compared to medical treatment only and there are a range of techniques now reported in the literature. Surgery is aimed at reducing the load on the temporohyoid articulation with the goal of reducing pain and preventing fracture or refracture of the petrous temporal bone. The surgical procedures are specialised and should be performed by suitably trained specialists.

In cases where bacterial otitis media/interna is suspected or confirmed, antimicrobial therapy with agents with high volumes of distribution should be selected to maximise penetration. Trimethoprim/sulphadiazine and chloramphenicol are examples of lipophilic antimicrobials with high volumes of distribution. Given the potential human complications with chloramphenicol exposure, trimethoprim/suphadiazine is the most frequently used antimicrobial.

Antimicrobials used

- Trimethoprim/ suphadiazine at 30 mg/kg PO q 12 h
- OR chloramphenicol at 100 mg/kg PO q 6 h

There is no evidence to support a specific duration of treatment, but 7 days is a reasonable first course.

Prognosis

Guarded. In a retrospective study of 33 medically treated cases, most horses had residual cranial nerve deficits and maximal improvement took one year or longer. In a study of 24 surgically managed cases, nearly 90% substantially improved within one year, with most improvement occurring within six months, but only 50% of cases returned to athletic performance.

Reference List

Maher O, MacDonald M, Aleman M. Surgical management of temporohyoid osteoarthropathy: 24 cases (1993-2008). Proc Amer Assoc Equine Pract. 2008;54:44-5. (405)

Walker AM, Sellon DC, Comelisse CJ, Hines MT, Ragle CA, Cohen N, et al. Temporohyoid Osteoarthropathy in 33 Horses (1993-2000). Journal of veterinary internal medicine. 2002;16(6):697-703. (406)

Koch C, Witte T. Temporohyoid osteoarthropathy in the horse. Equine veterinary education. 2014;26(3):121-5. (407)

Chapter 3: Vertebral body osteomyelitis

Authors: Laura Hardefeldt, Kellie Thomas, Stephen Page, Jacqui Norris, Glenn Browning, Leanne Begg

Key issues

1. A rare but life-threatening condition, predominately seen in foals.
2. A range of pathogens have been associated with the disease, but *R. equi* is over-represented in 2 - 8 month old foals, especially those with active rhodococcal pneumonia.

Vertebral body osteomyelitis is a rare but life-threatening condition in horses. The disease is thought to result from haematogenous spread of a pathogen in most cases, although trauma with subsequent bony infection can also occur. Foals are most commonly affected, but disease has been reported in adult horses, likely with a primary immunocompromising disease. The cervical and lumbar regions of the spinal column are the regions most commonly affected.

A number of different pathogens have been reported, but *Rhodococcus equi* appears to be over-represented in foals. Other pathogens include *E. coli*, *Salmonella* spp., *Actinobacillus* spp., *Streptococcus* spp. and others.

Diagnostics

Clinical signs include acute onset of pain or stiffness, sometimes ill-thrift, and neurological evidence of focal spinal cord compression with para- or tetra-paresis. Heat and pain may be detectable over the affected area, particularly if the cervical vertebrae are affected.

Radiographic signs of vertebral body osteomyelitis consist of proliferative new bone formation, demineralisation, sclerosis, soft tissue swelling and compression fractures. Radiographic changes may not be seen until 2 - 8 weeks after the onset of clinical signs. Advanced diagnostic imaging with computed tomography is useful but is not available in most areas of Australia. Thoracic radiographs should also be taken in 2 – 6-month-old foals, as radiographic evidence of pneumonia would support a diagnosis of *R. equi* osteomyelitis, but cases have been reported in the absence of lung lesions (see more on *R. equi* in Chapter 4).

Haematological changes are consistent with inflammation but are not specific for the disease.

Isolation of the organism in blood or urine can be attempted in cases where treatment is being pursued. Fine needle aspirates of the affected area can be submitted for cytology and culture.

Treatment

Medical therapy alone is unlikely to be successful. If attempted, blood and urine cultures should be used to guide therapy when positive. A sample of fluid obtained by fine needle aspiration of the affected area can also be submitted for culture. Where empirical antimicrobial therapy is necessary, selection should be appropriate for *R. equi* in foals in the at-risk age group (clarithromycin at 7.5 mg/kg PO q 12 h PLUS rifampicin at 5 mg/kg PO q 12 h). It is important to note that this combination does not have any Gram-negative coverage, and the addition of gentamicin is probably warranted.

In cases where *R. equi* is not suspected, broad-spectrum therapy with penicillin (procaine penicillin at 22,000 IU/kg IM q 12 h or benzyl penicillin at 12-16 mg/kg IV q 6 h) and gentamicin (6.6 mg/kg IV q 24 h for animals aged > 2 weeks) is suitable.

Surgical debridement of the lesion is probably necessary but increases the risk of fracture or collapse of the affected vertebrae. Stabilisation of the area is probably necessary and requires specialist surgical knowledge. Culture of the debrided material should guide antimicrobial therapy.

Nursing care is critical and typically needs to be intensive.

Antimicrobials used

- 2 - 8 month-old foals with suspected or confirmed *R. equi* disease:
    - clarithromycin at 7.5 mg/kg PO q 12 h PLUS rifampicin at 5 mg/kg PO q 12 h +/- gentamicin at 6.6 mg/kg IV q 24 h.

- In cases where *R. equi* is not suspected:

    - procaine penicillin at 22,000 IU/kg IM q 12 h or benzyl penicillin at 12-16 mg/kg IV q 6 h PLUS gentamicin at 6.6 mg/kg IV q 24 h for animals aged > 2 weeks, or 11 mg/kg IV q 36 h for foals < 2 weeks old.

Duration of therapy is unknown, but several weeks of therapy is likely necessary.

Prognosis

Grave. Successful treatment of one foal has been reported with an aggressive surgical technique.

Further reading

Lischer CJ. Successful treatment of vertebral body osteomyelitis in a foal: A highlight in equine surgery. Equine veterinary education. 2009;21(2):76-8. (408)

Crabtree JR, Jorgensen A. Cervical Vertebral Osteomyelitis With Secondary Septic Arthritis of the Atlantoaxial Joint in a Foal: A Case Report. Journal of equine veterinary science. 2012;32(9):599-606. (409)

Hu AJ, Grant B, Cannon J. Cervical vertebral osteomyelitis in a 4-month-old foal. Oxford, UK: Blackwell Publishing Ltd; 2009. Report No.: 0957-7734. (410)

Reference List

1. Southwood LL. Surgical antimicrobial prophylaxis: Current standards of care. Equine veterinary education. 2023;35(11):607-16.
2. Australian Commission on Safety and Quality in Health Care. Approaches to Surgical Site Infection Surveillance. Sydney: ACSQHC; 2017.
3. Uboh CE, Soma LR, Luo Y, McNamara E, Fennell MA, May L, et al. Pharmacokinetics of penicillin G procaine versus penicillin G potassium and procaine hydrochloride in horses. Am J Vet Res. 2000;61(7):811-5.
4. Hubbell JA, Muir WW, Robertson JT, Sams RA. Cardiovascular effects of intravenous sodium penicillin, sodium cefazolin, and sodium citrate in awake and anesthetized horses. Vet Surg. 1987;16(3):245-50.
5. Henderson ARP, Valverde A, Marchiori J, Tisotti T, Torrent A, Côté N, et al. Effect of rapid and slow intravenous injection of sodium penicillin on arterial blood pressure in isoflurane-anesthetized horses during surgery. Vet Anaesth Analg. 2025;52(2):200-7.
6. Busk P, Jacobsen S, Martinussen T. Administration of perioperative penicillin reduces postoperative serum amyloid A response in horses being castrated standing. Vet Surg. 2010;39(5):638-43.
7. Kilcoyne I, Watson JL, Kass PH, Spier SJ. Incidence, management, and outcome of complications of castration in equids: 324 cases (1998-2008). JAVMA. 2013;242(6):820-5.
8. Weese JS, Cruz A. Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital. Can Vet J. 2009;50:185-8.
9. Borg H, Carmalt JL. Postoperative septic arthritis after elective equine arthroscopy without antimicrobial prophylaxis. Vet Surg. 2013;42(3):262-6.
10. Desmaizières L-M, Martinot S, Lepage OM, Bareiss E, Cadoré J-L. Complications associated with cannula insertion techniques used for laparoscopy in standing horses. Veterinary Surgery. 2003;32(6):501-6.
11. Röcken M, Mosel G, Seyrek-Intas K, Seyrek-Intas D, Litzke F, Verver J, et al. Unilateral and bilateral laparoscopic ovariectomy in 157 mares: a retrospective multicenter study. Vet Surg. 2011;40(8):1009-14.

12. Mayhew PD, Freeman L, Kwan T, Brown DC. Comparison of surgical site infection rates in clean and clean-contaminated wounds in dogs and cats after minimally invasive versus open surgery: 179 cases (2007-2008). JAVMA. 2012;240(2):193-8.
13. Eugster S, Schawalder P, Gaschen F, Boerlin P. A prospective study of postoperative surgical site infections in dogs and cats. Vet Surg. 2004;33(5):542-50.
14. Maxson AD, Reef VB. Bacterial endocarditis in horses: ten cases (1984-1995). Equine veterinary journal. 1997;29(5):394-9.
15. Henderson B, Diaz M, Martins C, Kenney D, Baird JD, Arroyo LG. Valvular endocarditis in the horse: 20 cases (1993-2020). Canadian veterinary journal. 2020;61(12):1290-4.
16. Ewart S, Brown C, Derksen F, Kufuor-Mensa E. Serratia marcescens endocarditis in a horse. Journal of the American Veterinary Medical Association. 1992;200(7):961-3.
17. Buergelt CD, Cooley AJ, Hines SA, Pipers FS. Endocarditis in six horses. Veterinary pathology. 1985;22(4):333-7.
18. Nath LC, Anderson GA, Hinchcliff KW, Savage CJ. Serum cardiac troponin I concentrations in horses with cardiac disease. Australian veterinary journal. 2012;90(9):351-7.
19. Cawdell-Smith AJ, Todhunter KH, Perkins NR, Bryden WL. Exposure of mares to processionary caterpillars (Ochrogaster lunifer) in early pregnancy: An additional dimension to equine amnionitis and fetal loss. Equine veterinary journal. 2013;45(6):755-60.
20. Reimer J. Management of equine pericarditis. Equine veterinary education. 2013;25(7):334-8.
21. Sprayberry KA, Slovis NM. Sales performance and athletic outcome in young Thoroughbreds with pericarditis. Equine veterinary journal. 2017;49(6):729-33.
22. Pusterla N, Watson JL, Affolter VK, Magdesian KG, Wilson WD, Carlson GP. Purpura haemorrhagica in 53 horses. Veterinary record. 2003;153(4):118-21.
23. Waller AS, Sellon DC, Sweeney CR, Timoney PJ, Newton JR, Hines MT. Streptococcal Infections. In: Sellon DC, Long MT, editors. Equine Infectious Diseases. St Louis: Elsevier Saunders; 2013. p. 265-e4.
24. Müller CDVS, Lübke-Becker A, Doherr MG, Gehlen H. Influence of Different Types of Catheters on the Development of Diseases of the Jugular Vein in 45 Horses. Journal of equine veterinary science. 2016;46:89-97.
25. Russell TM, Kearney C, Pollock PJ. Surgical Treatment of Septic Jugular Thrombophlebitis in Nine Horses. Veterinary surgery. 2010;39(5):627-30.
26. Divers TJ. Prevention and treatment of thrombosis, phlebitis, and laminitis in horses with gastrointestinal diseases. The Veterinary clinics of North America Equine practice. 2003;19(3):779-90.
27. Knottenbelt DC. Vasculitis: just what does it mean? Equine veterinary education. 2002;14(5):247-51.
28. Wilson ME, Holz CL, Kopec AK, Dau JJ, Luyendyk JP, Soboll Hussey G. Coagulation parameters following equine herpesvirus type 1 infection in horses. Equine veterinary journal. 2019;51(1):102-7.
29. Johnston GCA, Lumsden JM. Antimicrobial susceptibility of bacterial isolates from 33 thoroughbred horses with arytenoid chondropathy (2005-2019). Veterinary surgery. 2020;49(7):1283-91.
30. Pujol R, Tessier C, Manneveau G, De Fourmestraux C. Suspected primary mycotic rhinitis and paranasal sinusitis in seven horses (2013–2019). Equine veterinary education. 2021;33(8):401-.
31. Watt DA. A Case of cryptococcal granuloma in the nasal cavity of a horse. Australian veterinary journal. 1970;46(10):493-4.
32. Roberts MC, Sutton RH, Lovell DK. A protracted case of cryptococcal nasal granuloma in a stallion Australian veterinary journal. 1981;57(6):287-91.
33. Lean NE, Ahern BJ. Antifungal non-invasive soak under general anaesthetic to treat fungal rhinitis in an Australian Quarter Horse gelding at pasture. Australian veterinary journal. 2018;96(8):297-301.
34. Davis EW, Legendre AM. Successful Treatment of Guttural Pouch Mycosis With Itraconazole and Topical Enilconazole in a Horse. Journal of Veterinary Internal Medicine. 1994;8(4):304-5.
35. Ludwig A, Gatineau S, Reynaud MC, Cadoré JL, Bourdoiseau G. Fungal isolation and identification in 21 cases of guttural pouch mycosis in horses (1998–2002). The veterinary journal (1997). 2005;169(3):457-61.
36. Watkins AR, Parente EJ. Salpingopharyngeal fistula as a treatment for guttural pouch mycosis in seven horses. Equine veterinary journal. 2018;50(6):781-6.
37. Jukic CC, Cowling NR, Perkins NR, Eps AW, Ahern BJ. Evaluation of the effect of laser salpingopharyngostomy on the guttural pouch environment in horses. Equine veterinary journal. 2020;52(5):752-9.
38. Kendall A, Bröjer J, Karlstam E, Pringle J. Enilconazole Treatment of Horses with Superficial Aspergillus Spp. Rhinitis. Journal of Veterinary Internal Medicine. 2008;22(5):1239-42.
39. Stewart AJ. Diagnosis and treatment of cryptococcal infections in horses. Equine Veterinary Education. 2020;32(11):576-9.

