Antimicrobial prescribing guidelines for pigs

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Foreword – antimicrobial prescribing guidelines for pigs

Antimicrobials have been a catalyst for unprecedented medical and societal advancement. However, the revolutionary healing power of antibiotics has resulted in widespread and often inappropriate use. This has led to the development of resistance to antimicrobials in many bacteria, with subsequent treatment complications and failures, and increased healthcare costs for both human and animal health. The Australian veterinary profession and livestock industries have a long history of addressing antimicrobial resistance (AMR). Their previous and ongoing work—a result of partnership across the animal sectors—has resulted in relatively low levels of AMR in our food animals.

In more recent times, we have been responsive to national and international guidelines to address this complex global challenge. In particular, the veterinary profession has worked in close cooperation with animal industries and governments to implement the seven objectives of Australia's First National Antimicrobial Resistance Strategy 2015-19 (National Strategy). The antimicrobial prescribing guidelines for pigs addresses the second objective of the National Strategy.

This objective requires us to '*implement effective antimicrobial stewardship practices across human health and animal care settings to ensure the appropriate and judicious prescribing, dispensing and administering of antimicrobials*'. These guidelines for the Australian pig veterinarian are a handy 'go-to' resource, as they have been developed specifically for Australian conditions and contain the most contemporary knowledge available on AMR. I commend the work of all involved in the development of these guidelines, and urge every pig veterinarian to become familiar with these to deliver the best possible veterinary service to the Australian pig industry.

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Image courtesy of Trent Hewson, TKOAH.

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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

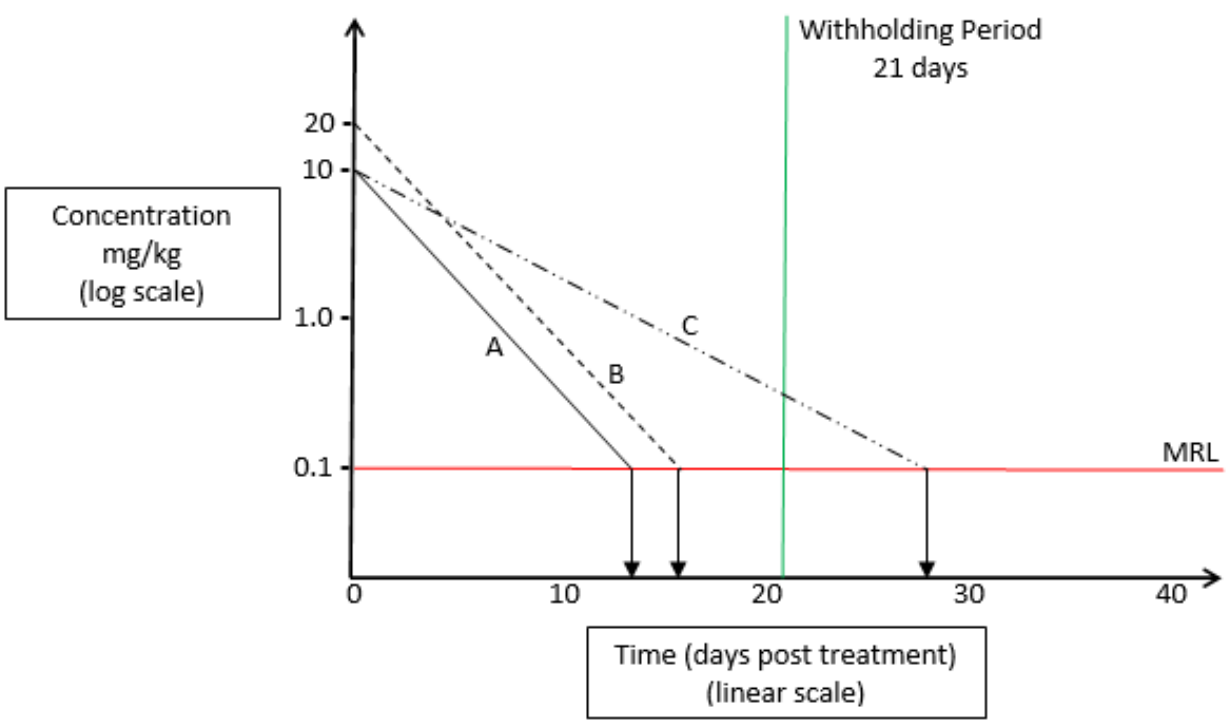
Evaluate veterinarians' prescribing practices continually, based on such information as the main indications and types of antimicrobials used in different animal species and their relation to available data on antimicrobial resistance and current use guidelines.

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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1 Antimicrobial stewardship guidelines for veterinarians working with pigs

1.1 Introduction

One of the key objectives of any antimicrobial stewardship program is to reduce the use of antimicrobials. Eliminating the unnecessary use of antimicrobials is an essential part of this equation. While other objectives include ensuring appropriate prescribing practice (such as using the narrowest spectrum of antimicrobial activity and minimising the duration of use) and ensuring optimal infection prevention and control, the best way to secure the use of antimicrobials for the future and to reduce selection pressures favouring resistant organisms is to reduce the overall amounts used.

Best practice pig farming relies on raising animals under high standards of hygiene, air quality, nutrition and management. These elements contribute to raising animals in ways that reduce the reliance on antimicrobials. It is fair to say that in the past, pigs have been placed in environments that have often failed to completely meet the pigs' requirements. For example, it has long been recognised that the best responses to antimicrobials were seen under conditions of poor hygiene. In addition, when diets were balanced for lysine, growth and feed efficiency, performances were no different from those achieved using carbadox.

These practices also resulted in a culture of controlling enteric and respiratory diseases with antimicrobials, rather than attending to underlying management, housing or hygiene deficiencies. Production policies that focus on financial returns per square metre compromise not only the biological performance of the herd, but also its health, and encourage greater antimicrobial use. In a world where there is little likelihood of novel antibacterial drugs becoming available for use in food animals, this production paradigm must change.

In addition to these pressures, there is close examination locally and globally of animal production practices that might contribute to transfer of antimicrobial resistance to human pathogens and the effects that interventions to reduce antibiotic use in food-producing animals might have on the level of antimicrobial resistant organisms in humans and animals.[1] The evidence suggests that many of the antimicrobial resistance problems in human medicine are not related to antimicrobial resistance in animals, and WHO,[2] having commissioned two meta-analyses of available published literature,[1,3] concluded that the quality of evidence supporting recommendations on reduced antimicrobial use in animals to mitigate AMR in human pathogens is low to very low. Nonetheless, it is reasonable that antimicrobial use should only be implemented when necessary.

Food production practices do intersect with human health. For animal production, antimicrobial use and resistance issues do relate to environmental contamination. Resistance develops in commensal bacteria and that increases the risk of transferring resistance to human pathogens. Of course, using antimicrobials in pig production systems increases the risk of further resistance developing in porcine pathogens.

Antimicrobial v Antibiotic

Antibiotics are substances produced by one organism to inhibit or kill another. Antimicrobials refers to drugs, such as the sulfonamides, that affect a wider range of organisms. They can also include the semi-synthetic drugs such as amoxicillin and fully synthesised drugs such as florfenicol. Zinc oxide is also antimicrobial, but few would class it as an antibiotic. In general, we have used the term antimicrobial to include both the antibiotics and their synthetic cousins that, on application to living tissue or by systemic administration, will selectively kill or prevent or inhibit growth of susceptible organisms.

1.2. Reducing antimicrobial resistance and improving the quality of antimicrobial use in animal production

Antimicrobial stewardship programs are one way that the animal production community can demonstrate its commitment to producing food in a way that does not place environmental or human health at risk, while ensuring that this shared resource is available when needed to protect animal health and welfare.

The easiest and most effective ways to reduce the use of antimicrobials in food animal production is to remove them from animal feeds. Many Australian pig producers stopped using antimicrobials in feed for growth promotion during the late 1990-2000 period. It may not have been part of a policy decision at industry level, but veterinarians around the country noticed changes in their clients' herds to the point that veterinarians were including antibacterial drugs in feed for disease control, largely of *Lawsonia intracellularis* and respiratory disease, and not for growth promotion. The effect on performance and the impact on resistance development may have been the same, but the focus had changed.

On many farms, pig producers lack the facilities to medicate via water across all age groups of pigs.

In seeking to reduce antimicrobial use, producers will be increasingly obliged to renovate their plumbing systems to enable medications to be delivered to specific sheds or specific areas in each shed to properly deliver medication to the target group. In addition, industry supported research will be helpful in guiding efficient delivery systems which minimise water wastage. Along the way, modification and improvements in cleaning programs and ventilation systems, reductions in group sizes, together with staff training, will drive further improvements in antimicrobial use.

1.3. Many producers worldwide have already reduced antimicrobial use

Many farms worldwide with a conventional health status successfully produce pigs with little use of specifically targeted medication by using commercially available vaccines, housing systems that meet best practice, and batch systems or all-in all-out pig flows. It is not the intention of stewardship programs to develop animal production systems that never use antimicrobials. This is not yet possible with current knowledge and resources in groups of many thousands of animals, although small groups may be produced in this way.

It will, however, be possible to substantially refine and reduce antimicrobial use.

Many producers and veterinarians are using novel ingredients as alternatives to antibiotics in feed or water. For example, the acidification of feed or water has been shown to be effective for prevention of post-weaning diarrhoea caused by enterotoxigenic *Escherichia coli*.[4-6] The use of directly fed microbial products, such as probiotics, to combat enteric disease, has some theoretical support, with some information available on use in other animal industries or in conference proceedings, but rigorous studies published in refereed journals are lacking. These novel ingredients or products may offer new alternatives for effective disease control but controlling disease outside of laboratory studies is very difficult and has not yet been convincingly demonstrated. Hence the use of probiotics, for example, have not been strongly endorsed in the sections in this guide on prevention strategies however, the generation of evidence to support the safe and effective use of alternatives is strongly encouraged. The medication strategies outlined in this publication are supported by the global technical literature and have already been applied in Australia.

Table 1: Antibacterial agents registered for antibacterial use in pigs by APVMA

ANTIBACTERIAL AGENT	CLASS	IMP# ASTAG 2018
Amoxicillin	Moderate spectrum penicillin	low
Apramycin	Aminoglycoside	med
Chlortetracycline	Tetracycline	low
Erythromycin	Macrolide	low
Flavophospholipol	Bambermycins	NHU*
Florfenicol	Amphenicol	low
Lincomycin	Lincosamide	med
Neomycin	Aminoglycoside	low
Olaquindox	Quinoxaline	low NHU*
Oxytetracycline	Tetracycline	low
Penethamate	Narrow spectrum penicillin	low
Penicillin (and salts)	Narrow spectrum penicillin	low
Salinomycin	Ionophore	low NHU*
Spectinomycin	Aminocyclitol	med
Sulfadimidine	Sulfonamide	low
Tiamulin	Pleuromutilin	low NHU*
Tilmicosin	Macrolide	low
Trimethoprim + sulfonamide (sulfadimidine/sulfadiazine/ sulfadoxine)	DHRI + sulfonamide	med
Tulathromycin	Macrolide	low
Tylosin	Macrolide	low

* No human use (NHU) of the antibiotic class in Australia

Importance according to Australian Strategic and Technical Advisory Group[7] (ASTAG) list

DHRI Dihydrofolate reductase inhibitors

Ceftiofur is a third generation cephalosporin that is rated by ASTAG as having HIGH IMPORTANCE, a rating assigned to "... 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 pigs. It is registered for use in cattle and carries the label restraint "DO NOT USE for mass medication: for individual animal treatment only". Label restraints take precedence over the rights of veterinarians to prescribe off-label.

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

By formally developing a treatment priority, it is possible to preserve more important medications, the drugs of high or critical importance, so that their antimicrobial efficacy is preserved.

This concept is well developed in human medicine, where a wide range of antimicrobial agents are available for use, but with relatively few medicines available for pigs, and neither colistin, fluoroquinolones nor cephalosporins registered for use in pigs, there are fewer to prioritise. For this reason, this guide provides advice on primary and secondary levels of treatment, but not tertiary levels of treatment.

In developing treatment priorities, the importance rating of the Australian Strategic and Technical Advisory Group[7] (ASTAG) on antimicrobial resistance has been consulted. 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 NHU, (Table 1). The World Health Organisation (WHO)[8] list is numbered from one to five, or highest to lowest of importance. First line treatments, for example those initiated while waiting for laboratory results, should use the lowest rated medications that are likely to be effective.

The WHO priority list varies from the ASTAG list, as it aims to address global issues, rather than the Australian context. The authors have elected to follow the ASTAG rating system as it is most relevant to the Australian situation.

In Australia, registered veterinarians are permitted to prescribe a medication for pigs if it is approved by the Australian Pesticides and Veterinary Medicines Authority (APVMA) for use in other food animals in Australia. Veterinarians are also permitted to prescribe a medication approved for use in pigs at levels or for 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 included on the label. For example, amoxicillin soluble powder is only registered for use in poultry, but it can be prescribed for pigs to treat *Haemophilus parasuis*. Salinomycin is registered for use at 25 ppm (zero days WHP) but is prescribed for pigs at 60 ppm to control *Brachyspira hyodysenteriae*. However, there are no publicly accessible studies in pigs supporting a WHP for this drug at this dose rate in pigs, and it is therefore the responsibility of the prescribing veterinarian to determine a suitable WHP. At the same dose rate in feed fed continuously to chickens there is zero WHP for meat. Where there

is an efficacious antimicrobial approved for pigs, the authors have favoured that product over an off-label prescription. Monensin is not registered in pigs and not recommended for use as no Maximum Residue Limit (MRL) has been approved for pigs anywhere in the world.

The treatment priority list is outlined in Table 3. Although there are only one or two first line treatments listed, any of the medications classified as low importance, NHU or MHU can meet this criterion. The higher importance rating of lincomycin, spectinomycin and trimethoprim should be noted. These rankings imply a need for significant changes from current practice, with these drugs being used less frequently than they currently are.

While the long-term focus must be to reduce the level of antimicrobial use in animal production, from a therapeutic perspective, the most problematic pathogens for pigs are *Actinobacillus pleuropneumoniae, B. hyodysenteriae and E. coli*. These pathogens severely affect pig farming profitability. Globally *A. pleuropneumoniae* isolates are increasingly resistant to the available treatments. For *B. hyodysenteriae*, Australian laboratory susceptibility testing shows that common isolates are no longer generally susceptible to tiamulin, lincomycin or tylosin, although there is still some field efficacy evidence for the first two. Because of this, the Australian industry has lost the capacity to fully control swine dysentery using medication programs. The susceptibility of *E. coli* has changed little over the last 20 years. Four antimicrobial drugs (apramycin, neomycin, amoxicillin and potentiated sulfonamides) still have reasonable levels of efficacy.[9] Solutions for the control of these three diseases will rely increasingly with approaches that by-pass the need for antimicrobial drugs. They will rest with vaccines, housing management, hygiene and dietary manipulation. For all the other pathogens the available antimicrobial drugs still offer good therapeutic outcomes. The main issue associated with antimicrobial use in animal production remains the environmental risk. That too is affected by the quantity of veterinary drugs used as well as the use of products such as zinc oxide or copper sulphate, which are added to diets for their antimicrobial activity.

