Antimicrobial susceptibility of bacterial isolates from ambulatory practice and from a referral hospital

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Abstract

Background: Responsible use of antimicrobials in equine practice relies on knowledge of common bacterial isolates and their antimicrobial sensitivities.

Objectives: To assess the frequency of bacterial resistance to a combination of parenteral penicillin and gentamicin and to trimethoprim and sulfamethoxazole for PO use in a selection of clinical isolates, and subsequently to determine the prevalence of resistance to antimicrobials that might then be used as alternatives to first-line antimicrobials for the same isolates.

Methods: Retrospective analysis of minimal inhibitory concentrations (MICs) of antimicrobials for 6354 bacterial isolates from 365 ambulatory practices and 519 isolates from a referral hospital. The MICs were used to indicate sensitivity or resistance to commonly used antimicrobials and the prevalences of resistance were compared between origin of the isolates, and among antimicrobial drugs.

Results: Isolates from the referral hospital were significantly \((P < .05)\) more likely to be resistant to the antimicrobials tested than those derived from ambulatory practice. Overall, 91% of the ambulatory isolates and 64% of the hospital isolates were sensitive to penicillin-gentamicin. For trimethoprim-sulfamethoxazole combination, 82% of the ambulatory practice isolates and 56% of the referral hospital isolates were sensitive.

Conclusions and Clinical Importance: Most isolates were sensitive to penicillin and gentamicin as well as trimethoprim-sulfamethoxazole. No predictable efficacious second choice antimicrobial was identified for those isolates resistant to the first-line antimicrobials. The likelihood of isolates being sensitive to second choice antimicrobials was variable but generally higher for ambulatory isolates compared to referral isolates. Bacterial identification and measurement of MIC are essential to make the appropriate antimicrobial choice.

KEYWORDS
antimicrobial, horse, MIC, practice, resistance

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Union Committee on Antimicrobial Susceptibility Testing; MIC, minimal inhibitory concentration; P-G, procaine penicillin with gentamicin sulfate combination; TMP-S, trimethoprim-sulfamethoxazole.
1 | INTRODUCTION

Antimicrobial use in veterinary practice has been linked to increased resistance in bacterial infections in both human and veterinary healthcare,1 and most especially in hospital practice.2,3 Clinicians should apply principles of antimicrobial stewardship when considering their choice of antimicrobials,4 which is not necessarily always the case currently in the United Kingdom (UK).5 In some other European countries such as Sweden or Denmark, critically important antimicrobials have legally enforced restricted use in veterinary medicine.6

The British Equine Veterinary Association guidelines for responsible antimicrobial use advise that first-line injectable antimicrobials should be a combination of procaine penicillin with gentamicin sulfate (P-G) in most infectious scenarios encountered in equine practice (www.beva.org.uk/protectme). Among the PO antimicrobials available, a trimethoprim-sulfadiazine (TMPS) combination is recommended for first-line use7 and is also the only licensed choice in horses in the UK.

Responsible use of antimicrobials is facilitated by in vitro antimicrobial susceptibility testing to inform antimicrobial choice. Breakpoints are determined based on the minimum inhibitory concentration (MIC) of an antimicrobial to separate isolates for which there is a high likelihood of treatment success (sensitive) versus those for which treatment is more likely to be ineffective (intermediate or resistant).5,9 International groups including the Clinical and Laboratory Standards Institute (CLSI) and the European Union Committee on Antimicrobial Susceptibility Testing (EUCAST) have published suggested breakpoints for clinical application based on pharmacokinetics and pharmacodynamics to predict clinical efficacy.10,11 However, very little specific data are available for horses, requiring some extrapolation from other species.12

Our aim was to examine the value of in vitro antimicrobial sensitivity testing in antimicrobial selection in both ambulatory and hospital practice. The prevalence of sensitivity to first-line antimicrobials (parenteral P-G and PO TMPS) was determined and subsequently the sensitivity to alternative antimicrobials was examined for the isolates found to be resistant to first-line choices. The hypotheses were that bacteria cultured from a hospital population would have lower prevalence of in vitro sensitivity compared to ambulatory isolates as previously described9 and that organisms resistant to P-G or TMPS still could be treated successfully with noncritically important antimicrobials such as tetracyclines.

