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How and When to Treat Endometritis With Systemic or Local Antibiotics

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1. Introduction
The decision to use antibiotics for the treatment of a reproductive problem in a mare is not always clear-cut or cookbook. Factors that may influence that decision include current duration of the pathology/infertility, previous treatment, previous infertility, previous experience, or even pressure from the owner to get the mare pregnant.

One of the key factors in treating endometritis is accurately diagnosing that a true bacterial infection is present. This stems from the potential difficulty in acquiring an accurate diagnostic sample from culture and/or cytology. Recently, Petersen, from Denmark, described the invasiveness of Streptococcus zoopneumaticus into the mare’s endometrium, discovering on analysis of uterine biopsies that Streptococcus was present deep within the endometrial tissue.1 Thus, it is possible to miss a diagnosis with sampling of the uterine lumen, or, if treatment is limited to intra-uterine therapy, the treatment course could be unsuccessful, especially if the antibiotic did not achieve deep-tissue antibiotic concentrations adequate to kill the organism. Unfortunately, there is no immediate answer regarding many bacterial organisms as to where they are located because investigators have yet to classify which organisms may be predisposed to superficial or more deep seated infections. Chronicity of infection may certainly predispose to deeper invading infections. There are also differences between mares with regard to location within the uterus or endometrium for bacterial infections. Infections may be localized to a specific area of the uterus or may encompass the vast majority of the luminal endometrium.

Antibiotics are used in the mare to treat potential or realized reproductive tract infections including vaginitis, cervicitis, endometritis, metritis, pyometra, and placentitis. Alternatively, infections may be associated with or classified as sexually transmitted diseases, post-mating-induced endometritis, acute or chronic endometritis, abortion-related, and/or bacterial and fungal infections.2 Antibiotics are administered either through intravenous/intramuscular routes or directly into the reproductive tract lumen. Antibiotics are naturally occurring or synthetic substances that inhibit the growth of or kill microorganisms. The definition may be limited to substances affecting bacteria or may also include fungi and protozoa. In this report, antifungals will be considered part of the antibiotic class.
There are some reviews of the use of antibiotics in mare reproduction. The choice of antibiotic should be based on culture and sensitivity patterns when possible or based on the most likely organism when a culture/sensitivity is not possible, as a client refusing the procedures. The most common bacteria isolated from the mare’s reproductive tract are Streptococcus equi, subspecies zooepidemicus (Gram positive), Escherichia coli (Gram negative), Klebsiella pneumonia (Gram negative), Pseudomonas aeruginosa (Gram negative), Staphylococcus aureus (Gram positive), and Bacteroides (Gram negative, anaerobe). S. equi subspecies zooepidemicus and E. coli are the number-1 and number-2 isolates in almost all reports. The most common fungi isolated from the mare’s reproductive tract are Candida spp. and Aspergillus spp.

There are many factors that may affect antibiotic effectiveness/clearance such as overwhelming microorganism numbers, presence of uterine fluid/debris, lack of uterine contractility, use of ecbolics, normality of uterine mucocilliary clearance mechanisms, cervical dilation, and dependency of the uterine horns. Disruptions of natural barriers to infection, such as previous cervical trauma/scarring, vestibulovaginal fold incompetence (windsucker), and poor vulvar conformation, may also contribute to continued bacterial/fungal contamination.

Intrauterine antibiotic therapy appears to have decreased in use, probably because of concerns about inducing secondary fungal infections and/or antibiotic resistance, and as the result of new information on the effectiveness of uterine lavage and the use of ecbolics, such as oxytocin and prostaglandins. Antibiotic therapies are now more targeted at specific organisms, are used with more specific disease processes, or are used in conjunction with methods to disrupt biofilms or after decreasing bacterial numbers with lavage techniques. This report will describe the results of an on-line survey of veterinarians concerning antibiotic use in mare reproduction and will correlate the results to the literature.

2. Materials and Methods

Two surveys were conducted with regard to the use of antibiotics in equine reproduction. The surveys were initiated to see what is commonly used in practice versus what is recommended in the literature. Both surveys were sent to the Equine Clinicians Network listserv (ecn@listserv.vetmed.wsu.edu), the American Association of Equine Practitioner’s listserv (aaep discussion@list.aaepp.org), the Equine Reproduction listserv (eqrepro-l@po.missouri.edu), and the American College of Theriogenologists listserv (ACTList@lists.theriogenology.org). The first was initiated in September 2008 (190 respondents) and the second was initiated in March 2009 (109 respondents). The second survey was performed to augment the first survey results. Sixty-one percent of participants in the second survey partook in the first survey.