1.4. Diseases considered

In any program considering a reduction in use of antimicrobials, it is prudent to focus on the "low hanging fruit". These recommendations focus on the most common diseases that veterinarians combat with antimicrobials. In addition, the focus is on removing medications from feed because, currently, this is how most of the medications are administered and generally requires a longer and less controllable duration of antimicrobial use and greater potential for environmental contamination. Table 2 shows the common diseases of pigs and the common age groups they affect. The disease and treatment priorities are presented in Table 3. The common diseases are represented. Others can be added in due course as success is demonstrated in the first phase of the stewardship program.

Table 4 shows the antimicrobial susceptibilities of common Australian porcine pathogens. Australian susceptibilities are presented where they are available, and where they are not available international peer reviewed data are included. The Danish Veterinary and Food Administration publishes a table of priority treatments much the same as is presented in these guidelines in Table 4.[9] In

addition, the advice provided in these guidelines is consistent with the recommendations of the joint scientific opinion of the European Medicines Agency and the European Food Safety Authority.[10]

It is obvious from the published literature that there is a dearth of recently published information on the susceptibility of common Australian porcine pathogens to antimicrobials. For this reason, veterinarians will, in prescribing medications, necessarily draw insight from both the global scientific literature and local laboratory susceptibility testing. The need for ongoing surveillance of resistance is clearly important.

1.5. Dose rates

This document provides guidance to veterinarians on prevention and treatment options for bacterial disease including the selection and use of antimicrobial products registered in Australia for use in pigs. 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 animals it is likely that best practice dose rates are not aligned with label dose rates for at least penicillin, potentiated sulfonamides and amoxicillin.[11] These products were first registered over 50 years ago. Even for veterinarians prescribing these antimicrobials at dose rates consistent with efficacy published in the scientific literature, there is no readily available data base that informs veterinarians of required WHPs to meet the MRL. It places any food animal veterinarian in a quandary regarding WHPs when prescribing, off-label, an antimicrobial at an optimal level for efficacy, and hence, minimising both the risk of developing resistance and potential residues that may affect trade. A solution to this challenge will likely require input from veterinarians, scientists, pharmaceutical industry, and the APVMA. A summary 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 pigs are presented in Table 5. Readers are referred to the APVMA web site and search engine PUBCRIS[26] for product specific information regarding dose rates and WHPs.

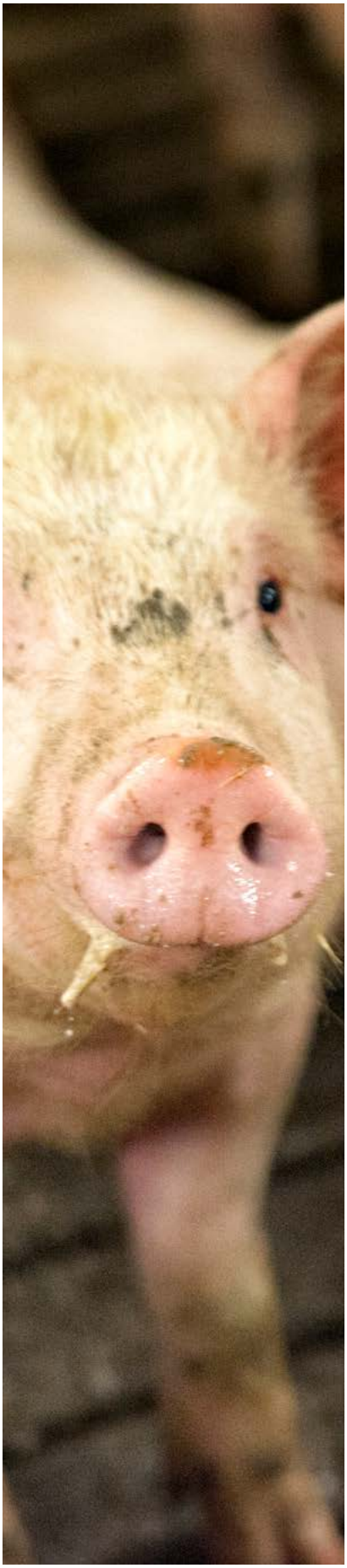


Table 2: Common pathogens or diseases of pigs and the ages in weeks at which they are most commonly seen

Age in weeks	Clinical signs	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Enterotoxigenic (non-haemolytic) *Escherichia coli*	Diarrhoea																					
Clostridium perfringens	Diarrhoea																					
(Rotavirus)	Diarrhoea																					
(Coccidiosis)	Diarrhoea																					
Enterotoxigenic and enterotoxaemic (haemolytic) *Escherichia coli*	Diarrhoea, sudden death																					
(Mulberry heart disease)	Sudden death																					
Streptococcus suis	Meningitis, lameness, sudden death																					
Haemophilus parasuis	Polyserositis, lameness, sudden death																					
Mycoplasma hyorhinis	Polyserositis, sudden death																					
Salmonellae	Diarrhoea, sudden death																					
Mycoplasma hyosynoviae	Lameness																					
(Porcine circovirus associated disease)	Sudden death, Ill thrift																					
Lawsonia intracellularis	Diarrhoea, ill thrift, sudden death																					
Brachyspira hyodysenteriae	Diarrhoea																					
Mycoplasma hyopneumoniae +	Coughing, sudden death																					
Actinobacillus pleuropneumoniae+	Coughing, sudden death																					
Erysipelas	Diamond skin lesions, lameness, sudden death																					

+ Includes secondary invaders, such as *Pasteurella multocida*, *Bordetella bronchiseptica*, *Streptococcus suis* and *Klebsiella pneumoniae*, which may exacerbate primary infections. Diseases or pathogens in parentheses are included for completeness, although they are not treated with antimicrobial drugs. In the last 20 years the global impact of the *porcine circovirus type 2* (PCV2) vaccines has been significant. In Australia, as elsewhere, their deployment has facilitated reduced reliance on antimicrobial treatments and metaphylaxis. In apparently normal herds PCV2 vaccines have reduced post weaning mortality rates by 3-6% without the need for concurrent antimicrobial treatment.[12]

Table 3: Common Australian pig pathogens and antimicrobial treatment options[13] and priority

Pathogen/disease	Clinical signs	Preventative elements	Primary treatment choice	Secondary treatment choice	Notes
Actinobacillus pleuropneumoniae	Coughing, sudden death	Vaccine, air quality, space allowance	Penicillin, amoxicillin	Florfenicol, tilmicosin, lincospectin tulathromycin	Cephalosporins not recommended
Brachyspira hyodysenteriae	Diarrhoea	Hygiene	Tiamulin	Lincomycin	Monensin is not recommended
Clostridium perfringens	Diarrhoea	Hygiene, thermal comfort, colostrum management	Penicillin, amoxicillin+	Florfenicol, tylosin	Cephalosporins not recommended
Enterotoxigenic (non-haemolytic) *Escherichia coli*	Diarrhoea	Vaccine, hygiene, thermal comfort, colostrum management	Fluids + oral neomycin or apramycin	Fluids + trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	
Enterotoxigenic or enterotoxaemic (haemolytic) *Escherichia coli*	Diarrhoea, sudden death	Live oral autogenous vaccine, thermal comfort, diet, organic acids in feed and/or water, bromelain extract	Neomycin, apramycin	Trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	Cephalosporins not recommended
Erysipelothrix rhusiopathiae	Diamond skin lesions, lameness, sudden death	Vaccine	Penicillin, amoxicillin	Tylosin, lincomycin	
Haemophilus parasuis	Sudden death, polyserositis, lameness	Air quality, space allowance, vaccination	Penicillin, amoxicillin	Florfenicol, tulathromycin	
Isospora suis	Diarrhoea	Hygiene, prophylactic toltrazuril	Toltrazuril		

Table 3: Common Australian pig pathogens and antimicrobial treatment options[13] and priority

Pathogen/disease	Clinical signs	Preventative elements	Primary treatment choice	Secondary treatment choice	Notes
Lawsonia intracellularis	Diarrhoea, ill thrift, sudden death	Vaccine, hygiene	Tylosin	Tetracycline, tiamulin, olaquindox, lincomycin	
Mycoplasma hyopneumoniae +	Coughing, sudden death	Vaccine, air quality, space allowance	Tiamulin	Tylosin, tilmicosin, lincomycin, tulathromycin	
Mycoplasma hyorhinis	Polyserositis, sudden death	Air quality, space allowance	Tetracycline, tiamulin	Tylosin or lincomycin	
Mycoplasma hyosynoviae	Lameness	Air quality, space allowance	Tetracycline, tiamulin	Tylosin or lincomycin	
Pasteurella multocida	Coughing, sudden death	Air quality, space allowance	Chlortetracycline, oxytetracycline, florfenicol, penicillin, amoxicillin	Trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	
Salmonellae	Diarrhoea, sudden death	Hygiene, thermal comfort, organic acids in feed and/or water	Neomycin	Trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	Cephalosporins not recommended
Streptococcus suis	Meningitis, lameness, sudden death	Air quality, space allowance	Penicillin	Florfenicol, tylosin, trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	Cephalosporins not recommended
Staphylococcus hyicus	Exudative epidermitis	Hygiene	Penicillin, amoxicillin	Tiamulin, trimethoprim-sulfonamide (sulfadimidine/ sulfadiazine/sulfadoxine)	

Table 4: Common Australian pig pathogens and their antimicrobial susceptibility

Pathogen	Clinical signs	Susceptibility
Actinobacillus pleuropneumoniae	Coughing, sudden death	[14]Australia 2015: 75% tetracycline resistance, 25% tilmicosin resistance, 8.5% amoxicillin and penicillin resistance
Clostridium perfringens	Diarrhoea	[15]Australia 1985: no resistance to penicillin, 75% of isolates resistant to tetracycline, 41% resistant to erythromycin and lincomycin. Multiple resistance common.
Brachyspira spp	Diarrhoea	[16]Australia 2002: for 76 Australian isolates tested by broth dilution, the minimum inhibitory concentration (MIC)^{90} for tiamulin was 1 mg/L; for valnemulin was 0.5 mg/L; for tylosin was > 256 mg/L; for erythromycin was > 256 mg/L; for lincomycin was 64 mg/L; and for clindamycin was 16 mg/L.
Erysipelothrix rhusiopathiae	Diamond skin lesions, lameness, sudden death	[17]Australia 2018: highly susceptible to amoxicillin. 20% isolates resistant to tetracyclines, 0.75% isolates resistant to lincospectin, penicillin and erythromycin
Escherichia coli	Diarrhoea, sudden death	[18]Australia 2004: widespread resistance to tetracycline and moderately common resistance (30–60%) to amoxicillin and sulfadiazine. [9]Denmark: 2016: susceptibility based on MIC^{90}; to amoxycillin in 67% of isolates; to apramycin in 78% of isolates; to neomycin in 72% of isolates; and to trimethoprim-sulfamethoxazole in 65% of isolates.
Haemophilus parasuis	Polyserositis, sudden death	[19]Australia 2014: elevated MICs for amoxicillin (1% isolates), penicillin (2% isolates), erythromycin (7% isolates), tulathromycin (9% isolates), tilmicosin (22% isolates), tetracycline (31% isolates,) and trimethoprim-sulfamethoxazole (40% isolates).
Lawsonia intracellularis	Diarrhoea, ill thrift, sudden death	[20]USA 2009: when tested for intracellular activity, carbadox, tiamulin and valnemulin were the most active antimicrobials, with MICs of ≤0.5 mg/L. Tylosin (MICs ranging from 0.25 to 32 mg/L) and chlortetracycline (MICs ranging from 0.125 to 64 mg/L) had intermediate activities and lincomycin (MICs ranging from 8 to >128 mg/L) had the least activity. When tested for extracellular activity, valnemulin (MICs ranging from 0.125 to 4 mg/L) was the most active against most *L. intracellularis* isolates. Chlortetracycline (MICs ranging from 16 to 64 mg/L), tylosin (MICs ranging from 1 to > 128 mg/L) and tiamulin (MICs ranging from 1 to 32 mg/L) had intermediate activities. Lincomycin (MICs ranging from 32 to >128 mg/L) had the least activity.
Mycoplasma hyorhinis	Sudden death, polyserositis, lameness	[21]Japan 1996: tiamulin had the highest activity with MICs of 0.2 to 0.78 mg/L, and 10% of isolates were resistant to all macrolide antibiotics tested.
Mycoplasma hyosynoviae	Lameness	[22]USA 2011: clindamycin (a lincosamide) had the highest activity and was most consistent inhibitory of all isolates, with a MIC^{50} of ≤ 0.12 mg/L. The MIC^{50} of tiamulin was ≤ 0.25 mg/L. For the macrolides, the MIC^{50} of tylosin and tilmicosin was ≤ 0.25 mg/L and ≤ 2 mg/L respectively but was ≤16µg/ml for tulathromycin. Spectinomycin and neomycin had an MIC^{50} of ≤4µg/ml. The MIC^{50} of tetracyclines was ≤ 2 mg/L. The MIC^{50} of florfenicol was ≤ 1 mg/L. All isolates were resistant to penicillin, amoxicillin, ceftiofur, trimethoprim/sulfamethoxazole, and sulphadimethoxine.
Mycoplasma hyopneumoniae	Coughing	[23]Thailand 2006-2011: resistance to antibiotics is increasing. The MIC of tiamulin was < 0.013 - 0.78 mg/L, with an MIC^{90} of 0.1 mg/L; the MIC of lincomycin was 0.025 - > 12.5 mg/L, with an MIC^{90} of 0.39 mg/L; the MIC of tylosin was 0.025 - >12.5 mg/L, with an MIC^{90} of 0.39 mg/L; the MIC of oxytetracycline was 0.78 - 12.5 mg/L, with an MIC^{90} of 6.25 mg/L; the MIC of chlortetracycline was 3.12 – 100 mg/L, with an MIC^{90} of 50 mg/L; and the MIC of florfenicol was 0.2 - 6.25 mg/L with an MIC^{90} of 1.56 mg/L.
Pasteurella multocida	Coughing, sudden death	Genetic basis for the resistance or elevated MICs of the majority of isolates of Australian porcine respiratory pathogens to amoxicillin, penicillin and tetracycline.[11] In the EU resistance is evident in 22% of isolates to tetracycline, 3% to potentiated sulfonamides and 1% to amoxicillin.[24]
Salmonellae	Diarrhoea, sudden death	[25]Australia 1975-1982: in porcine salmonella 4% of isolates were resistant to neomycin, 3% to ampicillin and 29% to tetracycline.
Streptococcus suis	Meningitis, lameness, sudden death	[26]Europe 2014: 81.8% of isolates were resistant to tetracycline. Resistance to amoxicillin/clavulanic acid, ceftiofur, enrofloxacin, tiamulin and tilmicosin was absent or <1%. Trimethoprim/sulfamethoxazole resistance was seen in 3 - 6% of isolates.