2 | MATERIALS AND METHODS

In this retrospective analysis, data were collected from all clinical samples submitted to The Liphook Equine Hospital Laboratory for culture and determination of antimicrobial sensitivity between January 2014 and December 2018.

Submitted samples were plated onto Columbia blood agar and MacConkey’s agar, colistin-nalidixic acid agar, or combinations thereof depending on sample type. Subcultures usually were prepared, depending on the purity of primary growth, to obtain pure cultures before suspending individual colonies in saline to a McFarlane standard of 0.5.

The suspension then was processed using a VITEK 2 analyzer (BioMerieux, Basingstoke, Hampshire, UK) for bacterial identification. Isolates were further examined after separating Gram-negative and Gram-positive bacteria using a different array of antimicrobials to determine MICs (AST-GN65, AST-GP73, BioMerieux). Antimicrobial susceptibilities were examined across a range of dilutions from 0.5 to 16 μg/mL for gentamicin, 0.06 to 16 μg/mL for benzylpenicillin, 0.1 to 320 μg/mL for trimethoprim-sulfamethoxazole (because sulfadiazine was not available for susceptibility testing on the analyzer used), 0.25 to 16 μg/mL for tetracycline, 0.25 to 8 μg/mL for cefotiofur, and 0.25 to 4 μg/mL for enrofloxacin. Antimicrobial breakpoints were selected from data provided by EUCAST and CLSI and used to categorize isolates as sensitive or resistant. For the purposes of analysis, isolates with MICs categorized as intermediate susceptibility were classified as resistant.11

All of the samples were categorized into different main anatomic sites of origin: skin/wounds (including fistulous withers, surgical incisions and IV catheters), respiratory (pleural fluid, bronchoalveolar lavage, tracheal wash, gullett pouch lavage, sinus fluid, nasal discharge), reproductive (cervix, clitoris, fetus, uterus, vulvar or vaginal discharge), abcesses (including dental, foot or septic pedal bone), urinary (bladder biopsy, urine), ocular, other (surgical implants; internal biopsy samples such as intestines, liver, stomach, ovary, peritoneal fluid, synovial fluid, penile swab, mammary discharge, diarrhea), or unknown origin.

The population of isolates found to be resistant to P-G was evaluated to determine the prevalence of sensitivity to other antimicrobials that might be selected as a second choice in practice consisting of TMPS, tetracycline, cefotiofur, and enrofloxacin. Not all isolates were tested against every antimicrobial, given that some would not be logical choices based on known pharmacodynamics. For example, gram-negative bacteria were not tested for sensitivity to penicillin. For Enterobacter spp, Enterococcus spp was not tested for cefotiofur, and Streptococcus spp was not tested for enrofloxacin and gentamicin.13,14

The population of isolates found to be resistant to TMPS was evaluated to determine the prevalence of sensitivity to other antimicrobials that might be selected as a second choice in practice based on known pharmacodynamics comprising tetracycline, cefotiofur, enrofloxacin, or P-G.

2.1 | Statistical analysis

Bacterial resistance to antimicrobials was compared between samples derived from ambulatory practices and those obtained from the referral hospital by using a Chi-squared test when appropriate (>5 expected cases) or a Fisher’s exact test, with a P value <.05 indicating a significant difference.

The prevalences of resistance to the second-choice antimicrobials in ambulatory and hospital practice also were compared with one another using a Chi-squared test when appropriate (>5 isolates) or a Fisher’s exact test, with a P value <.05 indicating a significant difference.

GraphPad Prism 8 software (GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California, www.graphpad.com) was used, with contingency tables to compare the data in ambulatory practice and in the referral hospital population, as well as second-choice antimicrobials in pairs.
A total of 6873 isolates were identified and their MICs determined during the study period. Of these, 6354 (92%) came from 345 different ambulatory practices and 519 (8%) came from a single referral hospital population.