40. Stewart AJ. Conidiobolus coronatus fungal upper respiratory infections in horses. Equine veterinary education. 2019;31(6):301-2.
41. Sellon DC, Long MT, Eds. Equine Infectious Diseases. 2nd ed. St Louis: Elsevier Saunders; 2013.
42. Gilkerson JR, Bailey KE, Diaz-Méndez A, Hartley CA. Update on Viral Diseases of the Equine Respiratory Tract. The Veterinary clinics of North America Equine practice. 2015;31(1):91-104.
43. Kydd JH, Lunn DP, Osterrieder K. Report of the Fourth International Havemeyer Workshop on Equid Herpesviruses (EHV) EHV-1, EHV-2 and EHV-5. Equine veterinary journal. 2019;51(5):565-8.
44. Gibson JS, Slater JD, Awan AR, Field HJ. Pathogenesis of equine herpesvirus-1 in specific pathogen-free foals: primary and secondary infections and reactivation. Arch Virol. 1992;123(3-4):351-66.
45. Gilkerson J, Jorm LR, Love DN, Lawrence GL, Millar Whalley J. Epidemiological investigation of equid herpesvirus-4 (EHV-4) excretion assessed by nasal swabs taken from thoroughbred foals. Veterinary microbiology. 1994;39(3):275-83.
46. Diaz-Mendez A, Viel L, Hewson J, Doig P, Carman S, Chambers T, et al. Surveillance of equine respiratory viruses in Ontario. Canadian journal of veterinary research. 2010;74(4):271-8.
47. Black WD, Wilcox RS, Stevenson RA, Hartley CA, Ficorilli NP, Gilkerson JR, et al. Prevalence of serum neutralising antibody to equine rhinitis A virus (ERAV), equine rhinitis B virus 1 (ERBV1) and ERBV2. Veterinary microbiology. 2007;119(1):65-71.
48. Hallowell KL, Hepworth-Warren KL, Dembek K. An updated description of bacterial pneumonia in adult horses and factors associated with death. Journal of veterinary internal medicine. 2024;38(5):2766-75.
49. Tomlinson JE, Reef VB, Boston RC, Johnson AL. Association of Fibrinous Pleural Effusion with Survival and Complications in Horses with Pleuropneumonia (2002–2012): 74 Cases. Journal of veterinary internal medicine. 2015;29(5):1410-7.
50. Raidal SL, Love DN, Bailey GD. Inflammation and increased numbers of bacteria in the lower respiratory tract of horses within 6 to 12 hours of confinement with the head elevated. Australian veterinary journal. 1995;72(2):45-50.
51. Racklyeft DJ, Love DN. Bacterial infection of the lower respiratory tract in 34 horses. Australian veterinary journal. 2000;78(8):549-59.
52. Raidal SL, Taplin RH, Bailey GD, Love DN. Antibiotic prophylaxis of lower respiratory tract contamination in horses confined with head elevation for 24 or 48 hours. Australian veterinary journal. 1997;75(2):126-31.
53. Muscatello G. Rhodococcus equi pneumonia in the foal – Part 1: Pathogenesis and epidemiology. The veterinary journal (1997). 2012;192(1):20-6.
54. Sanz M, Loynachan A, Sun L, Oliveira A, Breheny P, Horohov DW. The effect of bacterial dose and foal age at challenge on Rhodococcus equi infection. Veterinary microbiology. 2013;167(3-4):623-31.
55. Fenton CS, Buckley TC. Minimum inhibitory concentrations of erythromycin and rifampin for Rhodococcus equi during the years 2007-2014. IRISH VETERINARY JOURNAL. 2015;68(1):23-.
56. Fines M, Pronost S, Maillard K, Taouji S, Leclercq R. Characterization of mutations in the rpoB gene associated with rifampin resistance in Rhodococcus equi isolated from foals. Journal of clinical microbiology. 2001;39(8):2784-7.
57. Takai S, Takeda T, Nakano Y, Karasawa T, Furugoori J, Sasaki Y, et al. Emergence of rifampin-resistant Rhodococcus equi in an infected foal. Journal of Clinical Microbiology. 1997;35(7):1904-8.
58. Burton AJ, Giguere S, Sturgill TL, Berghaus LJ, Slovis NM, Whitman JL, et al. Macrolide- and rifampin-resistant rhodococcus equi on a horse breeding farm, Kentucky, USA. Emerging infectious diseases. 2013;19(2):282-5.
59. Huber L, Giguère S, Slovis NM, Carter CN, Barr BS, Cohen ND, et al. Emergence of Resistance to Macrolides and Rifampin in Clinical Isolates of Rhodococcus equi from Foals in Central Kentucky, 1995 to 2017. Antimicrob Agents Chemother. 2018;63(1).
60. Asoh N, Watanabe H, Tharavichitkul P, Sirisanthana T, Nagatake T, Fines-Guyon M, et al. Emergence of Rifampin-Resistant Rhodococcus equi with Several Types of Mutations in the rpoB Gene among AIDS Patients in Northern Thailand. Journal of Clinical Microbiology. 2003;41(6):2337-40.
61. Huber L, Giguère S, Cohen ND, Slovis NM, Hanafi A, Schuckert A, et al. Prevalence and risk factors associated with emergence of Rhodococcus equi resistance to macrolides and rifampicin in horse-breeding farms in Kentucky, USA. Veterinary microbiology. 2019;235:243-7.
62. Giguère S, Lee E, Williams E, Cohen ND, Chaffin MK, Halbert N, et al. Determination of the prevalence of antimicrobial resistance to macrolide antimicrobials or rifampin in Rhodococcus equi isolates and treatment outcome in foals infected with antimicrobial-resistant isolates of R equi. Journal of the American Veterinary Medical Association. 2010;237(1):74-81.
63. Val-Calvo J, Darcy J, Gibbons J, Creighton A, Egan C, Buckley T, et al. International Spread of Multidrug- Resistant Rhodococcus equi. Emerging infectious diseases. 2022;28(9):1899-903.

64. Riviere JE, Papich MG. Veterinary pharmacology and therapeutics. Tenth edition. ed. Hoboken, NJ: John Wiley & Sons Inc.; 2018.
65. Huber L, Giguère S, Hart KA, Slovis NM, Greiter ME, Dailey CA, et al. Association between antimicrobial treatment of subclinical pneumonia in foals and selection of macrolide- And rifampicin-resistant Rhodococcus equi strains at horse-breeding farms in central Kentucky. Journal of the American Veterinary Medical Association. 2021;258(6):648-53.
66. Sanz MG. Rhodococcus equi–What is New This Decade? The Veterinary clinics of North America Equine practice. 2023;39(1):1-14.
67. Muscatello G. Rhodococcus equi pneumonia in the foal – Part 2: Diagnostics, treatment and disease management. The veterinary journal (1997). 2012;192(1):27-33.
68. Ramirez S, Lester GD, Roberts GR. Diagnostic contribution of thoracic ultrasonography in 17 foals with Rhodococcus equi pneumonia. Veterinary radiology & ultrasound. 2004;45(2):172-6.
69. McCranken JL, Slovis NM, editors. Use of thoracic ultrasound for the prevention of Rhodococcus equi pneumonia on endemic farms. American Association of Equine Practitioners Annual Conference; 2009; Las Vegas, Nevada.
70. Venner M, Astheimer K, Lämmer M, Giguère S. Efficacy of Mass Antimicrobial Treatment of Foals with Subclinical Pulmonary Abscesses Associated with Rhodococcus equi. Journal of veterinary internal medicine. 2013;27(1):171-6.
71. Arnold-Lehna D, Venner M, Berghaus LJ, Berghaus R, Giguère S. Changing policy to treat foals with Rhodococcus equi pneumonia in the later course of disease decreases antimicrobial usage without increasing mortality rate. Equine veterinary journal. 2020;52(4):531-7.
72. Hillidge CJ. Use of erythromycin-rifampin combination in treatment of Rhodococcus equi pneumonia. Veterinary microbiology. 1987;14(3):337-42.
73. Jacks S, Giguere S, Gronwall RR, Brown MP, Merritt KA. Pharmacokinetics of azithromycin and concentration in body fluids and bronchoalveolar cells in foals. American journal of veterinary research. 2001;62(12):1870-5.
74. Womble AY, Giguère S, Lee EA, Vickroy TW. Pharmacokinetics of clarithromycin and concentrations in body fluids and bronchoalveolar cells of foals. American journal of veterinary research. 2006;67(10):1681-6.
75. Suarez-Mier G, GiguÈRe S, Lee EA. Pulmonary disposition of erythromycin, azithromycin, and clarithromycin in foals. Journal of veterinary pharmacology and therapeutics. 2007;30(2):109-15.
76. Wetzig M, Venner M, Giguère S. Efficacy of the combination of doxycycline and azithromycin for the treatment of foals with mild to moderate bronchopneumonia. Equine veterinary journal. 2020;52(4):613-9.
77. Giguère S, Berghaus LJ, Lee EA. Activity of 10 antimicrobial agents against intracellular Rhodococcus equi. Veterinary microbiology. 2015;178(3-4):275-8.
78. Cohen ND, Giguère S, Burton AJ, Rocha JN, Berghaus LJ, Brake CN, et al. Use of Liposomal Gentamicin for Treatment of 5 Foals with Experimentally Induced Rhodococcus equi Pneumonia. Journal of veterinary internal medicine. 2016;30(1):322-5.
79. Cohen ND, Slovis NM, Giguère S, Baker S, Chaffin MK, Bernstein LR. Gallium Maltolate as an Alternative to Macrolides for Treatment of Presumed Rhodococcus equi Pneumonia in Foals. Journal of veterinary internal medicine. 2015;29(3):932-9.
80. Giguère S, Cohen ND. Controversies in therapy of infections caused by Rhodococcus equi in foals. Equine veterinary education. 2018;30(6):336-41.
81. Muscat K, Venturini C, Giles C, Barton M, Muscatello G. Bacteriophages from Australian horse farms targeting Rhodococcus equi. Equine veterinary journal. 2021;53(S56):18-9.
82. Ainsworth DM, Eicker SW, Yeagar AE, Sweeney CR, Viel L, Tesarowski D, et al. Associations between physical examination, laboratory, and radiographic findings and outcome and subsequent racing performance of foals with Rhodococcus equi infection: 115 cases (1984-1992). J Am Vet Med Assoc. 1998;213(4):510-5.
83. Rakowska A, Cywinska A, Witkowski L. Current trends in understanding and managing equine rhodococcosis. Animals (Basel). 2020;10(10):1-12.
84. Giguere S, Hernandez J, Gaskin J, Miller C, Bowman JL. Evaluation of white blood cell concentration, plasma fibrinogen concentration, and an agar gel immunodiffusion test for early identification of foals with Rhodococcus equi pneumonia (vol 222, pg 775, 2003). Journal of the American Veterinary Medical Association. 2003;223(9):1300.
85. Passamonti F, Vardi DM, Stefanetti V, Marenzoni ML, Prato S, Cévese P, et al. Rhodococcus equi pneumonia in foals: An assessment of the early diagnostic value of serum amyloid A and plasma fibrinogen concentrations in equine clinical practice. The veterinary journal (1997). 2015;203(2):211-8.
86. Steiger RR, Williams MA. Granulomatous tracheitis caused by Conidiobolus coronatus in a horse. J Vet Intern Med. 2000;14(3):311-4.

