Tutorial Article

Current controversies in equine antimicrobial therapy

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Summary

Controversies exist regarding the use, misuse and potential overuse of antimicrobial treatments in foals and adults. When antimicrobials are required for treatment of infectious diseases, veterinarians should follow a logical approach and not simply reach for the newest drug. Targeted, single drug therapy is probably best, and culture and sensitivity testing should be undertaken. The most likely infectious agent, potential drug toxicities, and age-appropriate dose and route should be considered. The development of an increasing number of different multiple drug resistant pathogens requires that veterinarians use antimicrobial drugs responsibly to protect veterinary patients and the public at large.

Introduction

Appropriate antimicrobial use in the equine patient poses many specific challenges. Considerations prior to antimicrobial selection include poor oral absorption of many drugs, large total dosage (and therefore high cost) often required, and risk of adverse side-effects, the most common of which is antimicrobial-associated enterocolitis. In addition, drug disposition in the foal may be very different from that in the adult, with differences in oral absorption, volume of distribution, metabolism and clearance of many drugs. Knowledge and understanding of basic pharmacokinetics and pharmacodynamics in different age groups is, therefore, essential to appropriate use of antimicrobial agents. In addition, there is the question of development of antimicrobial resistance, which has important implications for both human and veterinary medicine. Many controversies exist regarding the current use of antimicrobials, including appropriate antimicrobial selection, and use of antimicrobials in certain clinical situations.

Antimicrobial selection

There is little information available regarding appropriate antimicrobial selection in the horse. First line antimicrobial agents for suspected or proven infection should generally be broad spectrum and have known efficacy against the most likely pathogens. First line antimicrobials are those that are appropriate for use in the absence of, or pending, culture and sensitivity results (Table 1). There are instances in which a first line antimicrobial does not need to be broad-spectrum, for example simple penicillin is an appropriate choice for treatment of suspected Streptococcus equi ssp. equi infections, where treatment is deemed necessary (Fig 1). Where possible, cultures should be obtained prior to antimicrobial administration, allowing selection of further antimicrobial agents on the basis of the

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Fig 1: Horse with nasal discharge (apparent in left nostril) due to infection with Streptococcus equi var. equi or 'strangles'. While this disease seldom requires antimicrobials, horses with severe systemic illness may require treatment.
specific sensitivity pattern of the organism in question, should initial therapy be unsuccessful.

The American College of Veterinary Internal Medicine (ACVIM) has published a consensus statement on antimicrobial drug use in veterinary medicine (Morley et al. 2005) recommending that veterinarians categorise antimicrobials used in their practice into primary, secondary, and tertiary use categories. Drugs assigned to the primary use category should include older drugs and those with a narrower spectrum of activity, e.g. simple penicillins, and these drugs should be used in the majority of infections. Drugs assigned to the secondary use category include newer drugs with an extended spectrum of activity, and those with added importance in the treatment of serious or frequently resistant infections in man. Drugs for which antimicrobial resistance appears to develop relatively easily, e.g. rifampin, should also be assigned to this class. Secondary use drugs should be reserved for cases where culture and sensitivity results indicate primary use drugs are not appropriate. Tertiary use drugs are those particularly important for human and animal health care, especially those most recently developed and those with extended spectra of coverage that are useful against the most resistant bacteria (for example methicillin resistant Staphylococcus aureus [MRSA]), with use limited to animals with clinically important infections caused by bacteria demonstrated resistant to all reasonable primary and secondary use drugs (Morley et al. 2005). It is important that secondary and tertiary category antimicrobial drugs are not used when a primary category drug could be just as effective.

