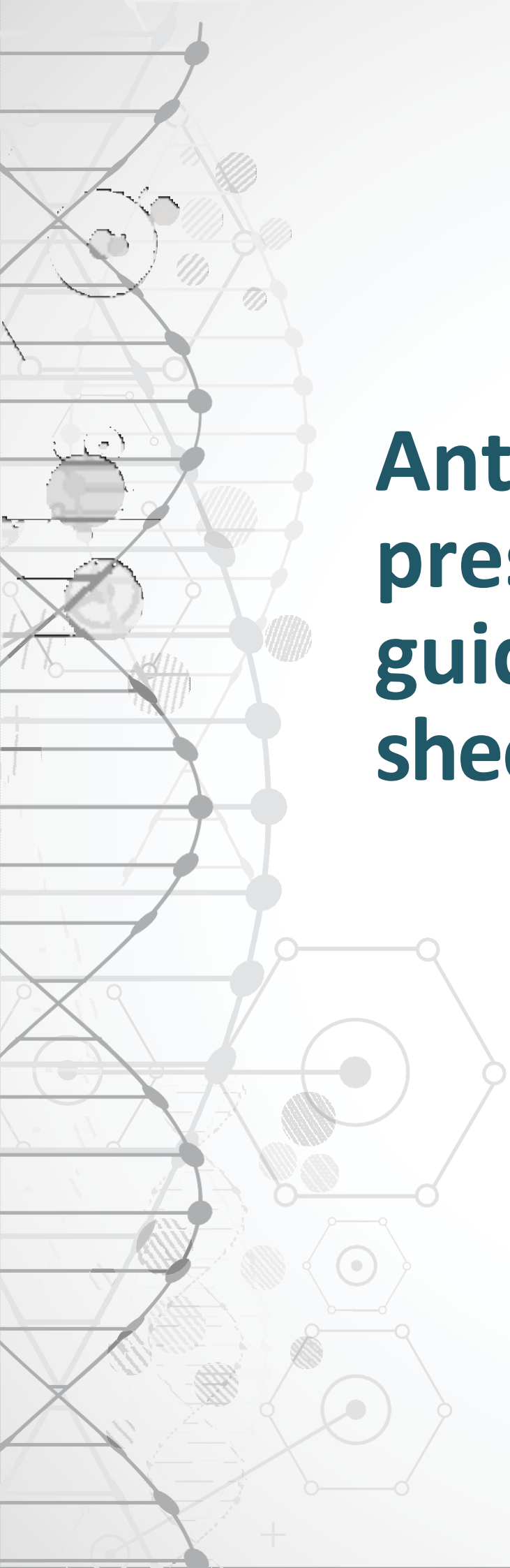

Antimicrobial prescribing guidelines for sheep

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Foreword – antimicrobial prescribing guidelines for sheep

Antimicrobial resistance (AMR) is a growing global threat that presents a serious risk to human and animal health. Resistance to antimicrobials occurs naturally in microorganisms. But it can be amplified by antimicrobial overuse, underuse, or poor management. Hence, the effective stewardship of antimicrobials—through appropriate and judicious manufacture, administering, dispensing, prescribing and disposal—is critical.

Here in Australia, the veterinary profession and food producing animal industries have a long history of addressing AMR, working diligently to ensure the safe and continued efficacy of antimicrobials. Their previous and ongoing work—a result of partnerships across the animal sector—has resulted in demonstrated low levels of antimicrobial resistant bacteria in food producing animals. It is encouraging that, in the United Kingdom's 2015 O'Neill Review into Antibiotic Resistance, Australia was ranked the fifth lowest for antibiotic use in agriculture among the 29 countries examined. Strict regulation on antimicrobial registration, high levels of biosecurity and extensive farming systems that do not favour bacterial disease also contribute to the low risk of AMR development from animals in Australia.

With the recent release of *Australia's National Antimicrobial Resistance Strategy – 2020 and Beyond* (2020 AMR Strategy), the veterinary profession will continue to play a critical role in how we minimise AMR. The antimicrobial prescribing guidelines for sheep seeks to 'ensure that coordinated, evidence based antimicrobial prescribing guidelines and best practice supports are developed and made easily available, and encourage their use by prescribers'.

These practical guidelines for Australian sheep veterinarians are designed to be a useful resource. They have been developed specifically for the Australian sheep industry and contain best-practice information to help clinical veterinarians make appropriate decisions when prescribing antimicrobials.

They encourage veterinarians to first pause and consider the need to use antimicrobials in the situation and whether there are effective non-antimicrobial alternatives. Prevention and control of infections through strict on-farm biosecurity minimises the need to use antimicrobials. Vaccination may also be available to control several important sheep diseases. If antimicrobial use is indicated, practitioners should consider the five rights – right drug, right time, right dose, right duration and right route. Using a lower rating or narrow-spectrum antimicrobial is the preferred approach, and you can also refer to the Australian Antibacterial Importance Ratings to help with these decisions.

I commend the work of all involved in the development of these guidelines and urge every sheep veterinarian to use this advice. In doing so, you'll help safeguard ongoing access to antimicrobials, ensure their long-term efficacy, deliver the best possible veterinary service to the Australian sheep industry, and play your role in the global response to AMR.

Dr Mark Schipp
Australian Chief Veterinary Officer
President of the OIE World Assembly

Dr Ray Batey BVSc, MSc, MANZCVS (Microbiology & Microbiological Disease), MAIMSc

For much of a 50+ year career as a veterinarian, Ray has been involved in a range of professional activities associated with sheep. This has included research on caseous lymphadenitis and ovine meat inspection standards, international projects, as a rural practitioner or consultant to individual producers, and as an adviser to service or support organisations of the sheep industry.

From teaching and working in both medical and veterinary microbiology, Ray developed a special interest in applying laboratory antimicrobial susceptibility testing to appropriate clinical use.

Appointment to a state reference group developing control of use regulation fostered an ongoing interest in managing risk from administering veterinary chemicals. This extended to undertaking investigations on behalf of and providing advice to a veterinary chemical company supplying products registered for sheep.

Ray has been convenor of continuous professional development for SCGV and its predecessor ASV, as well as presenting at national and international conferences and publishing in refereed scientific journals.

Dr Paul Nilon BVSc, MVS, MACVSc

Paul Nilon graduated in veterinary science in 1983 and completed a Masters with the Mackinnon Project in sheep and beef production in 1986. Since then Paul has worked in rural practice in 3 states, and for the last 15 years as a full time health and production adviser to sheep and beef clients in Tasmania, as well as the occasional gig with sheep and beef R & D corps, research projects with universities and pharmaceutical companies and some training and surveillance with the Tasmanian government.

Paul has been a member of state steering committees for footrot and OJD. He was a member of the Paraboss technical committee and contributes monthly to the Paraboss website. Paul has been trained to represent Wool Producers Australia on the CCEAD in the event of an exotic disease incursion. Paul was the president of the ASV and a committee member.

Paul cites the collegiality of a small, dedicated group of government and private vets and ag scientists as being an essential element to providing animal health and welfare, biosecurity, and production advice to the sheep industries in all states.

Professor Jacqueline Norris
BVSc MVS, PhD, FASM, MASID Grad Cert Higher Ed.

Jacqui is Professor of Veterinary Microbiology and Infectious Diseases and Associate Head of Research at the Sydney School of Veterinary Science, at the 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 zoo Felids and 6) Factors influencing antimicrobial prescribing behaviour of vets and health professionals.

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 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.

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 Chair of the International Organisation for Mycoplasmology.

He is a co-author of 280 peer reviewed research papers and book chapters, has edited two books on recent progress in understanding the mycoplasmas, and has co-supervised 60 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.

The 5R Framework for Good Antimicrobial Stewardship

Derived from: Page S, Prescott J and Weese S. *Veterinary Record* 2014;175:207-208.
Image courtesy of Trent Hewson, TKOAH.

Core principles of appropriate use of antimicrobial agents

While the published literature is replete with discussion of misuse and overuse of antimicrobial agents in medical and veterinary situations there has been no generally accepted guidance on what constitutes appropriate use. To redress this omission, the following principles of appropriate use have been identified and categorised after an analysis of current national and international guidelines for antimicrobial use published in the veterinary and medical literature. Independent corroboration of the validity of these principles has recently been provided by the publication (Monnier *et al* 2018) of a proposed global definition of responsible antibiotic use that was derived from a systematic literature review and input from a multidisciplinary international stakeholder consensus meeting. Interestingly, 22 elements of responsible use were also selected, with 21 of these 22 elements captured by the separate guideline review summarised below.

PRE-TREATMENT PRINCIPLES

1. Disease prevention

Apply appropriate biosecurity, husbandry, hygiene, health monitoring, vaccination, nutrition, housing, and environmental controls. Use Codes of Practice, Quality Assurance Programmes, Herd Health Surveillance

Programmes and Education Programmes that promote responsible and prudent use of antimicrobial agents.

2. Professional intervention

Ensure uses (labelled and extra-label) of antimicrobials meet all the requirements of a bona fide veterinarian-client-patient relationship.

3. Alternatives to antimicrobial agents

Efficacious, scientific evidence-based alternatives to antimicrobial agents can be an important adjunct to good husbandry practices.

DIAGNOSIS

4. Accurate diagnosis

Make clinical diagnosis of bacterial infection with appropriate point of care and laboratory tests, and epidemiological information.

THERAPEUTIC OBJECTIVE AND PLAN

5. Therapeutic objective and plan

Develop outcome objectives (for example clinical or microbiological cure) and implementation plan (including consideration of therapeutic choices, supportive therapy, host, environment, infectious agent and other factors).

DRUG SELECTION

6. Justification of antimicrobial use

Consider other options first; antimicrobials should not be used to compensate for or mask poor farm or veterinary practices.

Use informed professional judgment balancing the risks (especially the risk of AMR selection & dissemination) and benefits to humans, animals & the environment.

7. Guidelines for antimicrobial use

Consult disease- and species-specific guidelines to inform antimicrobial selection and use.

8. Critically important antimicrobial agents

Use all antimicrobial agents, including those considered important in treating refractory infections in human or veterinary medicine, only after careful review and reasonable justification.

9. Culture and susceptibility testing

Utilize culture and susceptibility (or equivalent) testing when clinically relevant to aid selection of antimicrobials, especially if initial treatment has failed.

10. Spectrum of activity

Use narrow-spectrum in preference to broad-spectrum antimicrobials whenever appropriate.

11. Extra-label (off-label) antimicrobial therapy

Must be prescribed only in accordance with prevailing laws and regulations.

Confine use to situations where medications used according to label instructions have been ineffective or are unavailable and where there is scientific evidence, including residue data if appropriate, supporting the off-label use pattern and the veterinarian's recommendation for a suitable withholding period and, if necessary, export slaughter interval (ESI).

DRUG USE

12. Dosage regimens

Where possible optimise regimens for therapeutic antimicrobial use following current pharmacokinetic and pharmacodynamic (PK/PD) guidance.

13. Duration of treatment

Minimise therapeutic exposure to antimicrobials by treating only for as long as needed to meet the therapeutic objective.

14. Labelling and instructions

Ensure that written instructions on drug use are given to the end user by the veterinarian, with clear details of method of administration, dose rate, frequency and duration of treatment, precautions and withholding period.

15. Target animals

Wherever possible limit therapeutic antimicrobial treatment to ill or at-risk animals, treating the fewest animals possible.

16. Record keeping

Keep accurate records of diagnosis (indication), treatment and outcome to allow therapeutic regimens to be evaluated by the prescriber and permit benchmarking as a guide to continuous improvement.

17. Compliance

Encourage and ensure that instructions for drug use are implemented appropriately

18. Monitor response to treatment

Report to appropriate authorities any reasonable suspicion of an adverse reaction to the medicine in either treated animals or farm staff having contact with the medicine, including any unexpected failure to respond to the medication.

Thoroughly investigate every treated case that fails to respond as expected.

POST-TREATMENT ACTIVITIES

19. Environmental contamination

Minimize environmental contamination with antimicrobials whenever possible.

20. Surveillance of antimicrobial resistance

Undertake susceptibility surveillance periodically and provide the results to the prescriber, supervising veterinarians and other relevant parties.

21. Continuous evaluation

Evaluate veterinarians' prescribing practices continually, based on such information as the main indications and types of antimicrobials used in different animal species and their relation to available data on antimicrobial resistance and current use guidelines.

22. Continuous improvement

Retain an objective and evidence guided assessment of current practice and implement changes when appropriate to refine and improve infection control and disease management.

Each of the core principles is important but **CORE PRINCIPLE 11 Extra-label (off label) Antimicrobial Therapy** can benefit from additional attention as veterinarians, with professional responsibility for prescribing and playing a key role in residue minimisation, must consider the tissue residue and withholding period (WHP) and, if necessary, export slaughter interval (ESI) implications of off-label use before selecting this approach to treatment of animals under their care (Reeves 2010; APVMA 2018).

The subject of tissue residue kinetics and calculation of WHPs is very complex requiring a detailed understanding of both pharmacokinetics (PK) and statistics, as both these fields underpin the recommendation of label WHPs. Some key points to consider when estimating an off-label use WHP include the following:

1 The new estimate of the WHP will be influenced by (i) the off-label dose regimen (route, rate, frequency, duration); (ii) the elimination rate of residues from edible tissues; and (iii) the MRL.

2 Approved MRLs are published in the MRL Standard which is linked to the following APVMA website page: https://apvma.gov.au/ node/10806

3 If there is an MRL for the treated species, then the WHP recommended following the proposed off label use must ensure that residues have depleted below the MRL at the time of slaughter.

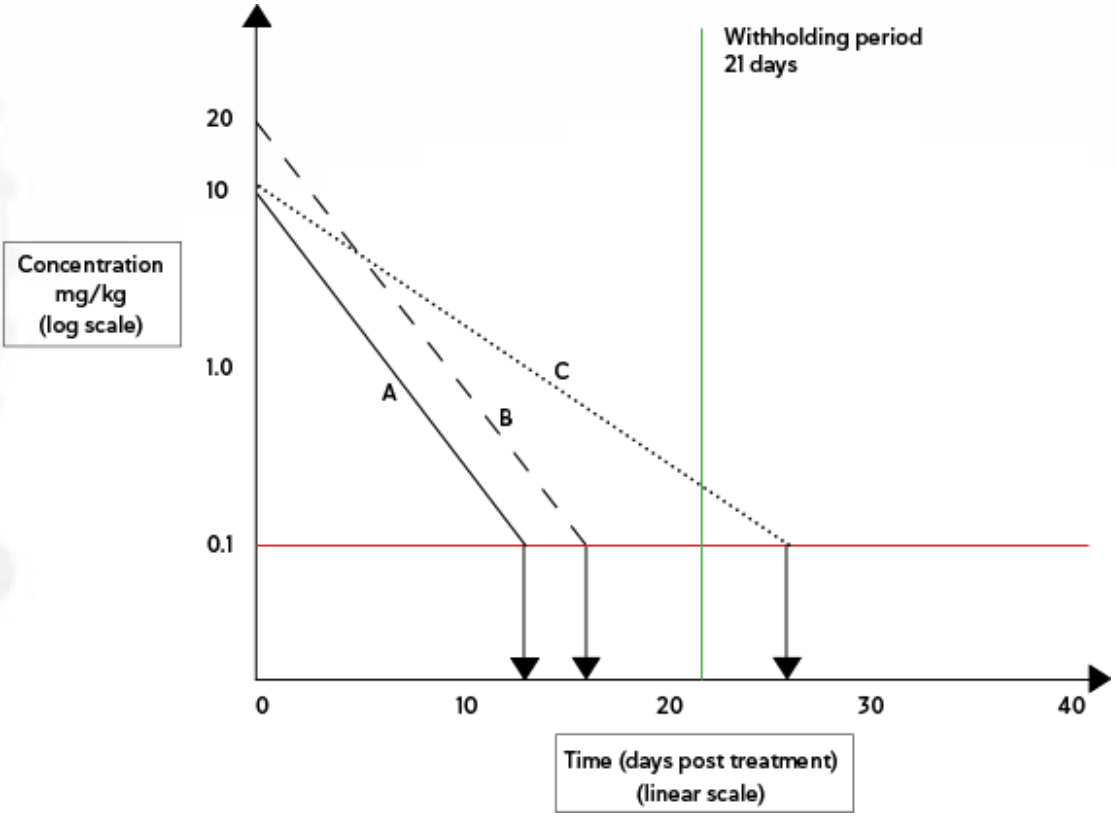
4 If there is no MRL for the treated species, then the WHP recommendation must ensure that no detectable residues are present at the time of slaughter.