### TABLE 1
Six thousand two-hundred fifty isolates from 345 ambulatory practices and 491 isolates from a referral hospital tested for Penicillin-Gentamicin (P-G) sensitivity alongside prevalence of sensitivity (F, female)

| Penicillin-Gentamicin | Total ambulatory | P-G tested | P-G sensitive | Total referral | P-G tested | P-G sensitive |
|-----------------------|------------------|------------|---------------|---------------|------------|---------------|
|                       | n%               | n%         | n%            | n%            | n%         | n%            |
| Skin/wounds           | 2151             | 2137       | 1915          | 89            | 291        | 271           |
|                       | 2137             | 2137       | 1915          | 89            | 291        | 271           |
| Respiratory           | 1267             | 1251       | 1148          | 92            | 108        | 106           |
|                       | 1251             | 1251       | 1148          | 92            | 108        | 106           |
| Reproductive F        | 330              | 305        | 280           | 92            | 5          | 5             |
|                       | 305              | 305        | 280           | 92            | 5          | 5             |
| Abscesses             | 790              | 764        | 708           | 93            | 54         | 52            |
|                       | 764              | 764        | 708           | 93            | 54         | 52            |
| Urinary               | 242              | 220        | 207           | 94            | 11         | 8             |
|                       | 220              | 220        | 207           | 94            | 11         | 8             |
| Ocular                | 170              | 168        | 155           | 92            | 4          | 4             |
|                       | 168              | 168        | 155           | 92            | 4          | 4             |
| Other                 | 324              | 319        | 300           | 94            | 34         | 33            |
|                       | 319              | 319        | 300           | 94            | 34         | 33            |
| Unknown               | 1094             | 1072       | 972           | 91            | 12         | 12            |
|                       | 1072             | 1072       | 972           | 91            | 12         | 12            |
| Total                 | 6354             | 6250       | 5585          | 91            | 519        | 491           |

### TABLE 2
Five thousand nine-hundred thirty isolates from 345 ambulatory practices and 489 isolates from a referral hospital tested for Trimethoprim-Sulfamethoxazole (TMPS) sensitivity alongside prevalence of sensitivity (F, female)

| Trimethoprim-sulfamethoxazole | Total ambulatory | TMPS tested | TMPS sensitive | Total referral | TMPS tested | TMPS sensitive |
|-------------------------------|------------------|-------------|----------------|---------------|-------------|----------------|
|                               | n%               | n%          | n%             | n%            | n%          | n%             |
| Skin/wounds                   | 2137             | 2001        | 1490           | 74            | 291        | 278           |
|                               | 2001             | 2001        | 1490           | 74            | 291        | 278           |
| Respiratory                   | 1267             | 1192        | 1035           | 87            | 108        | 99            |
|                               | 1192             | 1192        | 1035           | 87            | 108        | 99            |
| Reproductive F                | 330              | 314         | 248            | 79            | 5          | 4             |
|                               | 314              | 314         | 248            | 79            | 5          | 4             |
| Abscesses                      | 790              | 735         | 628            | 85            | 54         | 48            |
|                               | 735              | 735         | 628            | 85            | 54         | 48            |
| Urinary                        | 242              | 216         | 167            | 77            | 11         | 11            |
|                               | 216              | 216         | 167            | 77            | 11         | 11            |
| Ocular                         | 170              | 145         | 137            | 94            | 4          | 4             |
|                               | 145              | 145         | 137            | 94            | 4          | 4             |
| Other                          | 324              | 287         | 244            | 85            | 34         | 34            |
|                               | 287              | 287         | 244            | 85            | 34         | 34            |
| Unknown                        | 1094             | 1040        | 884            | 85            | 12         | 11            |
|                               | 1040             | 1040        | 884            | 85            | 12         | 11            |
| Total                          | 6354             | 5930        | 4833           | 82            | 519        | 489           |