Decisions to advance from a primary to a secondary or tertiary category drug should be based on either culture and sensitivity information, where available, or inadequate response to a lower category drug, after allowing sufficient time to evaluate the response. In general, the authors recommend a period of at least 48 h with no clinical or clinicopathological improvement prior to deeming an antimicrobial agent ineffective. In addition, the use of tertiary antimicrobials should be restricted to animals with a ‘reasonable chance of survival’. This consensus statement (Morley et al. 2005) should be studied in detail and used to develop prescribing guidelines for each individual practice. Guidelines for antimicrobial use in the authors’ hospital are included in Table 1. In addition to these guidelines, directed antimicrobial therapy should be used whenever possible, using culture and sensitivity techniques to target specific organisms. Further considerations for antimicrobial selection should include the availability of the drugs and whether the antimicrobial is licensed for use in the horse, or even any veterinary species. In addition, consideration should be given to the pharmacokinetic and pharmacodynamic profile of the drug, where known, as absorption and distribution varies significantly both within and between species. The authors are refraining from comment regarding the use of compounding pharmacies, as the controls and regulations of such pharmacies are disparate between regulating agencies on various continents and between countries on the same continent.

### Table 1: Example antimicrobial use policy

#### Primary use

- Penicillins
- Trimethoprim-sulphonamide
- Gentamicin (reserve for serious infections)
- Tetracyclines
- Metronidazole
- Erythromycin
- Rifampin (Never use as sole agent)

#### Secondary use

- Cefotaxime and other 3rd generation cephalosporins
- Enrofloxacin
- Ticarcillin + clavulanic acid
- Chloramphenicol
- Azithromycin
- Doxycycline

#### Tertiary use

- Imipenem
- 4th generation cephalosporins
- Other drugs used for the treatment of resistant bacteria, e.g. newer fluoroquinolones

### Association of antimicrobial drugs with enterocolitis and nephrotoxicity

There are many adverse drug reactions associated with antimicrobials, the most common of which is antimicrobial-
associated enterocolitis. Many clinicians hold very strong opinions on the association of certain antimicrobials with enterocolitis, but the fact remains that any antimicrobial drug has the potential to cause enterocolitis. Horses are especially prone to the development of antimicrobial-associated enterocolitis because of their poor oral absorption of many drugs, leading to large concentrations of active drug in the intestinal lumen (Papich 2003). However, drugs that are absorbed well orally or administered i.v., have also been associated with diarrhea because of biliary excretion or enterohepatic recycling, exposing the intestinal lumen to large concentration of the drug (Papich 2003). A decrease in anaerobic bacteria in the intestine leads to altered carbohydrate metabolism and the overgrowth of some potentially pathogenic bacteria, both of which may lead to diarrhea (Papich 2003). The most commonly implicated antimicrobials are presented in Table 2: it is important to note that, anecdotally, there appear to be geographical differences in the antimicrobial drugs most likely to cause enterocolitis. Local knowledge of antimicrobials commonly associated with enterocolitis in a specific region is, therefore, helpful for antimicrobial selection.

The administration of potentially nephrotoxic drugs to azotaemic animals is another controversial topic. Many of these animals will have prerenal azotaemia secondary to hypovolaemia, rather than intrinsic renal disease, although occult renal parenchymal disease may exist secondary to that hypovolaemia. In most cases, administration of nephrotoxic antimicrobial drugs (such as gentamicin and amikacin) can be avoided and other antimicrobial agents used in preference; there are, however, clinical situations in which complete nephrotoxic drug avoidance is not possible. The prescribing veterinarian should consider the ‘cost-benefit analysis’ of using such drugs in these animals; if the relative risk appears small, and the potential benefit great, potentially nephrotoxic drugs should be used with caution and frequent monitoring of renal function (including urinalyses and serial, daily if necessary, creatinine concentration determinations) performed. If aminoglycosides are used in the azotaemic patient, therapeutic drug monitoring, with particular attention paid to the ‘trough’ concentrations, should be carried out. Guidelines for therapeutic drug monitoring are outside the scope of this article, and the reader is referred to other texts (e.g. Dowling 2004).