5 Tissue residue kinetics may be quite different to the PK observed in plasma – especially the elimination half-life and rate of residue depletion. The most comprehensive source of data on residue PK is that of Craigmill et al 2006.

6 WHP studies undertaken to establish label WHP recommendations are generally undertaken in healthy animals. Animals with infections are likely to have a longer elimination half-life.

7. There are many factors that influence variability of the PK of a drug preparation, including the formulation, the route of administration, the target species, age, physiology, pathology, & diet.

8 The following figure provides a summary of typical effects on elimination rates associated with drug use at higher than labelled rates and in animals with infections.



An example of the relationship between the maximum residue limit (MRL) and tissue depletion following administration of a veterinary medicine. In a healthy animal (A), tissue depletion to the MRL often occurs at a time point shorter than the withholding period (WHP) that has been established for the 99/95th percentile of the population. In such an individual animal, if the dose is doubled, tissue depletion (B) should only require one more half-life and would most likely still be within the established WHP. However, if the half-life doubles due to disease or other factors, depletion (C) would now require double the normal WHP and may still result in residues exceeding the MRL (adapted from Riviere and Mason, 2011)

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Antimicrobial prescribing guidelines for sheep

Contents

SECTION 1

Chapter 1: Introduction

Nationally and globally there is close examination of animal production practices that might contribute to the transfer of antimicrobial resistance (AMR) to human pathogens, and the effects that interventions to reduce antimicrobial use in food-producing animals might have on the level of antimicrobial resistant organisms in humans and animals.[1] Most of the AMR problems in human medicine are not related to AMR in animals, and the World Health Organisation (WHO),[2] having commissioned two meta-analyses of available published literature,[1,3] concluded that the quality of evidence supporting recommendations on reducing antimicrobial use (AMU) in animals to mitigate AMR in human pathogens is low to very low.

Nevertheless, it is clear that antimicrobials should only be used when necessary. Using antimicrobials in sheep production systems increases the likelihood of resistance developing in ovine pathogens or commensals, with an associated potential for transfer to human pathogens or to pathogens in other animal species. Sheep production practices intersect with human health and the emergence of resistance from the use of antimicrobials in sheep production may also result in environmental contamination, particularly when treatment is implemented at flock level, especially when confinement feeding is practiced or when sheep are aggregated in saleyards or prior to live-export.

Improving the quality of antimicrobial use in animal production

Antimicrobial stewardship (AMS) programs are one way that the animal production community can demonstrate its commitment to producing food and fibre in a way that mitigates risk to the environment or human health, while ensuring that our shared antimicrobial resource continues to be available when needed to protect animal health and welfare.

It is not the intention of AMS programs to develop animal production systems that never use antimicrobials. This is not yet possible with current knowledge and resources, although a substantial proportion of sheep are likely to be produced in this way. However, it is possible to substantially refine and reduce AMU, with the overall aim of reducing selection pressures favouring resistant organisms and securing the use of antimicrobials for the future.

The key objectives of an AMS program are to:

- optimise the overall quantity of antimicrobials used,
- eliminate the unnecessary use of antimicrobials,
- ensure appropriate prescribing practices result in use of the most appropriate antimicrobial (or drug-of-first choice), dose rate, route, frequency and duration of treatment, and
- ensure optimal biosecurity and infection control.

To achieve these objectives for the sheep industry requires an understanding of the factors that may determine the occurrence of infectious disease in individual enterprises, as well as across the industry.

Profile of antimicrobial use in the Australian sheep industry

In Australia, sheep enterprises are conducted across a diverse range of geographic and climatic regions within limitations imposed by the quality and quantity of available fodder or water throughout the year. This is substantially influenced by large variations in climate, season and soil. Predation or risk of specific diseases also tend to restrict sheep production to certain parts of the country. There is a historical differentiation between wool and meat enterprises, although it is now generally accepted that meat production as lamb, hogget or mutton is a significant contributor to most sheep enterprises, with a major proportion of meat and offal being exported. Sheep production is generally based on extensive grazing systems with continuous access to pasture and appropriate supplementary feeding. Less frequently, sheep may be kept intensively and fed commercial or locally mixed rations for a range of commercial objectives.

The routine use of specifically targeted antimicrobial agents is very unlikely in Australian sheep enterprises, although it may be necessary for veterinarians to prescribe treatment to individuals or groups of animals on

farms when specific bacterial diseases, such as dermatophilosis or mastitis, are unresponsive to other interventions.

Best practice sheep production

Local circumstances, combined with the production system, define what constitutes best practice sheep production, with a lack of uniformity across the country in several key aspects that affect the occurrence or consequences of infectious disease, including stocking rates and whether animals are regularly moved to fresh areas for grazing (generally described as rotational grazing).

In some regions, best practice may include ewes or weaned lambs being congregated in temporary feedlots or at high stocking rate (confinement feeding) for short periods as determined by seasonal factors. High-value animals may also be housed and fed for variable lengths of time, including during critical growth periods, during preparation for and during exhibition, for the collection of semen or embryos, or for the production of ultra-fine wool.

The live export industry uses large sheep feedlots close to ports and there may be significant environmental contamination if antimicrobials are used in these feedlots.

Determinants of the occurrence, prevalence and treatment of infectious disease

Clinical conditions other than infectious disease tend to be the principal causes of morbidity or mortality in commercial sheep flocks, particularly parasitic, toxicological and nutritional disease. The treatment of infectious disease with antimicrobials may often require that concurrent non-infectious conditions also be addressed. However, specific diseases, such as virulent ovine footrot, may be a significant recurring challenge for some sheep enterprises or in some climatic regions.

In commercial sheep enterprises, the timing of regular annual husbandry events, such as mating, lambing and weaning, and procedures such as crutching and shearing, is frequently determined by anticipated seasonal constraints, or by other farming priorities, such as the demands of cropping. Husbandry procedures associated with increased risk of infectious disease on many farms include tail docking, castration, mulesing and dipping, which tend to be performed within a restricted time period after regular events such as lambing or shearing. In some remote areas, the difficulties of mustering may affect the timing of or age at which some procedures are performed, and this may affect the likelihood of infectious disease events.

Many bacterial or protozoal infections may be endemic or recur sporadically in individual flocks because of subclinical infection, such as with coccidia, *Dermatophilus congolensis* and salmonellae, or may originate from environmental contamination or sources, as is seen with *Erysipelothrix rhusiopathiae*. Normal microflora, such as *Streptococcus bovis*, may also contribute to the infectious disease burden due to the impact of high starch intake on the ruminal microflora when individual sheep or flocks consume substantial quantities of grain.

A general survey of sheep/ovine production animal veterinarians in Australia was undertaken in 2019 as part of the development of these guidelines. The data indicate that the administration of antimicrobials for the treatment, metaphylaxis or prophylaxis of infectious disease is neither widespread nor frequent across the Australian sheep industry, and that a small number of conditions, including

- kerato-conjunctivitis,
- foot abscess,
- pneumonia,
- virulent ovine footrot, and
- mycotic dermatitis (dermatophilosis)

are the most frequent reasons for veterinarians prescribing antimicrobial treatment within individual sheep enterprises (*unpublished data*).

In addition to this general survey, interviews were conducted in late 2019 across five Australian states with veterinarians who regularly treat sheep. The results were used to determine the impact on sheep enterprises of a range of conditions or circumstances that may or may not necessitate prescription of antimicrobials

(*unpublished data*). Participating veterinarians were asked to score the importance or urgency of the situation when a client sought advice on each nominated condition and indicate how often they were consulted about animals with each condition. The impact of each condition in the meat/wool and the dairy sectors was calculated as importance x frequency, although only two of the veterinarians were involved in the dairy sector. The median of these scores was the basis for ranking conditions as having moderate to high importance or occurring with medium to high frequency, as shown in Table 1. For the meat/wool sector these data summarise priority conditions across mainland Australia and thus present an overall view of likely requirement for antimicrobial treatment. However, these semi-quantitative median values do not adequately reflect that there may be substantial state, regional or local variations in the importance or frequency of some conditions.

While 19 conditions were deemed by veterinarians to be of moderate to high importance or urgency if encountered in dairy and/or meat/wool sheep enterprises, the median frequency of veterinarians being consulted was low for the majority (15/19 or 79%) of these. This supports the conclusion that the prescription and use of antimicrobials is likely to be infrequent in sheep enterprises, including for high impact diseases. It should be noted that, in this context, frequency refers to how often individual veterinarians encounter a disease, rather than overall prevalence or percentage of enterprises in which the disease occurs. For example, caseous lymphadenitis (CLA) is a relatively common infectious disease of sheep, but veterinarians are infrequently consulted about it. However, the results from the interviews suggest that CLA is important on those infrequent occasions when veterinarians are consulted, whether for individual cases or advice about a high prevalence of disease.

The substantial difference in impact between the meat/wool and the dairy sectors of some conditions, such as acute ruminal acidosis and interdigital trauma, suggests that prescribing veterinarians are required to take account of the enterprise type when a specific condition occurs or is diagnosed.

Table 1 – Clinical Conditions: importance and frequency of consultation about clinical conditions for which antimicrobial treatment may be indicated in sheep meat/wool or sheep dairy enterprises, ranked by median impact (importance x frequency).

Clinical condition or circumstance	Principal clinical effect or consequence	Median importance [a]	Median frequency [b]
Foot abscess	Subacute to chronic lameness; animal welfare	Moderate [c]	Medium
Fly-strike	Subacute exudative dermatitis; septicaemia; mortality	High	Low
Acute ruminal acidosis	Acute mortality, subacute diarrhoea, chronic lameness	Moderate	Low
Foot scald	Acute to subacute lameness	Moderate	Medium
Pinkeye	Acute to chronic keratoconjunctivitis; blindness	Moderate	Medium
Mastitis	Acute to chronic agalactia; ewe or lamb mortality	Moderate	Low
Virulent footrot	Severe acute to chronic lameness; animal welfare	High	Low
Pneumonia	Various, from illthrift to death; abattoir condemnation	Moderate	Medium
Salmonella, Yersinia	Acute to subacute diarrhoea; septicaemia; mortality	Moderate	Low
Infectious arthritis	Lameness; illthrift; abattoir condemnation	Moderate	Low
Uterine prolapse	Risk of intercurrent infection; ewe & lamb mortality	Moderate	Low
Caseous lymphadenitis	Pyogranulomas of lymph nodes and lungs; high value individual animals may require treatment.	Moderate	Low
Dermal grass seeds	Intercurrent infection, septicaemia; animal welfare	High	Low
Interdigital trauma[d]	Lameness; non-specific infection; reduced milk yield	Low	Low
Mycotic dermatitis	Chronic dermatitis; unable to shear; flystrike; lameness	Moderate	Low
Obstetrical	Risk of intercurrent infection; ewe & lamb mortality	Moderate	Low
Urinary/Urolithiasis	Frequently high value rams requiring surgical intervention; animal welfare	Moderate	Low
Spontaneous abortion	Pre-partum lamb mortality; agalactia	Moderate	Low
Tetanus	Post-husbandry event; poor prognosis for clinical disease; risk of additional cases	Moderate	Low

a. **Median importance** is derived from semi-quantitative estimates by responding veterinarians of importance (or urgency) if a client sought advice on the clinical condition or circumstance.
b. **Median frequency** is derived from semi-quantitative estimates by responding veterinarians of frequency of interaction with individual clients or affected animals relevant to the clinical condition or circumstance.
c. **Moderate (or Medium) and High** breakpoints are at 40% and 70% respectively of the maximum score for each of importance, frequency and impact.
d. **Scores for interdigital trauma** were LOW for meat/wool enterprises and overall. However, the impact score was HIGH for dairy enterprises and ranked above 5 other conditions of overall moderate importance.

Table 2 – Active ingredients for use in sheep – ASTAG ratings and formulations

ANTIMICROBIAL AGENT	CLASS	IMPORTANCE ASTAG 2018[4]	FORMULATIONS
AMOXICILLIN	Penicillins moderate-spectrum	Low	injection
BACITRACIN ZINC@	Polypeptides	Low	ear and eye ointment
CLOXACILLIN	Penicillins antistaphylococcal	Medium	eye ointment
ERYTHROMYCIN	Macrolides	Low	injection
FRAMYCETIN@	Aminoglycosides	Low	ear and eye ointment
NEOMYCIN	Aminoglycosides	Low	injection, topical lotion
OXYTETRACYCLINE	Tetracyclines	Low	injection, feed supplement, soluble powder, topical spray, aerosol, foaming pessary
PENETHAMATE HYDRIODIDE	Penicillins narrow-spectrum	Low	injection
PENICILLIN BENZATHINE	Penicillins narrow-spectrum	Low	injection
PENICILLIN PROCAINE	Penicillins narrow-spectrum	Low	injection
POLYMYXIN B@	Polymyxins	High	ear and eye ointment
SULFADIAZINE#	Sulfonamides and DHR inhibitors	Medium	injection, oral, pessary, bolus
SULFADIMIDINE#	Sulfonamides and DHR inhibitors	Medium	injection
SULFADOXINE#	Sulfonamides and DHR inhibitors	Medium	injection
TRIMETHOPRIM#	Sulfonamides and DHR inhibitors	Medium	injection, oral, pessary, bolus
VIRGINIAMYCIN	Streptogramins	High	wettable powder
LASALOCID	Ionophores	Low (NHU)	Solid feed supplement, liquid
MONENSIN	Ionophores	Low (NHU)	Feed supplement

@only available in a combination for topical use

only available as a combination of sulfonamide and trimethoprim, the combination is of ASTAG medium importance, individual agents are low importance.

Chapter 2: Appropriate treatment plan

Targeting treatments at the specific diseases or condition of concern helps preserve the efficacy of more important antimicrobials, the drugs of high or critical importance by reducing their use in situations where they are not needed. This concept is well developed in human medicine, where a wide range of antimicrobial agents is available for use. With relatively few medicines registered for use in sheep to prioritise, these guidelines provide advice principally on whether antimicrobial agents are required and the recommended primary treatment, but not on secondary or tertiary recommendations for treatment.

The Australian Strategic and Technical Advisory Group[4] (ASTAG) on AMR importance rating was used in developing these recommendations as the most relevant to the Australian situation. This rating ranks antimicrobials as having high, medium or low importance for use in humans. There are two other categories of minimum human use (MHU) or no human use (NHU). The WHO[5] list is numbered from one to five, from highest to lowest in importance, and varies from the ASTAG list, as it aims to address global issues, rather than the Australian context. First line treatments, for example those initiated while waiting for laboratory results, should use the lowest rated medications that are likely to be effective.

In Australia, registered veterinarians are permitted to prescribe a medication for sheep if it is approved by the Australian Pesticides and Veterinary Medicines Authority (APVMA) for use in sheep or other food animals in Australia. Veterinarians are also permitted to prescribe a medication approved for use in sheep at levels and durations that vary from those on the label if a suitable withholding period (WHP) can be applied, the prescription can be justified scientifically, and provided that the use does not contradict a restraint statement on the label. It is likely there will be no label meat WHP for such drugs or elevated dose rates in sheep, and it is therefore the responsibility of the prescribing veterinarian to determine a suitable WHP.

The treatment priority list is outlined in Table 3. An effective, approved antimicrobial is preferred over 'off-label' prescription. Although there may be only one or two first line treatments listed, in most situations medications classified as low importance, NHU or MHU can meet this criterion. The higher importance rating of lincomycin, spectinomycin and trimethoprim/sulfonamide should be noted. Trimethoprim/sulfonamide combinations are recommended as a first line treatment only for specified conditions, though it should be recognized that trimethoprim may not be a suitable antimicrobial agent for sheep as it has a very short elimination half-life.

While the long-term focus must be to reduce the level of AMU in animal production, from a therapeutic perspective, there are multiple, high-impact conditions in sheep for which treatment with antimicrobials is justifiable for reasons of animal health, welfare and productivity (Table 3). The differences in priority between dairy and meat/wool enterprises should be noted. These conditions are frequently only relevant to individual farms, rather than being industry-wide problems. The occurrence of many of these conditions is determined by environmental and other factors that may not be amenable to preventive management.