### TABLE 3
Six-hundred sixty five ambulatory isolates found to be resistant to Penicillin-Gentamicin (P-G) and tested for sensitivity to alternative antimicrobials (F, female; TMPS, trimethoprim sulfamethoxazole combination)

| Ambulatorypractice | P-G Resistant | TMPS tested | TMPS sensitive | Tetra-cycline sensitive | Ceflo-fur tested | Ceflofur sensitive | Enro-floxacin tested | Enrofloxacin sensitive |
|--------------------|--------------|-------------|----------------|-------------------------|-----------------|-------------------|----------------------|-----------------------|
|                    | n%           | n%          | n%             | n%                      | n%              | n%                | n%                   | n%                    |
| Skin/wounds        | 230          | 59          | 26             | 234                     | 39              | 17                | 134                  | 61                    |
| Respiratory        | 94           | 73          | 78             | 101                     | 63              | 62                | 35                   | 18                    |
| Reproductive F     | 22           | 11          | 50             | 25                      | 7               | 28                | 16                   | 6                     |
| Abscesses          | 51           | 25          | 49             | 56                      | 22              | 39                | 29                   | 16                    |
| Urinary            | 9            | 6           | 66             | 13                      | 6               | 46                | 5                    | 1                     |
| Ocular             | 10           | 5           | 50             | 12                      | 6               | 50                | 3                    | 2                     |
| Other              | 18           | 8           | 44             | 16                      | 6               | 38                | 10                   | 6                     |
| Unknown            | 95           | 51          | 54             | 100                     | 47              | 47                | 37                   | 19                    |
| Total              | 529          | 236         | 46             | 557                     | 196             | 35                | 269                  | 129                   |

3.1 | Comparison of ambulatory and referral isolates

Overall 5685 (91%) of the 6354 ambulatory isolates were sensitive to P-G (Table 1), and 4833 (82%) were sensitive to TMPS (Table 2). Of the 519 hospital isolates, 314 (64%) were sensitive to P-G (Table 3), and 275 (56%) were sensitive to TMPS (Table 4).
Prevalence of resistance to P-G was significantly different between ambulatory and referral isolates for all isolates combined \((P < .001)\) as well as for the subcategories of skin/wounds \((P < .001)\), respiratory \((P < .001)\), reproductive female \((P < .001)\), abscesses \((P < .001)\), ocular \((P < .001)\), other \((P = .05)\), and unknown \((P < .001)\).

Prevalence of resistance to TMPS was significantly different between ambulatory and referral isolates for all isolates combined \((P < .001)\), as well as for the subcategories of skin/wounds \((P = .003)\), respiratory \((P < .001)\), reproductive female \((P = .01)\), urinary \((P < .001)\), ocular \((P < .001)\), other \((P < .001)\), and unknown \((P < .001)\).

**TABLE 4** One thousand ninety seven ambulatory isolates found to be resistant to Trimethoprim-sulfamethoxazole (TMPS) and tested for sensitivity to alternative antimicrobials (F, female; P-G, Penicillin-Gentamicin association)