One example of potential benefit outweighing an apparently small risk is administration of polymyxin B to endotoxaemic animals. Polymyxin B is an antimicrobial agent used at subantimicrobial doses for treatment of endotoxaemia, and has proven to be efficacious, even when given after administration of endotoxin (Barton et al. 2004). Polymyxin B has potential nephrotoxic and neurotoxic effects (Raisbeck et al. 1989; MacKay et al. 1999). Interestingly, despite its commonly stated nephrotoxicity, this has not been demonstrated in the horse even when very large doses have been experimentally administered (up to 36,000 IU/kg BWI) (Raisbeck et al. 1989; Durando et al. 1994; MacKay et al. 1999; Parviainen et al. 2001; Moresey and MacKay 2006), and there are no reports of nephrotoxicity following polymyxin B administration in the equine veterinary literature. In spite of this, it is commonly recommended that polymyxin B should be used with care in azotaemic or hypovolaemic animals (Barton et al. 2004). Large doses have been associated with neurological side-effects, including ataxia, hypermetria and spasmodic coughing, seen at doses of 18,000 IU/kg BWI and above (Raisbeck et al. 1989), but not at 10,000 IU/kg BWI or less (Durando et al. 1994; Barton et al. 2004). Fortunately, polymyxin B binding of endotoxin occurs at much lower doses, and the recommended dose range is 5000–6000 IU/kg BWI q. 8–12 h i.v. (Durando et al. 1994; Parviainen et al. 2001; Barton et al. 2004). In light of the current evidence, and lack of reported cases of nephrotoxicity secondary to administration of polymyxin B, the authors consider its use appropriate for the treatment of endotoxaemia, even in those animals with prerenal azotaemia, alongside other supportive treatments.

### Antimicrobial use in neonates

In general, critically ill neonatal foals are considered immunocompromised patients with presumed sepsis until proven otherwise, and broad-spectrum antimicrobial therapy should therefore be provided (Paradis 1994). There is compelling evidence from human medicine that early provision of appropriate antimicrobial therapy increases survival (Ibrahim et al. 2000; Raghavan 2006), and the same is likely to be true of the septic equine neonate. In spite of this, clinicians need to avoid the ‘knee-jerk’ reaction to provide the best possible antimicrobial coverage, which may lead to the selection of extended spectrum drugs that should be reserved for more serious infections that do not respond to first-line drugs. Antimicrobials selected for these animals should be primary use drugs, preferably selected with an evidence-based approach with directed antimicrobial therapy, following years of information on blood culture isolates and sensitivity patterns in the local geographic area. If this is not possible, data should be extrapolated and guidelines taken from the many

<table>
<thead>
<tr>
<th>TABLE 2: Commonly implicated antimicrobials in antimicrobial-associated enterocolitis</th>
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<tbody>
<tr>
<td>Enrofloxacin</td>
</tr>
<tr>
<td>Trimethoprim-sulphonamide combinations</td>
</tr>
<tr>
<td>Oxytetracycline</td>
</tr>
<tr>
<td>Penicillin</td>
</tr>
<tr>
<td>Cefthiaxone</td>
</tr>
<tr>
<td>Doxycycline</td>
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<tr>
<td>Erythromycin</td>
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<tr>
<td>Neomycin</td>
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<tr>
<td>Lincomycin</td>
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<tr>
<td>Clindamycin</td>
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<tr>
<td>Moxifloxacin</td>
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<tr>
<td>Florfenicol</td>
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<tr>
<td>Tylosin</td>
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published studies available – treatment of the equine neonate is one of the few areas of equine medicine where much information is available regarding common isolates and potentially appropriate therapies (Platt 1973; Koterba et al. 1984; Wilson and Madigan 1989; Brewer and Koterba 1990; Paradis 1994; Raisis et al. 1996; Henson and Barton 2001; McKenzie and Furr 2001; Marsh and Palmer 2001; Stewart et al. 2002; Furr 2003; Sanchez 2005; Pusterla et al. 2006; Corley et al. 2007).