The disease and treatment priorities are presented in Table 3 with the common diseases represented. Meat WHP or export slaughter interval (ESI) will be the principal determinant of the primary drug for some treatments, such as when animals are being treated to facilitate salvage slaughter or when animals in feedlots undergo treatment. However, especially for wool producing sheep, there will often be a prolonged time to slaughter following treatment (months to years), and thus tissue residues become less relevant than the choice of the most appropriate drug or duration of action, or the practicalities of administration. For these reasons, long-acting injectable preparations of penicillin and oxytetracycline are frequently used.

There is a dearth of recently published information on the susceptibility of common Australian ovine pathogens to antimicrobials. Veterinarians will, in prescribing medications, necessarily draw insight from both the global scientific literature and local laboratory susceptibility testing. There is a need for ongoing surveillance of AMR in Australia and, wherever it is practical and appropriate, AMU should be preceded by culture and susceptibility testing.

Ceftiofur

Ceftiofur is a third-generation cephalosporin rated by ASTAG as having HIGH IMPORTANCE as a member of a class of antimicrobials considered "essential antibacterials for the treatment or prevention of infections in humans where there are few or no treatment alternatives for infections". These have also been termed "last resort" or "last line" antibacterials."

Ceftiofur is not registered by APVMA for use in sheep. It is registered for use in cattle and carries the label restraint "DO NOT USE for mass medication: for individual animal treatment only". As a general principle, *label restraints take precedence over the rights of veterinarians to prescribe off-label*.

Within a framework of AMS, use of ceftiofur in sheep should be reserved for rare and exceptional circumstances in individual sheep where culture and susceptibility testing of appropriate clinical samples indicates no suitable alternative.

Ceftiofur use cannot be justified to take advantage of NIL or very short WHP for milk or meat, respectively. The need for ceftiofur should be considered an alert to closely examine management practices and to develop and implement a health plan to prevent infection and improve animal health without the need for antibacterials of HIGH IMPORTANCE.

Dose rates

These guidelines provide guidance to veterinarians on prevention and treatment options for some common bacterial and protozoal diseases, including the selection and use of antimicrobial products registered in Australia for use in sheep, or those that are registered for other species and may be used in sheep.

Registered dose rates and corresponding WHPs are rarely, if ever, revised once a product is first registered. Based on recently published research in horses and small companion animals, it is likely that best practice dose rates are not always aligned with label dose rates, at the very least for penicillin, potentiated sulfonamides and amoxicillin.[6] These products were first registered over 50 years ago. There is no readily available database that informs veterinarians of required WHPs that ensure that the maximum residue level (MRL) is not exceeded when prescribing these antimicrobials at the higher dose rates consistent with efficacy, even when these higher dose rates have been published in the scientific literature.

For food animal veterinarians these circumstances create a quandary when attempting to establish the appropriate WHP to manage risk to human health or trade when prescribing of an antimicrobial off-label at an optimal level for efficacy, a key principle of AMS as it assists in minimising the risk of selection for resistance.

A solution to this challenge will likely require input from veterinarians, scientists, the pharmaceutical industry and the APVMA. Summaries of antimicrobial dose rates approved by APVMA at the time of product registration, together with literature based specific off-label use for products used in sheep, are presented in Table 3. Readers are referred to the APVMA web site and search engine PubCRIS[7] for product-specific information about dose rates and WHPs.

Antimicrobials in feed

The easiest and most effective ways to reduce the use of antimicrobials in food animal production is to remove them from animal feeds. Australian sheep producers do not use antimicrobials in feed for growth promotion, but antimicrobials have been used to manage the risk of ruminal acidosis associated with feeding moderate to high starch diets to ruminants. The feeding of grain or grain-based diets in sheep enterprises may be undertaken for a range of valid reasons, including:

- as a supplement to paddock grazing, particularly to overcome seasonal energy deficits,
- to ensure that the turnoff of sheep as lamb or mutton is of sufficient quantity or quality to meet market specifications,
- to utilise excess on-farm production, particularly grain that does not meet market specifications,
- to enhance the growth rate and/or performance of high value individual animals such as stud rams, or

- as a sole feed under conditions of drought or emergency, such as after a major fire.

Many commercial stock feeds available for feeding sheep now utilise a range of technologies that do not require the addition of antimicrobials to enable animals to adapt rapidly to the feed. This is an important innovation to reduce the overall use of these drugs in the sheep industry and should be fostered and encouraged by veterinarians providing advice to sheep enterprises.

It is frequently necessary to feed grain-based diets other than as commercial feeds. It is customary to progressively introduce these by initially limiting the quantities fed and/or by increasing the starch component of the ration over a period of at least 10 days. However, this may not be feasible in circumstances of emergency feeding.

The medication of feed with antimicrobials in these circumstances requires the prescribing veterinarian to have an adequate understanding of the justification and to exercise a high level of professional judgment.

It is inappropriate to rely on ongoing and extended use of antimicrobials as a routine approach to managing all grain based diets.

Oral antimicrobial dosing including as water medication

Considering the potential impact on ruminal microflora and variable absorption of some antimicrobial classes in ruminants following oral administration, the oral administration of antimicrobials is generally not appropriate for treating non-enteric infections. Medication through water may also be affected by considerable variation in individual water intake by sheep, and thus an appropriate dose rate may not be reliably achieved for individuals in a group, with the potential to contribute to treatment failure or the development of AMR through subtherapeutic doses.

Facilities to medicate via water may not be available on most commercial sheep farms, although in some regions and states, tank troughs are being increasingly adopted, especially when confinement feeding is being practiced. However, dosing as water medication may be feasible and is sometimes undertaken in special circumstances, particularly in the live-export industry.

Recommendations on oral medication of sheep with antimicrobials

Although it may sometimes be appropriate to treat all individual animals in a mob or flock during infectious disease outbreaks associated with high morbidity and/or mortality, veterinarians should consider alternatives to mass medication of sheep with antimicrobials in feed or water.

Considering the likely impact on ruminal microflora, including the selection for AMR, oral medication of sheep with antimicrobials should generally be limited to the treatment or management of enteric infections.

The oral use of broad-spectrum antimicrobials, such as the tetracyclines or the macrolides and related antimicrobials, is likely to adversely affect or disrupt the normal anaerobic microflora of the rumen and they should only be prescribed for oral or intra-ruminal use in exceptional circumstances. Oral medication should generally be limited to aminoglycosides and sulfonamides.

The treatment, metaphylaxis or prophylaxis of non-enteric infectious disease should be undertaken by systemic injection or by topical or local application, as appropriate.

General biosecurity considerations

Vaccination against bacterial diseases, such as those caused by the clostridia, caseous lymphadenitis and/or *Erysipelothrix rhusiopathiae*, is frequently, but not universally, practiced, and vaccines against virulent ovine footrot and campylobacteriosis may be administered in certain regions. Vaccination has a variable impact on reducing the need to prescribe or use antimicrobials in sheep across different enterprises and regions. As examples: vaccines against virulent ovine footrot may be prohibited in some jurisdictions; depending on the enterprise, a combination of vaccines and antibiotics may be used at different stages of the disease cycle for control; or antibiotics may be used on an individual animal or part flock basis for prevalence reduction prior to eradication or vaccination.

Many of the globally important high mortality infectious diseases of sheep do not occur Australia, and for those that do occur. the risk of contagious disease is best managed by biosecurity practices that prevent the introduction of the relevant pathogen and/or by husbandry systems that mitigate the likelihood of enzootic infections occurring or being expressed, rather than by medication with antimicrobials.

Important examples include clinical salmonellosis or anaemia due to *Mycoplasma ovis*, which are frequently triggered by nutritional or other stress events. Dermatophilosis (mycotic dermatitis), can occur frequently and at high prevalence, but is likely to be expressed in susceptible populations following the congregation of wet sheep during husbandry procedures that favour the dissemination of zoospores between subclinical cases and non-immune animals, such as lambs or hoggets.

It is a key role of veterinarians and a component of good AMS to provide advice to sheep enterprises on the impact of nutrition and husbandry on the likelihood of the occurrence or recurrence of infectious diseases.

For some diseases, such as virulent ovine footrot, it is an imperative of AMS to utilise epidemiological principles to eradicate the organism from infected flocks, if this is feasible, or to otherwise limit the expression of disease requiring antimicrobial treatment.

Dose rates, frequency of administration and duration of oral or parenteral treatment for antimicrobials registered for sheep

Anecdotal experience and survey data suggest that penicillin and oxytetracycline are the antimicrobial drugs most frequently prescribed for the treatment of bacterial disease of individual sheep, and that sulfonamides alone, or in combination with trimethoprim, are also commonly administered to treat high morbidity disease such as salmonellosis, as well as for individuals. Amoxicillin, neomycin and penethamate are currently prescribed infrequently.

An important objective in developing these guidelines is sustainable use of antimicrobials registered for sheep. This includes both efficient and effective administration, and preservation of efficacy.

Narrow spectrum penicillins

General considerations

Injectable forms of penicillin used in humans and animals include complexes with procaine or benzathine, as well as the soluble potassium salt of benzyl penicillin. The penethamate hydriodide form is also registered for use in animals in many countries.

Disregarding slow release formulations in oil, any change in the dose of penicillin does not increase or decrease the duration of effect by an equivalent proportion, but there is a more direct relationship with the maximum blood or tissue levels or C_{max}. Doubling the dose will usually double the maximum concentration but will only increase the duration of effect by one elimination half-life.

However, evidence demonstrates that the duration of time above the minimum effective concentration (MEC), rather than maximum plasma concentration (C_{max}), is the principal determinant of efficacy (ie penicillins are time-dependent antimicrobials).

Serious infections in humans may be treated with appropriate intravenous doses of soluble benzyl penicillin, with an underlying limitation being the renal excretion rate. Excretion can be modified to achieve higher C_{max} and duration of action using probenecid, although this is generally not used in domestic animals.

A second way to extend duration of action is by use of low solubility salts, such as procaine and benzathine, in equimolecular ratio to penicillin, which are injected intramuscularly and dissolve slowly at the site of injection.

Penethamate hydriodide is an ester of benzyl penicillin and a salt of a weak base (pKa 8.5) and consequently a high proportion appears in the plasma and tissue in a non-ionized form. Unlike other commonly used penicillins, plasma and tissue esterases release benzyl penicillin from penethamate in the target tissues, including at the site of infection.

There is considerable variation (up to 64 fold) in the mean minimum inhibitory concentration (MIC) for bacterial isolates reported as susceptible to benzyl penicillin. The MIC is very low for some ovine pathogens, including *Erysipelothrix rhusiopathiae*, group C & G streptococci, and non-penicillinase-producing staphylococci, making them highly susceptible.

Procaine penicillin

The key pharmacokinetic (PK) characteristic of the procaine-benzyl penicillin complex is delayed absorption. Data suggests that C_{max} is achieved at a relatively low plateau (compared to an equivalent dose of the potassium salt of benzyl penicillin) at about 4 hours, with plasma concentrations then gradually declining and with the drug still detectable, but often below the MEC, at 24 hours.

It is therefore reasonable to presume that when procaine penicillin is administered once daily, the plasma concentrations are likely to be below the MEC, particularly for those organisms in which the MIC of penicillin is higher, at the time the repeat doses are administered, with a lag of up to 4 hours before C_{max} is again attained. Accordingly, currently registered dose rates or frequencies of administration are likely to result in a suboptimal treatment regimen.

The WHP for meat is 5 days, while the export slaughter interval (ESI) is not established.

Dose rate, and frequency and duration of administration: The dose rate for registered procaine penicillin preparations is 12-15 mg/kg by intramuscular or subcutaneous injection, with a 24-hour frequency of dosing.

The prescribing veterinarian may need to take account of the site of infection and the MIC of the target organism in determining the dose rate, and the frequency and duration of administration for procaine penicillin, and this may include consideration of off-label use.

Long acting penicillin (LAP)

The currently registered products are a combination of procaine and benzathine penicillins.

The key PK characteristic of the benzathine-benzyl penicillin complex is more extended absorption from the site of injection. Benzathine penicillin results in a lower, but more prolonged, plateau of plasma concentrations than procaine penicillin due to the slower absorption from the site of injection.

The critical issue for the combinations is whether the plateau is above the MEC (or MIC) for sufficient time with the registered dose.

It is therefore reasonable to presume that long acting penicillin (LAP) will deliver a substantially lower C_{max} than procaine penicillin. The WHP for meat is 30 days, while there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rate for LAP preparations (2 ml/40 kg) contains half the dose of procaine penicillin of the procaine penicillin preparations (7.5 mg/kg) and a 5.75 mg/kg dose of penicillin as the benzathine complex – a total dose of 13.25 mg/kg. It is administered by intramuscular or subcutaneous injection.

The prescribing veterinarian may need to take account of the MIC of the target organism in determining dose rate of long acting penicillin and this may include consideration of off-label use.

Penethamate

Considering that the complex itself is absorbed, distributed and locally hydrolysed, penethamate would appear to have PK characteristics that are very different from those of procaine/benzathine penicillins, which may offer some advantages when treating susceptible bacteria with a higher penicillin MIC.

The WHP for meat is 5 days, while there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rate for penethamate is 15 mg/kg once daily.

Amoxicillin

Amoxicillin is a semi-synthetic broad-spectrum penicillin that is slightly less active against most Gram-positive bacteria than benzyl penicillin. Like penicillin, it is inactivated by the penicillinases of resistant staphylococci. However, *Listeria monocytogenes* is substantially more sensitive to ampicillin than to benzyl penicillin. Considering the similar spectrum of MIC's between ampicillin and amoxycillin, registered amoxycillin preparations might be preferred over penicillin for antimicrobial treatment of clinical listeriosis.

The key distinguishing characteristic of amoxicillin is an activity 4 to 8 times greater than that of benzyl penicillin against many Gram-negative pathogens. However, it is important to note that this is not the case for members of the *Pasteurellaceae*, including *Pasteurella, Mannheimia, Bibersteinia, Histophilus* and *Actinobacillus* spp. *Pseudomonas* spp. are resistant and *Klebsiella aerogenes* (a cause of necrotising Gram-negative infections) has a high level of intrinsic resistance.

Most registered veterinary preparations are a slow-release formulation in oil, providing prolonged tissue levels, but more frequent dosing may be needed for efficacy against Gram-negative infections.

Most registered preparations have a concentration of 150 mg/kg. One registered formulation contains 200 mg/mL.

Precautions for one registered preparation include that it must not be administered orally or by intra-ruminal injection, with a statement that limits use to parenteral injection, suggesting that it should not be used for treatment of ruminal acidosis.

The WHP for meat is generally 28 or 30 days, and there is no ESI established. One registered formulation has a WHP for meat of 14 days.

Dose rate, and frequency and duration of administration: The label dose rate and frequency of administration vary between registered preparations. The registered dose rates are 7-15 mg/kg, with a dosing interval of 48 hours (if required), for most Gram-positive pathogens, and 24 hours if the target organism is Gram-negative.

In comparison to procaine and benzathine penicillins, the properties of registered amoxicillin preparations and the dosing regimen may offer advantages in terms of ensuring a sufficient time of exposure to concentrations above MEC in tissues during therapy.

Oxytetracycline

General considerations

There are at least two distinct formulations of the hydrochloride salt of oxytetracycline, with some preparations registered to deliver prolonged duration of action (up to 48 hours) at an increased dose rate.

Oxytetracycline is also available in a registered long acting form as the dihydrate.

Oxytetracycline is known to affect osteocytes and amelocytes and cause discolouration of developing teeth. The label precautions on some registered preparations draw attention to this effect if treating growing lambs or ewes during late pregnancy.

Short acting oxytetracycline hydrochloride 100mg/mL

The WHP for meat is 14 or 15 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: Registered dose rates vary considerably from 2-9 mg/kg, with once daily administration for 3-5 days. The routes of administration advocated include subcutaneous, intramuscular, intraperitoneal and intravenous injection, but vary between preparations, with intravenous administration in sheep not supported on any label.

Formulation of oxytetracycline hydrochloride 100 mg/mL in polyvinylpyrrolidone (PVP)

There are two registered dose rates. The purpose of the higher dose rate is to provide greater duration of effect or extend the interval between dosing.

The WHP for meat is 10 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rates are variable. For once daily administration for 3-5 days, 3-8 mg/kg is advocated, and for extended duration of activity to up to 72 hours, a dose of 10-20 mg/kg.