87. Madison JB, Reid BV, Raskin RE. Amphotericin B treatment of Candida arthritis in two horses. Journal of the American Veterinary Medical Association. 1995;206(3):338-41.
88. Mullen KR, Fenn M, Hill JA, Alexander K, Gonzalez-Barrientos CR, Rodrigues-Hoffmann A, et al. Successful management of pneumonia and pyogranulomatous cranial mediastinitis due to Coccidioides species infection with fluconazole in a 3-year-old horse. Equine veterinary education. 2024;36(11):e270-e5.
89. Passler NH, Chan HM, Stewart AJ, Duran SH, Welles EG, Lin HC, et al. Distribution of voriconazole in seven body fluids of adult horses after repeated oral dosing. Journal of veterinary pharmacology and therapeutics. 2010;33(1):35-41.
90. Davis JL, Salmon JH, Papich MG. Pharmacokinetics and tissue distribution of itraconazole after oral and intravenous administration to horses. Am J Vet Res. 2005;66(10):1694-701.
91. Prades M, Brown MP, Gronwall R, Houston AE. Body fluid and endometrial concentrations of ketoconazole in mares after intravenous injection or repeated gavage. Equine veterinary journal. 1989;21(3):211-4.
92. Robinson NE, Sprayberry KA. Appendix 1 - Table of Common Drugs and Approximate Dosages. Robinson's Current Therapy in Equine Medicine. Seventh edition ed: Elsevier; 2015.
93. Baptiste KE. Antimicrobial Drug Use in Horses. In: Dowling PM, Prescott JF, Baptiste KE, editors. Antimicrobial Therapy in Veterinary Medicine. Sixth ed. New Jersey: Wiley-Blackwell; 2024.
94. White SD. Equine Bacterial and Fungal Diseases: A Diagnostic and Therapeutic Update. Clinical Techniques in Equine Practice. 2005;4(4):302-10.
95. Williams MM, Davis EG, KuKanich B. Pharmacokinetics of oral terbinafine in horses and Greyhound dogs: Pharmacokinetics of terbinafine horses and dogs. Journal of veterinary pharmacology and therapeutics. 2011;34(3):232-7.
96. Begg LM, Hughes KJ, Kessell A, Krockenberger MB, Wigney DI, Malik R. Successful treatment of cryptococcal pneumonia in a pony mare. Aust Vet J. 2004;82(11):686-92.
97. Martineau M, Castagnet S, Kokabi E, Tricot A, Jaÿ M, Léon A, et al. Detection of Mycoplasma spp. in horses with respiratory disorders. Equine veterinary journal. 2023;55(5):747-54.
98. Wood JLN, Chanter N, Newton JR, Burrell MH, Dugdale D, Windsor HM, et al. An outbreak of respiratory disease in horses associated with Mycoplasma felis infection. Veterinary record. 1997;140(15):388-91.
99. Uchida-Fujii E, Kinoshita Y, Niwa H, Maeda T, Nukada T, Ueno T. High prevalence of Mycoplasma equirhinis in Thoroughbred horses with respiratory symptoms in autumn 2018. Journal of Veterinary Medical Science. 2021:21-0163.
100. Martineau M, Kokabi E, Taiebi A, Lefebvre S, Pradier S, Jaÿ M, et al. Epidemiology and pathogenicity of M. equirhinis in equine respiratory disorders. Veterinary microbiology. 2023;287:109926-.
101. Gerber V, Tessier C, Marti E. Genetics of upper and lower airway diseases in the horse. Equine veterinary journal. 2015;47(4):390-7.
102. Couëtil LL, Cardwell JM, Gerber V, Lavoie JP, Léguillette R, Richard EA. Inflammatory Airway Disease of Horses—Revised Consensus Statement. Journal of veterinary internal medicine. 2016;30(2):503-15.
103. Kinnison T, McGilvray TA, Couëtil LL, Smith KC, Wylie CE, Bacigalupo SA, et al. Mild-moderate equine asthma: A scoping review of evidence supporting the consensus definition. The veterinary journal (1997). 2022;286:105865-.
104. Hinchcliff KW, Couetil LL, Knight PK, Morley PS, Robinson NE, Sweeney CR, et al. Exercise Induced Pulmonary Hemorrhage in Horses: American College of Veterinary Internal Medicine Consensus Statement. Journal of veterinary internal medicine. 2015;29(3):743-58.
105. Bayly W, Lopez C, Sides R, Bergsma G, Bergsma J, Gold J, et al. Effect of different protocols on the mitigation of exercise-induced pulmonary hemorrhage in horses when administered 24 hours before strenuous exercise. Journal of veterinary internal medicine. 2019;33(5):2319-26.
106. Wilkins PA. Equine multinodular pulmonary fibrosis: Diagnosis and treatment. Equine veterinary education. 2013;25(8):393-7.
107. Spelta CW, Axon JE, Begg A, Diallo ISI, Carrick JB, Russell CM, et al. Equine multinodular pulmonary fibrosis in three horses in Australia. Australian veterinary journal. 2013;91(7):274-80.
108. Williams KJ, Robinson NE, Lim A, Brandenberger C, Maes R, Behan A, et al. Experimental Induction of Pulmonary Fibrosis in Horses with the Gammaherpesvirus Equine Herpesvirus 5: e77754. PloS one. 2013;8(10).
109. Schwarz B, Schwendenwein I, van den Hoven R. Successful outcome in a case of equine multinodular pulmonary fibrosis (EMPF) treated with valacyclovir. Equine veterinary education. 2013;25(8):389-92.
110. Easton-Jones CA, Madigan JE, Barnum S, Maxwell LK, Taylor SD, Arnesen T, et al. Effect of valacyclovir on EHV-5 viral kinetics in horses with equine multinodular pulmonary fibrosis. Journal of veterinary internal medicine. 2018;32(5):1763-7.

111. Wong DM, Belgrave RL, Williams KJ, Del Piero F, Alcott CJ, Bolin SR, et al. Multinodular pulmonary fibrosis in five horses. Journal of the American Veterinary Medical Association. 2008;232(6):898-905.
112. Maxwell LK, Bentz BG, Gilliam LL, Ritchey JW, Pusterla N, Eberle R, et al. Efficacy of the early administration of valacyclovir hydrochloride for the treatment of neuropathogenic equine herpesvirus type-1 infection in horses. American journal of veterinary research. 2017;78(10):1126-39.
113. Craven A, Todd-Donato A, Stokol T, Liepman R, Glasberg I, Wilkins P, et al. Clinical findings and outcome predictors for multinodular pulmonary fibrosis in horses: 46 cases (2009-2019). Journal of veterinary internal medicine. 2024;38(3):1842-57.
114. Easton-Jones CA, Cissell DD, Mohr FC, Chigerwe M, Pusterla N. Prognostic indicators and long-term survival in 14 horses with equine multinodular pulmonary fibrosis. Equine veterinary education. 2020;32(11):41-6.
115. Wilkins PA, Otto CM, Baumgardner JE, Dunkel B, Bedenice D, Paradis MR, et al. Acute lung injury and acute respiratory distress syndromes in veterinary medicine: consensus definitions: The Dorothy Russell Havemeyer Working Group on ALI and ARDS in Veterinary Medicine. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2007;17(4):333-9.
116. Gough SL, Carrick J, Raidal SL, Keane S, Collins N, Cudmore L, et al. Chlamydia psittaci infection as a cause of respiratory disease in neonatal foals. Equine veterinary journal. 2020;52(2):244-9.
117. Raidal SL, McKean R, Ellul PA, Nielsen SG, Quinn CT. Effects of continuous positive airway pressure on respiratory function in sedated foals. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2019;29(3):269-78.
118. Floriano D, Watkins AR, Hopster K. Intratracheal oxygen administration increases FIO2 and PaO2 compared with intranasal administration in healthy, standing horses. American journal of veterinary research. 2022;83(5):450-4.
119. Dunkel B, Dolente B, Boston RC. Acute lung injury/acute respiratory distress syndrome in 15 foals. Equine veterinary journal. 2005;37(5):435-40.
120. Aas JA, Paster BJ, Stokes LN, Olsen I, Dewhirst FE. Defining the Normal Bacterial Flora of the Oral Cavity. Journal of Clinical Microbiology. 2005;43(11):5721-32.
121. Bailey GD, Love DN. Oral associated bacterial infection in horses: studies on the normal anaerobic flora from the pharyngeal tonsillar surface and its association with lower respiratory tract and paraoral infections. Veterinary microbiology. 1991;26(4):367-79.
122. Kennedy R, Lappin DF, Dixon PM, Buijs MJ, Zaura E, Crielaard W, et al. The microbiome associated with equine periodontitis and oral health. Veterinary research (Paris). 2016;47(1):49-.
123. Kern I, Bartmann CP, Verspohl J, Rohde J, Bienert-Zeit A. Bacteraemia before, during and after tooth extraction in horses in the absence of antimicrobial administration. Equine veterinary journal. 2017;49(2):178-82.
124. Mackintosh ME, Colles CM. Anaerobic bacteria associated with dental abscesses in the horse and donkey. Equine veterinary journal. 1987;19(4):360-2.
125. Bienert A, Bartmann CP, Verspohl J, Deegen E. Bacteriological findings for endodontical and apical molar dental diseases in the horse. Dtsch Tierarztl Wochenschr. 2003;110(9):358-61.
126. Sykora S, Pieber K, Simhofer H, Hackl V, Brodesser D, Brandt S. Isolation of Treponema and Tannerella spp. from equine odontoclastic tooth resorption and hypercementosis related periodontal disease. Equine veterinary journal. 2014;46(3):358-63.
127. Bartmann CP, Peters M, Amtsberg G, Deegen E. Dentogene Sinusitis durch gramnegative Anaerobier beim Pferd. Tierärztliche Praxis Ausgabe G, Grosstiere/Nutztiere. 2002;30:178-83.
128. Verdegaal EJMM, Heer Nd, Meertens NM, Maree JTM, Oldruitenborgh-Oosterbaan MMS. A right-sided bacterial endocarditis of dental origin in a horse. Equine veterinary education. 2006;18(4):191-5.
129. Bach FS, Bodo G, Kuemmerle JM, Bienert-Zeit A, Hainisch EK, Simhofer H. Bacterial Meningitis After Sinus Surgery in Five Adult Horses. Veterinary surgery. 2014;43(6):697-703.
130. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. J Am Dent Assoc. 2007;138(6):739-45, 47-60.
131. Rutherford SJ, Glenny AM, Roberts G, Hooper L, Worthington HV. Antibiotic prophylaxis for preventing bacterial endocarditis following dental procedures. Cochrane database of systematic reviews (Online). 2022;5(5):Cd003813.
132. Hall G, Heimdahl A, Nord CE. Bacteremia after oral surgery and antibiotic prophylaxis for endocarditis. Clin Infect Dis. 1999;29(1):1-8; quiz 9-10.
133. Daly CG. Antibiotic prophylaxis for dental procedures. Australian prescriber. 2017;40(5):184-8.

