Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

# Antimicrobial Resistance in Young New Zealand Horses

A thesis submitted in fulfilment of the requirements for the degree of a Master of Veterinary Science

Submitted 12<sup>th</sup> December 2014

Toombs-Ruane, Leah Jo

### **Abstract**

The emergence of bacteria that are resistant to antibiotics used in horses has been reported worldwide, including in Australia, the USA and United Kingdom. There is a lack of published comparative scientific information on the New Zealand equine population. However, recent individual cases of multi-drug resistant (MDR) bacterial infections reported by veterinarians have raised concerns about the situation in New Zealand. The use of antimicrobials coupled with less than ideal prescription practice in the horse industry may have led to inadvertent selection for MDR bacteria. An initial perspective on antimicrobial resistance in NZ is gleaned through a retrospective description of laboratory submissions in the form of a database analysis from 2004 to 2013/2014. In neonates (foals less than three weeks of age), the presence of MDR bacteria was identified in 37.5% (24/64) of foals; although 81.6% (102/125) of bacteria cultured from foals included in the study were sensitive to either penicillin or gentamicin. Of the respiratory samples from horses three-years-old and younger, the most commonly cultured bacteria were Staphylococcus species accounting for 40.1% (310/774) of isolates. These bacteria were sensitive to penicillin, ceftiofur and gentamicin for > 90% of isolates. Of all respiratory equine submissions, MDR bacteria were recovered from 39.2% (93/237) of horses. Using multiple correspondence analysis, MDR was associated with submissions from 2009-2014 and two-year-old horses from the Waikato region.

These two population groups were targeted specifically for examination due to the potentially severe consequences of bacterial disease in neonates (Chapter 3), and the anecdotal experience of high clinical use of antimicrobials in young horses, especially in the treatment of clinically apparent respiratory disease (Chapter 4). Multi-drug resistance was assessed as part of this work, and is presented in the systematic literature review (Chapter 2), and in both descriptive studies (Chapters 3 and 4). The results of the two retrospective descriptive studies presented show that there is a substantial proportion of submissions from young horses in New Zealand that grow multi-resistant bacterial isolates, and that there is decreased efficacy of commercially available antimicrobials in this country. The antimicrobial resistance reported in this study has potential clinical implications, and reflects the first step in a multifactorial approach to improve and maintain horse and human health.

## Acknowledgements

I owe an eternal debt of gratitude to my generous and wise supervisors Sarah Rosanowski, Jackie Benschop and Chris Riley (the dream team!). Special thanks to Sarah, who was always quick and astute in her critiques and advice (even from afar): I absolutely could not have done this without your help! Big and grateful thanks to Anna Kendall, Joe Mayhew and Kate Hill for their bright and shiny brains, which they allowed me to pick from time to time! For her statistical wisdom, and grace in agreeing to help me with the MCA, I owe Charlotte Bolwell a cake that I never quite got around to baking.

Thanks to the McGeorge Research Fund and the New Zealand Equine Research Foundation for providing funding for this project. Thanks also to NZVP and especially Isobel Gibson for her time and database expertise. And finally, a special thank you to all veterinarians in practice who have submitted samples for bacterial culture and sensitivity, as well as to those who will do so into the future.

And of course, thank you to my mum!