Table 5: Approved dose rates[27,28] and recommended off-label dose rates where the product is not registered for use in pigs

Drug	Route of administration	Dose rate	Duration	WHP**(Export Slaughter Interval [ESI])	Notes and evidence for off-label use
Amoxicillin	IM	7 mg/kg 15 mg/kg (long acting)	Daily for 3-5 days Repeat after 48 hours if required	14-28 days (no ESI issued) 28-30 days	WHP varies. Refer to product label.
Amoxicillin	Oral in water**	20 mg/kg	3-5 days	14 days (no ESI issued) Range: 2-14 days for different products	Off-label. Dose and WHP taken from UK registered product Stabox50% Oral Soluble Powder Pig for use against *Actinobacillus pleuropneumoniae*[29,30]
Amoxicillin	Oral in feed**	20 mg/kg 500 ppm in feed	5 days	14 days (no ESI issued)	Off-label. Dose and WHP taken from UK registered product Perlium Amoxival for use against *S. suis*[30,31]
Apramycin	Oral in water	25 mg/kg for neonates 12.5 mg/kg for weaners	3 days 7 days	14 days (no ESI issued)	Do not use for more than 14 days
Chlortetracycline	Oral in feed	400 ppm in feed	Maximum 7 days	7 days (no ESI issued)	In feed oral dose at odds with dose via water
Chlortetracycline	Oral in water	25 mg/kg	2-5 days	7 days (no ESI issued)	
Erythromycin	IM	2-6 mg/kg	3-5 days*	7 days (no ESI issued)	There are no label recommendations for duration of treatment
Florfenicol	IM	15 mg/kg	Two injections 48 hours apart	12 -18 days (ESI 12-22 days)	Check specific product label for ESI
Florfenicol	Oral in water	10 mg/kg	5 days	12 days (no ESI issued)	Label recommendation for respiratory disease treatment only
Florfenicol	Oral in feed	10 mg/kg 200 ppm	5 days	12 days (ESI 15 days)	15 mg/kg detailed in Burch[10] but there are no WHP published for this dose
Lincomycin	Oral in water	10 mg/kg 33 mg/L	Treat for 5 days after the disappearance of bloody stools (swine dysentery) for a maximum of 10 days	2 days (no ESI issued)	
Lincomycin	Oral in feed	40-110 ppm *B. hyodysenteriae* 220 ppm *M. hyopneumoniae*	A maximum of 21 days or, in the case of swine dysentery, until clinical signs disappear	1 day for 110ppm 2 days for 220 ppm (no ESI issued)	Highest dose (110 ppm) for clinical swine dysentery. 40 ppm for metaphylaxis of swine dysentery and controlled exposure of *Lawsonia intracellularis*.

Table 5: Approved dose rates[27,28] and recommended off-label dose rates where the product is not registered for use in pigs

Drug	Route of administration	Dose rate	Duration	WHP**(ESI)	Notes and evidence for off-label use
Lincomycin-spectinomycin	IM	15 mg/kg total combined antibiotic	3 days	21 days (No ESI issued)	
Lincomycin-spectinomycin	Oral in water	6.3 mg/kg Total combined antibiotic of 63 mg/L of water	Daily for 3-7 days	8 days (no ESI issued)	Do not use this medication simultaneously in both feed and water
Lincomycin-spectinomycin	Oral in feed	Total combined antibiotic of 44 ppm	3-7 days*	1 day (no ESI issued)	Do not use this medication simultaneously in both feed and water
Neomycin	IM	2-4 mg/kg	Every 6-12 hours for 3-14 days as indicated	15-30 days (no ESI issued)	Check product label – WHP varies
Neomycin	Oral in water	8-22 mg/kg	3-5 days	20 days (no ESI issued)	
Neomycin	Oral in feed	8-22 mg/kg 100-200 ppm	3-7 days	20 days (no ESI issued)	
Olaquindox	Oral in feed	100 ppm for pigs 3-10 weeks of age 50 ppm for 11+ weeks		12 -24 hours (ESI 28 days)	Metaphylactic treatment of proliferative enteritis at 50 ppm
Oxytetracycline Long acting	IM	20-30 mg/kg Engemycin: 10 mg/kg	Single treatment	28 days (ESI 28 days) Engemycin 10 days (no ESI issued)	Check product labels for dose, WHP and ESI
Oxytetracycline short acting	IM	4-9 mg/kg	Daily for 3-5 days	8 -14 days (ESI 8 days)	Check product label – WHP varies. Some do not have an ESI.
Oxytetracycline	Oral in feed	25 mg/kg 550-1100 ppm for leptospirosis 20 mg/kg 450 ppm other diseases	7-14 days	4 days (no ESI issued)	Check product label – WHP varies
Penicillin: short acting (procaine)	IM	12-15 mg/kg	Daily for 3-5 days	5 days (no ESI issued)	Higher doses up to 20 mg/kg are suggested in Diseases of Swine[32] and Veterinary Medicine[33], but there are no published Australian WHPs for this dose. FARAD offers 50 days.[34]
Penicillin: long acting (benzathine)	IM	13 mg/kg total penicillin	Single dose Repeat after 3 days	30 days (No ESI issued)	Higher doses up to 20 mg/kg are suggested in Diseases of Swine, but there are no published Australian WHPs for this dose. FARAD offers 50 days.

Table 5: Approved dose rates[27,28] and recommended off-label dose rates where the product is not registered for use in pigs

Drug	Route of administration	Dose rate	Duration	WHP**(Export Slaughter Interval [ESI])	Notes and evidence for off-label use
Salinomycin	Oral in feed	60 ppm for swine dysentery prophylaxis	Continuous	Nil for 25 ppm No WHP stated for 60 ppm in pigs (no ESI issued)	Toxic in combination with Tiamulin Statement of field efficacy[35] No adverse effect on human health or the environment.[36] Burch[10] states 15-60 ppm, but no WHP recommended. Zero WHP for meat of chickens at 60 ppm.[27]
Tiamulin	Oral in water	8.8 mg/kg – 25.5 mg/kg per 400L water for *B. hyodysenteriae* 17.6 mg/kg – 25.5 g/200L water for *M. hyopneumoniae*	3-5 days 6 days	5 days (no ESI issued)	Do not use concurrently with salinomycin or other ionophores Dose rates for *B. hyodysenteriae*, *M. hyopneumoniae* and *L. intracellularis* vary
Tiamulin	Oral in feed	50-100 ppm for treatment and control of *B. hyodysenteriae* 100 ppm for treatment of *M. hyopneumoniae*	5 days 10 days	5 days (No ESI issued)	Do not use concurrently with salinomycin or other ionophores Dose rates for *B. hyodysenteriae*, *M. hyopneumoniae* and *L. intracellularis* vary
Tilmicosin	Oral in water	15-20 mg/kg	5 days	7 days	
Tilmicosin	Oral in feed	8-24 mg/kg	14 days	14 days	Feed 7 days in advance of anticipated disease outbreak Bentonite may affect product efficacy
Tulathromycin	IM	2.5 mg/kg	One dose	14 days (ESI 26 days)	Do not treat again until at least 8 weeks after the last treatment. Culture and sensitivity recommended.
Tylosin	IM	5-10 mg/kg (*B. hyodysenteriae*)	Do not exceed 3 days treatment	3 days	
Tylosin	Oral in water	25 mg/kg (*B. hyodysenteriae*) 6-12 mg/kg (*L. intracellularis*)	7 days	(No ESI issued)	
Tylosin	Oral in feed	40-100 ppm	Up to 21 days for treatment of ileitis at 100 ppm	Nil (No ESI issued)	In practice 50 ppm in feed will permit controlled exposure to *L. intracellularis*[37]

*The labels for these products are unclear as to the recommended treatment duration. The durations here have been adjusted based on a consensus of best practice

**Always confirm and follow the WHP advice on the label of the registered product selected for use

2 Lameness in neonatal pigs in the first week of life

2.1. History and predominant clinical signs

Lameness in piglets in the first 3 days of life is common in those reared on abrasive concrete floors. The pigs suffer both abrasion of the skin over the carpus and the hock and erosion of the sole of the foot. The prevalence of erosions can be as high as 60%. Arthritis occurs in about 6% of pigs.[37] Pigs raised on wire floors can have traumatic penetrating injuries to the interdigital skin, and subsequent ascending infection. Approximately 1.5% of pigs die from arthritis before or within two weeks of weaning.[38]

The affected piglets show a painful shifting lameness from the time of the erosion on day one and struggle to compete or get to the udder quickly enough to suck before milk let down is completed. In time, many progress to weakness and succumb to starvation, diarrhoea or septicaemia, or are overlain. Others survive only to be euthanised as unviable animals at weaning or soon after.

The pathogens recovered are comprised largely of streptococci and staphylococci, with *E. coli* in a minority (about 5%). These pathogens are mostly susceptible to penicillin.

After the first week of age, the incidence of new lameness cases decreases significantly. By this stage, superficial carpal and hock abrasions have mostly completely healed. Arthritis may also have its genesis in infectious disease caused by *Haemophilus parasuis* or *Streptococcus suis*, or following teeth clipping or poor umbilical hygiene. This section refers only to the problem of abrasive or injurious floors.

2.2. Differential diagnoses

- Lameness and arthritis following sole abrasions
- Arthritis following teeth clipping or umbilical infection

Arthritis following teeth clipping or umbilical infection occurs later than lameness and arthritis following sole abrasions due to rough floors. Umbilical infections should be apparent at the same time as any arthritis if the septicaemia has resulted from an ascending umbilical infection. These pigs don't necessarily have abrasions of the sole.

2.3. Diagnostic tests

The lame pigs are easy to pick by observation alone. The less thrifty pigs are often missed as lameness cases, so it pays to pick up the individuals and examine them. It's important to look beyond any carpal abrasions, which are very common in new born pigs, to specifically check on the health of the foot itself.

2.4. Preventative strategy

The problem relates to rough abrasive floors, so the solution lies with resurfacing with polymer, rubber mats or large amounts of bedding.

When the condition presents in many piglets, veterinarians often prescribe penicillin, given at the same time as iron during piglet processing, to provide 'antibiotic cover' around the same time as the lesion is initiated. From an antimicrobial stewardship perspective, this is not recommended and instead the veterinarian should recommend environmental change (attending to floor surfaces) as soon as this is possible.

2.5. Treatment

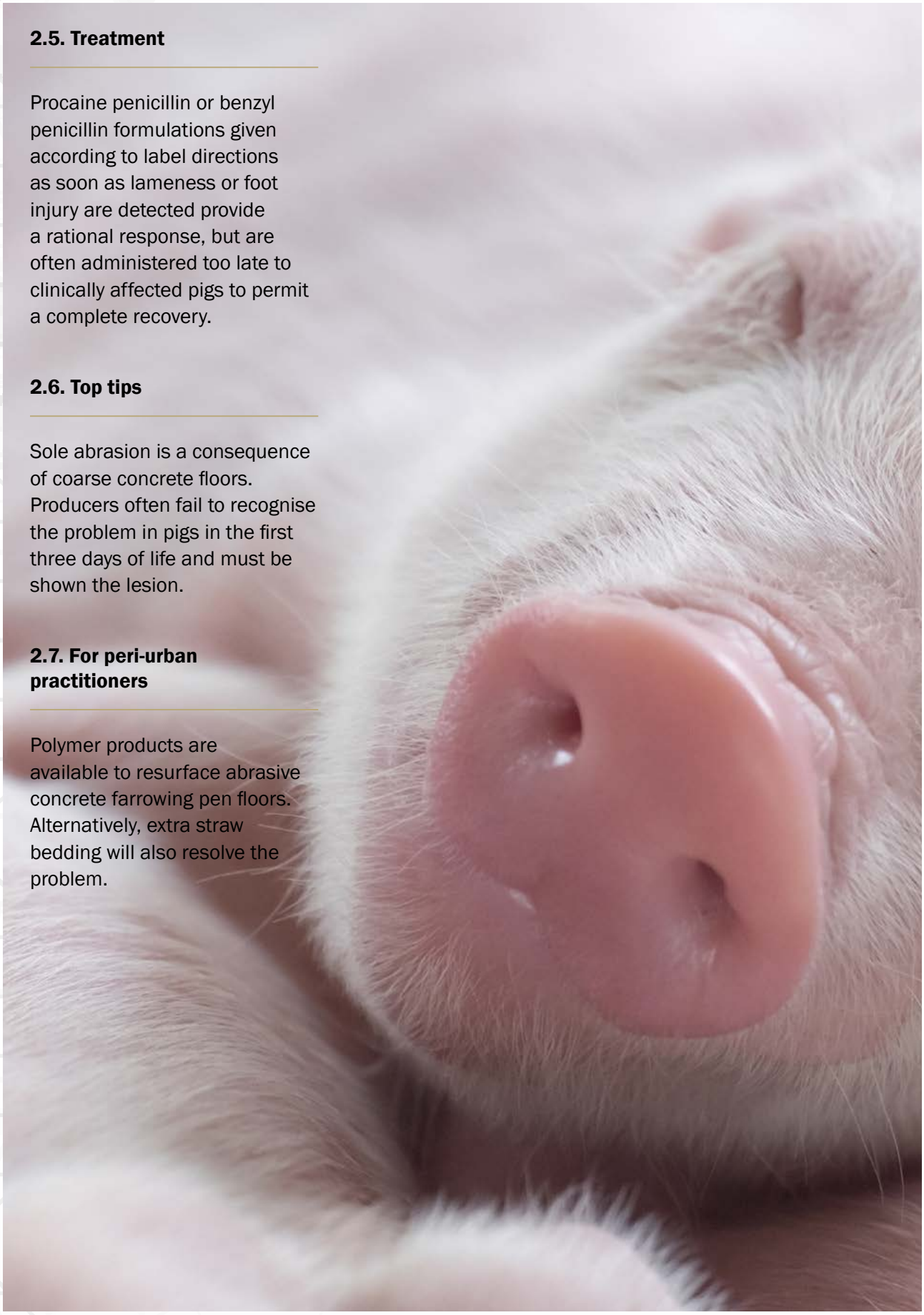
Procaine penicillin or benzyl penicillin formulations given according to label directions as soon as lameness or foot injury are detected provide a rational response, but are often administered too late to clinically affected pigs to permit a complete recovery.