134. Dixon PM, Parkin TD, Collins N, Hawkes C, Townsend N, Tremaine WH, et al. Equine paranasal sinus disease: a long-term study of 200 cases (1997-2009): treatments and long-term results of treatments. Equine Vet J. 2012;44(3):272-6.
135. Lowder MQ, Mueller POE. Periradicular dental disease in horses. Compendium on Continuing Education for the Practicing Veterinarian. 1999;21(9):874–6.
136. Tremaine H. Advances in the Treatment of Diseased Equine Cheek Teeth. The Veterinary clinics of North America Equine practice. 2013;29(2):441-65.
137. Pearce CJ. Treatment of maxillary cheek teeth apical infection caused by patent infundibula in six horses (2007–2013). Equine veterinary education. 2016;28(11):600-8.
138. Lundström T, Wattle O. Description of a technique for orthograde endodontic treatment of equine cheek teeth with apical infections. Equine veterinary education. 2016;28(11):641-52.
139. du Toit N, Pearce CJ. Long-term follow-up of equine incisor endodontic treatments using an orthograde technique. Journal of the American Veterinary Medical Association. 2023;261(S2):S96-S101.
140. Easley J, Dixon P, Toit Nd. Equine dentistry and maxillofacial surgery. 1st edition ed. Newcastle upon Tyne: Cambridge Scholars Publishing; 2022.
141. Jackson K, Kelty E. Recent advances in the treatment and prevention of equine peripheral caries. Journal of the American Veterinary Medical Association. 2023;261(S2):S79-S86.
142. Christiansen MS, Rosenmeier JG, Jensen DB, Lindegaard C. Standing equine cheek tooth extraction: A multivariate analysis of the effect of antibiotics on the risk of post-operative complications. Equine veterinary journal. 2023;55(6):968-78.
143. Potschka H, Richter A, Kroker R. Pharmaka zur Behandlung bakterieller Infektionen. Löscher W, Richter A, Potschka H (Hrsg), Pharmakotherapie bei Haus- und Nutztieren. Stuttgart: Enke; 2014. p. 282-330.
144. Kennedy RS, Dixon PM. The aetiopathogenesis of equine periodontal disease – a fresh perspective. Equine veterinary education. 2018;30(3):161-8.
145. Beste KJ, Lawhon SD, Chamoun-Emanuelli AM, Duff AH, Coleman MC, Griffin CE, et al. Culture-independent and dependent evaluation of the equine paranasal sinus microbiota in health and disease. Equine veterinary journal. 2020;52(3):455-63.
146. Townsend NB, Hawkes CS, Rex R, Boden LA, Barakzai SZ. Investigation of the sensitivity and specificity of radiological signs for diagnosis of periapical infection of equine cheek teeth. Equine Vet J. 2011;43(2):170-8.
147. DIXON PM, PARKIN TD, COLLINS N, HAWKES C, TOWNSEND N, TREMAINE WH, et al. Equine paranasal sinus disease: A long-term study of 200 cases (1997–2009): Ancillary diagnostic findings and involvement of the various sinus compartments. Equine Vet J. 2012;44(3):267-71.
148. Liuti T, Smith S, Dixon PM. Radiographic, computed tomographic, gross pathological and histological findings with suspected apical infection in 32 equine maxillary cheek teeth (2012–2015). Equine veterinary journal. 2018;50(1):41-7.
149. Barakzai S, Tremaine H, Dixon P. Use of Scintigraphy for Diagnosis of Equine Paranasal Sinus Disorders. Veterinary surgery. 2006;35(1):94-101.
150. Verwilghen D, Easley J, Zwick T, Uhlhorn M, Grulke S, Simhofer H, et al. Equine Suture Exostosis: A Review of Cases from a Multicenter Retrospective Study. Vet Sci. 2022;9(7).
151. Jehle MC, Biermann NM, Haltmayer E. Trephination versus Minimally Invasive Transnasal Approaches for the Diagnosis and Treatment of Sinus Disease in Horses. 2022. Report No.: 2306-7381.
152. Lydiksen CV, Christensen JI, Rosenmeier JG, Jensen DB, Lindegaard C. Equine dental sinusitis—A statistical analysis of the effect of antibiotics on dental sinusitis following dental extraction. Equine veterinary education. 2024;36(7):357-65.
153. Fielding CL, Higgins JK, Higgins JC, McIntosh S, Scott E, Giannitti F, et al. Disease Associated with Equine Coronavirus Infection and High Case Fatality Rate. Journal of veterinary internal medicine. 2015;29(1):307-10.
154. Horner S, Agne GF, Byrne DP, Bain ME, Lynch BM, Gow WR, et al. Case series report: Equine coronavirus in Australia. Australian Veterinary Journal. 2025;103(1-2):56-62.
155. Gomez D, Toribio R, Caddey B, Costa M, Vijan S, Dembek K. Longitudinal effects of oral administration of antimicrobial drugs on fecal microbiota of horses. Journal of veterinary internal medicine. 2023;37(6):2562-72.
156. Gohari IM, Arroyo L, Macinnes JI, Timoney JF, Parreira VR, Prescott JF. Characterization of Clostridium perfringens in the feces of adult horses and foals with acute enterocolitis. Canadian journal of veterinary research. 2014;78(1):1-7.
157. Hain-Saunders NMR, Knight DR, Bruce M, Byrne D, Riley TV. Genomic Analysis of Clostridioides difficile Recovered from Horses in Western Australia. Microorganisms. 2023;11(7).

158. Walshe N, Mulcahy G, Crispie F, Cabrera-Rubio R, Cotter P, Jahns H, et al. Outbreak of acute larval cyathostominosis – A "perfect storm" of inflammation and dysbiosis. Equine veterinary journal. 2021;53(4):727-39.
159. Goer JR, Harris PA, editors. How to minimize gastrointestinal disease associated with carboyhdrate nutrition in horses. AAEP Annual Convention; 2007; Orlando: American Association of Equine Practitioners.
160. van Galen G, Saegerman C, Hyldahl Laursen S, Jacobsen S, Andersson Munk M, Sjöström H, et al. Colonic Health in Hospitalized Horses Treated with Non-Steroidal Anti-Inflammatory Drugs – A Preliminary Study. Journal of equine veterinary science. 2021;101:103451-.
161. Karcher LF, Dill SG, Anderson WI, King JM. Right dorsal colitis. J Vet Intern Med. 1990;4(5):247-53.
162. Davis JL. Nonsteroidal anti-inflammatory drug associated right dorsal colitis in the horse. Equine veterinary education. 2017;29(2):104-13.
163. Lightbody KL, Austin A, Lambert PA, von Samson-Himmelstjerna G, Jürgenschellert L, Krücken J, et al. Validation of a serum ELISA test for cyathostomin infection in equines. International journal for parasitology. 2024;54(1):23-32.
164. Kopper JJ, Kogan CJ, Cook VL, Schott nHC. Outcome of horses with enterocolitis receiving oncotic fluid support with either plasma or hetastarch. Canadian veterinary journal. 2019;60(11):1207-12.
165. van Galen G, Hallowell G. Hydroxyethyl starches in equine medicine. Journal of veterinary emergency and critical care (San Antonio, Tex : 2000). 2019;29(4):349-59.
166. van Eps AW. Therapeutic Hypothermia (Cryotherapy) to Prevent and Treat Acute Laminitis. The Veterinary clinics of North America Equine practice. 2010;26(1):125-33.
167. Schoster A, Weese JS, Guardabassi L. Probiotic Use in Horses - What is the Evidence for Their Clinical Efficacy? Journal of veterinary internal medicine. 2014;28(6):1640-52.
168. Quattrini C, Bozorgmanesh R, Egli P, Magdesian KG. Fecal microbiota transplant for treatment of diarrhea in adult hospitalized horses—111 cases (2013–2018). Open veterinary journal (Tripoli, Libya). 2023;13(9):1135-40.
169. Mullen KR, Yasuda K, Divers TJ, Weese JS. Equine faecal microbiota transplant: Current knowledge, proposed guidelines and future directions. Equine veterinary education. 2018;30(3):151-60.
170. Niinistö K, Sykes BW. Diagnosis and management of sand enteropathy in the horse. Equine veterinary education. 2022;34(11):600-6.
171. Tennent-Brown BS, Wilkins PA, Lindborg S, Russell G, Boston RC. Sequential plasma lactate concentrations as prognostic indicators in adult equine emergencies. J Vet Intern Med. 2010;24(1):198-205.
172. Love S, Mair TS, Hillyer MH. Chronic diarrhoea in adult horses: a review of 51 referred cases. Vet Rec. 1992;130(11):217-9.
173. Murphy D, Reid SWJ, Love S. The effect of age and diet on the oral glucose tolerance test in ponies. Equine Veterinary Journal. 1997;29(6):467-70.
174. Divers TJ. Azathioprine - a useful treatment for immune-mediated disorders in the horse? Equine Veterinary Education. 2010;22(10):501-2.
175. Divers TJ, Barton MH. Chapter 13 - Disorders of the Liver. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine (Fourth Edition): W.B. Saunders; 2018. p. 843-87.
176. Smith MRW, Stevens KB, Durham AE, Marr CM. Equine hepatic disease: the effect of patient- and case-specific variables on risk and prognosis. Equine veterinary journal. 2003;35(6):549-52.
177. Peek SF, Divers TJ. Medical treatment of cholangiohepatitis and cholelithiasis in mature horses: 9 cases (1991-1998). Equine veterinary journal. 2000;32(4):301-6.
178. Seahorn TL, Cornick JL, Cohen ND. Prognostic indicators for horses with duodenitis-proximal jejunitis. 75 horses (1985-1989). J Vet Intern Med. 1992;6(6):307-11.
179. Steinman A, Gips M, Lavy E, Sinay I, Soback S. Pharmacokinetics of metronidazole in horses after intravenous, rectal and oral administration. Journal of veterinary pharmacology and therapeutics. 2000;23(6):353-7.
180. Collins A, Love RJ, Pozo J, Smith SH, McOrist S. Studies on the ex vivo survival of Lawsonia intracellularis. Swine Health and Production. 2000;8(5):211-5.
181. Dohrmann J, Hildebrand F, Straub J, Wadephul R, Pusterla N, Freise F, et al. Equine Proliferative Enteropathy in Weanling Foals on A German Breeding Farm: Clinical Course, Treatment and Long-Term Outcome. Journal of equine veterinary science. 2022;111:103873.
182. Sykes BW, Bowen M, Habershon-Butcher JL, Green M, Hallowell GD. Management factors and clinical implications of glandular and squamous gastric disease in horses. Journal of veterinary internal medicine. 2019;33(1):233-40.
183. Sykes BW, Hewetson M, Hepburn RJ, Luthersson N, Tamzali Y. European College of Equine Internal Medicine Consensus Statement-Equine Gastric Ulcer Syndrome in Adult Horses. Journal of veterinary internal medicine. 2015;29(5):1288-99.