| Ambulatory practice | TMPS resistant | Tetra-cycline sensitive | Tetracycline tested | n | % | Enrofloxacin sensitive | Enrofloxacin tested | n | % | Cefti-fur sensitive | Cefti-fur tested | n | % | P-G sensitive | P-G tested | n | % |
|---------------------|-----------------|-------------------------|--------------------|---|--|------------------------|---------------------|---|--|-------------------|-----------------|---|--|----------------|-------------|---|--|----------------|
| Skin/wounds         | 515             | 133                     | 26                 | 496 | 301 | 61                     | 366                 | 227 | 62 | 506               | 301             | 60 |
| Respiratory         | 150             | 90                      | 60                 | 68  | 40  | 59                     | 114                 | 90  | 79 | 158               | 125             | 79 |
| Reproductive F      | 68              | 34                      | 50                 | 58  | 47  | 81                     | 49                  | 29  | 73 | 64                | 51              | 80 |
| Abscesses           | 110             | 25                      | 32                 | 92  | 71  | 77                     | 68                  | 45  | 66 | 104               | 77              | 74 |
| Urinary             | 50              | 33                      | 66                 | 48  | 30  | 63                     | 24                  | 20  | 83 | 43                | 40              | 93 |
| Ocular              | 9               | 5                       | 56                 | 9   | 6   | 67                     | 6                   | 5   | 83 | 9                 | 5               | 56 |
| Other               | 44              | 17                      | 39                 | 40  | 29  | 73                     | 31                  | 20  | 65 | 41                | 30              | 73 |
| Unknown             | 157             | 63                      | 40                 | 108 | 75  | 69                     | 87                  | 35  | 40 | 156               | 110             | 71 |
| Total               | 1103            | 410                     | 37                 | 919 | 599 | 65                     | 745                 | 451 | 61 | 1081              | 739             | 68 |

**TABLE 5** One-hundred seventy seven referral hospital isolates found to be resistant to Penicillin-Gentamicin (P-G) and tested for sensitivity to alternative antimicrobials (F, female; TMPS, trimethoprim sulfamethoxazole combination)

| Referral hospital | P-G resistant | TMPS sensitive | Tetra-cycline sensitive | Tetracycline tested | n | % | Enrofloxacin sensitive | Enrofloxacin tested | n | % | Cefti-fur sensitive | Cefti-fur tested | n | % | P-G sensitive | P-G tested | n | % |
|-------------------|---------------|----------------|-------------------------|--------------------|---|--|------------------------|---------------------|---|--|-------------------|-----------------|---|--|----------------|-------------|---|--|----------------|
| Skin/wounds       | 130           | 14             | 11                      | 136                | 11 | 8 | 96                    | 31                  | 32 | 136               | 46              | 34 |
| Respiratory       | 17            | 2              | 22                      | 18                 | 2  | 11 | 9                     | 4                   | 44 | 16                | 10              | 63 |
| Reproductive F    | 0             | 0              | 0                       | 0                  | 0  | 0 | 0                     | 0                   | 0  | 0                 | 0               | 0  |
| Abscesses         | 6             | 2              | 33                      | 6                  | 1  | 17 | 3                     | 0                   | 0  | 7                 | 3               | 43 |
| Urinary           | 4             | 0              | 0                       | 4                  | 0  | 0 | 4                     | 0                   | 0  | 4                 | 3               | 75 |
| Ocular            | 0             | 0              | 0                       | 0                  | 0  | 0 | 0                     | 0                   | 0  | 0                 | 0               | 0  |
| Other             | 10            | 0              | 10                      | 0                  | 0  | 7 | 0                     | 9                   | 6   | 67                |                 |    |
| Unknown           | 2             | 0              | 3                       | 0                  | 0  | 1 | 0                     | 0                   | 3   | 2                 | 67              |    |
| Total             | 169           | 18             | 11                      | 177                | 14 | 8 | 120                   | 35                  | 29 | 175               | 70              | 40 |

**TABLE 6** Two-hundred fourteen referral hospital isolates found to be resistant to Trimethoprim-sulfamethoxazole (TMPS) and tested for sensitivity to alternative antimicrobials (F, female; P-G, Penicillin-Gentamicin association)