**Antimicrobial use in enterocolitis**

Many clinicians have very strong opinions on the use of antimicrobial agents in horses with enterocolitis. There are some conditions for which specific antimicrobial therapy is definitely indicated in enterocolitis; i.v. oxytetracycline for Potomac horse fever (Neorickettsia risticii) infection, and orally administered erythromycin (or clarithromycin azithromycin) and rifampin for diarrhoea secondary to infection with Rhodococcus equi.

Oral metronidazole has a specific indication in horses with enterocolitis for the treatment of clostridial diarrhoea. *Clostridium difficile* and *Clostridium perfringens* infections are commonly implicated in enterocolitis, especially with antimicrobial associated enterocolitis (Båverud et al. 1997; Donaldson and Palmer 1999; Weese and Stämpfli 2001). In the neonatal foal, clostridial toxins are commonly detected. Of 93 foals aged <30 days presenting to a referral hospital with diarrhoea, 34.6% had *Clostridium perfringens* and/or *Clostridium difficile* toxins present in their faeces (Hollis et al. 2008). Alongside this specific indication, metronidazole has been shown useful in acute, idiopathic colitis that developed in a veterinary hospital where 8 horses treated with metronidazole survived, and 5 of 7 horses that received other treatments, but did not receive metronidazole, died or had to be subjected to euthanasia (McCorum 1998). Use of metronidazole therefore appears rational in all horses with enterocolitis, with attention paid to potential development of neurological adverse effects when larger dosages are used. Although vancomycin is also an effective drug for treatment of clostridial infections, the authors do not recommend its use in the equine patient, especially when other options are available, as it is considered a tertiary use drug that should be reserved for the most severe infections and special circumstances, as detailed previously (Table 1).

Most clinicians would agree that, with a few notable exceptions, that the use of oral antimicrobials in animals with enterocolitis is generally contraindicated; however, the use of i.v. antimicrobials remains highly controversial. In neonatal foals with diarrhoea, the authors recommend initial blood culture followed by provision of broad-spectrum antimicrobial therapy. In foals aged <30 days presenting to a referral hospital with diarrhoea from 1990–2007, 50% were bacteraemic at presentation (Hollis et al. 2008). This percentage is higher than the reported incidence of bacteraemia in the overall population of foals presenting to referral hospitals (29–36%) (Marsh and Palmer 2001; Corley et al. 2005). It seems that foals with diarrhoea are at increased risk for bacteraemia, presumable due to bacterial translocation from a compromised gastrointestinal tract or as a primary cause of diarrhoea. The most common isolates from the study of neonatal foals with diarrhoea were *Enterococcus spp.*, *Pantoea agglomerans*, *Escherichia coli* and *Salmonella spp.* (Hollis et al. 2008), which is different to the most commonly isolated bacteria in the general population of critically ill neonatal foals (Marsh and Palmer 2001; Corley et al. 2005). This information may aid appropriate antimicrobial selection in these animals. It is generally accepted that bacteraemic foals should be treated with appropriate antimicrobials as soon as sepsis is suspected (Paradis 1994), as previously discussed.

The indications for broad-spectrum i.v. antimicrobial administration in mature horses with colitis are less clear. Sepsis, defined as the presence of infection and a systemic inflammatory response (Levy et al. 2001), is commonly present in mature horses with colitis, but, conversely, the combination of sepsis and bacteraemia is uncommonly reported in mature horses. The prevalence of bacteraemia in horses with colitis is unknown at this time, although Gram-negative bacteraemia in horses with endotoxaemia and altered gastrointestinal mucosal integrity appears to be uncommon (Moore and Morris 1992). Ten percent of normal human adults with uncomplicated enteric salmonellosis develop transient bacteraemia that is cleared by the body’s own defence mechanisms without the need for specific antimicrobial therapy (Ploutz and Church 2004); the clinical importance of bacteraemia in the mature horse, where detected, is unclear. Clinically important bacteraemia responsive to specific antimicrobial therapy has been reported in a horse with enteric salmonellosis, and should be considered in horses with colitis that are unresponsive to typical supportive therapy (Johns et al. 2006). The authors recommend collection of multiple blood cultures from all mature horses with diarrhoea that are not responsive to general supportive care, and consideration of specific treatment in those that are bacteraemic with potentially pathogenic organisms. In addition, i.v. antimicrobial treatment has been recommended in severely neutropenic patients with diarrhoea as these animals may be immunocompromised due to the peripheral neutropenia (Feary and Hassel 2006; Oliver and Stämpfli 2006); however, the association between administration of antimicrobials and faecal shedding of *Salmonella* spp. (Hird et al. 1986; House et al. 1999; Dargatz and Traub-Dargatz 2004) may make administration of antimicrobials inadvisable in certain hospital situations.

