Preliminary Evidence of Fetal Cortisol Production in Response to Inflammation in a Model of Equine Placentitis

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Experimentally induced fetal infection in mares increased expression of interleukin (IL)-1β, IL-18, IL-15, and interferon (IFN)-γ, and abortion increased expression of IL-1β, IL-18, IFN-γ, and inducible nitric oxide synthase in a site-dependent manner. Cortisol concentrations in fetal fluids increased substantially before spontaneous abortion in mares with fetal infection and placentitis or with fetal aseptic fibrinous pneumonia and placential edema. Authors’ addresses: Department of Veterinary Clinical Sciences, School of Veterinary Medicine (Lyle, Johnson, Eilts, Paccamonti) and the Department of Animal Sciences, College of Agriculture (Gentry, Godke), Louisiana State University, Baton Rouge, Louisiana 70803; and the Gluck Equine Research Center, Department of Veterinary Science, University of Kentucky, Lexington, Kentucky 40546 (Horohov); e-mail: slyle@lsu.edu. © 2009 AAEP.

1. Introduction
In a previous study, the hypothalamic-pituitary-adrenal axis (HPAA) in equine fetuses ≤295 days of age was immature and could not produce cortisol in response to adrenocorticotropic hormone (ACTH).1 In mares with induced ascending placentitis, prostaglandin F2α, and prostaglandin E2 were synthesized in response to pro-inflammatory cytokines and fetal cortisol.2 The objectives were to quantify equine-specific cytokines in chorioallantois tissue and cortisol concentrations in maternal plasma and fetal fluids from mares with in utero infection, with or without subsequent abortion.

2. Materials and Methods
In 13 adult pony mares, allantoic catheters were placed3 between 260 and 285 days of gestation,4 and mares were allocated to the following five treatments: 1 × 10⁷ CFU Streptococcus zooepidemicus (n = 3), 5.1 × 10⁸ CFU S. zooepidemicus (n = 1), 1 × 10⁷ heat-killed S. zooepidemicus (n = 3), 1 ml sterile phosphate-buffered saline (n = 3), and sham control groups (n = 3). Fetal fluid and maternal plasma were collected every 24 h, and cortisol concentrations were determined by radioimmunoassay. Four areas of the chorioallantois were collected at delivery and stored in RNA stabilization reagent, and expression of 11 equine-specific cytokines was determined.
3. Results and Discussion

Seven mares developed in utero infection, but six remained uninfected. Infection increased the expression of interleukin (IL)-1β, IL-18, IL-15, and interferon (IFN)-γ, whereas mares that aborted had increased expression of IL-1β, IL-18, IFN-γ, and inducible nitric oxide synthase (all increases were site dependent). In 12 mares (6 with and 6 without uterine infection), there was no significant linear relationship between cortisol concentrations in maternal plasma and fetal fluids. However, fetal cortisol concentrations increased substantially before abortion in three mares (two with fetal infection and placentitis and one with fetal aseptic fibrinous pneumonia and placental edema), confirming HPAA function at 80% gestation. All mares with increased fetal fluid cortisol concentrations had >25-fold increased expression of IL-1β at the cervical star, normal, and abnormal areas of the chorioallantois. These findings suggest that pro-inflammatory cytokines released secondary to uterine infection or inflammation may provide a signal for HPAA activation before 295 days of gestation.

This work was funded by the Equine Health Studies Program, School of Veterinary Medicine, Louisiana State University.

References