| Referral hospital | TMPS resistant | Tetra-cycline sensitive | Tetracycline tested | n | % | Enrofloxacin sensitive | Enrofloxacin tested | n | % | Cefti-fur sensitive | Cefti-fur tested | n | % | P-G sensitive | P-G tested | n | % |
|-------------------|----------------|-------------------------|--------------------|---|--|------------------------|---------------------|---|--|-------------------|-----------------|---|--|----------------|-------------|---|--|----------------|
| Skin/wounds       | 143            | 28                       | 20                 | 139 | 69 | 50                     | 84                  | 38 | 45 | 141               | 41              | 29 |
| Respiratory       | 24             | 5                        | 21                 | 23  | 14 | 61                     | 17                  | 9  | 53 | 25                | 13              | 52 |
| Reproductive F    | 0             | 0                        | 0                  | 0   | 0  | 0                     | 0                   | 0  | 0 | 0                 | 0               | 0  |
| Abscesses         | 16            | 8                        | 50                 | 15  | 10 | 67                     | 12                  | 7  | 58 | 15                | 9               | 60 |
| Urinary           | 12            | 6                        | 50                 | 12  | 6  | 50                     | 10                  | 2  | 20 | 10                | 2               | 20 |
| Ocular            | 0             | 0                        | 0                  | 0   | 0  | 0                     | 0                   | 0  | 0 | 0                 | 0               | 0  |
| Other             | 11            | 2                        | 18                 | 11  | 9  | 82                     | 16                  | 12 | 75 | 11                | 1               | 9   |
| Unknown           | 3             | 0                        | 0                  | 2   | 1  | 50                     | 1                   | 1  | 100 | 3                 | 1               | 33  |
| Total             | 209           | 49                       | 23                 | 202 | 110 | 55                     | 140                 | 69 | 49 | 205               | 67              | 33  |
3.2  Comparison of antimicrobials selected as second choice to resistant isolates

The prevalence of sensitivity to the various second-choice antimicrobials isolates found to be resistant to P-G or TMPS are listed in Tables 3–6. A significant difference (P < .05) was found between the prevalence of resistance to each antimicrobial used when compared in pairs for all except TMPS and ceftiofur (P = .41), enrofloxacin and P-G (P = .14), and ceftiofur and enrofloxacin (P = .59) for the ambulatory samples. A significant difference also was found between the rates of resistance to each antimicrobial used when compared in pairs for all except TMPS and tetracycline (P = .46), and ceftiofur and enrofloxacin (P = .38) for the hospital isolates.

4  DISCUSSION

We found that bacterial isolates collected from ambulatory practice were more likely to be sensitive to P-G and to TMPS than those collected from a referral hospital. We also found that where resistance to first-line antimicrobials was found, no second-choice antimicrobial was consistently predicted to be efficacious, with <68% of the isolates resistant to P-G or TMPS being found to be sensitive to any other antimicrobial.

The finding of higher resistance rates in isolates from a referral hospital compared to those obtained from ambulatory practices (Tables 1–4) also has been found in previous studies. It is especially important to establish MICs for isolates from within a hospital population because resistance genes are put under more environmental pressure as well as other factors such as greater potential for transmission of resistant strains or resistance determinants among hospitalized horses and for stress to precipitate increased shedding of resistant strains.5 It is especially important to establish MICs for isolates from within a hospital population because of a generally lower likelihood of antimicrobial efficacy. By the same reasoning, it is logical that we found protected antimicrobials such as enrofloxacin and ceftiofur to have a lower prevalence of resistance among isolates because they are used less commonly and therefore preferences for TMPS, doxycycline, or enrofloxacin. Although enrofloxacin showed lower rates of resistance among the isolates from ambulatory cases compared to the other PO drugs, the rates of resistance nevertheless were high enough to prevent any confidence that enrofloxacin would be efficacious in the absence of determining MIC data. Also, enrofloxacin is not licensed for use in horses, is firmly within the group of critically important antimicrobials, and therefore should be used only with very good evidence-based reasoning. For hospital referral practice, parenteral administration is rarely problematic, meaning that parenteral P-G frequently is used as a first-line choice, and parenteral TMPS or oxytetracycline could be suitable second-choice antimicrobials where resistance is seen to P-G. Although sensitivity rates of P-G-resistant isolates generally were quite poor to TMPS and tetracyclines (11 and 8%, respectively, Table 7), these drugs nonetheless should be selected when the MIC is found to be below the clinical breakpoints or when other circumstances exist that might promote efficacy of these drugs (eg, local application). Although where resistance is seen to P-G, TMPS, and oxytetracycline, the further choices of ceftiofur or enrofloxacin might be considered, the sensitivity rates of isolates to these 2 further protected antimicrobials were only 29 and 40%, respectively, reinforcing the fact that they would be poor speculative choices and only should be used based on MIC data.