3. Results and Discussion

Approximately 69% of survey participants stated that the primary way that mares are bred in their practice is by the use of fresh cooled semen, 27% are bred primarily by natural cover, 3% primarily with frozen semen, and 2% did not provide an answer. The number of years in practice was: <5 years, 7%; 5 to 10 years, 20%; 11 to 15 years, 13%; 16 to 20 years, 18%; >20 years, 39%; and no answer, 2%. The percentage of their practice that was devoted to equine reproduction was: <10%, 11%; 10% to 25%, 21%; 25% to 50%, 18%; 50% to 75%, 15%; >75%, 34%; and no answer, 1%. The larger number of practitioners in the >75% category probably reflects the distribution of the survey to two predominately reproductively oriented listservs (ACT and EqRepro). Veterinarians from 14 countries participated in the survey, with 70% of respondents practicing in the United States.

When asked which bacterial and fungal organisms they encountered most, the overwhelming answer for bacterial isolates were S. zooepidemicus, followed secondarily by E. coli. One practice stated that they had 80% β-hemolytic Streptococcus isolated from 1400 uterine cultures in their clinic. An antibiotic with both Gram-positive and Gram-negative properties may be appropriate for the treatment of uterine infections in those cases without culture. Fungal cultures, from survey results, yielded primarily Candida spp. followed secondarily by Aspergillus spp.

4. Intrauterine Usage of Antibiotics

Antibiotics may be placed into the uterus before or after breeding or in association with treatment of suspected or known uterine infections. Dosages for antibiotics commonly given intrauterine are presented in Table 1. Practitioners in the survey stated that antibiotics used before breeding were used for mares that were known to be problem breeders, mares that were repeat breeders, mares with uterine fluid before breeding, mares with excessive uterine edema, mares suspected of having an infection (awaiting culture/cytology results), mares suspected of having an infection (owners decline culture/cytology), or strictly at the owner’s request.

Survey participants stated that they used post-breeding antibiotics in situations in which they knew the mare had previous problems, in mares with uterine fluid, in those mares susceptible to post-mating-induced endometritis, in mares bred late in the breeding season, in mares with previous pregnancy loss, or as a routine procedure with a single dose of antibiotics, especially in natural cover situations. A study by Pycock found that pregnancy rates were better after a single dose of antibiotics (with/without oxytocin) after breeding, especially in older mares (>12 years) and mares...
mated at the first postpartum estrus. Some Thoroughbred farms may routinely use a single post-breeding antibiotic to limit bacterial contamination from natural cover.19

When asked how many days mares were commonly treated with intrauterine antibiotics, the responses were: 1 day (12%), 2 days (7%), 3 days (50%), 4 days (5%), 5 days (7%), 1 week (1%), other (13%), and no answer (5%). Those answering “other” may treat for 1 to 3 days, 3 to 5 days, number of days would depend on bacteria isolated, number of days would depend on presence of fluid, or would never treat a mare intrauterine. It has been recommended, based on endometrial biopsy, that treatment for mild intrauterine infections be performed for 3 days, moderate infections for 5 days, and severe infections for 7 days.13 The determination of how mares fit into these categories may not be clear in practice and would need to be subjectively based on clinical signs and possible cytologic examination because biopsy results may not be returned for a number of days. It has also been suggested that mares not be treated for more than 2 or 3 days after ovulation to decrease possible negative effects on corpus luteum progesterone secretion from prostaglandin released in response to endometrial antibiotic/solution irritation.13 Antibiotics should also not be used immediately before breeding because high concentrations of antibiotics may negatively affect sperm function.13

