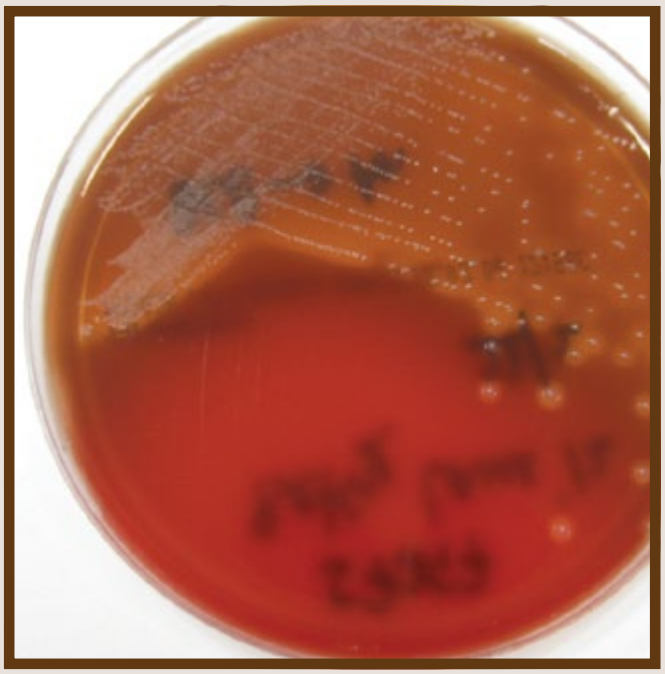
PROJECT SUMMARY

RURAL INDUSTRIES
Research & Development Corporation

Antimicrobial Susceptibility Patterns of Bacterial Isolates from Horses



by Dr Tony D Mogg

Background

In this project both retrospective and prospective approaches were used to investigate the most common types of bacteria that cause disease in horses in Australia and the antimicrobial susceptibility patterns of these bacteria. This project also investigated evidence for the development of antimicrobial resistance in bacterial pathogens of equine origin by comparing susceptibility patterns over time.

Who should be interested in the findings?

This report is highly relevant to veterinarians who treat horses, veterinary microbiologists and veterinary diagnostic laboratories, animal health authorities, pharmaceutical companies and the Australian horse industry.

Background

Bacterial diseases are common in horses worldwide and represent a significant proportion of all equine disease. Examples of common bacterial diseases include abscesses, respiratory tract infections (e.g. Strangles, "rattles", pneumonia and pleuropneumonia), intestinal infections (e.g. salmonellosis), reproductive infections (e.g. metritis and endometritis), skin infections (e.g. rain scald), corneal ulcers, joint ill and foal sepsis. These diseases result in significant animal suffering and possible death or euthanasia. Bacterial diseases also result in major economic losses as the result of the costs of treatment, loss of productivity (down-time from racing, breeding etc.) and horse wastage from the industry.

Antimicrobial drugs (a.k.a. antibiotics) are frequently administered to horses to treat or prevent bacterial infections. The antimicrobial susceptibility of many equine bacterial pathogens has been thought to be predictable, while for other bacteria the acquisition of antimicrobial resistance means that susceptibility to a particular drug may need to be tested (i.e. antimicrobial susceptibility testing). Over time, the use of antimicrobial drugs eliminates susceptible bacteria, leaving the resistant bacteria already present in the population. This process allows the spread of resistance genes resulting in drug-resistant bacteria. Acquired antimicrobial drug resistance has the potential to become a major problem in pathogenic bacteria in horses as has occurred in human medicine. The increasing incidence of bacterial resistance to antimicrobial drugs has been of major concern in human medicine in Australia and worldwide for many years (Commonwealth of Australia 1999, Commonwealth of Australia 2013, World Health Organization 2014). The development of antimicrobial resistance in pathogens of veterinary importance may have direct relevance to human disease due to the often close association between humans and horses.