The routes of administration include intramuscular or intravenous injection.

Long acting oxytetracycline dihydrate 200 mg/mL

The WHP for meat is consistently 42 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rate is 20 mg/kg (1 mL/10 kg) administered by deep intramuscular injection, preferably in the neck, with the total volume at any one site limited to 5 or 10 mL. If required, re-treatment is in 72 hours.

To attain an earlier and higher C_{max} during initial treatment, some registered labels advocate concurrent administration of a dose of oxytetracycline hydrochloride.

Long acting oxytetracycline dihydrate 300 mg/mL

The WHP for meat is 28 days, and the ESI is 28 days.

There are two registered dose rates. The purpose of the higher dose rate is to provide greater duration of effect or extend the interval between dosing.

Dose rate, and frequency and duration of administration: The registered dose rate is 20-30 mg/kg (1 mL/10-15 kg) administered by deep intramuscular injection, preferably in the neck, with the total volume at any one site limited to 5 or 10 mL.

Erythromycin

This macrolide antibiotic is mainly effective against Gram-positive aerobic, facultatively anaerobic and obligately anaerobic bacteria, mycoplasmas and Gram-negative anaerobes.

Most strains of *Campylobacter* spp. are very susceptible to erythromycin (low MIC), and it may be the drug of choice if antimicrobial treatment is required.

There is some evidence from human medicine of clinical effectiveness against facultatively intracellular organisms, including *Listeria* spp.

Many groups of anaerobic bacteria are particularly susceptible to erythromycin, so oral administration to animals with a functioning rumen is likely to have an adverse effect on the normal ruminal microflora. Oral formulations of erythromycin registered for pigs or poultry should not be prescribed for sheep.

The WHP for meat is short, at 3 days, but there is no ESI established.

Dose rate, and frequency and duration of administration: There is a variable registered dose rate of 2-5 mg/kg administered by deep intramuscular injection, with intravenous administration specifically contra-indicated. Repeat administration is at 24-hour intervals.

Neomycin

This aminoglycoside antibiotic is principally effective against Gram-negative aerobic or facultatively anaerobic bacteria and some Gram-positive pathogens, including staphylococci and actinomycetes.

Resistant pathogens include streptococci, clostridia and Gram-negative anaerobes. Aminoglycosides, including neomycin, have minimal effect against obligate anaerobes generally, including gastroenteric microflora, because they are not imported into the bacterial cell.

Neomycin is very poorly absorbed from the gastrointestinal tract after oral or intraruminal administration.

There is considerable variation in the meat WHP for registered preparations (10-30 days), and there is no ESI established.

Dose rate, and frequency and duration of administration: Renal toxicity of neomycin is related principally to duration and frequency of treatment rather than dose, and a maximum duration of treatment of 3 days for any parenteral treatment is advocated. The registered dose rate for parenteral use of neomycin is 2-4 mg/kg administered by intravenous or intramuscular routes. Label directions advocate repeat doses at intervals of 6-12 hours, but evidence supports treating at higher doses, but less frequently, for a short duration. Thus, using a dose rate of at least 4 mg/kg once daily for 1-3 days may be preferable.

Aminoglycosides, including neomycin, are specifically contra-indicated for use in the peritoneal cavity and should not be used in this way for contaminated surgery.

Procaine penicillin + neomycin combination

This preparation might be expected to be effective against bacteria susceptible to either penicillin or neomycin, but there may be indications where combining antibiotics from different classes, such as aminoglycosides and penicillins, may provide an apparent synergistic effect; for example, on the basis of clinical judgement, for overwhelming or life-threatening infections in individual animals.

The WHP for meat is 35 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The dose rate for procaine penicillin in this combination is 10 mg/kg, which is less than the registered dose for preparations containing only penicillin. The dose rate for neomycin is 5 mg/kg, which is 25% above the maximum dose for registered injectable neomycin preparations. This formulation is administered by intramuscular injection, with repeat doses at intervals of 24 hours and a maximum duration of treatment of 3 days.

Sulfonamide and related antimicrobial agents

General considerations

Sulfadimidine is not registered for use in sheep as a single agent, but is widely prescribed and used, particularly to treat enteric disease. No sulfonamide is registered as the sole active for use in sheep.

There are multiple registrations of sulfonamide combinations with trimethoprim.

Trimethoprim-sulfonamide combinations are effective against a wide spectrum of pathogenic Gram-positive and Gram-negative bacteria, but there are notable exceptions.

Erysipelothrix rhusiopathiae and *Leptospira interrogans* are intrinsically resistant and trimethoprim-sulfonamide combinations are generally ineffective against anaerobes.

The ASTAG rating of trimethoprim in combination with a sulfonamide is MEDIUM, while the ratings for most other antimicrobials registered for systemic use in sheep are low or NHU. This should be considered, particularly when alternative antimicrobial agents are available and regular or frequent treatment may be required, such as in a feedlot.

Trimethoprim-sulfadiazine combination for water medication

The registered preparation contains sulfadiazine at 400 g/kg and trimethoprim at 80 g/kg.

The WHP for meat is 14 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The registered daily dose rate is based on a target dose of 62.5 mg/kg.

There may be considerable differences in water intake by individual sheep. It may be reasonable to calculate an appropriate level of medication for sheep housed in sheds, but it would generally not be feasible to calculate levels of medication in other situations.

With appropriate dilution, it may be feasible to prescribe this preparation for oral dosing.

Trimethoprim-sulfadiazine bolus

A product containing sulfadiazine at 1 g and trimethoprim at 200 mg is registered and available for oral and intrauterine dosing of sheep.

The WHP for meat is 14 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: There is no registered oral dose rate for sheep, but one bolus per 40 kg is the general livestock dose and is equivalent to a dose of 30 mg/kg.

Trimethoprim-sulfadimidine for injection

A registered product containing sulfadimidine at 200 mg/mL and trimethoprim at 40 mg/mL is available.

The WHP for meat is 15 days with no ESI established for sheep.

Dose rate, and frequency and duration of administration: The registered dose rate is 24-36 mg/kg, administered by intramuscular injection with 24-hour interval between doses. Intravenous doing is not approved for sheep.

Trimethoprim sulfadoxine injection

Registered products containing sulfadoxine at 200 mg/mL and trimethoprim at 40 mg/mL are available.

The WHP for meat is 14 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rate is 24-36 mg/kg, administered by intramuscular or intravenous injection with 24-hour intervals between doses.

Trimethoprim-sulfadiazine injection

Registered products containing sulfadiazine at 400 mg/ml and trimethoprim at 80 mg/ml are available.

The WHP for meat is 28 days, and there is no ESI established.

Dose rate, and frequency and duration of administration: The registered dose rate is 16-24 mg/kg, administered by intramuscular or intravenous injection with 24-hour intervals between doses.

Feed additives

Monensin

The WHPs for meat (NIL or 24 hours) and the ESI (not established or 7 days) vary between registered products. There is a general label restraint for milk (DO NOT USE in sheep which are producing or may in the future produce milk that may be used or processed for human consumption).

Dose rate, and frequency and duration of administration: Monensin may be included in sheep feed at 5-20 g/tonne of prepared feed as a coccidiostat, principally in management systems in which lambs are reared or finished in sheds, or in other confinement feeding systems.

Rates above 20 g/tonne may suppress growth in lambs.

Lasalocid

The WHP for meat is 24 hours, and there is no ESI established. There is a general label restraint for milk.

Dose rate, and frequency and duration of administration: Lasalocid may be included in sheep feed at a preferred rate of 33 g/tonne of prepared feed (range 10-60 g/tonne) as a coccidiostat, principally in management systems in which lambs are reared or finished in sheds, or in other confinement feeding systems.

Virginiamycin

The streptogramin antimicrobials (to which virginiamycin belongs) are highly important in human medicine (ASTAG rating of 'high'[1]) for treatment of vancomycin-resistant staphylococcal and enterococcal infections. Accordingly, there is a risk of selection for AMR of significant concern to human health arising from the inclusion of virginiamycin in animal feeds, particularly if this is done on a routine or long-term basis.

The 2004 'APVMA *Review of the registration of products containing virginiamycin and their labels'*[2] found that there was an unacceptable risk that the use of virginiamycin for undefined periods of time will induce AMR in *Enterococcus faecium* in animals and poultry. Such resistant bacteria may colonise humans directly, or transfer genetic determinants of resistance to human pathogens, which may cause subsequent disease in humans.

Based on their review findings, the APVMA recommended cancelling the registration and label approvals of three products that had label claims relating to growth promotion, improved feed efficiency or both; and varying the conditions of label approval for virginiamycin feed premix products registered to reduce the risk of acidosis in sheep and cattle and prevent necrotic enteritis in chickens.

The APVMA decided to vary the labels of Eskalin Feed Premix for Cattle (APVMA 46049), Eskalin Wettable Powder Spray-On Feed Premix (APVMA 49111) and Eskalin 500 Feed Premix (APVMA 51354) to impose mandatory restrictions on off-label uses, limit the duration of use of the products to 28 days, and limit the number of re-treatments of virginiamycin in a 12-month period.

In 2005, the registrant of these three products with imposed label restrictions applied to the Administrative Appeals Tribunal (AAT) for a review of APVMA's decision. During the AAT proceedings, the registrant and the APVMA agreed that virginiamycin could be used prudently.

The AAT determined that the label changes set out above would not proceed. Instead, the labels would be varied to require that veterinarians must prescribe the three products in accordance with the Australian Veterinary Association's '*Code of Practice for Prescription and Use of Products which Contain Antimicrobial Agents*'[3] (the AVA Code). The AVA Code contains specific guidelines for the use of products that contain virginiamycin.

Further details of the APVMA's virginiamycin review can be found here: https://apvma.gov.au/node/12766

The only product with a claim for use in sheep is Eskalin Wettable Powder Spray-On Feed Premix (APVMA 49111).

The Label for Eskalin Wettable Powder Spray-On Feed Premix bears the following RESTRAINT statements:

> *"PRUDENT USE*
> *Prior to prescribing Eskalin Wettable Powder investigate the use of non-antibiotic options. If virginiamycin is indicated and selected for use, prescription must be consistent with the AVA Code of Practice for Prescription and Use of Products which Contain Antimicrobial Agents. Dosage regimens should be designed for each situation with an appropriate duration and frequency to minimize treatment failure while minimizing the emergence of antimicrobial resistance. Review farm records on the use of product containing virginiamycin to ensure compliance with prescribing instructions.*
>
> *NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL."*

[1] https://www.amr.gov.au/resources/importance-ratings-and-summary-antibacterial-uses-human-and-animal-health-australia
[2] https://apvma.gov.au/node/14231
[3] https://www.ava.com.au/siteassets/library/other-resources/ava-guidelines-for-prescribing-authorising-and-dispensing-veterinary-medicines-october-2013.pdf

In summary, labels for virginiamycin feed premix products contain mandatory restraints including that prescription must be consistent with the AVA Code.

The AVA Code includes, among others, the statements set out below. However, the AVA Code should be considered in full to ensure that prescription is consistent with the AVA Code in its entirety.

- Only use prescription antimicrobial agents to treat existing or anticipated diseases, not for long-term prophylaxis or production enhancement. Unless labelled for this purpose. (General section p 81)
- Minimise the duration and frequency of virginiamycin use as it is in the same class of agents as, and can cause cross resistance with, quinupristin-dalfopristin, an antibiotic used as a "last-line" therapy for important human infections. It should not be used for production enhancement. (General section p 82)
- Prescription antimicrobial agents to prevent digestive/physiological disorders such as ruminal acidosis should only be used in situations where management strategies such as dietary manipulation, grazing management and non-antibiotic treatments have failed. Such use should be regularly reviewed. (General section p 83)
- In all cases veterinarians must first consider management without antimicrobials. **If virginiamycin is considered essential, the treatment protocol must aim to minimise the duration and frequency of its use**. (Virginiamycin section, page 87)

Dose rate, frequency and duration of administration - risk management framework for use of virginiamycin:

Recommendations

The main justification for the use of virginiamycin is the introduction of sheep to grain-based diets (such as drought feeding) when, for animal welfare reasons, it is not possible to manage a more progressive induction.

One experimental study considering production aspects showed that virginiamycin only provides benefits in liveweight gain and wool growth in sheep fed a grain-based diet for the first 4 weeks after introduction to the diet.[8]

- Based on the prudent use label restraints, contents of the AVA Code, and high ASTAG rating of virginiamycin, the treatment protocol must aim to minimise the duration and frequency of its use.
- Treatment should be of the shortest duration possible whilst transitioning animals to a high grain diet.
- Virginiamycin should not be prescribed for routine use during the feeding of grain to ruminants.

As with all prescription animal remedies, virginiamycin should only be prescribed for a specific group of sheep or for individual sheep which are identifiable in the clinical records of the veterinarian. Written directions should include a statement that any medicated feed may not be fed to any animal other than those authorised by the prescription.

There is a Nil WHP for meat and milk when this product is used as per the label directions, and there is no ESI established.

SECTION 2: SYSTEMS AND SYNDROMES

The following chapters provide additional material on some of the more common and important diseases of sheep. This does not include all conditions listed in Table 3.

Chapter 3: Lameness

Foot abscess, infectious bulbar necrosis

Background/nature of infection/organisms involved

Foot abscess, affecting one or more feet, is a disease of high importance and frequency across meat/wool and dairy sheep enterprises. This extremely painful infection affects many flocks, particularly meat-sheep flocks, in the high rainfall areas. The major determinants are wet, muddy grazing conditions and mid to late pregnancy. The two most important causal organisms, *Fusobacterium necrophorum* and *Trueperella pyogenes*, are ubiquitous in sheep.

The pathogenesis involves initial necrosis within the subcutaneous tissue of the foot, extending to involvement of tendons and bone, creating a septic arthritis. The severe permanent damage done at this site often leaves sheep with eroded phalangeal bones and joint, and disfigured claws, so the sheep remain lame even after the infectious agents have been eliminated.

Although the incidence of foot abscess may not be high (up to 2% in some flocks), it should be regarded as a major animal welfare concern, a potent cause of pregnancy toxaemia and neonatal losses, and a serious cause of ram wastage.

Key issues

1. Intrinsic determinants of infection are size, body weight and condition, with ewes in late pregnancy or rams being most likely to be affected.
2. The principal extrinsic determinant of infection is prolonged grazing of water-logged pastures, leading to damage to interdigital skin.
3. There is a high probability of severe pain associated with foot abscess, representing a substantial risk to animal welfare.

Treatment

The principal purpose of treatment is to be curative and should be instituted early in the disease to minimise the involvement of key structures of the foot. In some flocks the purpose of treatment is salvage of affected animals, for example enabling severely affected ewes to rear a lamb before being culled.

Drainage, while logical, may be of limited value if infection has extended to involve key structures of the foot or claw.

Non-steroidal anti-inflammatory drugs (NSAIDs) are indicated to address animal welfare and may enable late pregnant ewes to continue grazing, preventing secondary pregnancy toxaemia. Only the NSAID meloxicam is currently registered for use in sheep.

Parenteral penicillin at high doses or oxytetracycline are the treatments of choice, but of limited efficacy unless affected sheep are detected and treated early. Intramammary cloxacillin (off-label) injected into draining fistulas may be of benefit.

See the relevant sections in the 'Appropriate treatment plan'chapter for dose rates, and frequency and duration of administration.

Prognosis

Early treatment is essential to ensure full recovery. Many ewes will become sound enough to continue productive lives in the flock. Affected rams are less likely to be able to work, particularly if hind feet are affected. In some flocks, this disease may be a significant contributor to ram wastage unless individuals are identified and treated early. It may be justifiable to recommend early euthanasia rather than treatment of severely affected animals.

Further reading

- West at al (2009)[10]: pp 274-277.

Virulent footrot

Background/nature of infection/organisms involved

This is a complex and devastating disease, with the essential causative bacterium being *Dichelobacter nodosus*, a fastidious, strictly anaerobic gram negative rod. Benign strains generally only cause inflammation of the interdigital skin up to the skin-horn junction near the heel, while virulent strains cause under-running from the heel, across the sole and up the walls of the hoof.

Virulence can be determined epidemiologically (if conditions are permissive for transmission) or using laboratory tests (for example, the elastase test). The virulence of an isolate as seen in the flock depends on the inherent virulence of the strain (which is believed to be stable), but is only apparent when the environmental conditions are appropriate for transmission.