Some clinicians advocate treatment of animals with documented *Salmonella* spp. infection, as treatment may kill existing organisms and prevent systemic infection; others argue that treatment is often unsuccessful, and may lead to release of more endotoxin secondary to bacterial killing,
Contribute to antimicrobial resistance, and further disturb colonic flora (Oliver and Stämpfli 2006). It has been shown that antimicrobial treatment does not reduce faecal shedding of Salmonella spp, even if the strain is sensitive to the antimicrobial agent used (van Duijkeren et al. 1995), and there is no evidence that antimicrobial therapy is beneficial in altering the course of salmonellosis in adult horses (Divers and Ball 1996). The decision to begin antimicrobial treatment on the basis of neutropenia, pyrexia and other signs of the systemic inflammatory response syndrome (SIRS) is further complicated by the fact that these signs also occur in response to endotoxaemia, extremely common in horses with diarrhoea. Horses are exquisitely sensitive to the effects of endotoxaemia and often appear to be endotoxaemic without evidence of bacteraemia, perhaps due to decreased blood culture sampling in the cases when compared to neonates. Based on the current evidence, the authors do not advocate the use of broad-spectrum antimicrobial agents for horses with salmonellosis or other causes of enterocolitis unless persistent bacteraemia is documented, or the animal is persistently and severely neutropenic (<10^9 cells/l). In addition, the authors do not recommend use of antimicrobial agents other than oral metronidazole even in the face of an epidemic of diarrhoea or on a property with a history of salmonellosis. Adult horses documented to be blood culture positive may benefit from directed antimicrobial treatment (Pellegrini-Masini et al. 2004; Johns 2008). Further work in this area is indicated. The antimicrobial agent should be based on the sensitivity of the isolated organism, where known.

**TABLE 3: Post operative infection (POI) risk categories with common isolates and suggested antimicrobial approaches**

<table>
<thead>
<tr>
<th>Risk of POI</th>
<th>Common pathogens</th>
<th>Suitable antimicrobials</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Staphylococcus</td>
<td>Penicillin</td>
<td>Prior to first incision only (&lt;3 h i.m., &lt;1 h i.v.)</td>
</tr>
<tr>
<td></td>
<td>Streptococcus</td>
<td></td>
<td>i.v., start &lt;1 h, prior to first incision, end within 24 h</td>
</tr>
<tr>
<td>Medium</td>
<td>Staphylococcus</td>
<td>Penicillin and gentamicin</td>
<td>i.v., start &lt;1 h, prior to first incision, end within 24 h</td>
</tr>
<tr>
<td></td>
<td>Streptococcus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gram-negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Streptococcus</td>
<td>Penicillin and gentamicin</td>
<td>i.v., start &lt;1 h, prior to first incision, end within 72 h</td>
</tr>
<tr>
<td></td>
<td>Gram-negative</td>
<td></td>
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</tr>
</tbody>
</table>

Low post operative infection (POI) risk – elective procedures without implants (arthroscopy, upper airway surgery, superficial urogenital procedures). Medium POI risk – nonarthroscopic elective orthopaedic procedures, urogenital procedures involving the peritoneum, procedures with minor implants (laryngoplasty, <3 lag screws) and emergency procedures without gross contamination or traumatic tissue damage. High POI risk – procedures requiring substantial implant materials (dynamic compression plate, mesh), procedures with gross contamination with infectious materials, procedures with persisting compromised tissue, immunocompromised patients (e.g. neonates). Adapted from Santschi (2006).

