A comparative efficacy trial for timethoprim-sulfamethoxazole, gentamicin and penicillin, using an ex vivo model of gestational disease

Katherine McKelvey, Megan Jacob, Mark Papich, Theresa Beachler, C. Scott Bailey
College of Veterinary Medicine, North Carolina State University, Raleigh, NC

Treatment of equine placentitis and other infectious reproductive diseases relies heavily on antibiotics. However, clinical efficacy of commonly used antibiotics is poor. In our laboratory, we developed an ex vivo model to study antibiotic efficacy under conditions characteristic of pregnancy and uterine disease.

In the current study, we aimed to test antibiotic efficacy of four antibiotics against *Escherichia coli* (EC) and *Streptococcus equi* subsp. *zooepidemicus* (SEZ) in Mueller Hinton broth (MHB), fetal fluids (FF) or purulent uterine fluid (PUF). Known concentrations of bacteria and two physiologically achievable concentrations (high [H]/low [L]) of trimethoprim-sulfamethoxazole (TMS), potassium penicillin (P; SEZ only), gentamicin sulfate (G), or P and G together were added to sterile autoclaved fluid. Each combination was incubated in triplicate for 8 hours, and serial dilutions were plated for quantitative assessment of bacterial load.

In PUF inoculated with EC, antibiotics were not effective, with greater than 3 log₁₀ growth in all samples. Bactericidal activity (3 log₁₀ reduction in bacterial concentration) was achieved by all antibiotics in MHB, and by either TMS or PGH in FF. Bactericidal activity against SEZ was achieved only by PGH, regardless of fluid-type. Penicillin alone (PH, PL) and PGL were bacteriostatic in all fluid types, while TMS and G lost efficacy against SEZ (bacterial growth at 8 hours) in PUF or PUF and FF, respectively.

These findings demonstrate a profound impact of physiologic fluids on antibiotic efficacy, with PG performing best under the study-conditions. Further work to understand the mechanisms by which these antibiotics are inhibited is warranted.

**Keywords:** Equine, placentitis, antibiotics, *Escherichia coli*, *Streptococcus equi* subsp *zooepidemicus*

**Acknowledgments**
Mitsu Suyemoto and Tonya Harris

**Reference**