

INSULIN DYSREGULATION: PLACENTAL CHANGES AND FOAL HEALTH

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This study investigates the role of equine metabolic syndrome on placental function and foal health and metabolic outcomes in order to develop effective treatment and management regimens.



Equine metabolic syndrome (EMS), characterized by insulin dysregulation, is the leading cause of laminitis, affects all horse breeds and is one of the most common diseases facing horse owners. However, we do not understand the impact of EMS in pregnant mares on her foal's health or metabolism. EMS is common in broodmares due to their diets, lack of exercise, and the practice of maintaining broodmares at a higher body condition to ensure that the foal is receiving adequate nutrition to grow. Humans suffering from diabetes, a similar condition to EMS, experience long bouts of high blood glucose and insulin levels, which have been shown to significantly change how the placenta functions. These changes increase the risk of the mother going into early labor, having difficulty giving birth, stillbirths, or the baby requiring hospitalization. Therefore, there is a gap in knowledge of the effects of a mare having EMS on placental function and foal health outcomes which prevents owners knowing how to manage their pregnant mares to have a healthy, athletic foal.

In this study, we will investigate the role that EMS has on placental function and foal health and metabolic outcomes in order to develop effective treatment and management strategies. We hypothesize that EMS leads to an increased risk of mare placental dysfunction, which is associated with health and metabolic outcomes in their offspring.

In Aim 1 we will assess the placenta at the microscopic level for changes in cellular structure and damage in mares with and without EMS. We hypothesize that placentas from EMS mares will have changes similar to what has been found in pregnant women with diabetes.

In Aim 2 we will assess changes in how genes are expressed (turned on or turned off) in the placenta of mares with and without EMS. We hypothesize that alterations in placental gene expression in pathways related to

inflammation, metabolism and growth will be associated with a mare's EMS status.

In Aim 3 we will compare events at birthing, neonatal health and metabolic outcomes between foals within their first year of life born from mares with and without EMS. We hypothesize that foals born to mares with EMS will have a higher incidence of adverse events in the first few days of life and changes in growth and insulin resistance in their first year. This is supported by evidence in horses that maternal obesity, a risk factor for EMS, leads to an increased incidence of poor-quality colostrum, fetal insulin resistance, and chronic inflammation.

This project will have a great impact on the horse industry as this is the first time that placental function will be assessed in EMS affected mares at both the cellular and genetic level. This will allow us to link foal health outcomes with placental dysfunction. This will also allow us to identify changes that can be screened during a mare's pregnancy to help guide timely treatment and management strategies. The impact on the horse industry will be notable as EMS affects all breeds, and nearly a quarter of broodmares. If EMS is a risk factor for placental dysfunction, resulting in failure of passive transfer or neonatal disease, early management strategies in mares could prevent foal loss and save owners \$5000-15,000 in hospitalization costs and emotional distress. Our strong team with expertise in neonatal, metabolic and reproductive health is well suited to assess the complexities afforded by maternal/ placental/fetal interactions in order to best identify treatment and management strategies needed to improve foal health outcomes.

Importance to the Equine Industry: The industry impact is notable as equine metabolic syndrome affects all breeds of horses and is the leading cause of laminitis, costing the equine industry over \$15 million dollars annually.

This number is continuing to rise as the reported prevalence of EMS has reached up to 25% in high-risk populations, with our preliminary data confirming that broodmares are amongst the high-risk groups. Impacts on foal health due to placental dysfunction, such as failure of passive transfer, sepsis or dummy foals can have a mortality of up to 25% and cost owners \$5000-15,000. Identification of EMS as a significant risk factor for the above has the potential to improve foal health and thus reduce the financial and emotional cost to owners.