Protective immunity (which can only be induced by vaccination, not by natural exposure) is fimbrial serogroup specific (with 10 serogroups, labelled A-M found in Australia), but the virulence of an isolate is not correlated with its serogroup.

There is some level of regulatory control of footrot in most jurisdictions. Consequently, veterinarians will need to be familiar with what is permissible in terms of therapeutics, vaccines and trading restrictions. Some jurisdictions mandate a specific test to determine virulence and consequent regulatory control.

Key issues

1. The definition of virulent footrot varies between states, but in broad terms virulent strains are those capable of causing under-running of the horn of the sole and wall of the foot (Score 3-5).[11]
2. Warmth and moisture are needed for virulent footrot to transmit and cause most damage.
3. There is variation between animals within a flock and between breed in susceptibility to footrot.

Treatment

The efficacy of antimicrobial treatment (number of cases cured or with a reduced lesion score) is improved by holding sheep on grating for 12 hours after injection and footbathing. No antimicrobial treatment regimen will result in eradication without inspection and culling. Antimicrobial therapy is rather a tool for reducing prevalence.

While good AMS suggests that only clinical cases should be treated, whole mob treatments may be needed if the prevalence is high (greater than about 40%) or if diagnosis of disease in individual sheep is difficult or creates animal welfare issues because of slow handling. Minor uses of antimicrobials for footrot include improving the mobility of infected ram flocks and as a quarantine measure for introduced rams.

Antimicrobials must be regarded as a treatment and control agent. Repeated use is not a route to whole-flock eradication.

Antimicrobials may be used in two main ways. Firstly, and most frequently, they are used to rapidly reduce the prevalence before starting eradication. Secondly, they are used to avert disasters, for example a high prevalence just before lambing. In both cases the key decision is whether to treat the whole flock or only affected sheep.

Antimicrobials of choice include long-acting oxytetracycline or erythromycin. Erythromycin is particularly useful if a short WHP is needed. Therapeutic efficacy is improved by holding sheep on grating for 12-24 hours after treatment.

The combination of lincomycin and spectinomycin as a soluble powder is not registered for use in sheep, but was used extensively in the late 1980s. Apart from being an off-label use, there have been problems associated with bacterial contamination during reconstitution of the product. This combination is no more efficacious than oxytetracycline or erythromycin. See the relevant sections in the ‘Appropriate treatment plan’ chapter for dose rates, and the frequency and duration of administration.

Prognosis

Footrot is a flock health condition. Cure rates after antimicrobial treatment of 80% or more have been reported for individual feet with lesions. In addition, some lesions may partially resolve. However, antimicrobials provide

no residual protection, so recovered sheep are susceptible to reinfection if they are re-exposed and seasonal conditions remain permissive.

Antimicrobials should be used as part of planned control and eradication programs, not as a crutch. Their use may be prohibited by regulatory imposts in some states.

Further reading

- Abbott, K. (2019)[12]: pp 418-441
- Anon[11]: https://footrotsydney.org/foot-scores/

Infectious arthritis

Background/nature of infection/organisms involved

Suppurative arthritis is generally a perinatal event, but may occur after lamb marking, dipping or shearing. Most cases are caused by opportunistically invading bacteria, including *E. coli, Fusobacterium necrophorum, Staphylococcus* spp., *Streptococcus* spp., and *Histophilus somni* (previously *Histophilus ovis*). The incidence is usually low, although larger perinatal outbreaks of polyarthritis caused by *H. ovis* have been recorded. Joint damage is often so severe that animals are left permanently lame and ill-thrifty.

Fibrinous arthritis has two causal agents:

- *Erysipelothrix rhusiopathiae*
- *Chlamydia pecorum*

C. pecorum may be associated with conjunctivitis (pink eye) but although the incidence may be high, it is usually a self-limiting disease with many cases recovering without treatment.

Key issues

1. *Erysipelothrix rhusiopathiae* can be transmitted at lamb marking or in contaminated dips.
2. *Chlamydia pecorum* causes a transmissible polyarthritis, particularly in the sheep-wheat and pastoral zones.

Treatment

Erysipelas arthritis can be controlled by attention to marking hygiene. While it is logical to improve hygiene, producers with intractable problems can vaccinate ewes to provide passive immunity to lambs. Some producers vaccinate ewes pre-lambing and/or lambs at marking. Before vaccinating it is important to get a definitive diagnosis (not all cases of post-natal polyarthritis are due to *E. rhusiopathiae)* and an estimate of the incidence to justify the cost of vaccination.

Antimicrobial treatment may well be effective if given early, but many cases have chronic joint damage that may only be discovered at slaughter or may render lambs chronically ill-thrifty. Problems are reduced by attention to hygiene in confined lambing areas and at marking. In cases of suppurative arthritis, early treatment with penicillin, erythromycin or oxytetracycline may aid some cases, but many cases are only detected at lamb marking or later.

Procaine penicillin is the antibiotic of choice.

In our interviews with them, veterinarians who regularly treat sheep indicated that long acting penicillin (procaine + benzathine) was occasionally prescribed for all lambs at marking in flocks with a history of post-marking lameness (suppurative or fibrinous) to prevent infections as a stop-gap while management changes were being implemented to improve hygiene. The prophylactic administration of antimicrobials for routine husbandry procedures is not supported other than in exceptional circumstances.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, and frequency and duration of administration.

Prognosis

Suppurative arthritis needs to be recognised and treated early. Many cases become permanently lame.

Fibrinous arthritis caused by *E. rhusiopathiae* requires early treatment. The prognosis is guarded.

Fibrinous arthritis caused by *C. pecorum* is often self-limiting and there is a good prognosis with or without treatment.

Further reading

- Abbott, K. (2019)[12]: pp 408-412.
- West at al (2009)[10]: pp 278-280; 274-277

Chapter 4: Skin, adnexa and eye

Mycotic dermatitis

Background/nature of infection/organisms involved

Dermatophilus congolensis, a Gram-positive branching bacterial rod, causes an exudative dermatitis, mostly in young merino sheep (called mycotic dermatitis or lumpy wool). The exudate clots to form a 'scab' at or just above the skin level, binding wool fibres together. The critical determinant of disease outbreaks is close contact between young, wet sheep, particularly if they are shedded wet after shearing, transported while wet or kept in close contact after dipping. Infection may result in anything from a few isolated clumps of scabs to scabbing over all the back and sides of the sheep.

D. congolensis can also cause a proliferative and exudative dermatitis (with attendant lameness) of the lower limbs, from the coronary band to the canon – so called strawberry footrot. This disease is associated with grazing wet pasture.

Key issues

1. Leads to devaluation of hogget fleeces, difficulty in shearing and is an important determinant of flystrike. Is best prevented by avoiding close contact between sheep when wet.

Treatment

Bacteriostats in dips (0.5% zinc sulfate) reduce transmission, but do not alleviate existing cases.

For exudative dermatitis oxytetracycline or erythromycin can be administered 6-8 weeks before shearing with the aim of 'lifting' scabs to allow shearing.

Strawberry footrot responds well to treatment with oxytetracycline and moving to drier paddocks.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, and frequency and duration of administration.

Prognosis

Sheep respond well to antimicrobial treatment, and repeat infections are rare. It is recommended that severely affected sheep are culled to reduce the risk of transmission to future generations of sheep.

Further reading

- West at al (2009)[10]: pp 361-365
- Abbott, K. (2019)[12]: pp 323-324, 413

Gangrenous mastitis

Background/nature of infection/organisms involved

This is a rapidly changing field. Veterinarians and producers are aware of gangrenous mastitis, but generally underestimate the importance and incidence of clinical, non-gangrenous mastitis and sub-clinical mastitis. *Staphylococcus aureus, Mannheimia haemolytica* and *Mannheimia glucosida* are both capable of causing gangrenous mastitis, while *M. haemolytica* and *M. glucosida* also can cause non-gangrenous mastitis. Staphylococci are also implicated in sub-clinical mastitis.

Limited data suggest that mastitis is more common in meat sheep than merinos. Whether this is breed disposition or environmental is largely unknown. Other determinants (mostly speculated) include higher levels of milk production, teat damage from coarse or abrasive pastures, damage to teats by infection with scabby mouth virus and drought feeding, where it is easy for lambs to spread mastitis while stealing a drink from the feeding ewes.

Key issues

1. Apart from mortality from gangrenous mastitis, or the culling of ewes that have lost half of their udder, the biggest production loss from mastitis is lamb mortality and ill-thrift. This may include pneumonia in lambs suckling mastitic ewes.

Treatment

In gangrenous mastitis cases, NSAIDs may help reduce toxaemic effects.

While clinical mastitis can be treated with intramammary medication and systemic antimicrobials, it is uncommon to perform culture and susceptibility testing, and there is a dearth of information on likely susceptibilities. However, there is at least one report of resistance to penicillin in both *Staphylococcus* and *Mannheimia* spp. Resistance to oxytetracycline has not been reported. In practice it is unlikely that flock sheep will be available for multiple treatments, so it is suggested that treatment with long acting oxytetracycline may be a good choice. If intramammary and systemic antimicrobials are administered, they should be complementary.

It is logical that clinical cases should be removed from the flock to reduce the risk of spread. Moreover, udders should be palpated annually (if the scale of the enterprise allows it) and ewes with lumpy udders culled. These are suggestions with little research to support them. Interventions such as intramammary treatment at weaning and using cell counts to identify subclinical cases are unlikely to be used in extensive flocks.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, and frequency and duration of administration.

Prognosis

Antimicrobial therapy is unlikely to alter the clinical course of gangrenous mastitis, but may protect the ewe against septicaemic extension of the infection.

Further reading

- Barber et al (2011)[13]: pp 95-98
- Abbott, K. (2019)[12]: pp 212-213
- West at al (2009)[10]: pp 303-305.

Ovine infectious keratoconjunctivitis/contagious ophthalmia

Background/nature of infection/organisms involved

This disease has distinct aetiological and geographical distributions. In the sheep-wheat and pastoral zones, surveyed veterinarians were concerned about *Chlamydia pecorum* and *Mycoplasma conjunctivae,* while in high rainfall areas *Moraxella* (previously *Branhamella*) *ovis* may be more important. There are reports of concomitant chlamydial pinkeye and chlamydial polyarthritis.

Key issues

1. Clinical progression from conjunctivitis to keratitis is rapid, and most sheep recover without treatment.
2. The incidence can be very high (greater than 50%).
3. Transmission is mostly by close contact, but dust and insects may also play a role.
4. Pinkeye may be an issue in feedlots when different lines of stressed sheep are introduced in dusty conditions.

Treatment

Because of the high prevalence and rapid clinical progression, treatment with antimicrobials is problematic. Yarding sheep for a part or whole flock treatment may induce new cases. Where *C. pecorum* or *M. conjunctivae* have been confirmed or could reasonably be suspected, oxytetracycline should be effective.

Tilmicosin (off-label) has been used against *M. conjunctivae* overseas (10 mg/kg). This drug can cause death in humans following self-injection and must be used carefully. While oxytetracycline aerosols and powders are popular therapeutics, there is little evidence demonstrating efficacy. There is a risk of serious damage to an ulcerated eye when it is treated with a high-pressure aerosol.

Cloxacillin eye ointments and/or injectable procaine penicillin are logical in cases where *M. ovis* is the confirmed or likely cause.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, and frequency and duration of administration.

Prognosis

Most situations in which spread is likely (close contact and/or dusty environment) are unavoidable. Feedlots may choose to move affected pens to pasture until the lot recovers. Most animals recover fully.

Further reading

- West at al (2009)[10]: pp 283-286
- Abbott, K. (2019)[12]: pp 320-322

Chapter 5: Gastrointestinal system

The involvement of bacteria and protozoa in gastrointestinal disease can present major diagnostic and therapeutic challenges. Many potential pathogens may be present as part of the normal microbial population of the ovine rumen or intestines with no evidence of clinical disease. Thus, any judgment on prescribing antimicrobials must depend not only on microbiological or laboratory detection, but on a review of the history, clinical examination, epidemiological observations and necropsy findings. Some pathogens have zoonotic potential and/or are notifiable. Moreover, there is increased focus on the potential for zoonotic pathogens to introduce new spectra of resistance to the human population.

Compared with intensive animal industries, there is little information on antimicrobial susceptibility and resistance in bacteria associated with ovine enteric disease. Therefore, clinicians are urged to be as thorough as reasonably possible to obtain accurate diagnoses, even if the results may be retrospective to actions.

The collection and submission of appropriate specimens from some diseases can contribute significantly to the knowledge base on the epidemiology of AMR in Australian livestock.

Acute ruminal acidosis

Background/nature of infection/organisms involved

Intrinsic determinants include appetite, hunger or periods of time off feed, the extent of ruminal fill with fibre (cellulose), ruminal buffering capacity, and whether the ruminal microbial population is adapted to the high-carbohydrate material being consumed.

Extrinsic determinants include availability of (usually unrestricted access to) a source of fermentable starch, including grain or mixed feeds, or to fruit with a high concentration of fermentable carbohydrates, principally starch, glucose, fructose and/or sucrose.

The risk of inducing ruminal acidosis varies between individual species and varieties of grain and the properties of the respective starch. Some fruits that are likely to be fed to sheep, particularly on joint horticulture/livestock enterprises or hobby farms, contain more than 75% fermentable carbohydrate on a dry matter basis (e.g. ripe apples and pears).[11]

In the presence of fermentable carbohydrate, aerotolerant anaerobic bacteria, particularly *Streptococcus bovis* and *Lactobacillus* spp., outcompete the strictly anaerobic ruminal bacteria to ferment carbohydrate, generating high concentrations of lactic acid.

Grain engorgement/carbohydrate overload is a common occurrence in at least two situations. Firstly, when sheep are improperly inducted to grain supplements, and secondly, in 'accidents', when sheep access grain spills. Details of the pathogenesis of acidosis are in all standard texts. In summary, the excess carbohydrate allows rapid overgrowth of bacterial species that generate lactic acid (principally *Streptococcus bovis* and *Lactobacillus* spp), leading to a fall in rumen pH and unfavourable conditions for survival of lactic acid consuming bacteria. The cardinal event is systemic acidosis. Other consequences are ruminal devitalisation, with ulceration, fungal invasion and liver abscessation.

Key issues

1. Multiple animals in various stages of clinical and subclinical disease are likely to be presented simultaneously.
2. Acute acidosis has been deemed to be of high importance and medium frequency, with impact for meat/wool sheep enterprises rated as high.
3. The risk of inducing ruminal acidosis varies between individual species and varieties of grain and the properties of the respective starch.

Treatment

Peracute and acute acidosis

Treatment consists of removing excessive grain by surgery or lavage and rectifying the systemic acidosis with appropriate fluid therapy. Intensive treatment on a mob basis is often impractical, so only high value animals are likely to be evacuated surgically or by lavage, and fluid therapy will only be oral.

Magnesium hydroxide or sodium bicarbonate may be administered orally or by intraruminal infusion. The former may reduce the direct absorption of lactate from the rumen.

The administration of NSAIDs to clinically affected animals may be indicated.

There may be benefit in giving parenteral oxytetracycline to prevent liver abscessation (usually caused by *Truperella pyogenes* and *Fusobacterium necrophorum*).

There is very little evidence to support a standard recommendation to administer procaine penicillin or virginiamycin orally or by intra-ruminal injection to clinically affected animals to reduce the numbers of streptococci.

Subacute and subclinical acidosis

The purposes of treating subacute cases are to restore normal ruminal function, including buffering capacity, and to minimise the further production of lactate. Magnesium hydroxide or sodium bicarbonate may be administered orally or by intraruminal infusion. The former may reduce the direct absorption of lactate from the rumen.

The feeding of roughage to animals that are still eating is beneficial in enhancing the buffer system and restoring normal ruminal bacterial populations.

There would appear to be some rationale, but limited evidence, to support the administration of antimicrobials, such as procaine penicillin or virginiamycin orally or by intra-ruminal injection to prevent further production of lactate by streptococci. *S. bovis* is a group D *Streptococcus* spp. and susceptible to moderate doses of neomycin, which is likely to have minimal effect on anaerobic microflora and may be administered by intraruminal injection.

Prevention/ metaphylaxis

The primary on-farm method of preventing acidosis involves progressive induction or adaptation to grain or other high-risk feedstuffs, whether it is being fed as a supplement or as the sole diet.