**Perioperative antimicrobials**

There is much information available on the use of perioperative antimicrobials in human surgical patients, and it is well documented that post operative infection leads to prolonged hospital stay, and increased morbidity, mortality, and cost of treatment in surgical patients (Southwood 2006). Aseptic and atraumatic surgical techniques remain the mainstay of successful outcome and prevention of infection, but the benefits of appropriate antimicrobial therapy in prevention of surgical site and distant infections cannot be disputed (Southwood 2006). For maximum efficacy, peak antimicrobial concentration should be present during the surgical procedure, and the surgical site infection rate in patients administered preoperative antimicrobials is significantly lower than in those administered antimicrobials following the surgical procedure (Classen et al. 1992; Esposito 1999). In horses, it has been recommended that prophylactic antimicrobials be administered 30 min prior to the start of the skin incision, and no more than 60 min prior to the start of the procedure (Dallap Schaer 2007). In addition, it is recommended that the dose be repeated if the length of the procedure is longer than 2 half-lives of the chosen antimicrobial (Dallap Schaer 2007). In human surgical patients, it is generally recommended that antimicrobial use be restricted to patients where the risk of infection is greater than 5% without prophylactic antimicrobial use (Esposito 1999), i.e. those surgeries that are clean-contaminated, contaminated or dirty, and when implants are used. In man, it has been recommended that empiric broad-spectrum antimicrobials should be used for 24–48 h with dirty or infected wounds, followed by a change to narrow-spectrum therapy based on culture and sensitivity of any isolated organisms, if available (Imahara and Nathens 2003). The optimal length of antimicrobial administration in other situations is less clear, but single dose prophylactic antimicrobial regimens appear to be as effective as a multiple-dose regimens (Esposito 1999). Within 24 h of surgery, the surgical site is considered sealed and resistant to the entry of microorganisms (Altemeier et al. 1968). Although the optimum duration of antimicrobial administration in veterinary patients undergoing clean-contaminated and contaminated surgical procedures, e.g. gastrointestinal surgery, is unknown, greater than 24 h of antimicrobial treatment is probably unnecessary in the majority of patients (Southwood 2006). Indeed, in human patients, prolonged use of antimicrobials does not reduce the prevalence of post operative infections, alters the skin and gastrointestinal flora, and encourages the development of antimicrobial resistance (Archer 1991; Harbarth et al. 2000; Takesue et al. 2002; Hoth et al. 2003). Guidelines for antimicrobial prophylaxis in the horse have been published (Santschi 2006) and are presented in Table 3.
Antimicrobial prophylaxis in travelling animals

There is recognised controversy as to the utility of administration of prophylactic antimicrobial agents to animals prior to long distance shipping as an attempt to prevent pleuropneumonia. There is a paucity of information on efficacy of prophylaxis with which to make evidence-based decisions. It is documented that the most important predisposing factor to lower respiratory disease is the lack of physical clearance of material when horses are restrained and unable to lower their heads, with the accumulation of bacteria and/or inflammatory exudate in the trachea being documented within 24 h of such restraint (Rackleyeff and Love 1990). It has been shown that such situations reduce tracheal mucocilliary clearance (Raidal et al. 1997), and that horses that are transported for 12 h without restraint showed no changes in the cytology or bacteriology of broncho-alveolar lavage fluid (Traub-Dargatz et al. 1988). The authors therefore feel that the emphasis should be placed on environmental modifications rather than antimicrobial prophylaxis.