2.6. Top tips

Sole abrasion is a consequence of coarse concrete floors. Producers often fail to recognise the problem in pigs in the first three days of life and must be shown the lesion.

2.7. For peri-urban practitioners

Polymer products are available to resurface abrasive concrete farrowing pen floors. Alternatively, extra straw bedding will also resolve the problem.



2.8. Case study
Reducing neonatal lameness by improving the flooring.

In old farrowing houses with deteriorating concrete floors, the cement wears away to expose the aggregate. For newborn pigs the surface is rough and abrasive. It soon wears away the tender soles of the feet. The injuries and bruising are clearly visible if the feet are inspected. If new concrete hasn't had a steel float finish a new floor surface can also be damaging for piglets. It is often exacerbated by the addition of oat husks as bedding as it has a sandpaper-like effect on the feet.

Wire mesh floors can cause penetrating wounds of the interdigital cleft. Sometimes, partly in error and partly to provide sows with firmer footing, wire mesh is installed upside down, with the result that the little spikes associated with hot-dipped galvanised iron coating penetrate the feet of neonatal pigs. Claws are also often damaged by sharp edges or joints that do not quite fit.

Producers faced with this problem eventually recognise that the best alternative is to replace the floor surface of the farrowing pen with plastic slats or plastic-coated expanded metal. Cast iron slats under the sow and plastic or wire mesh slats at the end of the creep area complete the floor construction. Some producers have had excellent results from renovation of old farrowing pen floors with terracotta tiles for the solid floor area. These are easy to clean and provide a non-slip surface for the sows. They are also safe for piglets. Others have sealed worn farrowing crate floors with resin to useful effect. Following these measures to improve the comfort, health and welfare of the pigs, preweaning mortality rates can be maintained well below 10%.

Experiments administering long acting penicillin to neonates at processing demonstrate subsequent reductions in requirements for lameness treatment before weaning. In a study in Victoria[39] involving 150 litters, the number of treated piglets was reduced from 0.33 per litter in controls to 0.08 per litter in the pigs given long acting penicillin in the first five days of life, and from 0.76 treatments per litter in controls to 0.34 treatments per litter in those given long acting penicillin between 5 days and weaning ($P < 0.05$). There was no effect on litter weaning weight, deaths per litter or deaths due to arthritis. The reduction in antibiotic treatment suggests the likely benefits if the floor surfaces could be improved and there was a reduction in foot infections. Alleviation of foot injury or arthritis and subsequent lameness improves the capacity of the pig to compete at the udder and suck. For example, a Bendigo study[40] found that 50% of the pigs dying with enteritis had intercurrent disease or disabilities, such as arthritis, respiratory disease, small birth weight or overlaying.

In a Swedish study[41] involving a herd with three different farrowing systems, 37 litters (390 piglets) were followed until 3 weeks of age to detect the presence of skin wounds and abrasions. The most severe abrasions on the carpus and the soles were seen in the system with a new solid concrete floor with slats over the dunging area. The lowest level of injuries was seen in a deep litter system with peat. Sole bruising was more common in the systems with concrete floors than in the deep litter system with peat, and the difference in prevalence was significant. The overall prevalence of lameness was highest in the system with new solid concrete floors with slats over the dunging area (9.4%), followed by the old solid concrete floor (7.5%). A lower prevalence ($P < 0.05$) was seen in the deep litter system with peat (3.3%). Lameness was diagnosed in every fourth litter in that system and in every second litter in the systems with concrete floors.

Where producers stop teeth clipping, published reports show no difference in post weaning performance.[42] Field reports from farms that stop teeth clipping show no change in preweaning mortality rate and indicate a reduction in polyarthritis, with a consequent reduction in ill thrifty pigs and reduced treatments for lameness (Cutler unpublished data).

3 Diseases where the main clinical sign is diarrhoea in newborn pigs up to four days of age

3.1. History and predominant clinical signs

Look for watery diarrhoea. It is the predominant clinical sign. Affected piglets can dehydrate rapidly. They are unable to compete at the udder, become progressively weak and die from dehydration or are overlain by the sow. The common aetiological agents are ubiquitous, so the litters of gilts, which may not have been exposed previously, are at higher risk. Where the sow is unwell, some degree of lactation failure will be a likely consequence. High risk piglets are those that have been fostered before receiving colostrum, those fostered after 24 hours that cannot compete for a teat, and those sucking a non-functional teat. Lightweight pigs are always at risk.

3.2. Differential diagnoses

- *E. coli* is a likely cause if the herd is unvaccinated. Some strains produce an adhesin involved in diffuse adherence (AIDA)[43] and colonise the lower gastrointestinal tract. They produce enterotoxins,[43] but appear to lack fimbriae. They could cause *E. coli* diarrhoea in vaccinated herds. A Canadian report suggested an AIDA *E. coli* pathotype prevalence of 20% in week old piglets with *E. coli* diarrhoea.
- Rotavirus infections are not uncommon, but rarely cause fatal disease unless other pathogens are present.
- Disease caused by *Clostridium perfringens* is difficult to diagnose. It relies on demonstration of toxin in the intestinal contents.
- *Clostridium difficile* is offered by some as a cause of neonatal diarrhoea, but it is difficult to culture and the evidence to support a role for it as a common pathogen, except where neonates have been treated with cephalosporins at birth, is not strong. Its presence in clinically normal animals confuses its direct role in causing disease.[44]

Even after exhaustive investigation, undifferentiated diarrhoea sometimes remains as the diagnosis for neonatal diarrhoea. Globally, transmissible gastroenteritis virus and infection with porcine epidemic diarrhoea virus warrant inclusion in the differential diagnosis, but neither of these pathogens is present in Australia.

3.3. Diagnostic tests

No thorough herd investigation is complete without a necropsy and histopathology, together with analysis of fresh tissues and gut content from several untreated, euthanised representative piglets, or freshly dead piglets, by culture and susceptibility testing. Rapid screening ELISAs for *E. coli* and PCR assays for the genes for the enterotoxins are readily available (Table 6). Toxin tests for the clostridia are available from specialist laboratories.

Table 6: Laboratory tests for diagnosis of diarrhoea in neonatal pigs

Disease	Necropsy, histopathology	Culture, serotyping, antimicrobial susceptibility testing	Other tests
Escherichia coli	✓	✓	ELISA for toxin, PCR for toxin genes
Rotavirus	✓		ELISA
Clostridium difficile	✓	✓	ELISA, toxin test
Clostridium perfringens	✓	✓	Toxin test, ELISA

3.4. Prevention

As with any enteric disease, farrowing pen hygiene (or fresh straw and a new site for outdoor sows) is a pivotal issue. Thermal comfort in a draft-free pen is essential. Vaccination of the dam is a core element for *E. coli* prophylaxis in very young piglets through production of IgG in colostrum and hence neutralisation of early *E. coli* colonisation of the gut. In older piglets the IgG effect has waned, and the piglets are reliant on lactogenic IgA.

Any factor affecting sow health and well-being will probably affect lactation performance. Udder soundness must be confirmed. The incorrect timing of any induced farrowing treatments must be ruled out.

3.5. Treatment

The first level of treatment must focus on colostral intake and access to a functional teat. At the same time, piglet vigour must be optimised through provision of a warm creep area.

The next step is to deliver fresh clean electrolytes, supplemented with glucose, in drinking bowls in the affected farrowing pens twice daily. Individual piglets can be treated orally by stomach tube if required.

Antimicrobial treatments based on culture and susceptibility testing of *E. coli* isolates with relevant fimbrial antigens is consistent with good practice. Although fluid-based treatment without supporting antimicrobials may ideally be the goal, current texts recommend early antimicrobial treatment to remove the pathogenic *E. coli*.[45]

Rotavirus infections are best dealt with by provision of oral fluid therapy delivered by bowl drinkers. Where the problem persists, exposure of pregnant sows, and particularly gilts, to faeces from affected litters or pens or from young weaned pigs likely to be excreting rotavirus offers a way forward by immunising the sow and increasing the likelihood of colostral immunity in subsequent litters.

The evidence base for treatment of the clostridial pathogens is very poor. Alternatives, such as penicillin treatment of affected litters and probiotics for prophylaxis or treatment, are anecdotally interesting but poorly researched. They lack formal confirmation of their value in the published literature.

Pending culture and susceptibility testing, in the case of *E. coli* the first line of treatment is oral neomycin or apramycin, or potentiated sulfonamide by injection or oral pump, at label recommendations.[13] Cephalosporins are NOT recommended. Their use in pigs is off label and contrary to the label restriction against mass medication. Selection

for extended spectrum beta lactamase or ESBL (for example cephalosporin) resistance is considered a significant adverse effect and the result of poor antimicrobial stewardship.

For prophylaxis efforts in basic environmental husbandry and sow farrowing house management, especially in terms of sow soundness and fostering management, are likely to be rewarded. Vaccines against alpha and beta toxoid containing *C perfringens type A* were protective in laboratory studies in Germany[46] but, in Australia, these vaccines are only available for poultry and their use untested in pigs.

3.6. Top tips

Thermal comfort, good hygiene, colostral intake, fostering management and sow nutrition, fitness and health underpin prevention of diarrhoea in neonatal pigs, as its aetiology is often multifactorial. Provision of fluids and electrolytes is critical in any treatment.

3.7. For peri-urban practitioners

Enterotoxigenic colibacillosis is usually a disease of the litters of parity one sows. It is unusual to see it in litters of sows of any parity farrowing in well-bedded huts on clean pasture or paddocks. In the unusual event of a pet pig requiring diagnosis, a faecal sample for an ELISA is a good start. In the absence of this, potentiated sulfonamides and fluids for three days are the way forward. Fluoroquinolones and cephalosporins are NOT recommended.

3.8. Case study: Using vaccines to reduce the severity of *E. coli* disease in neonatal pigs

This is well established news now. Most veterinarians, producers and people working on pig farms will not have known a time when *E. coli* vaccines were not available. In the late 1970s the discovery of the role of the adhesins in pathogenicity and their immunogenicity led to the development of the first killed *E. coli* vaccines. The first commercial vaccines against *E. coli* became available in Australia in the early to mid-1980s. Until then between 5 and 15% of all piglet deaths were due to enteritis. Those pigs that developed diarrhoea in the first 2 to 4 days of life had a mortality rate of about 22%.

The litters of gilts were most at risk, so herds that had high gilt populations regularly endured outbreaks of *E. coli* diarrhoea and preweaning mortality rates often exceeded 20%. The success of the *E. coli* vaccines in controlling the disease in the litters of parity one sows was recorded by Fahy et al[47] and is presented in Table 7.

This case study, although now quite old, heralded the arrival of the first of the new pig vaccines, including those against the bacterial pathogens *M. hyopneumoniae, A. pleuropneumoniae, H. parasuis and L. intracellularis*, and those against porcine parvovirus and PCV2. They demonstrate an early prophylactic approach to disease control and, over 30 years ago, a shift away from therapeutic approaches using antibiotics.

Table 7: The effect of killed *E. coli* vaccines given to sows on diarrhoea, treatments and deaths in piglets before weaning

Parameter	Whole cell vaccine	Purified pilus vaccine	Control
Number of sows	97	97	94
Piglets born alive	944	906	902
Litters with diarrhoea (%)	19.6***	21.6***	50
Scour days/litter	125***	166***	523
Severity score	54**	76**	387
Total treatments	133**	145**	1162
Deaths associated with diarrhoea	5.0%***	6.1%***	22.2%

***Significantly different from controls (P < 0.001, Chi-squared test)

**Significantly different from controls (P < 0.01, Student's t-test)

3.9. Case study: Eliminating ceftiofur use on a pig farm

The farm

The farm is a medium sized commercial sow breeder farm. It has conventional intensive housing, with facilities of varying ages and types. Sows are group housed for all of gestation. Litters are farrowed in conventional farrowing crates with a combination of plastic and metal flooring. The heating system, heat lamps and heated flooring are controlled by a remote system.

The herd has a conventional health status. There are no particular health challenges in the sow herd. The prevalence of clinical signs of diarrhoea (5% of litters) and ill-thrift in piglets (5%) falls within industry norms.

The breeding herd is vaccinated to control porcine parvovirus, leptospirosis, erysipelas and neonatal colibacillosis.

The issue

The management and treatment program for piglet scours comprised routine antimicrobial treatment of scouring litters. The farm had been prescribed different options for treatment, depending on the age at onset of diarrhoea and the severity of clinical signs.

The prescriptions specifically for "piglet scour" were Scourban® (proprietary blend of neomycin sulfate, streptomycin sulfate, sulfadimidine, sulfadiazine, hyoscine hydrobromide, pectin, calcium gluconate, potassium chloride, magnesium sulfate and sodium chloride), neomycin sulfate injection, trimethoprim-sulfadiazine injection and ceftiofur hydrochloride injection. The latter, which is not registered for use in pigs, but is used off-label, came with the specific instructions from the herd's prescribing veterinarian for use with "non-responsive scour – use only as last resort".

Routine veterinary review of animal health and treatment effectiveness following a change of ownership found a higher than expected use of ceftiofur at this farm. Inspection of farm records and questioning of staff revealed that all piglets were receiving a dose of ceftiofur by injection at 1 to 2 days of age, regardless of clinical signs of diarrhoea. In using ceftiofur outside the specific instruction, staff stated that, "scours have been bad recently." They had confidence that ceftiofur was effective for control.

Key points

Antibiotic use can be significantly reduced and refined following investigation of apparent overuse by:

- Confirming the diagnosis
- Assessing management
- Reviewing hygiene practices
- Developing and implementing protocols to improve management
- Introducing a targeted treatment plan

3 Diseases where the main clinical sign is diarrhoea in newborn pigs up to four days of age

Clinical findings

Review of the farm records revealed that piglet mortality rates had increased over the previous 4 weeks. Weaning weights were below target. Inspection of the animals and facilities revealed a prevalence of neonatal diarrhoea up to 10% in piglets from 1 to 4 days of age. Records indicated that all sows were routinely vaccinated pre-farrowing for *E. coli*. Culture of rectal swabs taken from untreated piglet diarrhoea cases yielded no bacterial pathogens.