Sheep with reduced feed intake over the previous days, such as during transport or drought, will benefit from *ad libitum* access to a high fibre ration, such as straw or cereal hay, over several days prior to introduction of a high-risk diet.

During confinement feeding, buffers (for example, bicarbonate) have been added to rations. Bentonite is often promoted as a buffer, but its therapeutic efficacy is unknown. Limestone and dolomite are added to rations to provide calcium, but their buffering capacity is limited.

There are three rumen-modifying products available: the antibiotic virginiamycin and the ionophores lasalocid and monensin. They can be added to the grain and grain-based pellets or included in premixes. All these products are useful when rapid grain induction is needed, but in most situations, they are unnecessary once sheep have adapted to their grain diets. Lot-fed lambs and drought-lotted sheep do well without rumen modifiers if properly inducted.

Virginiamycin is a streptogramin antibiotic. Members of this class of antibiotics are highly important in human medicine for treatment of vancomycin resistant staphylococci, and vancomycin resistant *Enterococcus* spp. Human health authorities are anxious that resistance is not selected in the normal flora of domestic animals and transferred to the human population. Therefore, it is critical that virginiamycin is used judiciously. See earlier section under “Feed Additives”, in the ‘Appropriate treatment plan’ chapter.

Many commercial manufactured feeds are now formulated to minimise the risk of ruminal acidosis without the inclusion of antimicrobials, particularly virginiamycin.

Prognosis

The prognosis in severely affected animals is likely to be poor, despite treatment. Euthanasia of severely affected animals may be preferable to treatment.

Further reading

- Constable et al (2017)[14]: Position 37735-38520.
- Abbott, K. (2019)[12]: pp 510-515
- Wills (1987)[15]: pp 523-526
- AVA 2013[16]: pp 81-90 (particular reference to pp 86-87)

Salmonellosis

Background/nature of infection/organisms involved

Clinical ovine salmonellosis caused by serovars of *Salmonella enterica* presents principally as high-morbidity enteric disease, but may also be expressed as acute mortality in the septicaemic form or result in spontaneous abortions. In our survey of veterinarians who regularly treat sheep (see Table 1), the impact of salmonellosis and yersiniosis together ranked in the top one third of clinical conditions likely to be treated with antimicrobials, even though veterinarians were less frequently consulted about these diseases.

There is clinical and research evidence that salmonellae may be present in the normal gastrointestinal microflora of ruminants, including sheep, and organisms may occur intracellularly within the mesenteric lymph nodes of clinically normal animals.

Intrinsic determinants of infection include nutritional status, frequently associated with intermittent feeding or periods of time off feed.

Extrinsic determinants of infection include a range of non-specific stressors, including concurrent disease, prolonged transport and major climatic or husbandry events.

The pathogenic effect of salmonellae is associated with attachment to the enteric epithelium, with more acute and severe disease seen if there is invasion from the intestine to cause bacteraemia or septicaemia.

The process to establish a diagnosis may vary between outbreaks because of the range of potential clinical manifestations. It is critical to collect appropriate samples for microbiological culture and antimicrobial susceptibility testing.

Salmonellosis is a stress related disease and predisposing events, or history may include sheep being pre-conditioned for shipping, during shipping, in drought lots or being fed grain, or feedlot lambs that have been transported long distances.

Key issues

1. Non-helminth enteric disease has been deemed to be of moderate importance but low frequency for meat/wool sheep enterprises.
2. Salmonellae have zoonotic potential and are among the most important causes of human food poisoning, and have commonly been associated directly or indirectly with animal products, including meat or milk.

Treatment (and advice to clients)

Veterinarians should inform clients of the zoonotic potential of *Salmonella enterica* and the implications of a diagnosis for their enterprise. Severe human salmonellosis, particularly involving immunocompromised individuals, may be treated with antimicrobials, so the development of resistance in *Salmonella* spp. and transfer to humans as a result of AMU in animals is an important risk.

Initial treatment is often undertaken without knowing antimicrobial susceptibility of the infecting strain. The principal purpose of treatment is curative, but the mode of treatment may depend on the morbidity or mortality rate and clinical manifestation(s).

Metaphylactic treatment of an affected mob may be undertaken to minimise the risk of clinical disease, or to minimise environmental contamination. This may include a consideration of the difficulty of yarding an affected mob for retreatment.

Antimicrobial treatment is unlikely to be effective against intracellular bacteria in lymph nodes, which may provide a focus of infection for recrudescence.

Evidence from various mammalian species suggests that oral antimicrobial treatment favours the persistence of *Salmonella enterica* in the gut. This is probably a result of the disruption of the normal microflora by antimicrobials. However, because ovine salmonellosis is an invasive disease associated with significant mortality, treatment with antimicrobials is usually required.

Oral sulfonamides or neomycin have minimal effect on normal anaerobic microflora. There is a high probability that field isolates of extensively grazed sheep will be susceptible to these drugs.

It is feasible to deliver neomycin by intra-ruminal injection, although this is an off-label use.

To treat the septicaemic form of salmonellosis, parenteral administration of trimethoprim-sulfonamide is recommended in the literature. However, recent evidence has demonstrated that trimethoprim is rapidly metabolised in sheep, and it is likely that efficacy is due to the sulfonamide component alone. Thus, an adequate oral dose of sulfadimidine (off label) may be appropriate for primary curative or metaphylactic treatment.

A high single dose of parenteral neomycin is also likely to be effective.

For animals under conditions of confinement feeding, mass medication with neomycin and/or electrolytes through the water supply may be appropriate, with individual sick animals being also treated parenterally with an antimicrobial.

High value individual animals with severe disease are likely to benefit from oral or intravenous electrolytes.

The treatment plan should be reviewed, and modified if required, as soon as the results of culture and antimicrobial susceptibility testing are available.

Ancillary treatments are generally impossible in a flock situation. Therefore, control under grazing conditions depends on reducing contamination by spreading sheep out and providing multiple watering points. Enterprises engaged in confinement feeding or feedlots should be advised to regularly clean water troughs during an outbreak and to institute this as a standard prophylactic procedure. Dilute acetic acid (vinegar) has been used in feedlots, although salmonellae are somewhat acid tolerant, or diluted hypochlorite might also be used. However, attention to physical cleaning should be emphasised. Affected pens of sheep should be quarantined for observation, treatment and management of WHPs (if treated), or released into paddocks to reduce transmission.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, frequency and duration of use.

Prophylaxis

Attending to the intrinsic and extrinsic determinants, including stressors, in the affected mob and other mobs on the farm would be expected to be preventive and/or minimise the risk of recrudescence of salmonellosis.

Major changes in nutrition or extended periods off-feed are major triggers for clinical or subclinical salmonellosis. Therefore, husbandry activities likely to lead to these circumstances should be a focus for advice to clients. Under intensive feeding conditions, the removal of shy feeders is also likely to reduce the risk of clinical salmonellosis.

Cleaning and disinfection of contaminated water troughs might be expected to limit cross-infection.

Prognosis

The prognosis in severely affected animals is likely to be poor, despite treatment.

Parenteral administration of antimicrobials to pyrexic animals and/or metaphylactic treatment would be expected to result in recovery of most treated animals and/or substantially reduced morbidity.

Further reading

- Constable et al (2017)[14]: Position 30160-31227 (Kindle version)
- West at al (2009)[10]: pp 322-328
- Abbott, K. (2019)[12]: p 517

Yersiniosis

Background/nature of infection/organisms involved

Enteritis due to *Yersinia pseudotuberculosis* or *Y. enterocolitica* is most common in the winter months (hence, winter scours) in young (merino) sheep. Morbidity may be high (up to 50%), but mortality is generally relatively low unless co-determinants are unaddressed.

As a differential diagnosis, enteritis in weaner sheep due to *Campylobacter jejuni* or *C. coli* is uncommon and occurs mainly over the summer-autumn period. Coccidiosis is discussed elsewhere in these guidelines.

While mortality is not generally as high as with salmonellosis, practitioners are urged to have culture and susceptibility testing performed to exclude enteric salmonellosis, helminthosis and coccidiosis.

Key issues

1. Determinants involve the nutritional status, including undernutrition, cold wet weather and scour worm burdens.

Treatment

The principal purpose of treatment is curative.

Common practice has been to treat affected animals, or the whole mob depending on the incidence, with oral sulfadimidine for coccidiosis or non-specific enteritis. In a recent study, 64% of *Y. enterocolitica* and 87% of *Y. pseudotuberculosis* isolates were resistant to sulfonamides. It is assumed that this has resulted from prolonged use of sulfadimidine without culture and sensitivity data, and perhaps because yersiniosis is often presumptively diagnosed as coccidiosis.

Therefore, the recommended antimicrobial is parenteral oxytetracycline. As with salmonellosis the decision is whether to only treat clinical cases or the whole mob.

See the relevant section in the 'Appropriate treatment plan' chapter for dose rate, frequency and duration of use.

Prognosis

Prognosis following treatment is favourable, provided nutrition and parasitism have been assessed and appropriately managed.

Further reading

- Stanger et al (2018)[17]: pp 176-183
- Constable et al (2017)[14]: Position 154040-154164
- West at al (2009)[10]: pp 127-128

Coccidiosis

Background/nature of infection/organisms involved

Enteritis due to *Eimeria* spp. *(*particularly *E. ovinoidallis and E. crandallis)* occurs in post-weaning lambs run under intensive conditions. It is of interest for two reasons: firstly, it is a relatively rare clinical condition, but is presumptively diagnosed when it is more likely that the clinical problem is salmonellosis or yersiniosis. This means that diagnosis should be based on clinical signs (dysenteric diarrhoea), oocyst counts and necropsy findings. Nematodosis should be excluded, as should yersiniosis and salmonellosis. Secondly, there is no sheep-registered product for treatment of coccidiosis in Australia, though the ionophores lasalocid and monensin are approved for prevention. Off-label use should be approached carefully with due consideration of WHPs.

Intrinsic determinants of infection are age and immune status - it mainly affects unweaned and weaned lambs, and the nutritional status, including undernutrition such as the failure of lactation by ewes.

Extrinsic determinants of infection include cold wet weather and concurrent nematode burdens.

Although coccidia oocysts are encountered during worm faecal egg counts, often in very large numbers from lambs, such findings are of minor significance and rarely diagnostic of clinical coccidiosis.

Clinical coccidiosis is generally diagnosed on history, clinical signs and necropsy findings of a substantial number of typical gut lesions. Salmonellosis, yersiniosis or helminthosis should be considered as differential diagnoses, or as concurrent or intercurrent disease(s).

Key issues

1. Enteritis due to *Eimeria* spp. is considered of low importance and frequency.
2. Prevention of coccidiosis in high risk situations can be achieved by use of the ionophores.

Treatment

The principal purpose of treatment is curative.

Whole or part flock treatment with oral sulfadimidine is the most common recommendation. Other possibilities include toltrazuril or amprolium. None of these is registered in sheep, so be mindful of WHP's and ESI's

Toltrazuril is registered for ovine coccidiosis in other countries and is an effective treatment with due consideration of WHPs (ESI for cattle is 75 days).

Prognosis

Prognosis following treatment is favourable if nutrition and parasitism have been assessed and appropriately managed. Moving animals to less contaminated pastures after treatment is advisable, including early weaning of lambs suckling ewes under nutritional stress.

Further reading:

- Abbott, K. (2019)[12]: pp 525-528

Enterotoxigenic E. coli

Background/nature of infection/organisms involved

Enteritis caused by enterotoxigenic *E. coli* (ETEC) is mostly a problem of lambs 1-4 days old in unhygienic lambing conditions. Infections may be concomitant with rotavirus and cryptosporidial infections. Deaths in older lambs (post weaning) attributed to *E. coli 077* have been reported in Tasmania, and 'watery mouth' has been reported worldwide. Both latter diseases are likely causes of endotoxaemic deaths. The nomenclature and pathophysiology of ETEC in sheep is explained by Abbott.

Most ETEC are species-specific. This contrasts with Shiga toxin producing *E.coli* (STEC) strains, which are a serious human health risks.

Key issues

1. There are few reports of clinical ETEC in Australian sheep flocks.
2. Outbreaks in unhygienic lambing sheds may lead to high morbidity and mortality.

Treatment

As infected lambs die rapidly, antimicrobial therapy is unlikely to be successful. *E. coli* is likely susceptible to a wide range of antimicrobials. Oxytetracycline has been recommended for other *E. coli* infections (notably, watery mouth).

Prophylaxis

Hygienic lambing sheds (or better still, lambing in paddocks) and ensuring adequate colostrum by providing the ewe with good nutrition are the mainstays of prevention.

Further reading

- Abbott, K. (2019)[12]: pp 520-523
- Constable et al (2017)[14]:143279-144755
- West at al (2009)[10]: p92

Campylobacteriosis

Background/nature of infection/organisms involved

Enteritis caused by *Campylobacter jejuni* or *C. coli* is rare compared with yersiniosis. It is mostly a summer/autumn disease of weaned sheep in the high rainfall zones and may be diagnosed as coccidiosis.

Treatment

Treatment with oral sulfadimidine will likely be successful. See the relevant section in the 'Appropriate treatment plan' chapter for dose rate, and frequency and duration of use.

Further reading

- Stanger et al (2018)[17]: pp 176-183

Chapter 6: Respiratory system

Bacterial pneumonia including aspiration pneumonia

Background/nature of infection/organisms involved

Post-weaning infections with *Mycoplasma ovipneumoniae and M. arginini are* common, but frequently asymptomatic. Slaughter lambs frequently have pleural adhesions that may require additional trimming of the carcass. Mycoplasmal infections are the precursor for invasion by pathogenic bacteria, usually *Mannheimia haemolytica* or *Pasteurella multocida.* These bacteria can cause exudative pneumonia that frequently ends in death. Non-fatal infections may reduce weight gain.

The determinants of pneumonia include handling in dusty conditions, transport and close confinement (e.g. feedlots, which are also often dusty). There is a distinct summer-autumn seasonality (hence summer pneumonia).

Key issues

1. Pneumonias are probably underdiagnosed and may be of greater health and economic consequence than recognised.
2. Systemic infections may occur as an extension of pneumonic (*Pasteurella multocida*) or intestinal (*Salmonella* spp.*)* disease or as stand-alone entities. They are relatively rare in Australia.

Treatment

Oxytetracycline is the most frequently recommended antimicrobial. Cephalosporins are not approved for use in sheep. The only macrolide approved for use in sheep is erythromycin, though tilmicosin and tulathromycin are used in cattle. Erythromycin is active against all the causal agents, but offers little advantage over oxytetracyclines except the short WHP. It should be noted that tilmicosin can cause death of humans following self-injection.

When only the clinical animals are treated, new cases may develop for some time. Therefore, there is an argument for whole mob treatment, unless the mob can be easily accessed for ongoing surveillance and treatment.

See the relevant sections in the 'Appropriate treatment plan' chapter for dose rates, frequency and duration of use.

Prophylaxis

Prevention aims to reduce close contact during dusty conditions. Yards and feedlots should have dust reduction systems. Handling sheep in the early morning and late afternoon may reduce dust exposure. Providing multiple shade points in open paddocks may reduce excessive mobbing. Observe the Land Transport guidelines. Vaccines against *Mannheimia* spp. in cattle have not been evaluated in sheep.

Aspiration pneumonia after dipping is now rare because plunge and shower dipping is in decline. There are usually multiple bacterial species involved, necessitating treatment with a broad spectrum antimicrobial. Treatment should only be given to animals showing signs of respiratory distress. Aspiration pneumonia after drenching is probably more common than realised. There are significant numbers of mortalities seen from inadvertent administration of organophosphate drenches by the intra-tracheal route and there is no reason to believe that other drenches are not also frequently delivered into the trachea. It is perhaps surprising that there are not more clinical consequences. As with post-dipping pneumonia, multiple bacterial species are involved so broad-spectrum antimicrobials should be used to treat clinically affected animals.

Prognosis

Treatment is mostly aimed at therapeutic cure of clinical cases, but whole flock treatment may prevent some new cases. The outlook is good, although residual pleural lesions may result in extra trim at slaughter.

Further reading

- West at al (2009)[10]: pp 112-119
- Abbott, K. (2019)[12]: pp 591-600

Chapter 7: Systemic infections

Background/nature of infection/organisms involved

Salmonellosis. Systemic salmonellosis is usually associated with enteric salmonellosis and is characterised by sudden death and/or abortion in pregnant ewes (to be distinguished from abortion caused by abortigenic serotypes such Brandenburg and Abortusovis). The common causal serotypes are the same as those for enteric salmonellosis.