Antimicrobials in Streptococcus equi ssp. equi infection (‘strangles’)

Veterinary opinion remains divided as to the utility of antimicrobial therapy in strangles infections. Potential indications for the use of antimicrobial agents in strangles include treatment of peracutely affected animals during an outbreak (those with <24 h pyrexia and no palpable lymphadenopathy), prophylactic treatment of unaffected in-contact animals, critical cases with life-threatening airway obstruction, cases with secondary purpura haemorrhagica, cases of metastatic infection (‘bastard’ strangles), as adjunctive therapy for guttural pouch empyema, and for the treatment of chronic carrier animals (Brazil 2005). It is the opinion of the authors that the guidelines in the recent ACVIM consensus statement on the treatment of strangles (Sweeney et al. 2005) should be followed. Although the majority of strangles cases require no more than supportive care, immediate antimicrobial therapy of new cases in the early acute phase, with fever and signs of depression, may be curative, prevent focal abscessation, and effective in controlling outbreaks (Sweeney et al. 2005). However, antimicrobial therapy inhibits synthesis of protective antigens and the development of protective immunity (Piche 1984) thereby rendering horses highly susceptible to reinfection if they remain exposed to infected animals (Sweeney et al. 2005).

There is much debate as to whether the administration of antimicrobials to animals with strangles infections predispose to the development of metastatic, or ‘bastard’, strangles. A recent review of this topic concluded that there is no clinical or experimental evidence to suggest that antimicrobial therapy in acute S. equi ssp. equi infection is associated with metastatic strangles (Ramey 2007). There appears to be less controversy regarding treatment during the later stages of clinical disease, or in cases with secondary complications. Once external lymphadenopathy is detected, antimicrobial therapy is probably contraindicated, as it prolongs the enlargement and eventual rupture of lymph node abscesses (Sweeney et al. 2005). Horses that develop complications from strangles infections should be treated symptomatically, with metastatic abscessation treated with appropriate antimicrobial therapy. The antimicrobial agent of choice is penicillin, to which S. equi is consistently sensitive, with laboratories noting no emerging antimicrobial resistance (Sweeney et al. 2005). Identified carrier animals, with clinically silent S. equi infection of the guttural pouches, should be treated with both topical and systemic penicillin to aid elimination of the infection (Sweeney et al. 2005).

TABLE 4: Control measures for MRSA colonisation and infection in horses

<table>
<thead>
<tr>
<th>Control principal</th>
<th>Control measure</th>
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<tbody>
<tr>
<td>Prevent introduction of infection</td>
<td>Screen all incoming cases</td>
</tr>
<tr>
<td></td>
<td>Consider barrier nursing until negative status established</td>
</tr>
<tr>
<td>Prevent transmission: Animal to man/man to animal</td>
<td>Hand hygiene and related measures</td>
</tr>
<tr>
<td></td>
<td>Hand washing</td>
</tr>
<tr>
<td></td>
<td>Alcohol-based hand sanitisers</td>
</tr>
<tr>
<td></td>
<td>Staff screening and treatment</td>
</tr>
<tr>
<td></td>
<td>Barrier nursing/isolation of all confirmed cases</td>
</tr>
<tr>
<td>Prevent transmission: Animal to animal</td>
<td>Isolation of all MRSA suspects and confirmed cases</td>
</tr>
<tr>
<td>Prevent transmission: Indirect</td>
<td>High standards of cleaning and disinfection</td>
</tr>
<tr>
<td></td>
<td>Hand touch surfaces</td>
</tr>
<tr>
<td></td>
<td>Stables and bedding</td>
</tr>
<tr>
<td></td>
<td>Dedicated equipment (headcollars, lead ropes, thermometers thoroughly disinfected between cases).</td>
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</table>

Adapted from Leonard and Markey (2008).
Methicillin resistant *Staphylococcus aureus*