Production had been good recently, with more sows farrowing than expected. This meant that turn-around time in the farrowing facilities was shortened to fit the extra sows in, meaning that cleaning, drying, disinfecting and "resting" time between litters was reduced, thus compromising hygiene. Necropsies of dead piglets revealed that few piglets had died as a direct result of diarrhoea, and that the elevated mortality rate was due to an increase in overlays. Inspection of the facilities revealed that piglets had abnormal resting patterns, away from the heated creep areas, putting them at higher risk of trauma from the sow.

The temperature of the heated areas varied from 38°C to 50°C, when the recommended temperature for neonatal piglets is 30°C to 32°C.

Sow feed intakes also varied. Many sows were over-eating soon after farrowing. They had hard or engorged udders.

Resolving the case

The temperature control of the piglets' heated area was immediately reviewed. It came to light that no staff had routinely checked the calibration of the controlled set point against the actual temperature in the pens. The temperature settings were re-calibrated and a protocol agreed to routinely check temperatures against set points.

Routine hygiene practices were reviewed. A cleaning, drying and disinfection regimen was agreed. It allowed time for these operations and more timely movement of sows due to farrow. Disinfectant use and dilution rates were reviewed. No change to the routine disinfection with glutaraldehyde and a quaternary ammonium compound was considered necessary.

A drying agent was introduced as part of the disinfection process - commercial product of chloramine, iron sulfate and copper sulfate in a bentonite base. No sow was moved into a pen that was still wet.

Periparturient sow feeding was reviewed. Sows were offered minimal feed on the day of farrowing and "stepped up" each day to limit over-eating.

Colostrum management and early fostering of piglets were reviewed. Staff were re-trained in best practice techniques. All piglets were allowed to consume adequate colostrum from their birth mother and fostering of piglets was only used if the piglet did not have a functional teat to use and it could be moved to another litter within which a functional teat was available. No piglet was moved more than once. Only emergency moves were performed later than 24 hours after birth.

Outcomes

Pre-weaning mortality decreased by approximately 3%. Recorded deaths caused by "scour" reduced from 30% of all deaths to less than 5% of all deaths. All piglet treatments were reduced. Total antimicrobial drug use on piglets reduced from a high of approximately 1.2 doses per piglet born alive to less than 0.1 doses per piglet born alive. Piglet diarrhoea was soon considered to not be an issue at this farm.

The most common treatment now for any piglet diarrhoea is to provide electrolytes and review the environment. Antibacterial treatment of piglet diarrhoea is limited to oral dosing of affected piglets with Scourban®.

Ceftiofur was removed from the routine treatment list. Its use was eliminated from the farm. The farm has not used any ceftiofur for more than 2 years, with no detrimental effect on pig health.

4 Diseases where the main clinical sign is diarrhoea from five days of age until weaning

4.1. History and predominant clinical signs

Diarrhoea in piglets older than one week of age may have a similar morbidity rate to that seen in younger piglets, but the mortality rate is lower. Hygiene factors play a role, but are more likely to affect coccidiosis than colibacillosis.[45] Sow health factors are less likely to be involved. Pathogenic *E. coli* will have F4 (K88) fimbriae. The serogroups of the *E. coli* commonly involved include 0139, 0141 and 0149, amongst others. Sudden death where diarrhoea may or may not be evident is a feature of acute infection with E. coli in this age group. Sudden death, commonly with haemorrhagic diarrhoea, is also a feature of infection with *Clostridium perfringens* type C in pigs at around ten days of age.

The earliest coccidiosis (*Isospora suis*) can occur is dependent on the age of infection. If the piglets ingest oocysts during their first day of life, then it is possible that infection of the ileum by intermediate stages of the parasite can occur by day 5. More usually, coccidiosis affects pigs between 7 and 10 days of age. Most commercial herds use toltrazuril prophylactically around days 3 to 5. By targeting the intermediate stages, the disease is effectively prevented.[44]

4.2. Differential diagnoses and tests

- *Escherichia coli*
- *Isospora suis*
- *Clostridium perfringens type C*

Where deaths are involved, the aetiology is likely to be *E. coli*. Otherwise *I. suis* joins *E. coli* in the differential diagnosis of diarrhoea in pigs between 5 days of age and weaning. *C. perfringens* type C causes acute necrotic enteritis in pigs around 10 days of age, so should be included on the list of possible diagnoses, but it is much less common than colibacillosis or coccidiosis.[48]

Involvement of *E. coli* is confirmed by culture, serotyping, and toxin typing by PCR. Susceptibility testing is useful for treatment. *I. suis* oocysts are evident in faeces, but they may only be found in about 30% of submitted samples. Histopathology is also helpful. Identification of the *C. perfringens* type C toxin in intestinal contents remains the definitive diagnostic criterion, but this is a task for specialised laboratories. Globally, transmissible gastroenteritis virus and porcine epidemic diarrhoea virus warrant inclusion in the differential diagnosis but neither of these two viral pathogens is present in Australia.

4.3. Predisposing causes

There is a knowledge gap about predisposing factors for this group of diseases. A failing or diminution of lactogenic antibody, or even a disturbance of the microbiota, is possibly at the heart of diseases caused by both *E. coli* and *C. perfringens*. For coccidiosis, hygiene is a major factor for all pigs. Rather than the sow being an important source, as is likely with *E. coli* and *C. perfringens*, pen floor and wall contamination is an important coccidiosis risk factor.

4.4. Preventative strategies

Thorough cleaning and drying of farrowing pens before new sows are introduced remains the cornerstone of control of all three of these diseases. For outdoor sows, moving the farrowing hut for each farrowing and providing ample clean bedding yields the same result.

Where *E. coli* are involved, the sows can be vaccinated with a live autogenous oral vaccine during pregnancy if the disease persists. *C. perfringens* type C toxoid vaccines have been developed in Europe. Two separate studies demonstrated that the vaccines, one experimental and one commercial, improved survival by 30% and prevented further losses from *C. perfringens* in field outbreaks. The vaccines were used in the face of outbreaks on different farms once the disease had been diagnosed.[49,50] In Australia the

only registered *C. perfringens* type C vaccines are approved for sheep and cattle. While their use is theoretically sound these vaccines have not been assessed in controlled laboratory or field studies in pigs.

Other approaches (probiotics, acidification of sow diets and administration of exogenous proteases for neonates) lack credible field studies.

4.5. Treatment

Prompt treatment, at first with neomycin or apramycin at label recommendations, and then based on culture and susceptibility testing for *E. coli*, together with fluids, is recommended. The clostridia generally respond well to penicillins. Cephalosporins of any generation are NOT recommended due to label restraints. In any case the narrow spectrum penicillins are favoured over the broader spectrum cephalosporins.[13] Toltrazuril given about 4 days ahead of the first expected clinical signs contains coccidiosis effectively.

4.6. Top tips

Thorough cleaning and drying of farrowing pens or provision of clean ground and straw before new sows are introduced remains the cornerstone of control for enteric disease.

4.7. For peri-urban practitioners

It is unusual for enteric disease to cause disease in piglets in very small herds in which only one or two sows are farrowing. As numbers increase coccidiosis may emerge. If this is suspected and toltrazuril is not available, the best approach is to provide ample fluids and give the pigs time to recover naturally. At the same time hygiene and bedding practices can be overhauled.

4.8. Management: Diarrhoea in piglets between five days of age and weaning

Enterotoxigenic *E. coli* (O149, F4 [K88], toxins Sta, Stb and/or Lt) cause acute disease in 7 to 10-day old pigs. Many die suddenly in a state of shock, with blue extremities and low body temperature. Often the *E. coli* are resistant and do not respond to any registered antimicrobial drugs.

The differential diagnosis includes mulberry heart disease, *S. suis septicaemia* and *H. parasuis*, but the presence of diarrhoea, dehydration and the isolation of haemolytic *E. coli,* together with the absence of other lesions, leads to rapid diagnostic resolution.

Oral fluid therapy, with electrolyte replacement solutions containing glucose, is useful for the treatment of dehydration and acidosis. Prevention of enteric *E. coli* infection should be aimed at reduction of the numbers of pathogenic *E. coli* in the environment by good hygiene, maintenance of optimal environmental conditions, and provision of a plentiful supply of colostrum at birth and ensuring a high level of immunity.[44]

Colostrum and milk contain non-specific bactericidal factors and specific antibody (IgG and IgA) that inhibit the adherence of pathogenic *E. coli* to the intestine. If the dam has not been vaccinated or exposed to the pathogenic *E. coli* present in the environment of the piglets, her colostrum and milk lack specific antibodies and the piglets are susceptible to infection.

In support of this, where the disease is problematic, feeding sows a live autogenous 24-hour culture of *E. coli* using UHT milk as the culture medium effectively immunises the sow, inducing production of IgA antibodies in the milk. Veterinarians in Australia and abroad have found this method effective in overcoming this disease. The cultures are fed about 5 weeks ahead of farrowing to permit the sow time to develop antibodies.[48]

Under experimental conditions transmission can be prevented by implementing strict hygienic measures, but in the field routine cleaning and disinfection are usually insufficient to break the cycle of infection with *E. coli*. There are only limited data on the susceptibility of *E. coli* isolates to commonly used disinfectants.

According to a Danish study, faecal isolates of *E. coli* from livestock did not appear to have developed resistance to benzalkonium chloride, hydrogen peroxide, chlorhexidine, formaldehyde or zinc chloride.[51] However, Beier and others detected reduced susceptibility to chlorhexidine in virulent *E. coli* isolates from newborn pigs with diarrhoea and found that this was correlated with resistance to gentamicin and streptomycin.[52]

Low ambient temperatures in the farrowing house also increase the severity of disease. In newborn pigs kept at temperatures of less than 25 °C, intestinal peristaltic activity is greatly reduced, and passage of bacteria and protective antibodies through the intestine is delayed.[53] Pathogenic *E. coli* will cause more severe diarrhoea in pigs kept at temperatures below 25 °C than in pigs kept at 30 °C. The same principles apply for bigger suckling pigs. A dry, warm environment also reduces the moisture available for survival and growth of *E. coli.*

Dietary acidifiers, such as citric, fumaric, lactic, propionic, benzoic and formic acids, can have beneficial effects in the pig gastrointestinal tract. The use of organic acids in weaned piglets is associated with a reduction in stomach pH.[4] This will generate a hostile gastric environment for bacterial survival. It is tempting to try to reduce *E. coli* burdens and hence excretion by feeding organic acids to sows. Unfortunately, the technical literature provides no support for this approach.

5 Diseases where the main clinical sign is diarrhoea after weaning

5.1. History and predominant clinical signs

Diarrhoea is a common clinical sign in weaned pigs. Depending on the severity of the disease, it may be accompanied by an increase in the mortality rate for the group. The form, colour and presence or absence of blood or mucus in the faeces, together with the age of the affected animals, can provide a useful guide to differential diagnoses.[54]

Ill thrift accompanies all the differential possibilities. Sudden deaths with or without diarrhoea occur.

5.2. Differential diagnosis

- *Escherichia coli*
- *Salmonella* spp
- *Lawsonia intracellularis*
- *Brachyspira pilosicoli*
- *Brachyspira hyodysenteriae*
- *Trichuris suis*

In the first 7 to 14 days after weaning *E. coli* is the most likely cause of diarrhoea.[44] The organisms themselves are ubiquitous so disease results from a complex interaction of predisposing factors. Thermal comfort, air quality, food intake, protein digestibility and amino acid balance, water quality, and the loss of lactogenic immunity may all play a role.

High dietary zinc levels suppress *E. coli* populations but also select for methicillin, tetracycline and sulfonamide resistance genes,[55-57] which can be detected in up to 30% of *E. coli* isolates. Diagnosis rests on the demonstration of the fimbrial antigens and the O serogroups associated with virulent strains, and detection of the genes encoding the specific enterotoxins associated with virulence.[45]

Salmonella Typhimurium and other *Salmonella* serotypes are not uncommon pathogens, either alone or in association with porcine circovirus type 2, but infection is more common than disease. Infection and disease are seen at about 6 weeks of age and can persist for extended periods.

L. intracellularis is ubiquitous and natural infection commonly occurs between 7 and 11 weeks of age. While most pigs are infected in this period, many do not show clinical signs, which is typically a moderate diarrhoea of variable consistency. Milder cases are difficult to detect and may manifest as wasting pigs or failure to thrive.[58]

Infection with *B. pilosicoli, B. hyodysenteriae* and possibly other brachyspires can be seen from about 7 to 8 weeks of age but is more common in older pigs. Both cause diarrhoea, but mucus and blood in the sloppy diarrhoea of pigs infected with *B. hyodysenteriae* are important diagnostic indicators.[54]

Necropsy and histopathology are important diagnostic elements. Culture and antimicrobial susceptibility testing are used for all pathogens except *L. intracellularis*, the definitive diagnosis of which relies on qPCR on tissue or faeces. Because *L. intracellularis* is an obligate intracellular bacterium requiring use of cell culture techniques to grow *in vitro*, susceptibility testing is not performed routinely, so treatments (see below) are guided by the scientific literature, rather than laboratory results.

E. coli can be typed using ELISAs for fimbrial antigens and PCR assays for toxins. PCR assays are performed on cultures to differentiate *B. hyodysenteriae* from *B. pilosicoli*. Culture is difficult and susceptibility testing is expensive to perform.

Trichuris suis infection can be confirmed on the basis of gross pathology and is preferred to faecal egg counts as these can be unreliable indicators.

5.3. Preventative strategy

Post-weaning colibacillosis has been researched globally but clarity about specific predisposing factors, or even treatments, remain elusive in many cases. It is a multifactorial disease, with the thermal environment, hygiene, nutrition, physiological development, weaning stress, preweaning exposure, lactogenic immunity, weaning age and the gut microbiota all playing a role. Of these, ensuring thermal comfort, ensuring that dietary protein is highly digestible, and dietary acidification are first level measures that can be applied on-farm. Live oral vaccines given to pigs at 10 to 14 days of age are successful, but care must be taken to ensure that the live organisms that are inoculated carry the fimbrial antigens and are free of the toxin genes, as determined by PCR. Use of water or feed acidification as control measures is supported by limited peer reviewed studies, but a clear understanding of the mechanisms is lacking.[5] The acids do appear to increase water consumption and protein digestibility. The latter may well be the critical factor.