184. Vokes J, Lovett A, Sykes B. Equine Gastric Ulcer Syndrome: An Update on Current Knowledge. Animals (Basel). 2023;13(7):1261.
185. Javsicas LH, GiguÈRe S, Freeman DE, Rodgerson DH, Slovis NM. Comparison of Surgical and Medical Treatment of 49 Postpartum Mares with Presumptive or Confirmed Uterine Tears. Veterinary surgery. 2010;39(2):254-60.
186. Diekstall M, Rohde C, Rijkenhuizen ABM. Post-partum uterine rupture: Standing repair in three mares using a laparoscopic technique. Equine veterinary education. 2020;32(6):319-24.
187. Odelros E, Kendall A, Hedberg-Alm Y, Pringle J. Idiopathic peritonitis in horses: A retrospective study of 130 cases in Sweden (2002-2017). Acta veterinaria scandinavica. 2019;61(1):18-.
188. Alonso JdM, Esper CS, Pantoja JCF, Rosa GdS, Giampietro RR, dos Santos B, et al. Accuracy of differences in blood and peritoneal glucose to differentiate between septic and non-septic peritonitis in horses. Research in veterinary science. 2020;132:237-42.
189. McTernan SP, Heller J, Clulow JR, Gannon L, Huang R, Tidd N, et al. The prevalence, serotypes and antibiograms of Salmonella isolates on Thoroughbred stud farms in New South Wales and Victoria. Australian Veterinary Journal. 2025;n/a(n/a).
190. Kilcoyne I, Magdesian KG, Guerra M, Dechant JE, Spier SJ, Kass PH. Prevalence of and risk factors associated with Salmonella shedding among equids presented to a veterinary teaching hospital for colic (2013–2018). Equine veterinary journal. 2023;55(3):446-55.
191. Goni JI, Hendrix K, Kritchevsky J. Recovery of Salmonella bacterial isolates from pooled fecal samples from horses. Journal of veterinary internal medicine. 2023;37(1):323-7.
192. Kelmer G. Update on Treatments for Endotoxemia. The Veterinary clinics of North America Equine practice. 2009;25(2):259-70.
193. Belknap JK, Durham AE, Belknap JK, Geor RJ. Overview of Laminitis Prevention. Hoboken, NJ, USA: John Wiley & Sons, Inc; 2017. p. 421-6.
194. Kusser WC, Ishiguro EE. Effects of aminoglycosides and spectinomycin on the synthesis and release of lipopolysaccharide by Escherichia coli. Antimicrobial Agents and Chemotherapy. 1988;32(8):1247-50.
195. Hart KA, Barton MH. Adrenocortical Insufficiency in Horses and Foals. The Veterinary clinics of North America Equine practice. 2011;27(1):19-34.
196. Anderson MJ, Ibrahim AS, Cooper BR, Woolcock AD, Moore GE, Taylor SD. Effects of administration of ascorbic acid and low-dose hydrocortisone after infusion of sublethal doses of lipopolysaccharide to horses. Journal of veterinary internal medicine. 2020;34(6):2710-8.
197. Peek SF, Semrad S, McGuirk SM, Riseberg A, Slack JA, Marques F, et al. Prognostic value of clinicopathologic variables obtained at admission and effect of antiendotoxin plasma on survival in septic and critically ill foals. J Vet Intern Med. 2006;20(3):569-74.
198. Bailey K. Investigation of the infectious causes of diarrhoea in Australian thoroughbred foals: University of Melbourne; 2017.
199. Slovis NM, Elam J, Estrada M, Leutenegger CM. Infectious agents associated with diarrhoea in neonatal foals in central Kentucky: A comprehensive molecular study. Equine veterinary journal. 2014;46(3):311-6.
200. Flood JA, Collins NM, Russell CM, Cuming RS, Carrick JB, Cudmore LA. Blood culture isolates and antimicrobial sensitivities from 1621 critically ill neonatal foals (2005–2022). Australian veterinary journal. 2025;103(4):163-70.
201. Wong DM, Wilkins PA. Equine Neonatal Medicine. New Jersey: John Wiley & Sons, Inc; 2024.
202. Mckenzie HC. Chapter 20: Disorders of foals. In: Reed S, Bayley W, Sellon D, editors. Equine Internal Medicine. 4 ed. Michigan: Elsevier; 2018. p. 1365-459.
203. Dunkel B, Corley KTT. Pathophysiology, diagnosis and treatment of neonatal sepsis. Equine veterinary education. 2015;27(2):92-8.
204. McCoy AM, Lopp CT, Kooy S, Migliorisi AC, Austin SM, Wilkins PA. Normal regression of the internal umbilical remnant structures in Standardbred foals. Equine veterinary journal. 2020;52(6):876-83.
205. Reig Codina L, Werre SR, Brown JA. Short-term outcome and risk factors for post-operative complications following umbilical resection in 82 foals (2004–2016). Equine veterinary journal. 2019;51(3):323-8.
206. Dunkel B, Palmer JE, Olson KN, Boston RC, Wilkins PA. Uroperitoneum in 32 foals: Influence of intravenous fluid therapy, infection, and sepsis. Journal of veterinary internal medicine. 2005;19(6):889-93.
207. Kablack KA, Embertson RM, Bernard WV, Bramlage LR, Hance S, Reimer JM, et al. Uroperitoneum in the hospitalised equine neonate: retrospective study of 31 cases, 1988-1997. Equine veterinary journal. 2000;32(6):505-8.
208. Hyman SS, Wilkins PA, Palmer JE, Schaer TP, Piero FD. Clostridium perfringens Urachitis and Uroperitoneum in 2 Neonatal Foals. Oxford, UK: Blackwell Publishing Ltd; 2002. Report No.: 0891-6640.
209. Rendle DI, Durham AE, Lloyd D, Summerhays GES, Hughes KJ. Long-term management of sabulous cystitis in five horses. Veterinary record. 2008;162(24):783-7.

210. Zakia LS, Gomez DE, Kenney DG, Arroyo LG. Sabulous cystitis in the horse: 13 cases (2013-2020). Canadian veterinary journal. 2021;62(7):743-50.
211. Laverty S, Pascoe JR, Ling GV, Lavoie JP, Ruby AL. Urolithiasis in 68 horses. Vet Surg. 1992;21(1):56-62.
212. MacLeay JM, Kohn CW. Results of quantitative cultures of urine by free catch and catheterization from healthy adult horses. Journal of veterinary internal medicine. 1998;12(2):76-8.
213. Sprayberry KA. Cystoscopy. In: Slovis NM, editor. Atlas of equine endoscopy. St Louis (MO): Mosby; 2004. p. 169-82.
214. Cauvin ERJ, Munroe GA. Septic osteitis of the distal phalanx: findings and surgical treatment in 18 cases. Equine veterinary journal. 1998;30(6):512-9.
215. Cillán-García E. Can septic pedal osteitis be managed in the standing patient? Equine veterinary education. 2015;27(5):277-.
216. Dyson SJ, Ross MW. Diagnosis and management of lameness in the horse. Second edition. ed. St. Louis, Mo: Elsevier/Saunders; 2011.
217. Peek SF, Semrad SD, Perkins GA. Clostridial myonecrosis in horses (37 cases 1985-2000). Equine veterinary journal. 2003;35(1):86-92.
218. Durward-Akhurst SA, Valberg SJ. Immune-Mediated Muscle Diseases of the Horse. Vet Pathol. Los Angeles, CA: SAGE Publications; 2018. p. 68-75.
219. Gillespie CC, Adams SB, Moore GE. Methods and Variables Associated with the Risk of Septic Arthritis Following Intra-Articular Injections in Horses: A Survey of Veterinarians. Veterinary surgery. 2016;45(8):1071-6.
220. Smith LCR, Wylie CE, Palmer L, Ramzan PHL. Synovial sepsis is rare following intrasynovial medication in equine ambulatory practice. Equine veterinary journal. 2019;51(5):595-9.
221. Pezzanite LM, Hendrickson DA, Dow S, Stoneback J, Chow L, Krause D, et al. Intra-articular administration of antibiotics in horses: Justifications, risks, reconsideration of use and outcomes. Equine veterinary journal. 2022;54(1):24-38.
222. Cox KS, Nelson BB, Wittenburg L, Gold JR. Plasma, subcutaneous tissue and bone concentrations of ceftiofur sodium after regional limb perfusion in horses. Equine veterinary journal. 2017;49(3):341-4.
223. Beccar-Varela AM, Epstein KL, White CL. Effect of Experimentally Induced Synovitis on Amikacin Concentrations after Intravenous Regional Limb Perfusion. Veterinary surgery. 2011;40(7):891-7.
224. Biasutti SA, Cox E, Jeffcott LB, Dart AJ. A review of regional limb perfusion for distal limb infections in the horse. Equine veterinary education. 2021;33(5):263-77.
225. Crosby DE, Labens R, Hughes KJ, Nielsen S, Hilbert BJ. Factors Associated With Survival and Return to Function Following Synovial Infections in Horses. Frontiers in veterinary science. 2019;6:367-.
226. Walmsley EA, Anderson GA, Muurlink MA, Whitton RC. Retrospective investigation of prognostic indicators for adult horses with infection of a synovial structure. Australian veterinary journal. 2011;89(6):226-31.
227. Ferris DJ, Frisbie DD, McIlwraith CW, Kawcak CE. Current joint therapy usage in equine practice: A survey of veterinarians 2009. Equine veterinary journal. 2011;43(5):530-5.
228. Werner LA, Hardy J, Bertone AL. Bone gentamicin concentration after intra-articular injection or regional intravenous perfusion in the horse. Veterinary surgery. 2003;32(6):559-65.
229. Freeland RB, Morello SL, DeLombaert M, Rajamanickam V. Influence of intravenous regional limb perfusion with amikacin sulfate on Staphylococcus aureus bioburden in distal limb wounds in horses. Veterinary surgery. 2017;46(5):663-74.
230. Redding LE, Elzer EJ, Ortved KF. Effects of regional limb perfusion technique on concentrations of antibiotic achieved at the target site: A meta-analysis. PloS one. 2022;17(4):e0265971.
231. Adler DMT, Nielsen AT, Olsen C, Verwilghen D, Damborg P, Olsen RH. Local anesthetics and antibiotics display synergistic and antagonistic drug interactions against pathogens causing septic arthritis in horses. American journal of veterinary research. 2025:1-8.
232. Lloyd KC, Stover SM, Pascoe JR, Baggot JD, Kurpershoek C, Hietala S. Plasma and synovial fluid concentrations of gentamicin in horses after intra-articular administration of buffered and unbuffered gentamicin. Am J Vet Res. 1988;49(5):644-9.
233. Bonilla AG, Causeret L, Torrent-Crosa A. Pharmacokinetics of ceftiofur in the metacarpophalangeal joint after standing intravenous regional limb perfusion in horses. Canadian veterinary journal. 2021;62(9):975-81.
234. Hyde RM, Lynch TM, Clark CK, Slone DE, Hughes FE. The influence of perfusate volume on antimicrobial concentration in synovial fluid following intravenous regional limb perfusion in the standing horse. Canadian veterinary journal. 2013;54(4):363-7.
235. Deniaud M, Tee E. Susceptibility pattern of bacterial isolates in equine ulcerative keratitis: Implications for empirical treatment at a university teaching hospital in Sydney. Australian veterinary journal. 2023;101(3):115-20.