Forty-three percent of practitioners would increase the volume of antibiotic solution infused to between 50 to 100 mL before infusion: 8% used whatever volume the antibiotic originally came with; 19% added extra volume but kept the total less than 50 mL; 11% added extra liquid so that the final volume was less than 100 mL; 7% simply added their antibiotic to their lavage solution; 6% did not answer the question; 8% provided an alternative answer of “other,” which included leaving some lavage solution in the uterus and simply adding antibiotics to that, using a 250-mL bottle for infusion with antibiotics added, or using a 10-mL or 20-mL total volume. The literature has suggested intrauterine infusion volumes ranging from 30 to 200 mL to achieve distribution throughout the uterine lumen.3 Six grams of ticarcillin, for instance, has a higher intrauterine concentration over time when a 250-mL volume is infused rather than a 60-mL volume.20 With large volumes, however, reflux of fluid back through the cervix could occur, diminishing the overall dose. A more appropriate recommendation may be to maximize the volume of distribution of an antibiotic while factoring in the relative size and position of the uterus. Multiparous mares would naturally require more volume of distribution, whereas nulliparous mares should require less. With a dependent uterus, infused fluids tend to pool in the base of the uterine horns, making it difficult to achieve uniform coverage of the endometrium; con-

Table 1. Intrauterine Antibiotic Dosages

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Antibacterial Antibiotics</th>
<th>Major Bacterial Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>1 to 2 grams</td>
<td>Buffer with sodium bicarbonate or 150- to 200-mL solution</td>
<td>Gram negative</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1 to 3 grams</td>
<td>Use soluble product, may be irritating when concentrated</td>
<td>Gram positive and E. coli</td>
</tr>
<tr>
<td>Cefiofur sodium</td>
<td>1 gram</td>
<td>Can be irritating</td>
<td>Gram positive and Gram negative</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>2 to 3 grams</td>
<td>Acidic: Need to dilute and/or buffer</td>
<td>Gram positive and Gram negative</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>1 to 3 grams</td>
<td></td>
<td>Gram negative</td>
</tr>
<tr>
<td>Neomycin</td>
<td>2 to 4 grams</td>
<td></td>
<td>Gram negative</td>
</tr>
<tr>
<td>Potassium penicillin</td>
<td>5 million international units</td>
<td></td>
<td>Gram positive</td>
</tr>
<tr>
<td>Procaine penicillin</td>
<td>4.5 to 6 million international units</td>
<td>Concern about residue left in uterus</td>
<td>Gram positive</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>3 to 6 grams</td>
<td>Infuse with 150- to 200-mL solution</td>
<td>Gram positive, Pseudomonas</td>
</tr>
<tr>
<td>Ticarcillin with clavulanic acid</td>
<td>3 to 6 grams</td>
<td>β-Lactamase inhibitor, infuse with 150- to 200-mL solution</td>
<td>Same as ticarcillin plus more Gram positive (Staph, Bacillus, Enterobacter)</td>
</tr>
</tbody>
</table>

Drug | Dosage | Antifungal Antibiotics q 24 Hours for 7 Days | Comment |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>100 to 200 mg</td>
<td>Polyene, dilute in &gt;100-mL solution, mix well</td>
<td></td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>400 to 700 mg</td>
<td>Azole, tablets usually crushed and mixed with solution</td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>100 mg</td>
<td>Azole, may need to adjust pH to avoid acidic nature</td>
<td></td>
</tr>
<tr>
<td>Miconazole</td>
<td>500 to 700 mg</td>
<td>Azole</td>
<td></td>
</tr>
<tr>
<td>Nystatin</td>
<td>0.5 to 2.5 million international units</td>
<td>Polyene, Dilute in sterile water, not saline to avoid precipitates, mix well</td>
<td></td>
</tr>
</tbody>
</table>
sequently, systemic antimicrobials may be a good choice in these mares.

The most common antibiotic in the survey used for intrauterine treatment before receiving culture/antibiotic sensitivity results was ceftiofur (21%), followed by gentamicin (19%), ticarcillin with clavulanic acid (13%), ampicillin (12%), other (12%), procaine penicillin (5%), amikacin (5%), potassium penicillin (3%), and ticarcillin (3%). Nine percent of survey participants did not answer this question. The category “other” included combination of penicillin and gentamicin (2%), penicillin and neomycin (2%), ampicillin and gentamicin (1%), oxytetracycline, framomycin, framyctin, cefquinome, cefazolin, or chloramphenicol. Interestingly, procaine penicillin was used even though there are no reported dosages listed in most antibiotic reviews. Some practitioners had concern about residues that may be left within the uterus with the use of the procaine penicillin suspension. Enrofloxacin has been given intrauterine without causing more than a moderate inflammatory response, but there are other reports that the basic pH of enrofloxacin is very irritating to the endometrium. Differences in reports may be due to the formulation studied in various countries and dosage; thus, caution should still be exerted when considering intrauterine enrofloxacin, or, alternatively, systemic enrofloxacin should be used.