In pigs, post weaning diarrhoea (PWD) can be controlled using various preventative strategies without using antimicrobials (Table 8). Feed supplements, such as organic acids, prebiotics, probiotics, synbiotics, dehydrated porcine plasma, antimicrobial peptides, specific egg yolk proteins from vaccinated hens, and bacteriophages, have been used in weanling pigs to enhance growth, feed efficiency and to reduce PWD. The short chain and medium chain fatty acids and long chain polyunsaturated fatty acids have been shown to improve gut function in the face of inflammatory conditions. Supplementation of diets with butyrate may be a promising way to promote intestinal health.[59,60] Zinc oxide, once considered a suitable non-antibiotic antimicrobial substance, faces environmental heavy metal contamination issues as well as selecting for antimicrobial resistance genes.[61] Under the conditions of a Spanish study, a single dose of bromelain, a proteolytic extract from pineapple stems (registered as Detach), given at weaning was as effective as in-feed zinc oxide in reducing the prevalence of diarrhoea and antibiotic treatments post-weaning compared to untreated pigs.[62]

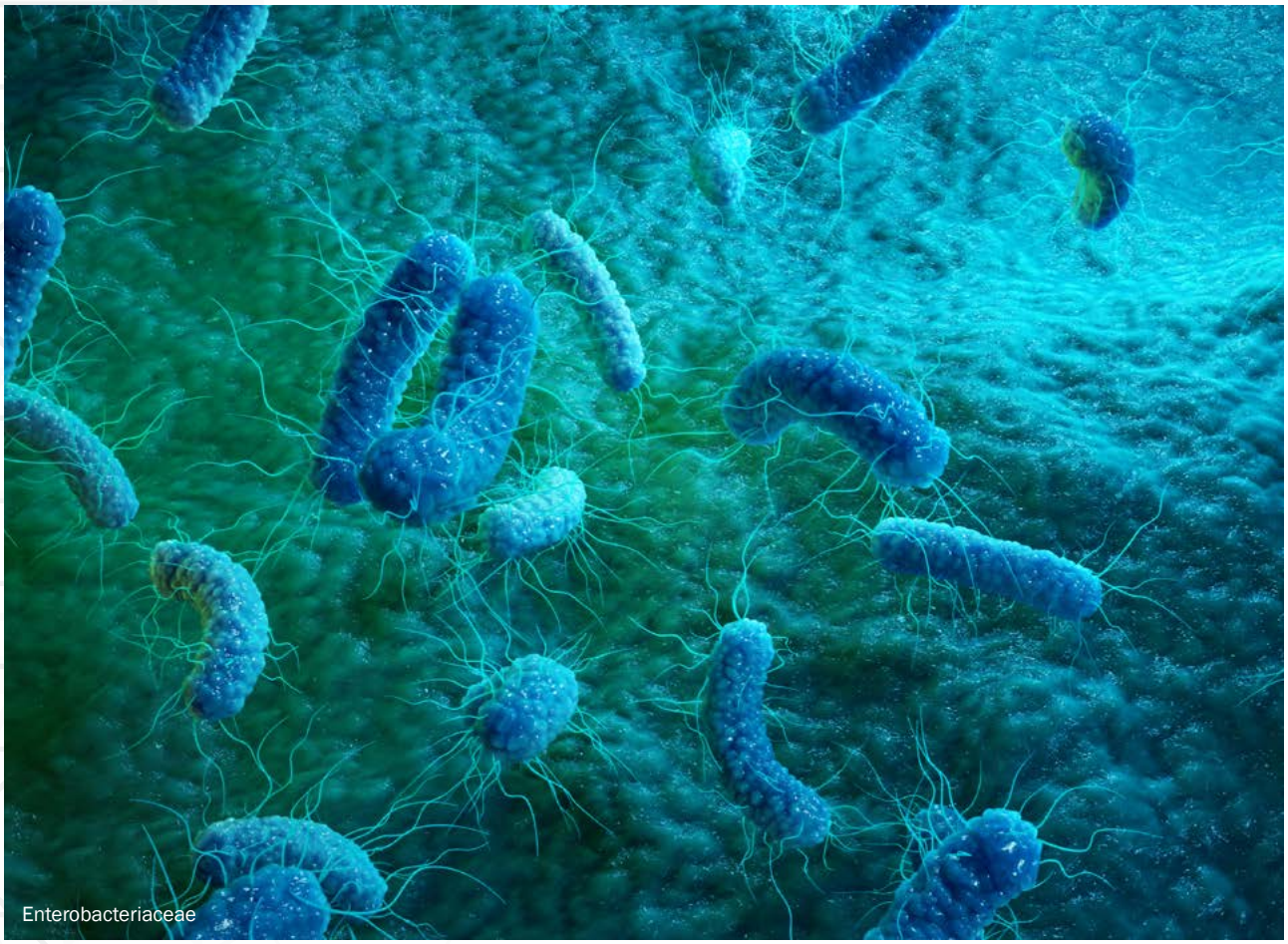
Dietary acidification with citric, fumaric, lactic, propionic, benzoic or formic acids can have beneficial effects in the pig gastrointestinal tract. The use of organic acids in weaned piglets is associated with a reduction of stomach pH, but the effects vary with the acid.[63] Organic acids promote the conversion of pepsinogen into pepsin in the stomach of pigs, and promote the activity of this enzyme. Decreasing the intestinal pH is probably not a primary effect of feeding organic acids in pigs. Risley et al did not detect a significant decrease in the pH of the small intestine in 3-week-old weanling pigs fed a diet supplemented with 1.5% fumaric or citric acid.[64] Addition of organic acids to weaned pig diets can improve growth performance and health[65] as well as the local immunity in the jejunum epithelium. It has reported that regardless of the specific organic acid used in the feed, these compounds reduce the incidence and severity of diarrhoea in pigs, and improve the performance of the treated group compared to that of the negative control group.[5]

Salmonellae commonly infect pigs and disease can follow. There is a complex interaction between the intestinal microflora, colonisation with *Salmonella* and disease. Diet and the environment play a role. Improving pen hygiene and reducing stress by improving thermal comfort are time-honoured *Salmonella* control measures. The addition of organic acids to the diet or water supply has yielded apparent prophylactic and therapeutic success in the field, but the evidence from the published literature lacks consistency.[66]

There is some evidence that the gut population of salmonellae is limited by acidification. Feeding a coarsely ground meal, rather than pellets, to pigs changes the physicochemical and microbial properties of the content in the stomach, which decreases the survival of salmonellae during passage through the stomach.[67] There is also evidence that inclusion of acids reduces seroprevalence, but, while it might prevent outbreaks, acidification will not treat outbreaks of disease.[68]

L. intracellularis is ubiquitous. The age of infection, as assessed by serum antibodies, can be delayed by antimicrobial treatments for other endemic diseases. A live oral vaccine, given individually or in liquid feed or in water using a proportioner, is available and its efficacy in preventing disease is supported in the literature by field experiences, but results can be mixed. Pen hygiene is an important element in disease control.[4] Historically the disease has been controlled by treatments just prior to peak periods of *L. intracellularis* infection that occurs on many farms at around 8-11 weeks. Alternatively, periods of about 3 weeks exposure interspersed with periods of in-feed treatment with tiamulin (120 ppm), tylosin (100 ppm) or lincomycin (110 ppm) can be effective but the disease still occurs if exposure to infection is not achieved.[58] Historically periods of medication at sub therapeutic levels for six weeks have permitted both exposure and the acquisition of active immunity but prevented clinical disease. However, given the availability of an effective vaccine, antimicrobial treatments must be considered poor stewardship.

B. hyodysenteriae and *B. pilosicoli* are widespread. Hygiene and space allowance are important elements in prevention, although both diseases can persist on farms even when these factors are addressed. Boiled rice has been shown to be prophylactic, but its availability is limited.[69]



Enterobacteriaceae

Table 8: Benefits and limitation of the major alternative feed strategies for the control of post-weaning diarrhoea in pigs[65,70]

Strategies	Benefits	Limitations
Zinc oxide	Inhibits bacterial adhesion to the intestinal mucosa	High levels can increase PWD
	Stimulates growth rate	Heavy metal contamination of soil
	Maintains intestinal mucosal integrity	Bacterial resistance selection
	Modulates immune functions	Co-resistance with antimicrobial drugs
Organic acids	Decreases pH in the stomach	Exact modes of action still unknown
	Improves growth performance	Antimicrobial activities differ between acids
	Reduces PWD	
Prebiotics, probiotics and synbiotics	Improve intestinal health	Contradictory studies on their effectiveness
	Improve growth performance	Lack of information on the potential synergism between prebiotics and probiotics
	Reduce ETEC: F4 attachment to the ileal mucosa	
	Reduced diarrhoea	
Spray dried plasma (SDP)	Reduce the markers of intestinal inflammation	High cost
	Maintain mucosal integrity	
	Requires rigorous control during the preparation process	
	Improve growth performance	Potential source of viral pathogens
	Reduce incidence and severity of diarrhoea	
Antimicrobial peptides	Decrease diarrhoea	Bacterial resistance
	Reduce the markers of intestinal inflammation	
	Enhance immune function	
	Cocktails of AMPs might be used to mitigate selection for resistance	
Specific egg yolk antibodies	Improve growth performance	High cost
	Decrease diarrhoea	Antibodies may not be directed against the ETEC strains present on some farms
	Maintain intestinal mucosal integrity	
Bacteriophages	Reduce *E. coli* mucosal adhesion	Narrow spectrum of activity
	Maintain intestinal mucosal integrity	Development of bacterial resistance
	Decrease diarrhoea	A combination of phages is needed
Proteolytic enzyme Bromelain	Treatment causes proteolytic disruption to K88 (F4) glycoprotein receptors and prevents *E. coli* attachment to the small intestine mucosa	Treatment efficacy may be limited to about 30 hours[62,70]

5.4. Treatment

E. coli: In the face of clinical disease, antimicrobial treatment based on culture and susceptibility testing, supported by electrolyte supplements and acidification, are recommended. First line treatments include neomycin or apramycin at label recommendations. Cephalosporins are NOT recommended.

L. intracellularis: First line therapy with a range of drugs, including tylosin, olaquindox, tiamulin, or the tetracyclines, is very effective. Lincomycin is a second level medication and is unlikely to be superior to tiamulin. Olaquindox is problematic for some businesses because of occupational health issues. Allergic contact dermatitis and photocontact dermatitis have been reported following occupational exposure to olaquindox.[71]

B. pilosicoli and *B. hyodysenteriae* are best treated on an empirical basis. Routine sensitivity tests are not done, but specialised laboratories have found that some strains of *B. hyodysenteriae* are resistant *in vitro* to tiamulin, tylosin and lincomycin. Field experience indicates good control and therapeutic effect with tiamulin at label recommendations. *B. pilosicoli* responds clinically to olaquindox, tiamulin and lincomycin, but resistance can occur in this pathogen as well.

Once clinical brachyspiral diarrhoea is under control, according to field reports, salinomycin at 60 ppm (off-label) in the feed effectively controls the disease but there are no approved WHPs for this dose rate and the prescribing veterinarian is therefore responsible for determining and providing an appropriate WHP. From an international trade perspective using salinomycin presents an unquantified risk. However, the product is used at this dose rate in chickens with a nil WHP for meat. Monensin is not recommended because there is no MRL for this ionophore in pigs. Ionophores (for example salinomycin), and tiamulin are toxic in combination in pigs. Concurrent treatment must be avoided.

5.5. Top tip

Administration of tiamulin in feed at 55 ppm for three weeks or in water at label recommendations for three days to weaned pigs in all-in all-out systems, combined with high hygiene standards, prevents swine dysentery caused by *B. hyodysenteriae* in growing and finishing pigs.

5.6. For peri-urban practitioners

The enteric diseases are unusual in weaned pigs in small numbers in small herds. The highest risk is post-weaning colibacillosis and this is best averted with high quality diets for pigs after weaning.

5.7. Case study: Controlling *Lawsonia intracellularis*

Love recognised porcine adenomatosis in growing pigs[72] as part of the same syndrome associated with the *Campylobacter*-like-organisms that caused proliferative haemorrhagic enteropathy in young breeding gilts.[73] Marr detected wasting and lesions in pigs at slaughter that were missed as subclinical cases in younger growing pigs on-farm.[74] Through the 1970s and 1980s the disease was kept largely in check almost universally by the addition of antimicrobials to pig diets, resulting in additional growth rates of about 3-10%, depending on age.

Periodically veterinarians would withdraw antibiotics from pig feeds, but invariably unwittingly created an environment in which large populations of susceptible pigs were exposed to this ubiquitous pathogen. This resulted in substantial reductions in growth rate and increases in mortality rates that resulted in significant losses. Every 1% increase in mortality rate costs a herd about $3.00 per pig. Every reduction of just 10 grams/day in growth rate costs about $1.50 per pig.[75] Hence, in a 500-sow herd producing about 200 pigs per week, a mortality rate attributable to this disease of 2% costs about $1200/week. Add to this a minimum of about $300/week in weight lost and the costs rise further, to the point where, over a 3-6 week outbreak, the likely costs can be conservatively estimated to be $4500 - $9000.

When the disease was well controlled with antimicrobial drugs, naïve populations of valuable young breeding stock emerged, and when these animals were eventually fed unmedicated diets they succumbed to acute haemorrhagic enteropathy.

Control of the disease stagnated until McOrist et al[76] identified the aetiological agent and work by Collins et al,[77] amongst others, through the late 1990s and early 2000s resulted in the availability of routine diagnostic serological and PCR assays. Veterinarians then became confident about removing antimicrobial drugs from the diets of growing and finishing pigs. Exposure to the pathogen could be monitored serologically. Treatment could be instituted promptly in water in the event of a failure in the controlled exposure strategy. Indeed, during this period, in large farming systems, medications were removed from the diet of weaned pigs between 3 and 10 weeks of age. Tylosin was added to diets of growing pigs at 40 ppm between 10 and 13 weeks of age (depending on the epidemiology of the organism in the herd,) to permit exposure while containing the clinical expression of disease.

In the knowledge that exposure had largely occurred by about 14 weeks of age, finisher pigs were left unmedicated. These changes, facilitated by the availability of diagnostic tests and the desire of farmers to produce pigs without in-feed antibiotic treatment, led to a reduction of 85% in the amount of antimicrobials fed to pigs on these sites.

In 2004, Kroll and others demonstrated the efficacy of an avirulent live vaccine against *L. intracellularis*.[78] Many veterinarians have successfully deployed this vaccine in herds in Australia. In high health status herds free of respiratory disease this has facilitated production without recourse to antimicrobial drugs in-feed after weaning, and, in some herds, without using antimicrobial drugs in water either. In these herds, from time to time, apparent increases in the prevalence of lesions of proliferative enteritis at slaughter to approximately 15% occur (Gleeson unpublished data). This is addressed on-farm by attention to vaccination technique. It highlights the importance of active disease surveillance at slaughter, monitoring health status with necropsies, serological testing of high-risk age groups and staff training in vaccine delivery.