236. Reed Z, Thomasy SM, Good KL, Maggs DJ, Magdesian KG, Pusterla N, et al. Equine keratomycoses in California from 1987 to 2010 (47 cases). Equine veterinary journal. 2013;45(3):361-6.
237. Chalder RH, Knott T, Rushton JO, Nikolic-Pollard D. Changes in antimicrobial resistance patterns of ocular surface bacteria isolated from horses in the UK: An eight-year surveillance study (2012-2019). Veterinary ophthalmology. 2020;23(6):950-6.
238. Martinez PS, Whitley RD, Plummer CE, Richardson RL, Hamor RE, Wellehan JFX. In vitro antifungal susceptibility of Fusarium species and Aspergillus fumigatus cultured from eleven horses with fungal keratitis. Veterinary ophthalmology. 2022;25(5):376-84.
239. Wehrman RF, Gemensky-Metzler AJ, Zibura AE, Nyhart AB, Chandler HL. Objective evaluation of the systemic effects of topical application of 1% atropine sulfate ophthalmic solution in healthy horses. Journal of the American Veterinary Medical Association. 2017;251(11):1324-30.
240. Williams LB, Pinard CL. Corneal ulcers in horses. Compend Contin Educ Vet. 2013;35(1):E4.
241. Brooks DE, Plummer CE. Diseases of the Equine Cornea. In: Gilger BC, editor. Equine Ophthalmology. Hoboken, New Jersey: John Wiley & Sons; 2022. p. 253-440.
242. Hampson ECGM, Gibson JS, Barot M, Shapter FM, Greer RM. Identification of bacteria and fungi sampled from the conjunctival surface of normal horses in South-East Queensland, Australia. Veterinary ophthalmology. 2019;22(3):265-75.
243. Sherman AB, Clode AB, Gilger BC. Impact of fungal species cultured on outcome in horses with fungal keratitis. Veterinary ophthalmology. 2017;20(2):140-6.
244. Galera PD, Brooks DE. Optimal management of equine keratomycosis. Vet Med (Auckl). 2012;3:7-17.
245. Rebhun WC. Corneal stromal abscesses in the horse. J Am Vet Med Assoc. 1982;181(7):677-9.
246. Proietto LR, Plummer CE, Maxwell KM, Lamb KE, Brooks DE. A retrospective analysis of environmental risk factors for the diagnosis of deep stromal abscess in 390 horses in North Central Florida from 1991 to 2013. Veterinary ophthalmology. 2016;19(4):291-6.
247. Smith KM, Pucket JD, Gilmour MA. Treatment of six cases of equine corneal stromal abscessation with intracorneal injection of 5% voriconazole solution. Veterinary ophthalmology. 2014;17(1):179-85.
248. Henriksen MDL, Andersen PH, Plummer CE, Mangan B, Brooks DE. Equine corneal stromal abscesses: An evolution in the understanding of pathogenesis and treatment during the past 30 years. Equine veterinary education. 2013;25(6):315-23.
249. Hurn SD, Turner AG. Ophthalmic examination findings of Thoroughbred racehorses in Australia. Veterinary ophthalmology. 2006;9(2):95-100.
250. Gerding JC, Gilger BC. Prognosis and impact of equine recurrent uveitis. Equine veterinary journal. 2016;48(3):290-8.
251. Charnock LN, Keys DA, McMullen RJ. Clinical findings associated with blunt ocular trauma in horses: a retrospective analysis. Veterinary ophthalmology. 2022;25(1):52-61.
252. Habin DJ. Equine traumatic uveitis. Equine veterinary education. 1994;6(3):122-7.
253. Allbaugh RA. Equine recurrent uveitis: A review of clinical assessment and management. Equine veterinary education. 2016;29(5):279-88.
254. Hanson RR. Management of burn injuries in the horse. The Veterinary clinics of North America Equine practice. 2005;21(1):105-23.
255. Herbert EW. Findings and strategies for treating horses injured in open range fires. Equine veterinary education. 2018;30(4):177-86.
256. Marsh PS. Fire and Smoke Inhalation Injury in Horses. The Veterinary clinics of North America Equine practice. 2007;23(1):19-30.
257. Garcia JAG, Chavez AMG, Grados JDJO. Topical Antimicrobial Agents for the Prevention of Burn-Wound Infection. What Do International Guidelines Recommend? A Systematic Review. World journal of plastic surgery. 2022;11(3):3-12.
258. Cuttle L, Pearn J, McMillan JR, Kimble RM. A review of first aid treatments for burn injuries. BURNS. 2009;35(6):768-75.
259. Malik KI, Malik MAN, Aslam A. Honey compared with silver sulphadiazine in the treatment of superficial partial-thickness burns. International wound journal. 2010;7(5):413-7.
260. Wilkes EJA, Woolsey HE. Chapter 85.1: Management of Burns in Horses. In: Orsini J, Grenager N, editors. Equine Emergencies. Fifth ed. Philadelphia: Saunders Elsevier; 2026.
261. Adam EN, Southwood LL. Primary and secondary limb cellulitis in horses: 44 cases (2000-2006). Journal of the American Veterinary Medical Association. 2007;231(11):1696-703.
262. Levine DG, Epstein KL, Ahern BJ, Richardson DW. Efficacy of Three Tourniquet Types for Intravenous Antimicrobial Regional Limb Perfusion in Standing Horses: Tourniquet Types for Regional Limb Perfusion in Horses. Veterinary surgery. 2010;39(8):1021-4.
263. Braid HR, Ireland JL. A cross-sectional survey of the diagnosis and treatment of distal limb cellulitis in horses by veterinary surgeons in the United Kingdom. Equine veterinary education. 2021;34(6):e234-e44.

264. Herd RP, Donham JC. Efficacy of ivermectin against cutaneous Draschia and Habronema infection (summer sores) in horses. Am J Vet Res. 1981;42(11):1953-5.
265. Scott DW, Miller WH. Parasitic diseases. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.
266. Scott DW, Miller WH. Environmental Skin Disease. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.
267. Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. Fourth Edition ed: Elsevier Inc; 2018. p. 1159-216.
268. Pilsworth RC, Knottenbelt D. Dermatophilosis (rain scald). Equine veterinary education. 2007;19(4):212-4.
269. Scott DW, Miller WH. Bacterial skin disease. Equine Dermatology. Second ed. Philadelphia: Elsevier Saunders; 2011.
270. Oesch S, Kaiser-Thom S, Vidondo B, Gerber V. Owner reported clinical signns and treatment decisions in equine pastern dermatitis. SAT ASMV. 2022;164(5):401-12.
271. Gerber V, Kaiser-Thom S, Oesch S. Equine pastern dermatitis: a narrative review on clinical presentation, diagnosis, risk factors, prevention, and therapeutic approaches. Journal of the American Veterinary Medical Association. 2023;261(S1):S58-S65.
272. Loreto ES, Tondolo JS, Zanette RA, Alves SH, Santurio JM. Update on pythiosis immunobiology and immunotherapuy. World Journal of Immunology. 2014;4(2):88-97.
273. Rashmir-Raven AM. Chapter 18 - Disorders of the Skin. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine (Fourth Edition): W.B. Saunders; 2018. p. 1159-216.
274. Herzog FE. The effect of Lactobacillus containing gel on the clitoral microbiome of the mare: Louisiana State University; 2024.
275. Timoney PJ. Contagious equine metritis. Comparative Immunology, Microbiology and Infectious Diseases. 1996;19(3):199-204.
276. Scholtz M, Guthrie AJ, Newton R, Schulman ML. Review of Pseudomonas aeruginosa and Klebsiella pneumoniae as venereal pathogens in horses. Equine Veterinary Journal. 2024;n/a(n/a):1-11.
277. Storme J, Brookes VJ, Gunn A. Is there evidence demonstrating venereal transmission of clitoral Pseudomonas aeruginosa in horses? Veterinary record. 2023;192(11):444-6.
278. Morris LHA, McCue PM, Aurich C. Equine endometritis: a review of challenges and new approaches. Reproduction (Cambridge, England). 2020;160(5):R95-R110.
279. Canisso IF, Segabinazzi LGTM, Fedorka CE. Persistent Breeding-Induced Endometritis in Mares—A Multifaceted Challenge: From Clinical Aspects to Immunopathogenesis and Pathobiology. International Journal of Molecular Sciences. 2020;21(4):1432.
280. Troedsson MHT. Uterine clearance and resistance to persistent endometritis in the mare. Theriogenology. 1999;52(3):461-71.
281. Frontoso R, De Carlo E, Pasolini MP, van der Meulen K, Pagnini U, Iovane G, et al. Retrospective study of bacterial isolates and their antimicrobial susceptibilities in equine uteri during fertility problems. Research in Veterinary Science. 2008;84(1):1-6.
282. Ferris RA. Current understanding of bacterial biofilms and latent infections: A clinical perspective. Rev Bras Reprod Anim. 2017;41:74-80.
283. Donlan RM, Costerton JW. Biofilms: Survival Mechanisms of Clinically Relevant Microorganisms. Clinical Microbiology Reviews. 2002;15(2):167-93.
284. Davis HA, Stanton MB, Thungrat K, Boothe DM. Uterine bacterial isolates from mares and their resistance to antimicrobials: 8,296 cases (2003–2008). Journal of the American Veterinary Medical Association. 2013;242(7):977-83.
285. Olsen I. Biofilm-specific antibiotic tolerance and resistance. European Journal of Clinical Microbiology & Infectious Diseases. 2015;34(5):877-86.
286. Petersen MR, Rosenbrock A, Osborne M, Bojesen AM. High Prevalence of Subclinical Endometritis in Problem Mares– Effect of Activation and Treatment on Fertility. Journal of Equine Veterinary Science. 2018;66:117.
287. Hoffmann C, Ellenberger C, Mattos RC, Aupperle H, Dhein S, Stief B, et al. The equine endometrosis: new insights into the pathogenesis. Anim Reprod Sci. 2009;111(2-4):261-78.
288. Snider TA, Sepoy C, Holyoak GR. Equine endometrial biopsy reviewed: Observation, interpretation, and application of histopathologic data. Theriogenology. 2011;75(9):1567-81.
289. Pascoe RR. CHAPTER 23 - Vulvar Conformation. In: Samper JC, Pycock JF, McKinnon AO, editors. Current Therapy in Equine Reproduction. Saint Louis: W.B. Saunders; 2007. p. 140-5.
290. Scoggin CF. Not just a number: effect of age on fertility, pregnancy and offspring vigour in thoroughbred brood-mares. Reprod Fertil Dev. 2015;27(6):872-9.
291. Katila T. Evaluation of diagnostic methods in equine endometritis. Reproductive Biology. 2016;16:189-96.