If we examine some of the more common antibiotics used in practice, one report found that 19% of β-hemolytic Streptococcus (includes S. zooepidemicus) were susceptible to gentamicin, whereas 96% of E. coli were susceptible. One hundred percent of their β-hemolytic Streptococcal isolates were susceptible to ampicillin and penicillin G, whereas 96% of E. coli were susceptible to ampicillin. Ceftiofur was not examined in this study. A separate study looked at intrauterine ceftiofur in mares, demonstrating good antimicrobial activity and no increase in uterine inflammation, through biopsy.

Ticarcillin with clavulanic acid has been examined for intrauterine use and found that the clavulanic acid portion does not maintain adequate intrauterine concentrations and thus this formulation may be questionable for intrauterine use. They also discovered that intrauterine ticarcillin declined rapidly and probably would require multiple-day dosing for adequate coverage.

Aminoglycosides have an acid pH that will irritate the endometrial lining. It is suggested that aminoglycosides be buffered to a more neutral pH, with an equal volume of 7.5% sodium bicarbonate. Forty-three percent of practitioners added sodium bicarbonate, whereas 38% increased the volume of infusion as a means to moderate the acidic effects, and 10% did not add anything to the aminoglycoside. If saline is used to increase the volume of infusion to dilute the effect of a lower pH, it should be noted that saline has a pH of ~5.5. A more suitable diluent may be lactated Ringers solution, which has a neutral pH.

Aminoglycosides should not be mixed with β-lactam antibiotics. Precipitates may form on combination, or, more importantly, aminoglycosides may cause a nucleophilic opening of the β-lactam ring, which then combines with an amine group from the aminoglycoside, resulting in a biologically inactive amide. Although the two drugs are synergistic in controlling Gram-positive (β-lactams) and Gram-negative (aminoglycosides) infections when given systemically, it is not completely understood how effective they are when placed together into the uterine lumen. In addition, penicillin G (potassium or procaine) is inactivated by acids, so if penicillin and an aminoglycoside are used together in an unbuffered form, the penicillin may be less effective because of the low pH environment caused by the aminoglycoside. From survey results, it appears that quite a few practitioners (34%) mix the two classes of drugs together in the same syringe (20%) or the drugs are given intrauterine at the same time (14%). For maximum effectiveness, mixing these drugs intrauterine should be discontinued, and the drugs should be given either systemically or separated in time by an unknown number of hours if given intrauterine. It is also not recommended to mix the two classes of drugs in lavage solutions. Interestingly, there are many semen extenders that combine potassium penicillin and amikacin. This practice may also result in somewhat diminished antibiotic effectiveness. Conversely, of the aminoglycosides, gentamicin has a high rate of inactivation when mixed with certain β-lactams, whereas amikacin is only slightly inactivated.

When asked about which antifungal intrauterine drug they used before receiving culture results, the majority of practitioners (32%) would not use an antifungal drug but instead opted for a betadine solution lavage, lufenuron, or, less commonly, a dilute vinegar lavage. If an antifungal drug was used, then the most common responses included clotrimazole (17%), nystatin (11%), miconazole (10%), fluconazole (8%), and amphotericin B (3%). No answer was provided by 19% of the respondents. Only 53% of practitioners submitted fungal cultures for sensitivity assay. Not having proper antibiotic sensitivity patterns to determine the most appropriate therapy may explain, in part, why fungal uterine infections are difficult to treat. The reasons stated for not submitting fungal cultures for a sensitivity assay are the length of time to receive result; had success with iodine lavage; all seem sensitive to amphotericin B; inability to obtain fungal sensitivities from the lab; the relative infrequency with which fungal infections were encountered precluded sensitivity testing; just treated Candida infection with nystatin; or treating appears to work just fine. There are a number of laboratories that offer fungal sensitivity patterns, including the laboratory at Cornell University. There was also concern from practitioners
that in vitro sensitivity patterns may not correlate with in vivo effectiveness. It would appear that within the group of polyene antifungal antibiotics, amphotericin B (96% susceptibility for all fungal organisms) and nystatin (100% susceptibility) are good choices, whereas clotrimazole (80% susceptibility) or ketoconazole (81% susceptibility) are good choices when using azole antifungal antibiotics. Polyene antibiotics are generally considered fungicidal, whereas azole antibiotics are fungistatic, unless at higher doses. Some practitioners try to avoid intrauterine antifungal treatments with the concern that repeated intrauterine treatment may make the mare more susceptible to reinfection or prolonged inflammation. An alternative would be oral antifungals, which may be expensive.