6 Diseases where the main clinical sign is coughing

6.1. History and predominant clinical signs

Coughing in pigs is common on farms infected with *M. hyopneumoniae*. The organism has an immunosuppressive effect and, despite vaccination, on many farms pneumonia is a reality in growing pigs.[79,80] Respiratory disease is the major cause of morbidity and mortality in this age group.

Pigs can start coughing in the nursery when they become infected with *H. parasuis* or *S. suis*. Infection with *M. hyopneumoniae* occurs at around the same time but is rarely a major problem until the pigs enter the grower phase. Respiratory disease is always worse in sheds holding large populations of animals and in continuous flow facilities.[81] Poor shed and ventilation system maintenance routines make things worse. More than 400 pigs per group is a risk factor for lesions at slaughter and increased mortality rates.[79] *P. multocida* and *B. bronchiseptica*, which are rarely pathogenic alone,[82] often together with resident streptococci and *H. parasuis*, combine with *M. hyopneumoniae* to cause bronchopneumonia. This affects feed intake and feed conversion efficiency, and commonly results in death.[82]

A. pleuropneumoniae (APP) can follow *M. hyopneumoniae* as a concurrent pathogen or can be a serious primary pathogen. When it is involved, disease is acute. Pigs die suddenly, within 24 hours of infection, and bleeding from the snout is evident at necropsy because of the effects of the haemolytic and necrotising toxins produced by APP and the resultant fibrinous pleuropneumonia.[83]

In those animals that survive, the forced respiration that accompanies severe pleurisy is commonly evident. Ill thrift is a common sequela. At slaughter as many as 40% of the pigs in APP-affected herds have pleurisy to a degree that requires trimming at slaughter (Gleeson unpublished data).

In these herds, despite vaccinations and medications in water, many pigs require individual treatments.

Coughing is also apparent in weaned pigs infected with ascarid intermediate stages when hygiene is poor. Disease caused by *Metastrongylus* species is unusual but must be considered where pigs are raised on dirt or where earthworms can survive.

6.2. Differential diagnosis

- *Mycoplasma hyopneumonia* and *Pasteurella multocida*
- *Mycoplasma hyopneumoniae* and *Actinobacillus pleuropneumoniae*
- *Actinobacillus pleuropneumoniae* alone
- *Ascaris suum* or metastrongyles in association with the pathogens above

PCV2 can exacerbate respiratory disease after infection with either APP or *M. hyopneumoniae*, but most herds vaccinate against PCV2 and the available vaccines are reliably effective.

The predominant lesion associated with APP is a fibrinous pleuropneumonia.

APP and *M. hyopneumoniae* are differentiated based on necropsy lesions, histopathology, culture for APP and tissue PCR for a definitive diagnosis. Severe bronchopneumonia and pleurisy can follow infection with *P. multocida* and the lesion can be confused with that caused by APP. While generally reliable, culture of APP can be difficult, so tissue PCR is always recommended for diagnosis.

Serology for APP and *M. hyopneumoniae* can provide an indication of herd prevalence and the age at which animals seroconvert.

Migrating ascarid intermediate stages must be considered in straw-bedded and free-range pigs. Lung worms (*Metastrongylus* species), although uncommon in mainstream herds, must be considered in pigs raised on dirt. Faecal egg counts and *post mortem* examinations provide useful differentiation.

6.3. Preventative strategy

For any respiratory disease, the underlying environmental elements of hygiene, air quality and space allowance are pivotal. Over and above these, control of respiratory disease is improved in those herds that can run all-in-all-out systems and group sizes of less than 400 pigs.[84] Batch farrowing systems also provide a way of segregating age groups and managing all-in all-out pig flows. Where continuous flow systems operate, and where group numbers are large, respiratory disease requires considerable technical intervention to control effectively.

Commonly farms are infected with both *M. hyopneumoniae* and APP. Prompt treatment with appropriate injectable antibiotics is essential because the progression of disease caused by APP is so rapid and therefore daily inspection of pens in the grower and finisher sections of the farm is necessary. Concurrent treatment with non-steroidal anti-inflammatory drugs mitigates against the extreme inflammatory response and provides pain relief.

Vaccines for *M. hyopneumoniae* are partially effective, but do not eliminate the need for therapy. An APP vaccine is also available and effective against some common serotypes. Where failures occur, an autogenous vaccine can be a useful alternative.

6.4. Treatment

The cephalosporins are NOT recommended at any level.

Even if the primary target is *M. hyopneumoniae*, treatment is generally focused on the secondary pathogens. While diagnostics and culture and susceptibility testing are proceeding, individual treatments with injectable penicillin provide the first line of treatment, followed by injectable amoxicillin, tulathromycin or florfenicol. Individual treatments can be supported by water medication with amoxicillin.

For *M. hyopneumoniae*, and when infection is uncomplicated, as can occur in pigs in the weaner section, tiamulin, tylosin, tetracyclines or tilmicosin in water for three days for the affected group are all appropriate as first line treatments. Culture and susceptibility testing of *M. hyopneumoniae* is not a routine laboratory procedure and is generally not attempted. However, resistance has been detected overseas to macrolides and tetracyclines. Where secondary pathogens are involved, treatment is based on culture and susceptibility testing of these organisms. *P. multocida* is a common target. Second line treatments include injectable or oral potentiated sulfonamides.[13]

For treatment of APP, guidance from culture and susceptibility testing is needed. First line in-water treatment can be achieved with amoxicillin, tilmicosin, florfenicol or the tetracyclines.

The roundworms respond well to levamisole, morantel or ivermectin.

6.5. Top tips

Effective control of respiratory disease will languish in the face of poor environmental and pig flow management. Fix the underlying problem and the respiratory diseases can be controlled by vaccination and short periods of in-water treatment at high risk times.

6.6. For peri-urban practitioners

Respiratory disease is rarely serious in small numbers of pigs in backyard herds. When coughing is evident parasites must be considered.

6.7. Case study: Reducing antimicrobial use for respiratory disease in growing and finishing pigs

The farm

A growing and finishing farm for a medium sized breeder herd. Pigs arrived at the farm at 12 weeks of age and were grown through to market weight. The health status was moderate for respiratory disease, with historical challenges of endemic infection with *M. hyopneumoniae* and APP (single serovar only). The farm routinely vaccinated progeny stock (as piglets) against *M. hyopneumoniae*. Groups of pigs were delivered to the site each week and were sold by weight. The historical mortality rate for this site varied between 2% and 4%, with seasonal "spikes" to 6%.

The issue

Respiratory disease was the main health challenge on this farm. Clinical signs of coughing and ill-thrift were common in the growing and finishing phase, with the prevalence of clinical signs in different groups ranging from 10% to 20%. Even though the herd was known to be infected with APP, no specific control measures for this pathogen were in place, except for in-feed medications, because historically it had not been found to be implicated in mortality or morbidity.

High levels of antimicrobial medication were used in the weaner phase for control of respiratory and enteric diseases that were considered separate issues to the respiratory disease on the finisher farm. In-feed medication was used for a total of 63 days out of the 84 days placement for the average pig in the growing and finishing phase prior to mid-2012. This medication was chlortetracycline (400 ppm) and tylosin tartrate (100 ppm). This equated to approximately 50 antimicrobial doses per 100 kg liveweight** for pigs at this farm. Group water medication (amoxicillin or tilmicosin) and individual injectable medication (penicillin or florfenicol) were also used if clinical signs exceeded expected prevalence or severity. This commonly resulted in an extra 8 to 10 doses per 100 kg liveweight, resulting in average antimicrobial usage of 59 doses per 100 kg liveweight.

KEY POINTS

Antimicrobial use was significantly reduced and refined following application of good husbandry and management principles that included:

- A confirmed diagnosis
- Assessing the management of pig groups
- Reviewing piggery facilities and the environment
- Developing and implementing protocols to improve the management of pig groups and facilities
- Introducing a targeted treatment plan

In mid-2012 the mortality rate spiked at close to 12%. To control the mortality rate the level of antimicrobial use was increased. Further medications were added to feed and the frequency of water dosing was also increased. These measures increased the average antimicrobial use to 92 doses per 100 kg liveweight. This increased level of medication continued through to mid-2013, but the mortality rate increased again to 6% (Figure 1).

Clinical findings

The increases in mortality rate, caused by acute respiratory disease occurred despite the increase in treatments. Necropsies and cultures revealed mixed infection with APP, *P. multocida* and *S. suis*. Lungs were PCR positive for *M. hyopneumoniae*. Serology profiles of the population revealed that seroconversion to both *M. hyopneumoniae* and APP (carrying the ApxIV toxin gene) peaked around 15 weeks of age.

Until mid-2014, the number of pigs placed each week in the system varied from 452 to 2216 each week (mean 1558, standard deviation 185.6).

The temperature settings for ventilation control varied between sheds and times of the year. Ventilation equipment controllers were poorly calibrated and poorly maintained.

Resolving the case

Facility and equipment maintenance were reviewed. Curtains were repaired or replaced. Controllers were calibrated and repaired to ensure temperature and ventilation settings were appropriate for each age group. Batch size and distribution were reviewed.

The vaccination strategy was changed to improve respiratory disease control. The first and second vaccinations for *M. hyopneumoniae* were moved from 5 and 20 days of age to 20 and 63 days of age. Autogenous APP vaccination was introduced at 63 and 84 days of age.

The pig flow was revised to ensure greater consistency in the number of pigs placed each week. Since mid-2014, the number of pigs placed each week has varied from 1790 to 1912 (mean 1840, standard deviation 24.5) (Figure 2).

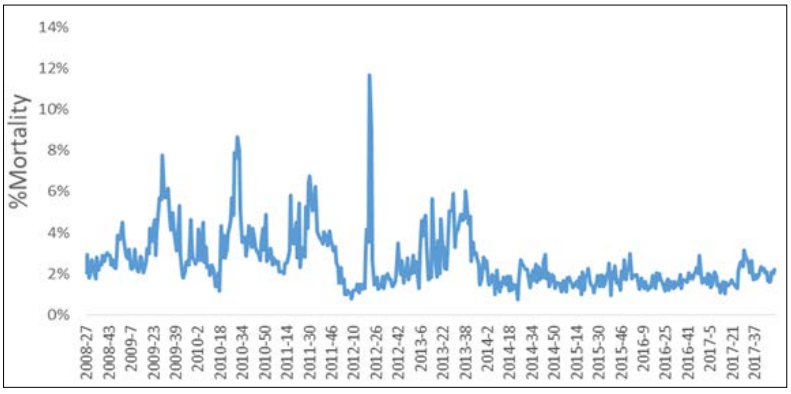
As the site was populated with pigs vaccinated using the new program, medications were strategically reduced. Continuous in-feed medications were replaced with strategic water medication for groups.

Staff training in recognising early signs of disease and appropriate individual treatment was introduced and continually reinforced.

Outcomes

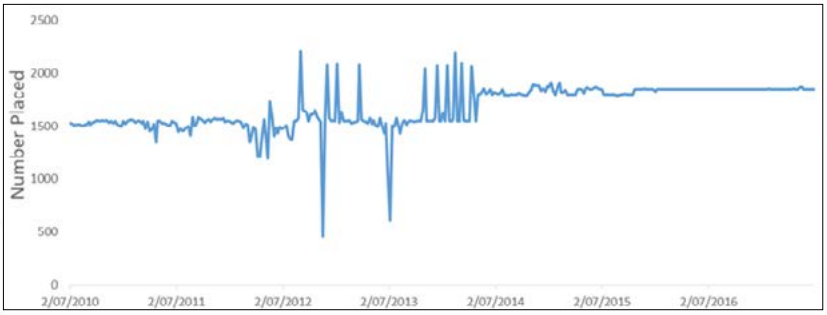
Average antimicrobial use for the last 2 years has been 6.2 doses per 100 kg liveweight (1.7 injectable doses and 4.5 in-water doses) using the same active ingredients as above. The farm now uses no in-feed medication. Respiratory disease on the farm is now well controlled and mortality is stable at around 2%.

Figure 1: Mortality rate in grow finish pigs per week



** 50 kg pig given 2 label doses of antimicrobial = 1 dose per 100 kg.

Figure 2: Number of pigs placed in the system each week



7 Diseases where the main clinical sign is sudden death in pigs between weaning and ten weeks of age

7.1. History and predominant clinical signs

While the mortality rate in recently weaned pigs can be as low as 2 to 3%, episodes of higher rates of mortality can occur. On most farms, deaths in the weaner house occur at a higher prevalence than in the growing and finishing sections, but the reverse can also be seen.

Close examination of the group in which peak mortalities occur is rewarding and usually identifies relevant clinical signs. Diarrhoea, signs referable to central nervous system (CNS) disease (inability to stand, incoordination, trembling, convulsions, head tilt, circling, paddling, nystagmus, opisthotonos), respiratory signs (coughing, forced inspiratory effort), and polyarthritis all signal the common infectious diseases occurring in the post-weaning period between weaning and 10 weeks of age. Fever (rectal temperature more than 40°C) is a common finding.

While most *E. coli* are part of the herd commensal microflora, the pathogenic *E. coli* associated with oedema disease can be traced to herds of origin. *H. parasuis*, *S. suis* and *M. hyorhinis* appear to be widespread and endemic in most herds.

7.2. Differential diagnosis

- Enterotoxigenic *Escherichia coli*
- Oedema disease (endotoxaemic *Escherichia coli*)
- *Haemophilus parasuis*
- *Streptococcus suis*
- *Mycoplasma hyorhinis*
- Salmonellosis
- Mulberry heart disease

Clinical signs are an indicator of the likely aetiology. In large herds all the common diseases can occur at once.

H. parasuis, S. suis and *M. hyorhinis* are common pathogens of pigs after weaning. *H. parasuis* and *M. hyorhinis* typically cause a polyserositis.[85] *S. suis* typically causes meningitis, but septicaemia, arthritis and pneumonia can also be seen.[86] In older pigs that recover from the acute disease, endocarditis is a common finding. *H. parasuis* also causes meningitis, but meningitis is not caused by *M. hyorhinis*. It can be argued that polyserositis is more likely to be seen with *H. parasuis* than *S. suis*.[80,87] A definitive diagnosis relies on necropsy and histopathology, supported by culture and susceptibility and PCR on affected tissues.

Oedema disease, caused by haemolytic *E. coli* (serogroup O138, O139 or O141 strains carrying the F18 fimbriae), is included in this group because the disease is associated with toxaemia.[45] If diarrhoea develops it is of short duration, but it precedes anorexia, swollen eyelids, ataxia, recumbency and death. The degree of oedema varies with the strain. There is usually no fever. PCR assays can be used to detect the gene encoding the STx2e toxin responsible for the toxaemia.