### **Abbreviations**

**ACVIM** American college of veterinary internal medicine

**AMR** Antimicrobial resistance

**CC** Clonal complex

CI Confidence interval

CIA Critically important antimicrobial

**ESBL** Extended-spectrum beta-lactamase

**OR** Odds ratio

MCA Multiple correspondence analysis

MDR Multi-drug resistance

MIC Minimum inhibitory concentration

MLST Multi-locus sequence typing

MPI Ministry for primary industries

MRCoNS Methicillin resistant coagulase-negative Staphylococcus species

MRS Methicillin resistant Staphylococcus species

MRSA Methicillin resistant Staphylococcus aureus

NZ New Zealand

**OIE** World organiation for animal health (office international des epizooties)

PCR Polymerase-chain reaction

**PFGE** Pulse-field gel electrophoresis

PMQR Plasmid-mediated quinolone resistance

**PRISMA** Preferred reporting items for systematic reviews and meta-analysis

SVARM Swedish veterinary antimicrobial resistance monitoring

**TMPS** Trimethoprim-sulfonamide combination (i.e. trimethoprim-sulfamethoxazole, trimethoprim-sulphadiazine)

VRE Vancomycin resistant Enterococcus

WHO World health organisation

# Contents

1 INTRODUCTION	1
1.1 Overview	1
1.2 Motivation for this study: a clinical perspective	2
1.3 A brief review of antimicrobial resistance in horse populations	3
1.3.1 General results of equine culture and sensitivity	3
1.3.2 Antimicrobial use and stewardship	
1.3.3 Selected research into equine bacterial resistance	9
1.4 Summary of objectives	13
2. SYSTEMATIC REVIEW: HOW IS MULTI-DRUG RESISTANO	
IN EQUINE POPULATIONS?	15
2.1 Abstract	15
	15
2.2 Introduction	15
2.3 Methodology	17
2.4 Results	19
2.5 Discussion	36
2.6 Conclusions	38
3. ANTIMICROBIAL SENSITIVITY OF BACTERIA ISOLATED	_
NEONATAL FOAL SAMPLES SUBMITTED TO A NEW ZEALA VETERINARY PATHOLOGY LABORATORY	
VETERINART TATHOLOGI LADORATORI	
3.1 Abstract	39
3.2 Introduction	40
3.3 Materials and Methods	41
3.3.1 Data collection	41
3.3.2 Case selection	41
3.3.4 Culture and sensitivity, identification and classification	42
3.3.5 Antimicrobial sensitivity and multi-drug resistance definition	42
3.3.6 Data analysis	42
3.4 Results	43
3.4.1 Overall submissions	43
3.4.2 Specimens	45

3.4.3 Culture results	45
3.4.4 Sensitivity results	
3.5 Discussion	40
3.6 Conclusions	50
4. ANTIMICROBIAL SENSITIVITIES OF AER	ORIC ISOLATES FROM
RESPIRATORY SAMPLES OF YOUNG NEW Z	
SUBMITTED TO A VETERINARY PATHOLOG	
SODIVILLED TO IT VETERAL WIRE THE SECOND	
4.1Abstract	51
4.2 Introduction	52
4.3 Materials and methods	53
4.3.1 Data collection	
4.3.2 Case selection	
4.3.3 Culture and sensitivity, identification and classification	
4.3.4 Data analysis	
4.4 Results	56
4.4.1 Demographics	
4.4.2 Samples	
4.4.3 Culture results	
4.4.4 Sensitivity results	
4.4.5 Multi-drug resistance	
4.4.6 Statistical analysis	
4.4.7 Multiple correspondence analysis	
4.5 Discussion	62
4600	
4.6 Conclusions	05
5. GENERAL DISCUSSION	67
5.1 Introduction	67
5.2 Limitations of thesis	68
5.4 Future directions	69
6 REFERENCES	71

# Tables

<b>Table 1.1</b> Selected published antimicrobial sensitivities of bacteria cultured from horses
Table 2.1 Quality criteria for grading of studies and publications 18
Table 2.2 Studies reporting equine bacterial multi-drug resistance      23
<b>Table 3.1</b> Demographic information of eligible foal submissions in the study of antimicrobial sensitivity of bacteria isolated from neonatal foal samples submitted to a New Zealand veterinary pathology laboratory
<b>Table 3.2</b> Antimicrobial sensitivity data from positive cultures of 64 foals in the study of antimicrobial sensitivity of bacteria isolated from neonatal foal samples submitted to a New Zealand veterinary pathology laboratory
<b>Table 3.3</b> Multi-drug resistant (MDR) isolates in the study of antimicrobial sensitivity of bacteria isolated from neonatal foal samples submitted to a New Zealand veterinary pathology laboratory
<b>Table 4.1</b> Demographic submission information from 289 horses from which respiratory samples for culture and sensitivity were submitted to a New Zealand laboratory
<b>Table 4.2</b> Antimicrobial sensitivity of isolates from 237 equine respiratory submissions
Figures
<b>Figure 2.1</b> Flowchart to determine studies of equine MDR included for qualitative assessment by systematic review following PRISMA guidelines
<b>Figure 2.2</b> Number of equine MDR studies by geographical region 2004-2014
<b>Figure 2.3</b> Number of equine MDR studies by bacterial type over the time-period of the systematic review 2004-2014
<b>Figure 2.4</b> Equine MDR study score distribution over years 2004-2014
<b>Figure 4.1</b> Multiple component analysis in two dimensions, using a joint method, of 773 bacterial isolates cultured from NZ horses