Lufenuron is a chitin inhibitor that has been used off-label for treatment of fungal intrauterine infections at the intrauterine dose of 540 mg of lufenuron suspension in 60 mL of sterile saline. It should be noted that lufenuron affects the wall of growing fungi and may not be appropriate for treatment of mature infections because chitin is already formed in fungal cell walls with mature infections. A better approach may be to treat with an antifungal antibiotic and then, at the end of treatment, place lufenuron intrauterine to prevent new growth. The effectiveness of lufenuron still remains in question.

Uterine lavage with either iodine or vinegar is a component of therapy for many veterinarians when treating fungal infections. Forty percent of veterinarians used a dilute iodine solution for lavage (24% added iodine to saline, 16% iodine added to lactated Ringers solution). The percentages of iodine in lavage solutions in the survey range from 0.02% (2 mL of 10% iodine per liter) to 0.5% (50 mL of 10% iodine per liter). A 0.2% solution of intrauterine iodine has been associated with endometrial inflammation and fibrosis. A 0.01% to 0.05% solution of iodine still maintains antimicrobial activity without the associated inflammation and fibrosis. This equates to 1 to 5 mL of 10% iodine in 1000 mL of sterile saline. Practitioners should be cautious of the higher-concentration intrauterine iodine solutions. Twenty-two percent of veterinarians used a dilute vinegar solution (15% of practitioners added vinegar to saline, 7% added it to lactated Ringers solution). When using vinegar, saline would be a more appropriate lavage solution if the desire is to lavage with a lower pH solution. Addition of 20 mL of white vinegar to 1000 mL of saline (2% v:v solution) will reduce the pH from ~5.5 to ~3, whereas it has little effect on the pH of lactated Ringers solution.

Intrauterine antibiotics and lavage should be avoided within 4 hours of breeding so that spermatozoa are not negatively affected by the drugs/solutions themselves or the vehicles in which they are delivered. Four hours after insemination, spermatozoa are located in the oviduct, and intrauterine treatment at this time does not have a negative effect on fertility. Most practitioners in the survey appeared aware of this, with only 16% of them placing antibiotics within 4 hours after insemination. Most practitioners (37%) naturally waited past 4 hours after breeding as their next examination, and thus treatment of the mare was not until the next day.

5. Systemic Antibiotics

The decision to use systemic antibiotics either in combination with intrauterine, after intrauterine, or instead of intrauterine antibiotics may be due to personal preference, desire to prolong the treatment period, because the organism is not susceptible to nonirritating drugs, or to avoid manual reproductive tract manipulations. From the on-line survey, systemic antibiotics are chosen when intrauterine treatments go beyond 3 to 5 days, when treating mares with metritis, when treating mares with contaminated caudal reproductive tracts, when treating mares with anatomical defects of the caudal reproductive tract, or occasionally when treating mares with fungal infections. It was thought that systemic antibiotics negate the need to invade the uterus, possibly avoiding the chances of iatrogenically placed bacteria/fungi. The downsides to using systemic antibiotics are increased costs and inconvenience from having to dose at the animal’s full body weight, possibly treating multiple times per day, and potential adverse effects on gastrointestinal bacterial flora. A very small number of practitioners thought that it was not good veterinary practice to place antibiotics intrauterine, since systemic antibiotics work well, do not cause endometrial irritation, and do not lead to further contamination.

Dosages for antibiotics commonly used systemically are presented in Table 2. Trimethoprim sulfa-diazine, ceftiofur, and a combination of penicillin and gentamicin were the most common antibiotics administered from the survey. Trimethoprim sulfamethoxazole (30 mg/kg, per os, q 12 hours) was found to provide adequate antibiotic concentrations in fetal tissues in mares with placentitis. In a separate study, ceftiofur dosed at 2 mg/kg q 12 hours intramuscularly did not obtain endometrial tissue levels; however, it has been suggested as a potential treatment for mares with placentitis. In cattle, ceftiofur has achieved in endometrial tissue minimal inhibitory concentrations after subcutaneous administration. A study by Murchie et al. found that penicillin G potassium and gentamicin sulphate administered intravenously achieved adequate allantoic fluid concentrations in pregnant pony mares. Enrofloxacin has also been used in mares with more resistant bacteria. Enrofloxacin should not be used in pregnant mares.
because of effects on developing cartilage. Doxycycline has also been demonstrated to achieve adequate endometrial concentrations above the minimum inhibitory concentration for *S. equi* subspecies *zooepidemicus*. Antifungal antibiotics may be administered systemically. Amphotericin B is fairly caustic as the result of a low pH and must be given via nasogastric intubation or diluted and given slowly intravenously. Oral fluconazole has been recommended for treatment of *Candida* spp., whereas oral itraconazole has been suggested for treatment of *Aspergillus* spp.