Pigs with oedema disease are usually in good condition. They respond poorly to treatment. The lesions of oedema around the stomach and colon, as well as in other sites, are highly suggestive of oedema disease. The degenerative angiopathy caused by the toxin explains, in part, the anorexia when it occurs in the brain hunger centres. It also explains how the vascular damage leads to oedema.

Sometimes pigs with enterotoxigenic *E coli* die acutely without showing signs of diarrhoea. Necropsy findings will uncover the acute signs of a fluid filled bowel and dehydration. Culture will invariably reveal *E. coli* that are positive on ELISA for fimbrial antigens and PCR assays for toxin genes.

7 Diseases where the main clinical sign is sudden death in pigs between weaning and ten weeks of age

Pigs with acute salmonellosis will show characteristic focal or diffuse necrotic enteritis. Diarrhoea is usually evident in the group. The definitive diagnosis is based on culture with supporting pathology.

7.3. Preventative strategy

This set of post-weaning diseases are influenced strongly by environmental considerations. The underlying environmental elements of hygiene, air quality and space allowance are pivotal. In addition, the requirements of newly weaned pigs for a thermoneutral environment has considerable influence on performance, even though experimental studies have failed to demonstrate an effect of cold stress on the occurrence of oedema disease. However, efforts to achieve thermal comfort may also result in poor air flow or volumes. While thermal comfort might be achieved, the reduced quality of the air can lead to adverse respiratory health outcomes. In parallel with these elements, poor hygiene and high concentrations of ammonia can also contribute to adverse outcomes. Both elements, together with tight space allowances and large populations, magnify the risk of transmission, particularly of *S. suis*, *H. parasuis* and the mycoplasmas.

Prophylactic measures most likely to achieve results against oedema disease include administration of *E. coli* probiotics, which act as live autogenous vaccines when made from isolates that do not produce the Stx2e toxin but do express the fimbrial antigen. Other central elements relate to diets. Some favour low protein high fibre diets, but their sustainability is questionable. Acidification has had equivocal success in reducing the impact of oedema disease, possibly because of the highly regulated pH close to the mucosal surface where the *E. coli* attach[1,2].

A commercial vaccine is available for the control of *H. parasuis* in weaned pigs, but it can also be given to sows to extend maternally derived immunity past the high-risk period post-weaning. The success of vaccination is serovar dependent.

7.4. Treatment

The cephalosporins are NOT recommended at any level.

Oedema disease: Any antimicrobial treatment is based on culture and susceptibility testing. Zinc oxide, once a possibility for prophylaxis, selects for multiple resistance to other antimicrobials, so has little long-term future in control. None of the probiotics have been shown to be effective. Field success with the organic acids is limited. Consideration of an imbalance of the microbiota as a predisposing factor is attractive, but little can be found in the published literature yet to support its manipulation as a treatment in populations of animals.

H. parasuis and *S. suis:* Disease caused by these two pathogens often respond well to penicillin - particularly the streptococci. Amoxicillin in water is a first line treatment, but as antimicrobial resistance is a growing problem in *H. parasuis*,[88] culture and susceptibility testing are needed.

M. hyorhinis: is increasingly diagnosed aided by the availability of new PCR assays. Tiamulin can be used with confidence, based on its activity against other mycoplasmas. Unfortunately, it is unlikely to be efficacious against *H. parasuis*, so the diagnosis must be definitive.

7.5. Top tips

Resolution of oedema disease cases is time consuming, difficult and complex. It involves working closely with the herd nutritionist, in the first instance, to secure a highly digestible diet. Attention to the environment for newly weaned pigs is critical. Autogenous vaccines are an ideal solution, as identified in the case study below.

7.6. For peri-urban practitioners

Colibacillosis in recently weaned pigs is unusual. Cleaning between groups of pigs is a central element in prevention and control.

7.7. Case study: Controlling systemic disease in weaner pigs without antimicrobials

The farm

This was a farrow-to-finish farm producing approximately 700 weaned pigs per week. It had a conventional health status. Enteric and respiratory disease were well controlled. Progeny pigs were vaccinated against *M. hyopneumoniae* and PCV2 as piglets. Weaner pigs were housed in naturally ventilated facility with supplemental heat. Common post-weaning bacterial infections were controlled by medication. The mortality rate (2%) had been stable in the weaner phase to 9 weeks of age.

The issue

Following farrowing house upgrades and alteration of the weaner facility to increase capacity, the farm began to see sudden deaths in weaner pigs about 2-3 weeks after weaning. Commonly the better pigs were found dead. The mortality rate increased from the expected 2% to above 5%, peaking in one batch at 10%.

Clinical findings

There were no changes in clinical signs of respiratory or enteric disease in any batch. Staff could not describe any clinical signs in the pigs that died. Deaths appeared to be sudden, without premonitory signs.

Necropsy findings revealed organ changes and generalised lesions consistent with toxaemia. Gross oedema of the mesocolon and serosa of the stomach were evident. Eyelids and facial regions were swollen. The presumptive diagnosis of oedema disease was confirmed by culture of toxigenic serotype O:139 *E. coli* and positive PCR assays for the genes for LT1, ST1, ST2, EAST, STx2E, AIDA and F18. The isolate was resistant to amoxicillin, apramycin, florfenicol, neomycin, tetracyclines, tilmicosin, tulathromycin, tylosin, lincomycin, and lincomycin/spectinomycin. The isolate was susceptible to ceftiofur.

Resolving the case

It was considered inappropriate and impractical to manage this issue with antimicrobial treatment. The facilities, equipment and environment for weaner pigs were reviewed. Feed and water access were upgraded. Temperature and ventilation control were improved to reduce stress on weaned pigs. Water dosing systems were installed for each weaner room.

KEY POINTS

Control of devastating disease caused by bacterial infection in weaner pigs when no common antimicrobials were of any use was achieved by:

- Diagnostic investigation of causative factors
- Assessing management and housing of pig groups
- Review of the feed and water supply
- Development and implementation of a management plan based on diagnostic findings and an understanding of disease biology
- Introduction of a disciplined disease management plan

Acid (potassium diformate) inclusion in feed was increased from 2 kg/T to 12 kg/T, with some positive effect on disease control, but the mortality rate still reached 8% in some batches.

Repeated culture of rectal swabs from pigs on this farm and PCR toxin gene testing of haemolytic *E. coli* isolates eventually identified a single O:139 isolate that was PCR assay negative for genes for LT1, ST1, ST2, EAST and STx2E. This isolate was PCR positive for the genes for AIDA and F18. Essentially the isolate bore the attachment antigens, but not the genes for toxin production.

This isolate was cultured and fed to weaned pigs as a probiotic or an avirulent live vaccine in the water supply for one week immediately post-weaning (1 x 10^9 colony forming units per pig per day for 7 days). Dosing with this non-toxigenic *E. coli* isolate is now routine for each batch of weaned pigs on this farm.

There was an immediate effect. Sudden deaths ceased in treated groups. Weaner phase exit weights increased by 2 kg per pig on average. Culture of rectal swabs from treated pigs yielded both toxigenic and non-toxigenic *E. coli* serotype O:139 isolates from normal pigs.

The improvement in health and growth of weaned pigs gave the farm managers confidence to remove all antimicrobial medication from the feed and use strategic water dosing of amoxicillin for the control of common post-weaning bacterial infections such as *H. parasuis* and *S.suis.*

Outcomes

The signs of oedema disease are now absent from the farm. Weaner phase mortality remains stable at around 1.5%. The farm uses no in-feed medication. Acid inclusion has returned to 2 kg per tonne in feed.

8 Diseases where the main clinical signs are skin lesions

Age: All ages

8.1. History and predominant clinical signs

The most common contagious bacterial skin disease of pigs is erysipelas. The diamond-shaped lesions are commonly seen in growing pigs, replacement breeding stock and mature sows. Sows are vaccinated on most farms, but the growing pigs are usually unvaccinated and hence depend on maternal antibody for protection. In naïve animals or in herds in which vaccinations have been missed, both infected neonatal pigs and sows can develop diamond skin lesions. All ages are at risk but growing pigs from 12 to 22 weeks of age are most likely to be affected. It is also a zoonotic disease.[89]

The disease is caused by *Erysipelothrix rhusiopathiae*. Up to 40% of growing pigs carry the organism asymptomatically, but clinical disease periodically emerges in 10-30% of a group of growing pigs. Clinical signs (fever, cutaneous haemostasis, inappetence, depression, diamond skin lesions, lameness and abortion in pregnant sows) appear within 24 hours of exposure. The mortality rate is variable, but if the pigs are left untreated it can be high. Trimming losses at slaughter because of the skin lesions are considerable.[90]

The organism commonly reaches the body via the tonsils. Septicaemia follows infection. This leads to widespread vascular thrombosis that can extend to small diamond lesions in the cortex of the kidney and localisation of the pathogen on the cardiac valves. It causes synovitis 4 to 10 days after exposure, localises in joints and disease progresses to fibrinous exudation, severe fibrosis and destruction of the articular cartilage over a period of months.[91] Affected joints can be culture negative, but the arthritic lesions continue to progress. As a result, trimming at slaughter due to erysipelas may also involve joints.

8.2. Differential diagnosis

When the diamond skin lesions appear in several pigs in the same pen the signs are pathognomonic. From time to time porcine dermatosis and nephropathy syndrome, characteristically associated with PCV infection, might be confused with erysipelas, but lack the uniformity of the rhomboid lesion of erysipelas.

Rhomboid lesions can also occasionally be caused by other bacterial species, such as members of the *Pasteurellaceae* that can establish bacteraemias in pigs.

The early signs of acute infection, which may appear in a group before the diamond skin lesions appear, resemble those of any pig with septicaemia or viraemia, so a differential diagnosis that includes classical swine fever and porcine reproductive and respiratory syndrome must be considered.

8.3. Diagnostic tests

A diagnosis of erysipelas rests on clinical signs, vaccination history, numbers affected, necropsy findings consistent with a septicaemia, histopathology (widespread vascular lesions and microthrombi), and culture of the lesions or PCR.

8.4. Preventative strategy

Killed vaccines are available and while failures occur at an individual animal level, vaccine failures are unusual at a herd level. Protection is best against the acute disease and less effective against arthritis.[92] The breeding herd should be vaccinated. In an era of antimicrobial stewardship, a strong case can be made for vaccinating pigs at weaning. This will remove the need to periodically treat individual pigs with penicillin by injection or add medications to feed or water to contain disease outbreaks. It will also significantly reduce losses due to carcass condemnations or trimming at slaughter. An attenuated vaccine that can be delivered orally has been developed but is not yet registered in Australia.[93,94]

The organism survives in soil for short periods. It is carried in fish meal and by a wide range of birds and mammals, including seagulls, chickens, turkeys, sheep and mice. Hence strategies that prevent the mixing of species and awareness of the additional risk during mouse plagues assist in control.

Good sanitation is part of good management practice but becomes more important in controlling the disease during and after an outbreak. Contamination of feed or bedding with *Aspergillus* spp. and the release of aflatoxins can increase susceptibility.

8.5. Treatment

The treatment of choice is penicillin by injection for individual pigs as soon as clinical signs are seen. Long acting penicillin can be used in young pigs. Older pigs require a medication with a shorter withholding period. Penicillin and tylosin are first line treatments with short withholding periods. Lincomycin injections are a second line treatment and appropriate for treatment of cases occurring close to slaughter because of the very short WHP.

Field experience shows that tylosin at 100 ppm in-feed (off-label) protects against clinical disease and has a zero-withholding period. Water medication for three days with amoxicillin, tylosin or the tetracyclines is commonly effective, although resistance has been reported to the latter two.

8.6. Top tips

A punch biopsy in the centre of the skin lesion provides excellent material for culture.

8.7. For peri-urban practitioners

Early detection and prompt treatment are the cornerstone of recovery from erysipelas. For many people with just one or two pigs the logistics of vaccination are just too hard to justify in the face of very low risk. A rapid response to penicillin is a good diagnostic indicator.

8.8. Case study: Reducing trim loss at slaughter without sustained antimicrobial use in finishing pigs

The farm

A finishing site taking 400 pigs per week from 10 weeks of age to sale. All pigs were raised on bedding over dirt floors. The pigs had a high health status – they were free of *M. hyopneumoniae*, APP, swine dysentery and internal and external parasites.

The issue

Feedback to the farm from the abattoir about the trimming of carcasses revealed an increase in trimming for arthritis or swollen joints. There was also an increase in skin trimming. At slaughter up to 2% of pigs had some skin trimming each week. Leg and joint trimming rose to approximately 25% of slaughtered pigs, accounting for a loss of more than 1% in carcass weight across sold batches.

Clinical findings

The farm was inspected for any issues that could be causing traumatic joint injury. Steps to the feed pad were in disrepair, so some groups had further than normal to step for feed and water. No clinical signs consistent with erysipelas (diamond skin lesions, fever, lethargy) were reported or found on farm. Treatment records indicated that there had not been any recent change in the number or type of treatments for any group of pigs. Clinical signs of lameness were absent in pre-sale and finisher pigs.

Pigs inspected at slaughter had normal viscera. Trimmed joints had excess sero-sanguinous fluid when incised. The synovial membranes of affected joints were grossly thickened. Samples of joint fluid and synovium were taken for laboratory analysis. Results were negative on culture for any bacterial pathogens, but PCR positive for *E. rhusiopathiae*. Histopathological examination of joint tissue revealed resolving changes consistent with bacterial infection.

Resolving the case

Despite the absence of clinical signs on the farm, the main cause of the joint lesions found at slaughter was considered to be erysipelas. A decision was made to vaccinate pigs against erysipelas. The first dose was given at 8 weeks of age (pre-delivery to the finishing farm) and the second at 12 weeks of age, to coincide with the movement of the pigs between sheds. Finisher feed was medicated with tylosin (100 ppm, nil WHP) for the period until vaccinated pigs came through to sale. The steps to feed pads were repaired, allowing easy access to resources for all pigs.

KEY POINTS

Control of production losses caused by sub-clinical bacterial infection was achieved by:

- A diagnostic investigation into causative factors
- Assessing the management and housing of pig groups
- Using strategic medication for short term infection control
- Developing and implementing a management plan based on the diagnostic findings and an understanding of disease biology
- Introducing a disciplined disease management plan that included a vaccination plan

Outcomes

Slaughter trimming for arthritis or joint and skin conditions returned to normal levels as soon as the vaccinated pigs came through. The farm continues to vaccinate against erysipelas. No medications have been used for erysipelas control since vaccination commenced.

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