Strict application of MIC data to predict clinical efficacy or inefficacy sometimes may mislead because the many assumptions underlying the prediction of sensitivity and resistance might not always be correct. The so-called 60-90 rule often is quoted as a guide, which states that bacterial infections with in vitro prediction of efficacy to a particular antimicrobial will resolve in 90% of patients treated with that antimicrobial, whereas 60% of bacterial isolates with predicted resistance still might respond well. There are many instances and reasons why bacteria with apparent in vitro resistance to an
antimicrobial actually might respond well clinically to that antimicrobial. These factors include the host’s own immunity, which contributes to bacterial clearance, but also pharmacokinetic properties that might favor antimicrobial accumulation at a particular site of infection. For example, urinary excretion of TMP and P-G will lead to especially high urinary concentrations and clinical efficacy against urinary tract isolates even when in vitro testing might suggest resistance. This divergence between in vitro test results and clinical efficacy is likely to be even more pronounced for infections that are amenable to topical or local treatments (eg, intra-ocular, intra-uterine, dermal, IV regional perfusion) because local concentrations will be many times higher than could be achieved by systemic administration. For example, an isolate with an MIC for gentamicin of 16 μg/mL would be predicted to be highly resistant based on efficacy requiring attainment of 128 to 160 μg/mL gentamicin (8-10 times the MIC) in the locality of the infection, which is unachievable with systemic administration. However, such local concentrations are relatively easily achievable by topical treatment. Local treatments also will decrease the incidence of adverse effects on the fecal microbiota and the development of antimicrobial-associated diarrhea. Another important consideration is the synergistic action of some antimicrobial combinations leading to better clinical efficacy than would be expected based on the spectrum of each antimicrobial taken separately. For example, trimethoprim and penicillin demonstrate synergism when given along with aminoglycosides.

Conversely, there are instances and reasons why bacteria with apparent in vitro sensitivity to an antimicrobial may not respond well clinically to that antimicrobial. Infections may occur at sites poorly accessible to the chosen antimicrobial or potentially antagonistic factors may impair the pharmacodynamic properties of the antimicrobial in question. Additionally, suppressive or antagonistic drug interactions can occur when poorly selected polypharmacy is employed. A more intriguing strategy for improving antimicrobial sensitivity involves the concept of collateral drug sensitivity where a bacterial strain that has acquired resistance to 1 class of antimicrobials (especially aminoglycosides) may sometimes simultaneously become more sensitive to other antimicrobials.

Prudent use of antimicrobials hopefully will promote good efficacy in clearing bacterial infections while limiting the increase in bacterial resistance. Many facets contribute to achieving this balance beginning with correct identification of the specific pathogenic threats, and followed by careful selection of appropriate antimicrobials, which requires awareness of their pharmacokinetic and pharmacodynamic properties as well as their MICs for specific pathogens. Prioritization of nonprotected antimicrobials always should be practiced where supported by the considerations discussed above, thus conserving additional antimicrobials for clinical situations for which no other choices exist. Selection of antimicrobials in the absence of supportive data increases the risk of inefficacy along with subtherapeutic exposure, which contributes to the prevalence of resistance. When budgetary constraints dictate speculative selection, there is rarely any justification for the use of protected antimicrobials.

Our study reconfirmed previous evidence of higher rates of antimicrobial resistance in isolates from an equine hospital compared to ambulatory practices. Additionally, we found that when resistance was found to first-line antimicrobial choices, the choice of subsequent antimicrobials could not be predicted with confidence and always should be based on MIC data rather than speculation.

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CONFLICT OF INTEREST DECLARATION
Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION
Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION
This was a retrospective study of clinical data for which prior consent was obtained.

HUMAN ETHICS APPROVAL DECLARATION
Authors declare human ethics approval was not needed for this study.

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