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There is a paucity of published studies investigating equine bacterial infections across a range of body systems and age groups within the one geographical area. Equally, there is little data examining patterns and changes in the antimicrobial susceptibility of these bacterial isolates over time. Most published studies focus on specific bacterial isolates, body systems or antimicrobial agents, and often originate in Europe or North America. Studies originating in Australia are not common and the results of "local" studies often conflict with research performed overseas. These geographic differences highlight the need for an Australian study that investigates bacterial isolates over multiple body systems and ages, and also investigates changes in antimicrobial susceptibility patterns that have developed over time.

Aims/Objectives

The specific objectives of this project were to:

1. identify the most common bacterial isolates from various sites of culture, specific age groups and particular disease processes in horses;
2. identify the antimicrobial susceptibilities of the common disease-producing bacteria in horses; and
3. identify changes in the antimicrobial susceptibility of bacteria isolated from equine diseases to commonly used antimicrobial drugs over time.

This research provides valuable data on which to base recommendations for the use of antimicrobial drugs in horses in Australia, with the aims of increasing the efficacy of empirical (prior to culture and susceptibility testing) therapy and delaying the development of antimicrobial resistance.

Methods Used

This project consisted of two parts, a retrospective analysis of archived microbiology records and a prospective analysis of the antimicrobial susceptibility of bacterial pathogens collected during the course of the project. The retrospective analysis involved identification of the common bacterial isolates for different body systems, age groups and disease processes, and qualitative assessment of each isolate's antimicrobial susceptibility, using archived data from samples collected from horses submitted to the University of Sydney University Veterinary Teaching Hospital Camden. Examination of this data allowed investigation of retrospective trends in antimicrobial susceptibility over time. The prospective analysis involved the qualitative and quantitative assessment of antimicrobial resistance by comparing susceptibility patterns in β-haemolytic *Streptococcus* spp. collected by Scone Veterinary Diagnostic Laboratory during the course of the project with those of "historic" bacteria available from a collection of freeze dried isolates held by the University of Sydney Faculty of Veterinary Science.

Results/Key findings

Key findings include:

- Documentation of increasing antimicrobial resistance over time – this is the first study in Australia to definitively identify an increase in resistance to commonly used antimicrobial drugs by several significant equine bacterial pathogens.
- An overall low percentage susceptibility by most common equine bacterial pathogens to many commonly used "first-line" antimicrobial drugs and lack of predictable susceptibility by most of the common bacterial isolates.
- Clinically relevant differences between the most common bacterial isolates and antimicrobial susceptibility patterns identified in this study compared to previous reports in the veterinary literature, most of which originate from outside of Australia.

Implications for Relevant Stakeholders

The results of both the retrospective and prospective components of this project have substantiated the need for "local" studies of bacterial isolates and antimicrobial susceptibility, as these data cannot always be extrapolated from studies performed outside of Australia. Similarly, both components of this project have provided evidence for the development of antimicrobial resistance in multiple bacterial types that commonly cause clinically significant infections in horses in Australia.

Very few bacterial isolates evaluated in the retrospective study demonstrated "predictable" antimicrobial susceptibility and none of the most common isolates had 100% susceptibility to commonly used "first-line" antimicrobial drugs. Additionally, the overall percentage susceptibility to antimicrobial drugs commonly used in equine practice was low for all of the most common bacterial isolates. The lack of predictable susceptibility and overall low percentage susceptibility confirms the importance of basing antimicrobial therapy in all cases of bacterial infection on culture and susceptibility testing of appropriately collected samples. The development of antimicrobial resistance and the concomitant decrease in efficacy of "first-line" antimicrobial drugs will undoubtedly have negative animal welfare and economic impacts. It is possible that the development of antimicrobial resistance in bacteria that cause disease in horses may have negative impacts in human medicine, either through zoonotic infections or the transmission of resistance from equine to human pathogens.

