

ENDOTOXEMIA: Two Approaches Robert J. MacKay, BVSc, PhD

Robert J. MacKay, BVSc, PhD has been leading a team of scientists at the University of Florida in the study of "Production and Application of Specific Antibodies to Equine Tumor Necrosis Factor: Relevance to Equine Endotoxemia". This study has received funding from the American Association of Equine Practitioners and Morris Animal Foundation.

PROBLEM: Horses are peculiarly susceptible to the effects of a molecule called endotoxin. Endotoxin is part of the bacteria which live normally in the intestine of all animals. Sometimes, because the intestinal wall is damaged, endotoxin escapes from the intestine and enters the blood stream causing endotoxemia. Once endotoxin contacts blood, the defense of the affected horse are so thoroughly activated and misdirected that the horse essentially kills itself. Thus, in many cases of colic, salmonella, diarrhea, and blood poisoning of foals, the principle reason that horses die is the complicating effect of endotoxemia. Even though the response to endotoxin is complicated and overwhelming, it has been found that a single molecule, called tumor necrosis factor (TNF) sets all other events in motion.

FINDING: The investigators hypothesized that neutralizing TNF with an anti-TNF antibody might prevent the lethal effects of endotoxemia. They developed a technique to isolate TNF from the plasma of horses. They were able to separate out enough TNF to inoculate some mice and produced a cell line capable of producing indefinite amounts of antibody against horse TNF. They showed that it could neutralize TNF in two

situations, in the knee-joints and the bloodstream of horses.

In both cases a positive clinical effect of treatment was demonstrated. In the latter case, the scientists believe that the beneficial effect was so marked that the antibody has the potential to save the lives of horses with endotoxemia.

Michelle Henry Barton, DVM, led another team of scientists investigating endotoxemia with funding from Morris Animal Foundation at the University of Georgia in the study "The Effect of Pentoxifylline on Equine Endotoxemia".

PROBLEM: Colic is the leading cause of death in horses and is associated with the absorption of bacterial endotoxin into the blood. These endotoxins are deadly because they activate blood cells to make mediators, which in turn cause shock by altering the blood flow to vital organs.

FINDING: The scientists studied the effect of a drug, pentoxifylline, on the ability of horse blood to make mediators when exposed to endotoxin in a test tube. It was found that pentoxifylline reduced the production of harmful mediators. These results suggest that pentoxifylline may be a beneficial drug for the treatment of endotoxemia in horses.

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