292. Heil BA, van Heule M, Thompson SK, Kearns TA, Oberhaus EL, King G, et al. Effect of Sampling Method on Detection of the Equine Uterine Microbiome during Estrus. Veterinary Sciences. 2023;10(11):644.
293. LeBlanc MM. How to Perform and Interpret Findings From a Low-Volume Uterine Flush. AAEP Proceedings. 2011;57:32-6.
294. Riddle WT, LeBlanc MM, Stromberg AJ. Relationships between uterine culture, cytology and pregnancy rates in a Thoroughbred practice. Theriogenology. 2007;68(3):395-402.
295. Petersen MR, Skive B, Christoffersen M, Lu K, Nielsen JM, Troedsson MHT, et al. Activation of persistent Streptococcus equi subspecies zooepidemicus in mares with subclinical endometritis. Veterinary Microbiology. 2015;179(1):119-25.
296. LeBlanc M. Advances in the Diagnosis and Treatment of Chronic Infectious and Post–Mating-Induced Endometritis in the Mare. Reproduction in Domestic Animals. 2010;45(s2):21-7.
297. Ferris RA, Wittstock SM, McCue PM, Borlee BR. Evaluation of biofilms in gram-negative bacteria isolated from the equine uterus. Journal of Equine Veterinary Science. 2014;34(1):121.
298. Katila T. Onset and Duration of Uterine Inflammatory Response of Mares after Insemination with Fresh Semen. Biology of Reproduction. 2018;52(monograph_series1):515-7.
299. Scoggin CF, Burden CA, Schnobrich MR, Bradecamp EA. A single post-mating infusion of penicillin does not improve pregnancy rates in maiden Thoroughbred broodmares. Clinical Theriogenology. 2017;9(1):53-8.
300. Karam KM, Alebady AS, Alhilfi HO, Al-Delemi DH. Comparative study utilizing different post-breeding treatment regimens in cyclic Arabian mares. Vet World. 2021;14(11):2863-8.
301. Rose BV, Firth M, Morris B, Roach JM, Wathes DC, Verheyen KLP, et al. Descriptive study of current therapeutic practices, clinical reproductive findings and incidence of pregnancy loss in intensively managed thoroughbred mares. Animal reproduction science. 2018;188:74-84.
302. LeBlanc MM. The current status of antibiotic use in equine reproduction. Equine Veterinary Education. 2009;21(3):156-67.
303. Ferris RA, McCue PM, Borlee GI, Loncar KD, Hennet ML, Borlee BR. In Vitro Efficacy of Nonantibiotic Treatments on Biofilm Disruption of Gram-Negative Pathogens and an In Vivo Model of Infectious Endometritis Utilizing Isolates from the Equine Uterus. J Clin Microbiol. 2016;54(3):631-9.
304. Dascanio JJ, Schweizer C, Ley WB. Equine fungal endometritis. Equine Veterinary Education. 2001;13(6):324-9.
305. Rogan D, Fumuso E, Rodríguez E, Wade J, Sánchez Bruni SF. Use of a Mycobacterial Cell Wall Extract (MCWE) in Susceptible Mares to Clear Experimentally Induced Endometritis With Streptococcus zooepidemicus. Journal of Equine Veterinary Science. 2007;27(3):112-7.
306. Perkins N, Threlfall W. Mastitis in the mare. Equine Veterinary Education. 2010;5:192-5.
307. McCue PM, Wilson WD. Equine mastitis - a review of 28 cases. Equine Veterinary Journal. 1989;21(5):351-3.
308. McCue P, Sitters, S. Lactation. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2277-90.
309. Ginther O. How ultrasound technologies have expanded and revolutionized research in reproduction in large animals. Theriogenology. 2014;81(1):112-25.
310. Pugh DG, Magnusson RA, Modransky PD, Darnton KR. A case of mastitis in a young filly. Journal of Equine Veterinary Science. 1985;5(3):132-4.
311. Gee Erica K. MPM. Mastitis. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2738-41.
312. McKenzie RA, Brown OP. Avocado (Persea americana) poisoning of horses. Aust Vet J. 1991;68(2):77-8.
313. Canisso IF, Podico G, Ellerbrock RE. Diagnosis and treatment of mastitis in mares. Equine Veterinary Education. 2021;33(6):320-6.
314. Trela M, Domańska D, Witkowska-Piłaszewicz O. Diagnostic Use of Serum Amyloid A in Dairy Cattle. Agriculture. 2022;12(4):459.
315. Schiemann V, Bartmann C. Mastectomia in the horse- Indication and surgical procedure. Pferdeheilkunde. 2004;20:506-10.
316. Blanchard TL, Elmore RG, Kinden DA, Berg JN, Mollett TA, Garcia MC. Effect of intrauterine infusion of Escherichia coli endotoxin in postpartum pony mares. Am J Vet Res. 1985;46(10):2157-62.
317. Ferrer MS, Palomares R. Aerobic uterine isolates and antimicrobial susceptibility in mares with post-partum metritis. Equine Veterinary Journal. 2018;50(2):202-7.
318. Ferrer MS, Pozor MA. How to Manage the Post-Partum Mare with Metritis—Lessons Learned from a Retrospective Bacteriological Study. Proceedings of the American Association of Equine Practitioners. 2018;64:236-9.

319. Crabtree J. Peripartum problems in mares 2. Postpartum problems. In Practice. 2012;34(8):462-71.
320. Tukia E, Wagner B, Vainio K, Mönki J, Kareskoski M. The Effect of Uterine Lavage on Soluble CD14, Chemokine Ligand 2, and Interleukin 10 Levels in Mares With Postpartum Metritis. Journal of Equine Veterinary Science. 2021;98:103365.
321. Carrick J, editor Assessment and treatment of placentitis. College Science Week Scientific meeting, Equine Chapter proceedings 2007; Gold Coast.
322. Carrick JB, Perkins N, Zalucki MP. Causes of abortion in Australia (2005-2012) – proportion of cases due to Equine Amnionitis and Foetal Loss (EAFL). Journal of Equine Veterinary Science. 2014;34:212-4.
323. LeBlanc MM. Ascending placentitis in the mare: an update. Reprod Domest Anim. 2010;45 Suppl 2:28-34.
324. Troedsson MH, Macpherson ML. Placentitis. In: McKinnon AO SE, Vaala WE, Varner DD, editor. Equine Reproduction, 2nd ed. 2. Hoboken NJ2011. p. 2359–67.
325. Lofstedt R. Abnormalities of pregnancy. In: McKinnon AO SE, Vaala WE, Varner DD, editor. eds Equine Reproduction, Vol 2 2nd ed. Hoboken NJ: Wiley-Blackwell; 2011. p. 2441–53.
326. Troedsson M, Miller L. Equine placentitis. Pferdeheilkunde. 2016;32:49-53.
327. Macpherson ML. Treatment strategies for mares with placentitis. Theriogenology. 2005;64(3):528-34.
328. Hong CB, Donahue JM, Giles RC, Jr., Petrites-Murphy MB, Poonacha KB, Roberts AW, et al. Etiology and pathology of equine placentitis. J Vet Diagn Invest. 1993;5(1):56-63.
329. Erol E, Sells SF, Williams NM, Kennedy L, Locke SJ, Labeda DP, et al. An investigation of a recent outbreak of nocardioform placentitis caused abortions in horses. Vet Microbiol. 2012;158(3-4):425-30.
330. El-Sheikh Ali H, Ball B, Carleigh, Fedorka C, Scoggin K, Schnobrich M, et al. Nocardioform Placentitis: A Continuing Question. 2021.
331. Todhunter K, Perkins N, Wylie R, Chicken C, Blishen A, Racklyeft D, et al. Equine amnionitis and fetal loss: The case definition for an unrecognised cause of abortion in mares. Australian Veterinary Journal. 2009;87(1-2):35-8.
332. Begg AP, Carrick J, Chicken C, Blishen A, Todhunter K, Eamens K, et al. Fetoplacental pathology of equine abortion, premature birth, and neonatal loss due to Chlamydia psittaci. Vet Pathol. 2022;59(6):983-96.
333. El-Hage C, Legione A, Devlin J, Hughes K, Jenkins C, Gilkerson J. Equine Psittacosis and the Emergence of Chlamydia psittaci as an Equine Abortigenic Pathogen in Southeastern Australia: A Retrospective Data Analysis. Animals (Basel). 2023;13(15).
334. Renaudin CD, Troedsson MHT, Gillis CL, King VL, Bodena A. Ultrasonographic evaluation of the equine placenta by transrectal and transabdominal approach in the normal pregnant mare. Theriogenology. 1997;47 2:559-73.
335. Reef V, Vaala W, Worth L, Sertich P, Spencer P. Ultrasonographic assessment of fetal well-being during late gestation: Development of an equine biophysical profile. Equine Veterinary Journal. 2010;28:200-8.
336. Bucca S, Fogarty U, Collins A, Small V. Assessment of feto-placental well-being in the mare from mid-gestation to term: Transrectal and transabdominal ultrasonographic features. Theriogenology. 2005;64(3):542-57.
337. Begg A CJ, Shearer P, Stewart M Visual atlas of the gross pathology of equine reproductive loss 2022 [First:[Available from: https://agrifutures.com.au/product/visual-atlas-of-the-gross-pathology-of-equine-reproductive-loss/
338. Ousey JC, Houghton E, Grainger L, Rossdale PD, Fowden AL. Progestagen profiles during the last trimester of gestation in Thoroughbred mares with normal or compromised pregnancies. Theriogenology. 2005;63(7):1844-56.
339. Santschi EM, LeBlanc MM, Weston PG. Progestagen, oestrone sulphate and cortisol concentrations in pregnant mares during medical and surgical disease. J Reprod Fertil Suppl. 1991;44:627-34.
340. Ryan PL, Christiansen DL, Hopper RM, Bagnell CA, Vaala WE, Leblanc MM. Evaluation of systemic relaxin blood profiles in horses as a means of assessing placental function in high-risk pregnancies and responsiveness to therapeutic strategies. Ann N Y Acad Sci. 2009;1160:169-78.
341. Canisso IF, Ball BA, Cray C, Williams NM, Scoggin KE, Davolli GM, et al. Serum amyloid A and haptoglobin concentrations are increased in plasma of mares with ascending placentitis in the absence of changes in peripheral leukocyte counts or fibrinogen concentration. Am J Reprod Immunol. 2014;72(4):376-85.
342. Coutinho da Silva MA, Canisso IF, MacPherson ML, Johnson AE, Divers TJ. Serum amyloid A concentration in healthy periparturient mares and mares with ascending placentitis. Equine Vet J. 2013;45(5):619-24.