Pasteurellosis. Systemic infection with *Mannheimia haemolytica, Pasteurella multocida* or *Bibersteinia trehalosi* (formerly *Pasteurella haemolytica* biotype T or *Pasteurella trehalosi*) may be an extension of pneumonic syndromes or a stand-alone clinical event. The stand-alone event is most common in lambs 2 days to 2 months of age.

Septicaemic infections with *Histophilus somni* (previously *Histophilus ovis*). These ubiquitous bacteria have been associated with a range of septicaemic conditions including polyarthritis, meningitis, abortion, mastitis, neonatal mortality and epididymitis. It is a diagnosis for those looking for a high distinction in specialist examinations.

Treatment

Treatment recommendations are the same as for enteric salmonellosis: trimethoprim-sulfonamide parenterally, sulfadimidine orally, or neomycin orally via the watering system if whole mob metaphylactic treatment is required. Reducing stocking density, particularly around watering points, and providing adequate nutrition may help quell an epidemic and prevent new outbreaks. As with enteric salmonellosis, culture and susceptibility testing should be done to provide retrospective information and to alter therapeutic choice if needed. Systemic infections with *Pasteurella, Mannheimia or Histophilus* should be susceptible to oxytetracycline or erythromycin.

Prognosis

Most sheep with systemic bacterial infections are found dead or *in extremis*. Valuable animals should be treated with an antimicrobial and supportive therapy (fluids and NSAIDs). Whole mob treatment may cure early cases and break the transmission cycle.

Further reading

- Constable et al (2017)[14]: Positions 30609 – 30655, 30681, 30729 (salmonellosis) 155055 – 155137 (*Histophilus somnus*); 155386-155415: (Pasteurellosis).

Chapter 8: Male and female urogenital tract infections

Female

Bacterial abortion

The most common agents are *Campylobacter fetus* ss. *fetus, C. jejuni* and *Toxoplasma gondii.* Less common agents are *Listeria monocytogenes* and *L. ivanovi,* and very occasionally *Yersinia pseudotuberculosis and Histophilus somni.* Abortion specific serotypes of salmonella (*S.* Abortusovis, *S.* Brandenburg*)* have not been reported in Australia, although abortion may occur as a consequence of enteric/systemic salmonellosis. A *Leptospira* spp. is a rare cause of abortion. Enzootic abortion (*Chlamydia abortus) and Neosporum caninum* have not been diagnosed as causes of ovine abortion in Australia. The role of Q fever (as a cause of abortion or ill-health) is largely uninvestigated in sheep, but may receive more attention in the future.

Campylobacter abortion can cause large losses. Lambs are aborted in the last 4-6 weeks of pregnancy and some lambs are born with diminished viability. Campylobacteriosis is mostly a problem of high rainfall areas and concentrated grazing. Intensive rotational grazing and droughtlotting favour spread. Abortion storms may claim 5-50% of lambs. Circumstantial evidence suggests that there may be embryonic loss (differences between scanning and marking that cannot be accounted for by perinatal mortality) without signs of overt abortion. Additionally, flocks that have suffered abortion events may have inapparent, ongoing losses. Toxoplasmosis is also more of an issue in high rainfall areas (survival of oocysts and closer settlement increasing contact with cats). Abortion is most common in 1 and 2 year old sheep, as they have had less opportunity to seroconvert through exposure to contamination. Abortion storms are usually associated with feeding contaminated grain (open grain bins) or hay. Listerial abortions are associated with feeding spoiled silage (particularly pit silage). Occasional cases may occur at pasture.

Aborted ewes may have a mixed species metritis after aborting and, if this is identified, it can be treated with penicillin or oxytetracycline parenterally augmented by intrauterine treatments that complement the parenteral treatment.

Key issues

1. Campylobacter abortion can cause large losses.
2. Listerial abortions are usually associated with feeding spoiled silage.
3. There are no antimicrobial treatments or vaccines for toxoplasmosis.

Treatment

The issue with abortion storms is whether to institute whole-mob antimicrobial therapy in an attempt to quell the emerging epidemic. This approach is favoured in New Zealand and by some Australian veterinarians, but there is scant evidence of its value. Oxytetracyclines and erythromycin are the favoured drugs for campylobacter abortions. Penicillins, erythromycin or oxytetracycline should be effective against *Listeria* spp. but there are no reports of part or whole flock treatment in the face of an outbreak.

Prophylaxis

Campylobacter abortion storms should be managed by spreading sheep out, picking up as much of the aborted foetuses and membranes as possible, and removing ewes that have aborted from the mob. Campylobacteriosis is preventable by using a bivalent vaccine ahead of pregnancy or by exposing maidens and non-pregnant mobs where no abortion has occurred to sheep that have aborted. Whether to vaccinate is a complicated rubric involving evidence of suboptimal reproductive performance, risks posed by intensive grazing and drought-lotting, geographic location and past history of abortions.

As Australia does not have a registered vaccine for toxoplasmosis, control relies on cat control (a problematic option) and avoiding feeding contaminated supplements (hay or grain contaminated with cat faeces) during pregnancy. Logically, but unproven, exposing young sheep before first joining to pastures likely to be

contaminated with faeces or supplements known to be contaminated with faeces may promote immunity. Monensin (15 mg/hd/d) has been used overseas as a prophylactic measure during pregnancy.[10]

Prognosis

Most ewes survive abortion with or without treatment. Some develop metritis, particularly after toxoplasmal abortion. Whole flock treatment in the face of an abortion storm depends on a diagnosis and treating early in the outbreak.

Further reading

- West at al (2009)[10]: pp 64-70
- Abbott, K. (2019)[12]: pp 179-181

Male

Epididymitis

The major agents are *Brucella ovis, Actinobacillus seminis* and *Histophilus somni.* Brucellosis is refractory to treatment and should be managed by testing and culling. *A. seminis* and *H. somni* most often cause a transient epididymitis in young rams. However, a proportion may develop more severe, persistent lesions. While antimicrobials are unlikely to resolve chronic lesions (and culling is recommended), oxytetracycline has been recommended in studs trying to ensure product integrity.

Pizzle rot and knob rot

Pizzle rot (balanoposthitis) is an ulcerative inflammation of wethers, and occasionally rams, grazing legume pastures. The causal agent is *Corynebacterium renale.* Testosterone injections can be used to treat and prevent pizzle rot in wethers. Some animals may require pizzle slitting to provide drainage. *Corynebacterium* spp. are predictably sensitive to procaine penicillin. Testosterone treatment is contraindicated in rams and so procaine penicillin is the treatment of choice.

Knob rot (ulcerative balanitis) is an occasional issue in ram mobs. The glans penis becomes haemorrhagic and ulcerated. *Histophilus somni* and *Corynebacterium* spp. have been implicated, but evidence for any necessary bacterial cause is slight. Oxytetracycline can be given as an antimicrobial cover.

Further reading

- West at al (2009)[10]: pp 14-15, 32-34
- Abbott, K. (2019)[12]: pp 175-176, 570-571
- Watt et al (2016)[18]: Online http://www.flockandherd.net.au/sheep/reader/ulcerative-balanitis.html

Chapter 9: Central nervous system

Listeriosis

Listeria monocytogenes is the cause of listeriosis. Listeria are a saprophytic gram-positive bacteria that multiply in poorly made silage (pH > 4.5) or water-spoiled silage. It is also occasionally reported from paddocks with long, wet grass, or where hay residues are left to rot. Listeria are also at home in the gut and faecal shedding may be a source of contamination.

Listeria enter the trigeminal nerve via the oral mucosa and ascend the nerve to the brain. Clinical signs include unilateral facial paralysis and circling.

Listeria are susceptible to procaine penicillin and oxytetracycline, but the likelihood reaching the site of infection in the CNS at an appropriate concentration needs to be considered. Erythromycin may be better at crossing the blood-brain barrier. In any event, treatment is unlikely to be successful unless commenced early in the clinical course.

Feeding well-made, unspoiled silage, and cleaning up hay waste should reduce infection. In larger outbreaks it is speculated that faecal contamination may be an additional problem.

Prognosis

The outlook is guarded to poor. Early recognition and treatment produces the best results.

Further reading

- West at al (2009)[10]: pp 342-343
- Abbott, K. (2019)[12]: pp 476

Tetanus

As in all species, tetanus occurs when *Clostridium tetani* contaminates wounds and elaborates a toxin that causes hyperaesthesia and tetany. Outbreaks are associated with lamb marking, and occasionally other procedures. Prevention is through attention to marking hygiene, vaccinating ewes to provide good passive immunity and vaccinating lambs for active immunity. In high risk situations, sheep can be given antitoxin as a prophylactic measure 100 U (lambs) or 500 U (adult sheep). High value sheep with clinical tetanus may be treated with antitoxin, muscle relaxants and procaine penicillin. The prognosis is poor.

Further reading

- West at al (2009)[10]: pp 312-313
- Abbott, K. (2019)[12]: pp 477

Chapter 10: Blood and Lymphatics

Infectious haemolytic anaemia/eperythrozoonosis

Infection with *Mycoplasma ovis* causes haemolytic anaemia in immunologically naive sheep. Up to 90% of flocks in southern Australia are chronically infected. Insect vectors spread infection and it is suggested that contaminated marking equipment may also spread infection. Susceptible sheep of all ages can be affected, but clinical signs are most often seen in lambs. Cases are anaemic and weak, failing the "muster test". Oxytetracycline is the antimicrobial of choice. However, mustering of mobs may kill more sheep than leaving them unmustered in paddocks, provided they have easy access to feed and water.

Further reading

- Abbott, K. (2019)[12]: pp 587-588

Table 3: Bacterial and protozoal diseases of sheep - antimicrobial choices

The references are provided for those requiring more information on a disease or condition. They are not meant to be a comprehensive review resource for either the disease condition or the antimicrobial recommendations. The references are listed with the most useful first. The list of references is at the end of the guidelines.

System or syndrome	Disease	Most common pathogen	Recommended primary treatment	Comments, ancillary treatments, prevention
Lameness	Foot abscess/ infectious bulbar necrosis[10]	*Fusobacterium necrophorum* *Trueperella (Actinomyces) pyogenes*	Parenteral: Procaine or penethmate penicillin. Oxytetracycline LA Long acting penicillin Topical: Cloxacillin	Common debilitating condition of rams and pregnant ewes in wet conditions. Early treatment critical. Check for toe abscess. Ancillary treatment with NSAIDs provides pain relief, including to prevent secondary pregnancy toxaemia. Foot bathing out of yards may reduce prevalence. Keep ewes on dry pastures and lamb at lighter bodyweights.[10]
	Foot scald/ ovine interdigital dermatitis, including infection with benign footrot (score 2 or less)[12]	*Fusobacterium necrophorum* *Dichelobacter nodosus* *Trueperella pyogenes*	Antimicrobials generally not prescribed Parenteral: Procaine penicillin LA oxytetracycline	Although flock prevalence may be high (particularly in spring) antimicrobials are seldom employed. Foot bathing (10% zinc sulfate) and providing dry paddocks cures most cases. Sheep "self-cure" with a return to dry conditions.
	Virulent footrot[11,12,19,20]	*Dichelobacter nodosus*	Parenteral: Oxytetracycline LA Erythromycin Procaine penicillin 42 mg/kg	Efficacy of antimicrobial treatment enhanced by leaving sheep on concrete or boards for 12-24 h post injection. Erythromycin particularly useful if a short WHP needed. Antimicrobial treatment confined to four scenarios: - whole or part flock treatment to reduce prevalence before eradication. - salvage of a disastrous situation (e.g. high prevalence pre-lambing). - quarantine treatment of imported rams. - pre-joining treatment of infected rams. For a review of prevention, control and eradication of virulent footrot.[12]
	Septic arthritis: fibrinous/non-suppurative[10,12]	*Erysipelothrix rhusiopathiae*	Parenteral: Procaine penicillin or	*E. rhusiopathiae* infection may occur peri-natally, post-marking/mulesing or post-

			penethamate (*E. rhusiopathiae* is very susceptible with a very low MIC)	dipping. Post-dipping lameness may be due to lymphangitis and local pain, although arthritis also occurs. Attend to marking and dipping hygiene. Peri-natal or post-marking/mulesing infection may be managed by vaccinating ewes pre-lambing and lambs at marking. **Maternal antibodies may be waning by the time of marking**.
		Chlamydia pecorum	Oxytetracycline LA	Transmits from animal to animal, particularly in dusty conditions. Susceptible to oxytetracycline LA. Often self-limiting and self-curing.[10,12,14]
	Septic arthritis: suppurative[10,12]	*E. coli* *Fusobacterium necrophorum* *Trueperella pyogenes* *Histophilus somni* *Actinobacillus seminis* *Staphylococcus.* spp. *Streptococcus* spp.	Parenteral: Oxytetracycline LA Procaine penicillin or penethamate	Most commonly a peri-natal infection, may be associated with foot abscess in the ewes, but may occur post marking, shearing or dipping. Check lambing and procedural hygiene. With high prevalence (more than a few percent) culture and sensitivity essential to give appropriate treatment. Often, joint changes limit antimicrobial efficacy.[12]
	Strawberry footrot[12]	*Dermatophilus congolensis*	Parenteral: Oxytetracycline LA Erythromycin	Sporadic disease of young sheep. Foot bathing may stop transmission. Many sheep self-cure. Erythromycin is the drug of choice if a short WHP is needed.
	Major tissue damage: deep shearing cuts and dog bites, burn injuries	Non-specific infection	Parenteral: Procaine penicillin or penethamate LA penicillin Oxytetracycline LA	Debride wounds. Establish drainage. Euthanasia may be preferable if soft tissue or foot damage is extensive.
	Interdigital trauma/grass seeds	Non-specific infection	Parenteral: Oxytetracycline LA Procaine penicillin or penethamate LA	Antimicrobials rarely, if ever, required, but treatment of individuals with involvement of fascia or tendon sheaths may be required. Remove grass seed from feet; move to less seedy paddocks. Manage grass seeding with slashing, spray topping and pasture renovation.
Skin, adnexa	Flystrike/ cutaneous myiasis[12]	Non-specific infection	Parenteral: Procaine penicillin or penethamate Penicillin LA Oxytetracycline	As flystrike is a flock problem, antimicrobial treatment is reserved for high value animals showing signs of sepsis/toxaemia. Concurrent treatment with NSAIDs

				recommended. For information on prevention and insecticidal treatments see flyboss.com.au.
	Mycotic dermatitis/ lumpy wool[10,12]	*Dermatophilus congolensis*	Parenteral: Oxytetracycline Erythromycin	Antimicrobials given to extensive cases to "lift scabs" to allow shearing. Prevention by avoiding close contact between wet, shorn sheep after shearing or dipping. Bacteriostats can be added to dips and shorn sheep are occasionally sprayed with zinc sulfate. Rarely a problem beyond 1 year of age.
	Mastitis, including gangrenous mastitis[10,12,13]	*Staphylococcus. aureus* *Mannheimia haemolytica* *Mannheimia glucosida* *Actinobacillus* spp. *Streptococcus* spp.	Parenteral: Procaine penicillin or penethamate Oxytetracycline LA or Intramammary: Cloxacillin Oxytetracycline	*S. aureus*, *M. haemolytica* and *M. glucosida* are the most common causes of gangrenous mastitis, but other organisms are associated with mastitis and occasionally gangrenous mastitis. Antimicrobial treatment limited to valuable sheep in the acute phase. Establish drainage; watch for secondary fly strike. NSAIDs for toxaemic sheep.
	Scabby mouth/ contagious pustular dermatitis/ contagious ecthyma	Secondary non-specific infection	Parenteral: Oxytetracycline LA Procaine penicillin or penethamate	Rarely, if ever, requires antimicrobial treatment. Lesions self- limiting and self-curing. Vaccinate. Remove sheep from paddocks with abrasive plants (thistles). Individual young lambs with severe scabbing of lips or oropharyngeal lesions from sucking ewes with teat lesions may benefit from treatment with penicillin LA.
	Malignant oedema[12]	*Clostridium* spp.	Parenteral: Procaine penicillin or penethamate	Various *Clostridium* spp. may infect after fighting, wound contamination and obstetric intervention. Occasionally slow onset of signs allows antimicrobial treatment. Control with vaccination.
Eye	Contagious ophthalmia/ pinkeye[10,12]	*Chlamydia pecorum* *Mycoplasma conjunctivae* *Moraxella ovis*	Parenteral: Oxytetracycline LA Topical: Cloxacillin	Can affect all age groups with high incidence. Summer/autumn bias, but can occur any time. Role of *Moraxella ovis* as primary pathogen is uncertain, so treatment with cloxacillin may not work. Rapid, spontaneous recovery often occurs without treatment.