### 7. Treatments to Augment Antimicrobial Therapy

Uterine lavage is recommended to remove uterine debris and bacteria/fungi and to enhance uterine contractility. DMSO lavages may be useful to augment antimicrobial tissue penetration and to disrupt microbial biofilms. Acetylcysteine and kerosene have also been suggested as possible mucolytic agents. Biofilms are aggregates of bacteria and/or fungi encased in an adherent polymeric matrix, which may inhibit antibiotic penetration. Biofilms have been known to form with *Pseudomonas aeruginosa*, *E. coli*, *S. aureus*, *K. pneumonia*, and *Candida* spp.

Tris-EDTA has been demonstrated to act synergistically with antimicrobials by increasing the membrane permeability of bacteria to these drugs. Uterine lavage with Tris-EDTA, either alone or in combination with antibiotics, should be considered with resilient infections or in cases with antibiotic-resistant organisms.

### 8. Conclusions

Veterinarians should base antibiotic therapy on sensitivity testing. Consideration should be given to antibiotic therapy alternatives such as proper breeding management, use of uterine lavage, and oxytocin/prostaglandin treatment. Biofilm formation should be appropriately treated to enable antibiotic access to bacteria/fungi. With a plan, antibiotic usage can be minimized and treatment success optimized. The main issues identified from the on-line survey of veterinarians are the mixing of intrauterine β-lactam and aminoglycoside antibiotics, the use

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**Table 2. Systemic Antibiotic Dosages**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>10 mg/kg q 24 h</td>
<td>IV or IM</td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>29 mg/kg q 12 to 24 h</td>
<td>IV or IM</td>
<td></td>
</tr>
<tr>
<td>Ceftiofur</td>
<td>2 to 4 mg/kg q 12 to 24 h</td>
<td>IV or IM</td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>10 mg/kg q 12 h</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>5.5 mg/kg q 24 h</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.5 mg/kg q 24 h</td>
<td>Per os</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.0 mg/kg q 12 h</td>
<td>Per os</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>6.6 mg/kg q 24 h</td>
<td>IV or IM</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>15 to 25 mg/kg</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>6.6 mg/kg q 12 h</td>
<td>IV, dilute and give slowly</td>
<td></td>
</tr>
<tr>
<td>Potassium penicillin</td>
<td>22,000 IU/kg q 6 h</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Procaine penicillin</td>
<td>22,000 IU/kg q 12 h</td>
<td>IM, only 10 mL per injection site</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim sulfa</td>
<td>30 mg/kg q 12 h</td>
<td>PO</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>0.3 to 0.9 mg/kg q 24 to 48 h</td>
<td>IV</td>
<td>Polyene, Dilute and give slowly</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>14 mg/kg loading, then 5 mg/kg q 24 h</td>
<td>IV or per os</td>
<td>Azole</td>
</tr>
<tr>
<td></td>
<td>Alternatively, 2 grams q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>5 mg/kg q 12 to 24 h</td>
<td>IV or per os</td>
<td>Azole, oral suspension more bioavailable than capsules</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>20 mg/kg q 12 h in 0.2 N HCl</td>
<td>Per nasogastric intubation</td>
<td>Azole, irritant if given per os due to low pH; need to place into stomach</td>
</tr>
</tbody>
</table>

IV, intravenous; IM, intramuscular; PO, per os; IU, international units.
of higher concentrations of iodine solutions intrauterine, the use of lactated Ringers solution with vinegar for uterine lavage, and the treatment of mares less than 4 hours after breeding with intrauterine antibiotics. Consideration should be made toward the idea that organisms may develop deep-seated infections within the endometrium, possibly making systemic antibiotic administration a better choice in chronically infected mares.

References and Footnote

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*Coutinho da Silva M. Personal communication, 2010.