343. Canisso IF, Ball BA, Scoggin KE, Squires EL, Williams NM, Troedsson MH. Alpha-fetoprotein is present in the fetal fluids and is increased in plasma of mares with experimentally induced ascending placentitis. Anim Reprod Sci. 2015;154:48-55.
344. LeBlanc MM, Giguère S, Lester GD, Brauer K, Paccamonti DL. Relationship between infection, inflammation and premature parturition in mares with experimentally induced placentitis. Equine Vet J Suppl. 2012(41):8-14.
345. Bailey CS, Macpherson ML, Pozor MA, Troedsson MH, Benson S, Giguere S, et al. Treatment efficacy of trimethoprim sulfamethoxazole, pentoxifylline and altrenogest in experimentally induced equine placentitis. Theriogenology. 2010;74(3):402-12.
346. Rebello SA, Macpherson ML, Murchie TA, LeBlanc MM, Vickroy TW. Placental transfer of trimethoprim sulfamethoxazole and pentoxifylline in pony mares. Animal Reproduction Science. 2006;94(1-4):432-3.
347. Murchie TA, Macpherson ML, LeBlanc MM, Luznar S, Vickroy TW. Continuous monitoring of penicillin G and gentamicin in allantoic fluid of pregnant pony mares by in vivo microdialysis. Equine Vet J. 2006;38(6):520-5.
348. Macpherson ML, Giguère S, Pozor MA, Burden CA, Berghaus LJ, Berghaus RD, et al. Evidence for anti-inflammatory effects of firocoxib administered to mares with experimentally induced placentitis. Am J Reprod Immunol. 2021;86(1):e13396.
349. Bailey CS, Sper RB, Schewmaker JL, Buchanan CN, Beachler TM, Pozor MA, et al. Uterine artery blood flow remains unchanged in pregnant mares in response to short-term administration of pentoxifylline. Theriogenology. 2012;77(2):430-6.
350. Palmer E, Chavatte-Palmer P, Duchamp G, Levy I. Lack of effect of clenbuterol for delaying parturition in late pregnant mares2002. 797-9 p.
351. Sielhorst J, Roggel-Buecker U, Neudeck KC, Kahler A, Rohn K, Luettgenau J, et al. Effect of Acetylsalicylic Acid on Uterine Blood Flow, Gestation Length, Foal Birth Weight and Placental Weight in Pregnant Thoroughbred Mares - A Clinical Pilot Study. J Equine Vet Sci. 2022;118:104107.
352. Bommana S, Polkinghorne A. Mini Review: Antimicrobial Control of Chlamydial Infections in Animals: Current Practices and Issues. Front Microbiol. 2019;10:113.
353. Fedorka CE, Scoggin KE, Ruby RE, Erol E, Ball BA. Clinical, pathologic, and epidemiologic features of nocardioform placentitis in the mare. Theriogenology. 2021;171:155-61.
354. Santschi EM, Adams SB, Robertson JT, DeBowes RM, Mitten LA, Sojka JE. Ovariohysterectomy in six mares. Vet Surg. 1995;24(2):165-71.
355. Lu KG. Pyometra. In: McKinnon AO SE, Vaala WE, et al, editor. Equine Reproduction Second Edition. 2: Wiley-Blackwell; 2011. p. 2652-4.
356. LeBlanc M, Causey R. Clinical and Subclinical Endometritis in the Mare: Both Threats to Fertility. Reproduction in Domestic Animals. 2009;44(s3):10-22.
357. Naguib M, Rais B, Adzahan N, Armiladiana M, Adamu L. Equine Pyometra: A Case Report. IOSR Journal of Agriculture and Veterinary Science (IOSR-JAVS) IMPACT FACTOR 1485. 2013;2:2319-72.
358. Köhne M, Tönissen A, Unruh C, Pruß D, Sieme H. Occurrence of Intrauterine Purulent Concrements in a Maiden Mare—A Case Report. Journal of Equine Veterinary Science. 2020;95:103278.
359. Cozens ER. Pyometra and complete vaginal adhesion in a miniature horse. Can Vet J. 2009;50(9):971-2.
360. Brinsko S, Act D. How to Perform Uterine Lavage: Indications and Practical Techniques. Proc Am Assoc Equine Pract. 2001;47.
361. McNaughten J, Pozor M, Macpherson M, Kelleman A, Woodward E, Troedsson M. Effects of topical application of misoprostol on cervical relaxation in mares. Reprod Domest Anim. 2014;49(6):1057-62.
362. Krohn J, Ennen S, Hospes R, Nieth J, Wehrend A. Use of a cervical stent for long-term treatment of pyometra in the mare: A report of three cases. Reprod Domest Anim. 2019;54(8):1155-9.
363. Sharma S, Thapak S. Chronic pyometra in a thoroughbred mare. Veterinary Practitioner. 2010;11:116-7.
364. Arnold CE, Brinsko SP, Varner DD. Cervical wedge resection for treatment of pyometra secondary to transluminal cervical adhesions in six mares. J Am Vet Med Assoc. 2015;246(12):1354-7.
365. Prestes NC, et al. . Total Hysterectomy as Treatment for Recurrent Chronic Pyometra in Mares With Total Cervical AdhesioneCase Report. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2018;63:61-4.
366. O'Brien P. Retained Fetal Membranes In: Sprayberry KAR, N.E., editor. Robertson's Current Therapy In Equine Medicine 7th Edition: WB Saunders Co LTD; 2015. p. 713-6.
367. Asbury AC LM. The fetal membranes. In: McKinnon AO VJ, editor. Equine Reproduction. 1st Edition. Philadelphia: Lea & Febiger; 1992. p. 510-6.

368. Canisso I, Rodriguez J, Sanz M, Silva M. A Clinical Approach to the Diagnosis and Treatment of Retained Fetal Membranes with an Emphasis Placed on the Critically Ill Mare. Journal of Equine Veterinary Science. 2013;33.
369. Threlfall W. Retained Fetal Membranes. In: McKinnon AO SE, Valla WE, Varner DD, editor. Equine Reproduction. 2nd Edition: Blackwell Publishing LTD; 2011. p. 2520-9.
370. Provencher R, Threlfall WR, Murdick PW, Wearly WK. Retained fetal membranes in the mare: A retrospective study. Can Vet J. 1988;29(11):903-10.
371. Sevinga M, Barkema HW, Stryhn H, Hesselink JW. Retained placenta in Friesian mares: incidence, and potential risk factors with special emphasis on gestational length. Theriogenology. 2004;61(5):851-9.
372. Vandeplassche M, Spincemaille J, Bouters R. Aetiology, pathogenesis and treatment of retained placenta in the mare. Equine Vet J. 1971;3(4):144-7.
373. Pozor M. Equine placenta – A clinician's perspective. Part 1: Normal placenta – Physiology and evaluation. Equine Veterinary Education. 2015;28(6):327-34.
374. Pozor M. Equine placenta - A clinician's perspective. Part 2: Abnormalities. Equine Veterinary Education. 2016;28(7):396-404.
375. Brinsko SP. Common procedures in broodmare practice: what is the evidence? Vet Clin North Am Equine Pract. 2007;23(2):385-402.
376. Sevinga M, Barkema HW, Hesselink JW. Serum calcium and magnesium concentrations and the use of a calcium-magnesium-borogluconate solution in the treatment of Friesian mares with retained placenta. Theriogenology. 2002;57(2):941-7.
377. Burns SJ JN, Martin JE, et al, editor Management of retained placenta in mares. Am Assoc Equine Pract; 1977.
378. Samper JC PT, editor How to deal with dystocia and retained placenta in the field. Proceedings of the 58th annual convention of the AAEP; 2012; Anaheim CA.
379. Cuervo-Arango J, Newcombe J. The Effect of Manual Removal of Placenta Immediately after Foaling on Subsequent Fertility Parameters in the Mare. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2009;29:771-4.
380. Burden CA, Meijer M, Pozor MA, Macpherson ML. Fetal Membrane Removal in the Mare: Proactive Versus Reactive Approaches. Vet Clin North Am Equine Pract. 2019;35(2):289-98.
381. Rapacz-Leonard A, Paździor-Czapula K, Raś A, Tadeusz R, Janowski T. Retained Fetal Membranes in Heavy Draft Mares Associated with Histological Abnormalities. Journal of Equine Veterinary Science - J EQUINE VET SCI. 2012;32.
382. Meijer MAJ, Macpherson ML, Dijkman R, editors. How to use umbilical vessel water infusion to treat retained fetal membranes in mares2015.
383. Warnakulasooriya DN, Marth CD, McLeod JA, Hanlon DW, Krekeler N. Treatment of Retained Fetal Membranes in the Mare-A Practitioner Survey. Front Vet Sci. 2018;5:128.
384. Frazer G. Post partum complications in the mare. Part 2: Fetal membrane retention and conditions of the gastrointestinal tract, bladder and vagina. Equine Veterinary Education. 2010;15:91-100.
385. Sevinga M, Hesselink JW, Barkema HW. Reproductive performance of Friesian mares after retained placenta and manual removal of the placenta. Theriogenology. 2002;57(2):923-30.
386. Varner DD, Blanchard TL, Brinsko SP, Love CC, Taylor TS, Johnson L. Techniques for evaluating selected reproductive disorders of stallions. Animal reproduction science. 2000;60:493-509.
387. Hull BL, Vogel SR. Seminal Vesiculitis. Veterinary Clinics of North America: Food Animal Practice. 2008;24(2):267-72.
388. Scheeren VFC, Sancler-Silva YFR, El-Sheikh Ali H, Kastelic JP, Alvarenga MA, Papa FO. Update on Seminal Vesiculitis in Stallions. Journal of equine veterinary science. 2020;94:103234-.
389. Fennell LC, McKinnon AO, Savage CJ. Cryopreservation of semen from a stallion with seminal vesiculitis. Equine Veterinary Education. 2010;22(5):215-9.
390. Samper JC, Tibary A. Disease transmission in horses. Theriogenology. 2006;66(3):551-9.
391. Morrell JM, Rodriguez-Martinez H. Practical Applications of Sperm Selection Techniques as a Tool for Improving Reproductive Efficiency. Veterinary medicine international. 2010;2011:1-9.
392. Morrell JM, Geraghty RM. Effective removal of equine arteritis virus from stallion semen. Equine Veterinary Journal. 2006;38(3):224-9.
393. Morrell JM, Klein C, Lundeheim N, Erol E, Troedsson MHT. Removal of bacteria from stallion semen by colloid centrifugation. Animal reproduction science. 2014;145(1-2):47-53.
394. Sancler-Silva YFR, Monteiro GA, Ramires-Neto C, Freitas-Dell'aqua CP, Crespilho AM, Franco MMJ, et al. Does semen quality change after local treatment of seminal vesiculitis in stallions? Theriogenology. 2020;144:139-45.
395. Malaluang P, Åkerholm T, Nyman G, Lindahl J, Hansson I, Morrell JM. Bacteria in the healthy equine vagina during the estrous cycle. Theriogenology. 2024;213:11-8.

396. LeBlanc MM. Common Peripartum Problems in the Mare. Journal of Equine Veterinary Science. 2008;28(11):709-15.
397. Papa FO, Melo CM, Monteiro GA, Papa PM, Guasti PN, Maziero RRD, et al. Equine Perineal and Vulvar Conformation Correction Using a Modification of Pouret's Technique. Journal of Equine Veterinary Science. 2014;34(3):459-64.
398. Newcombe JR. CHAPTER 2 - The Follicle: Practical Aspects of Follicle Control. In: Samper JC, Pycock JF, McKinnon AO, editors. Current Therapy in Equine Reproduction. Saint Louis: W.B. Saunders; 2007. p. 14-21.
399. Bailey CS, Fallon L, Wang W, Borst L, Timoney J. Serum and Colostral Antibody Responses of Pregnant Mares to Salmonella Bacterins and Colostral Antibody Transfer to Their Foals. Journal of equine veterinary science. 2012;32(9):575-8.
400. Barrandeguy M, Parreño V, Lagos Mármol M, Pont Lezica F, Rivas C, Valle C, et al. Prevention of rotavirus diarrhoea in foals by parenteral vaccination of the mares: field trial. Dev Biol Stand. 1998;92:253-7.
401. Imagawa H, Kato T, Tsunemitsu H, Tanaka H, Sato S, Higuchi T. Field Study of Inactivated Equine Rotavirus Vaccine. Journal of Equine Science. 2005;16(2):35-44.
402. Powell DG, Dwyer RM, Traub-Dargatz JL, Fulker RH, Whalen JW, Srinivasappa J, et al. Field study of the safety, immunogenicity, and efficacy of an inactivated equine rotavirus vaccine. Journal of the American Veterinary Medical Association. 1997;211(2):193-8.
403. Toth B, Aleman M, Nogradi N, Madigan JE. Meningitis and meningoencephalomyelitis in horses: 28 cases (1985-2010). Journal of the American Veterinary Medical Association. 2012;240(5):580-7.
404. Viu J, Monreal L, Jose-Cunilleras E, Cesarini C, AÑOr S, Armengou L. Clinical findings in 10 foals with bacterial meningoencephalitis. Equine veterinary journal. 2012;44(s41):100-4.
405. Maher O, MacDonald M, Aleman M. Surgical management of temporohyoid osteoarthropathy: 24 cases (1993-2008). Proc Amer Assoc Equine Pract. 2008;54:44-5.
406. Walker AM, Sellon DC, Comelisse CJ, Hines MT, Ragle CA, Cohen N, et al. Temporohyoid Osteoarthropathy in 33 Horses (1993-2000). Journal of veterinary internal medicine. 2002;16(6):697-703.
407. Koch C, Witte T. Temporohyoid osteoarthropathy in the horse. Equine veterinary education. 2014;26(3):121-5.
408. Lischer CJ. Successful treatment of vertebral body osteomyelitis in a foal: A highlight in equine surgery. Equine veterinary education. 2009;21(2):76-8.
409. Crabtree JR, Jorgensen A. Cervical Vertebral Osteomyelitis With Secondary Septic Arthritis of the Atlantoaxial Joint in a Foal: A Case Report. Journal of equine veterinary science. 2012;32(9):599-606.
410. Hu AJ, Grant B, Cannon J. Cervical vertebral osteomyelitis in a 4-month-old foal. Oxford, UK: Blackwell Publishing Ltd; 2009. Report No.: 0957-7734.