Methicillin resistant *Staphylococcus aureus* (MRSA) is a significant, international problem in human medicine, and appears to be an emerging problem in equine medicine. MRSA infections have been reported in horses in many countries, and transmission between horses and man has been identified (O’Mahoney et al. 2005; Weese et al. 2005a, b, 2006a; Cuny et al. 2006). At present, the epidemiology of infection and colonisation of horses is poorly understood (Weese and Lefebvre 2007). In a recent study, MRSA was isolated from 5.3% of 2283 horses admitted to a tertiary referral hospital; 50.8% were isolated at admission. Clinical infections attributable to MRSA occurred in 11.7% of these horses, with horses colonised at admission were more likely to develop clinical MRSA infection than those not colonised at admission. Clinical infections included septic arthritis, jugular catheter site infection, wound infection, pneumonia, mastitis, rhinitis and body wall abscesses (Weese et al. 2006b). In addition, risk factors for community-associated MRSA colonisation of horses presenting to an equine hospital have been identified, including: previous colonisation of the horse, previous identification of colonised horses on the same farm, antimicrobial administration within 30 days, admission to the neonatal intensive care unit, and admission to services other than the surgery service. As more epidemiological information becomes available and ‘high risk’ patients are identified, appropriate control measures will be possible to reduce animal to man and animal to animal transmission.

It is the impression of the authors that MRSA infections in horses cause significant morbidity, but rarely cause mortality. Whilst the majority of identified cases of clinical disease caused by MRSA in the authors’ hospital appear to be catheter site infections that do not require systemic treatment, wound and post operative infections seem to be the most commonly reported manifestations of MRSA infections in horses (Leonard and Markey 2008). Prior to treatment of clinical infections, it should be determined whether local treatment may be adequate, as local treatment with chlorhexidine and 1% acetic acid have been successfully used to treat incisional and wound infections (Weese 2004). If specific treatment is required, directed antimicrobial therapy selected according to the sensitivity pattern of the isolated organism is preferred.

It is the opinion of the authors that particular attention should be paid to controlling MRSA in horses, guidelines for which are presented in Table 4. Surveillance methods should be considered in any equine hospital, in order to identify community acquired strains and document nosocomial infections. In horses, the nasal passage appears to be the most common site of colonisation (Weese 2004). Therefore any screening programme should involve cultures of nasal swabs. The question then arises as to whether to attempt eradication of colonisation to reduce the risk of further transmission and the development of clinical disease. The manner by which this should be undertaken is unclear, and colonisation is transient in most adult horses (Weese 2004) so treatment of colonised but clinically unaffected animals is often regarded as unnecessary. In addition, antimicrobial therapy of colonised horses may be inadvisable, as MRSA isolates rapidly develop resistance, and there are only limited antimicrobial options available for use (Weese 2004). Intranasal antimicrobials are most commonly used for eradication in man; however, the difficulty of applying topical antimicrobials to the entire nasal passage of the horse makes this a questionable treatment in this species (Weese 2004). Nebulisation of antimicrobials may be a viable alternative where eradication is desirable (Weese 2004). Eradication of MRSA colonisation has been successfully performed on a horse farm with a policy of segregation, infection control precautions and repeated testing (Weese and Rosseau 2005), suggesting that these measures would be sufficient in a hospital situation. At present the authors consider it appropriate to use barrier nursing techniques on identified carrier animals in order to limit spread of MRSA, but do not advise specific treatment unless clinically important infections have been identified.

Regardless of the approach to screening for and treatment of MRSA infections, there is little doubt that early institution of appropriate surveillance and other infection control measures should be used to attempt to limit the impact of MRSA in veterinary medicine (Weese 2004), and it is the responsibility of each individual institution to ensure that these measures are taken.

**Conclusions**

There are many controversial topics in the field of antimicrobial use in equine patients, and as evidence-based medicine becomes more commonplace in veterinary medicine, the answers to many of the aforementioned problems may become available. In the meantime, veterinarians should use antimicrobials prudently and select appropriate drugs for maximum efficacy, in order to slow the development of potentially devastating multidrug resistant bacteria.

**References**