Recommendations

Veterinarians prescribing antimicrobial drugs for the treatment of bacterial infections in horses have obligations to multiple stakeholders including, but not limited to, the patient and the general horse population, the owner(s) and other members of the horse industry, and the general community. While recommendations for "appropriate" antimicrobial therapy in equine practice have been previously described (Mogg 2009a, Mogg 2009b), the results of this project provide further valuable data on which to base formulation of an antimicrobial treatment regimen.

Recommendations for the clinical use of antimicrobial drugs in horses:

1. Avoid the administration of systemic antimicrobial therapy unless there is definitive evidence that a bacterial pathogen is present
   and/or substantial evidence is available from clinical, laboratory or other diagnostic procedures to suggest a bacterial aetiology for the disease process being treated.
2. Perform culture and susceptibility testing in all cases of suspected bacterial infection. Collect appropriate samples for culture and susceptibility that are likely to yield results representative of the microbial population at the site of the infection and ensure appropriate handling of samples.
3. Base antimicrobial treatment regimens on culture and susceptibility test results. Do not rely upon "predictable" susceptibilities for any bacterial isolate! This recommendation applies to all bacteria, including those that in the past have been thought to have predictable susceptibility patterns (e.g. β-haemolytic *Streptococcus* spp.). Susceptibility testing is vital for directing the appropriate use of "first-line" antimicrobial drugs (e.g. gentamicin, tetracycline and trimethoprim and sulphonamide combinations), especially for the treatment of gram negative bacteria.
4. Avoid the use of third-generation cephalosporin (e.g. ceftiofur) and fluoroquinolone (ciprofloxacin and enrofloxacin) antimicrobial drugs as "first-line" therapy. Ideally administration of these drugs should only be used based on culture and susceptibility testing, or in cases of life-threatening infections or previous treatment failure. Both of these antimicrobial classes have been assigned a "High" EAGAR (Expert Advisory Group on Antimicrobial Resistance) importance rating (NHMRC 2006). Antimicrobial drugs with a "High" rating are essential antibiotics for treatment of human infections where there are few or no alternatives for many infections, and therefore veterinary use of such drugs should be limited. This project documented a significant increase in resistance to ceftiofur by *Escherichia coli* and to enrofloxacin by *Pseudomonas* species. Restraint in prescribing third-generation cephalosporins and fluoroquinolones as "first-line" therapy may assist in slowing the further development of such resistance, and hence preserve the longevity of these drugs as effective antimicrobials for the treatment of serious resistant infections in equine practice. *continues overleaf*

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Recommendations for continued surveillance of antimicrobial resistance and education:

1. Develop a national antimicrobial drug resistance surveillance programme to provide on-going data regarding equine bacterial pathogens and their antimicrobial susceptibility patterns. This would involve the collection of data from multiple university and/or commercial veterinary laboratories across Australia, and would provide on-going guidelines for antimicrobial therapy in horses and strategies to prevent antimicrobial resistance. National monitoring of antimicrobial resistance in horses is important to ensure optimal use of currently registered antimicrobial drugs and thus conserve their effective "life-span"; encourage interactions between the horse industry, the veterinary profession and pharmaceutical companies to develop long-term strategies for antimicrobial therapy in horses; and provide data on the prevalence and antimicrobial susceptibility of equine bacterial pathogens relevant to human medicine (e.g. *Staphylococcus aureus*, *Escherichia coli,* and *Salmonella* spp.).
2. Encourage appropriate antimicrobial susceptibility testing to identify trends in resistance to significant equine and human pathogens (e.g. routine inclusion of oxacillin in susceptibility panels for coagulase positive *Staphylococcus* spp. isolated from horses to screen for MRSA [Axon et al. 2011]).
3. Develop compulsory antimicrobial stewardship training in undergraduate and postgraduate veterinary school curricula so that graduates are aware of their responsibilities in minimising the development of antimicrobial resistance, and have the skills to identify, definitively diagnose and effectively treat clinically relevant infections in all animal species.

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For more information

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