	Grass seed trauma	Non-specific infection	Topical: Cloxacillin	Remove grass seeds. Antimicrobial treatment rarely needed.
Gastrointestinal tract	Acute acidosis[12,14-16]	*Streptococcus bovis* and other lactogenic species Non-specific infection of the rumen wall and liver abscessation	Intraruminal: Virginiamycin (ELU) Procaine penicillin (ELU) Parenteral: Oxytetracycline LA Procaine penicillin or penethamate	Antimicrobial treatment with virginiamycin or procaine penicillin aimed at reducing overgrowth of *S. bovis* has been advocated, but there is little evidence of its efficacy. Treatment consists of: 1. Removing or neutralising the ruminal grain (rumenotomy, oral alkalising agents: MgOH, MgO NaHCO3). 2. Correcting dehydration and systemic acidosis with oral/parenteral fluid therapy. 3. Parenteral oxytetracycline may limit infection of the liver and other organs by *Trueperella pyogenes* and *Fusobacterium necrophorum*. See section on prophylaxis for prevention.[12]
	Bacterial enteritis: Salmonellosis Yersiniosis Campylobacteriosis[12,14,17]	*Salmonella* spp. *Yersinia pseudotuberculosis* *Yersinia enterocolitica* *Campylobacter jejuni* *Campylobacter coli*	Parenteral: Trimethoprim-sulfonamide Oxytetracycline LA Oral: Sulfonamides Neomycin in water or intra-ruminal injection	Aetiology may be partially determined by consideration of age of sheep affected and other aspects of the epidemiology (see Ref 2 PP 517-531). Cultural confirmation essential, particularly given concerns about antimicrobial resistance in salmonellas. If morbidity and mortality dictate speculative treatment, consider trimethoprim/sulfonamide combinations or oxytetracycline LA parenterally, or neomycin orally. Most bacterial enteropathic infections have background stressors - intestinal parasites, poor nutrition, crowding, cold wet weather. These must be eliminated. Spread sheep out if salmonellosis is suspected. Many field isolates of *Yersinia* spp. are resistant (*in vitro*) to sulfonamides, but are mostly sensitive to oxytetracyclines. **Note: *Salmonella* spp. *Campylobacter* spp and *Yersinia* spp. are all potential zoonoses.**
	Coccidiosis[12]	*Eimeria ovinoidallis* *Eimeria crandallis*	Oral: Sulfadimidine (ELU) Toltrazuril (ELU)	Occurs mostly in post-weaning lambs 2-6 months of age. Often mistakenly diagnosed when a bacterial enteritis is the cause.

				Diagnosis should be based on high oocyst counts (>10^5) plus necropsy findings. Provide dry watering points and reduce crowding in paddocks and around feeders. Eliminate other stressors, particularly intestinal parasites. **<u>Note</u>: none of the recommended antimicrobials are registered for oral use in sheep in Australia. Off-label prescriptions should have generous WHPs.** There is no MRL for toltrazuril in sheep approved in Australia. If use is considered essential/critical, an appropriately long WHP must be imposed. In countries with an MRL for sheep, the WHP varies from 42-48 days. Some multiple of this WHP may be appropriate.
	Enterotoxigenic *E. coli*[10,12,14]	Enterotoxigenic *E. coli*	Oral: Sulfadimidine (ELU) Neomycin	Disease of lambs born in unhygienic sheds. Antibiotics of limited efficacy. Attend shed hygiene
Respiratory	Bacterial pneumonia, summer pneumonia, enzootic pneumonia[10,12]	*Mycoplasma ovipneumoniae* *Mycoplasma arginini* *Mannheimia haemolytica* *Pasteurella multocida* Non-specific pathogens	Parenteral: Oxytetracycline LA	Most bacterial pneumonias are facilitated by infection with *Mycoplasma* spp., which commonly cause mild lesions in lambs and hoggets, but little clinical disease (although weight gain may be slowed). Secondary infection with *Mannheimia* spp. or *Pasteurella* spp. causes severe exudative pneumonia with variable incidence, but potentially high mortality. It occurs mostly in post-weaning lambs and hoggets with a distinct summer-autumn seasonality (hence summer pneumonia). Avoid yarding and handling sheep in dusty conditions: handle at dawn and dusk; water yards.
	Aspiration pneumonia/ post-dipping pneumonia[10,12]	Non-specific infection	Parenteral: Oxytetracycline LA	Occurs post plunge-dipping and occasionally post-drenching. May lead to gangrenous pneumonia. Examine dipping/drenching technique.
Systemic bacterial diseases/ sudden death	Salmonellosis[14]	*Salmonella enterica* serotype Typhimurium	Parenteral: Trimethoprim sulfonamide Oral or intra-ruminal:	Generally, part of an enteric Salmonellosis syndrome. Reduce stocking rate; remove stressors. Generally, will need to treat clinical cases before

			Sulfadimidine Neomycin	culture and sensitivity results are available.
	Pasteurellosis[14]	*Pasteurella multocida* *Bibersteinia* (*previously Pasteurella*) *trehalosi*	Parenteral: Procaine penicillin or penethamate Oxytetracycline LA	Systemic pasteurellosis is rare in Australia. May occur in feedlots and after sudden changes to better feed. Most lambs are found dead. Early intervention with antimicrobial treatment critical.
	E. coli[10]	Non-enterotoxigenic *E. coli* (watery mouth)	Parenteral: Oxytetracycline	Disease of day-old lambs. Very few survive long enough to get treatment. Colostrum protective. Second peak of deaths occasionally recorded at 3-8 weeks old.
	Histophilus septicaemia[14]	*Histophilus somni*	Parenteral: Oxytetracycline LA	Rare cause of septicaemia, occasionally with meningitis and polyarthritis. Often found dead. Treatment unlikely to be successful.
Female urogenital tract	Bacterial abortion[10,12]	*Campylobacter fetus* ss *fetus* *Campylobacter jejuni* *Listeria monocytogenes* *Listeria ivanovii* *Yersinia pseudotuberculosis*	Parenteral: For *Campylobacter* Erythromycin Oxytetracycline LA. For *Listeria*: amoxicillin or erythromycin For yersiniosis, oxytetracycline or amoxicillin	Campylobacter abortion associated with high density feeding (controlled grazing, drought lots, grain trails). Abortion storms can be slowed by reducing stocking density, collecting aborted foetuses and membranes and removing ewes that have aborted from the flock. Whole-flock antimicrobial treatments in the face of an outbreak have been recommended, but their value is not certain. Small proportion of ewes will have post-abortion metritis, which may warrant antimicrobial treatment. Bivalent vaccine available. Listerial abortion is associated with feeding spoiled silage. Antimicrobial treatment to stop an outbreak of unknown value. Rare. Value of antimicrobials unknown unless abortions are associated with enteric infection.
	Salmonellosis	*Salmonella enterica* serotype Typhimurium *Salmonella enterica* serotype Dublin	Parenteral: Trimethoprim - sulfonamide Oral: Sulfadimidine Neomycin	Abortion due to enteric or systemic infection with *Salmonella* spp. Antimicrobial choice should be based on culture and sensitivity. Oral neomycin may be used to stop spread. Remove stressors. Reduce stocking rate. Abortion-specific *Salmonella* serotypes

				such as Abortusovis and Brandenburg not found in Australia.
	Toxoplasmosis[10,12]	*Toxoplasma gondii*	Monensin orally.	No vaccine available in Australia. Monensin orally (15 mg/day) has been shown to reduce abortion incidence on chronically infected properties (overseas)[10]
	Vaginal/ uterine prolapse	Non-specific infection	Parenteral: Procaine penicillin Penicillin LA Oxytetracycline LA	
	Septic metritis	Non-specific infection	Parenteral: Oxytetracycline LA Procaine penicillin or penethamate Penicillin LA Intrauterine: Oxytetracycline Cephalosporins	Metritis most common after abortion, obstetric intervention or dystocia, but can occur with exposure to phytoestrogens. Intrauterine treatment includes pessaries (oxytetracycline), off-label use of a cephalosporin formulation registered for intrauterine use in cattle or custom lavage with an antibiotic.
Male urogenital tract	Epididymitis[10,12]	*Actinobacillus seminis* *Histophilus somni*	Parenteral: Oxytetracycline LA or amoxicillin	These infections are often transient and mostly not detected in young rams. A proportion of infected rams will develop notable epididymitis that persists. Culling is the best option. Antimicrobials have been used in stud flocks to reduce transmission and aid resolution. The efficacy is unknown.
	Balanoposthitis / pizzle rot[10,12]	*Corynebacterium renale*	Parenteral: Procaine penicillin or penethamate	Parenteral testosterone can be used as a preventative therapy in wethers, but not rams. Individual cases may need irrigation with disinfectants and (occasionally) slitting of the prepuce.[10,12]
	Ulcerative balanitis/ knob rot[18]	*Corynebacterium* spp. *Histophilus somni*	Parenteral: Procaine penicillin or penethamate	These bacteria have not been proven as a necessary or sufficient cause but have been isolated. Culling may be necessary for unresponsive cases.[18]
Central nervous system and neuromuscular diseases	Listeriosis[10,12]	*Listeria monocytogenes*	Parenteral: Erythromycin	Usually associated with spoiled silage, occasionally long wet grass and hay residue. *Listeria* spp. are sensitive to erythromycin which may be effective against organisms

				within phagocytes, but treatment must be given early.[10,12]
	Meningitis, brain and spinal cord abscessation[12]	*Histophilus somni* Non-specific infections	Parenteral: Procaine penicillin or penethamate Oxytetracycline	May be part of a systemic *Histophilus somni* infection, but more likely to be associated with non-specific infection perinatally or post-marking.[12]
	Tetanus[10,12]	*Clostridium tetani*	Parenteral: Procaine penicillin	Potentially can be triggered by any wound, but most likely after marking, when maternally acquired antibody has waned and lambs have little active immunity. Valuable animals can be treated with antitoxin and penicillin, but treatment must be early.
Blood and lymphatics	Infectious haemolytic anaemia[12]	*Mycoplasma ovis*	Parenteral: Oxytetracycline	The decision is whether to stress sheep by yarding for treatment or leave them undisturbed in the paddock. Most veterinarians recommend the latter. If it is a regular occurrence, examine marking hygiene.[12]
Prophylactic and metaphylactic antimicrobial use	Surgery	Non-specific infection	Parenteral: Procaine penicillin or penethamate Oxytetracycline LA Long acting penicillin	May be given if sterile conditions cannot be guaranteed for routine procedures (e.g. laproscopic artificial insemination, vasectomy), or if surgery involves contaminated sites (e.g. wound management, rumenotomy). Particular care is required to only use an appropriate formulation if using antimicrobial agents in the peritoneal cavity or joints. Aminoglycosides are usually contraindicated.
	Routine husbandry	Non-specific infection	Parenteral: Procaine penicillin or penethamate Long-acting penicillin	Lambing and marking in unhygienic conditions may dictate treatment with antimicrobials. While it is logical to suggest improving the hygiene, a small number of producers may have difficult conditions to work in, making prophylactic antimicrobials a good animal welfare choice.
	Footrot	*Dichelobacter nodosus*	Parenteral: Oxytetracycline LA	Antimicrobial treatment can be used as a biosecurity measure when rams are introduced onto a farm. It is a supplement to foot bathing and quarantine.
	Acidosis/grain overload/induc	*Streptococcus bovis* and other lactogenic species	Oral in medicated feed:	Rumen microbial modifiers allow rapid induction to grain, but they are generally not needed if

	tion to grain feeding[16]		Virginiamycin (ELU) Lasalocid	producers have time to introduce slowly and/or use buffers. Virginiamycin use should be reserved for exceptional and unpredictable circumstances while other management measures are instituted. Refer to the virginiamycin section under the appropriate treatment plan chapter.
	Bacterial enteritis	*Salmonella* spp. *Campylobacter* spp. *Yersinia* spp.	Parenteral: Trimethoprim-sulfonamide Oral: Sulfadimidine (ELU)	In outbreaks, clinical discretion may dictate whether to treat clinically affected animals or the whole mob. While there are no set trigger point considerations, include the incidence at time of diagnosis, ability to isolate clinical cases and ability to rehandle the mob when additional cases develop.
	Pneumonia	*Mannheimia* spp. *Pasteurella* spp.	Parenteral: Oxytetracycline LA	As with bacterial enteritis there may (occasionally) be a need for whole mob treatment with a high incidence, high risk of spread (e.g. feedlots) and limited opportunity for retreatment.
	Bacterial abortion	*Campylobacter* spp.	Erythromycin Oxytetracycline	Evidence for the value of whole mob/flock antimicrobial treatment in the face of an outbreak is limited.

Table 4: Diseases for which antimicrobial treatment is not or only rarely given

System or Syndrome	Disease	Most common pathogen	Comments, ancillary treatments, prevention
Skin, adnexa	Fleece rot	*Pseudomonas aeruginosa*	An infection of the fleece rather than the skin. The causative organism is not susceptible to most available antimicrobials and treatment is complicated by the inability to get effective antimicrobial concentrations to the site. Reduce prevalence by selection.
Gastrointestinal tract	Ovine Johnes Disease[12]	*Mycobacterium avium* subspecies *paratuberculosis*	Antimicrobials totally ineffective. Managed by vaccination, culling and biosecurity. **Johnes disease is a notifiable disease in Australia.**
	Cryptosporidiosis[12]	*Cryptosporidium parvum*	Occasional disease of lambs born in confinement. No currently registered antimicrobial or antiparasitic chemicals for sheep are known to be effective.
	Melioidosis[12]	*Burkholderia pseudomallei*	Treatment with sulfonamides or antimicrobials is not appropriate particularly considering the necessity for a prolonged duration of treatment and the complexity of monitoring the response. Although initially diagnosed in sheep in Australia, goats and camelids may be particularly susceptible as sentinel animals in an endemic area.
Systemic diseases	Anthrax[14]	*Bacillus anthracis*	Rapidly fatal. *Do not attempt treatment.* Please note that vaccinal efficacy may be diminished by prior or concurrent treatment with penicillins and some other antimicrobials. There is a place for prophylaxis for high value animals on a property where anthrax has occurred, but a decision on use must be made in conjunction with the relevant State or Territory government managing the incident. **Anthrax is a notifiable disease in Australia.**
	Clostridial septicaemias and toxaemias	*Clostridia* spp.	This includes the clinical syndromes of pulpy kidney, black disease, black leg, braxy and other clostridial toxaemias. Rapid death follows toxin elaboration from bacterial overgrowth. Control by vaccination and removing specific determinants (e.g. type of food, liver fluke control).

	Caseous lymphadenitis[12]	*Corynebacterium pseudotuberculosis*	Present in the majority of Australian sheep flocks as pyogranulomas, mainly in lymph nodes and lung, which generally do not respond to antimicrobial treatment. This is an occupational zoonosis that is invariably treated by surgical removal of affected lymph nodes. Discharging superficial lesions in valuable animals may be treated by antiseptic irrigation, mainly to enable healing of the skin over the granuloma, but this will not achieve resolution of the lesion. Control by vaccination and attention to hygiene when dipping and shearing, as well as handling youngest animals first.
	Tuberculosis	*Mycobacterium avium* complex	*M. bovis* has been eradicated from Australia. Members of *M. avium* complex are an occasional cause of non-contagious tuberculous lesions. **Tuberculosis is a notifiable disease in Australia.**
Urogenital	Leptospirosis[10,21]	*Leptospira interrogans* serovars Hardjo and Pomona	Rarely diagnosed in Australia, but occasionally associated with haemolytic anaemia and perhaps abortion.
	Brucellosis[10]	*Brucella ovis*	Treatment unrewarding. Eradication by testing and culling and using accredited sources of rams.
	Toxoplasmosis[10]	*Toxoplasma gondii*	Causes abortion and peri-natal death. No known treatment. Monensin (15 mg/hd/d) may provide chemoprophylaxis during pregnancy.

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