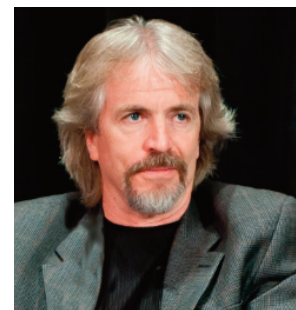


RESEARCH UPDATE 6

Ongoing and recent projects funded by Grayson-Jockey Club Research Foundation



Dr. James Belknap, The Ohio State University: Developments in Laminitis Studies

Summary---

The funding by the Grayson-Jockey Club Research Foundation and the NTRA (Barbaro Fund) of our last two projects on the efficacy of cryotherapy in laminitis has allowed us to bring to fruition a great deal of effort by many investigators over several decades. This has furthered our understanding of laminitis and to truly bring to the forefront the first laminitis therapy which has passed thorough scientific rigor as an effective therapy for laminitis. Laminitis is a disease in which the hoof wall separates from the soft tissue attached to the distal phalanx (coffin bone), resulting in the distal phalanx undergoing a crippling displacement towards the ground surface of the hoof. Although laminitis is one of the most common diseases that leads to the humane destruction of the horse, treatments for the disease were frustratingly unsuccessful for the past few decades, mainly due to fact that we did not understand the pathophysiology of the disease we were attempting to treat.

Scientific Detail:

One type of laminitis, sepsis-related laminitis, occurs in horses suffering from diseases which lead to absorption of bacteria (or their toxins) through a compromised intestinal wall as occurs in enterocolitis/diarrhea, and severe surgical conditions of the intestinal tract such as colon torsions. At the same time my laboratory was investigating the inflammatory pathways involved in sepsis-related laminitis in the early 2000's (the GJCRF funded my first study on laminar inflammatory changes in laminitis), Chris Pollitt and Andrew van Eps were performing their first studies on the safety and efficacy of cryotherapy (digital hypothermia induced by immersing the digits and lower limbs in an ice bath). Although the use of cryotherapy on equine digits had been studied for over ten years by other investigators using the very short time periods used for cryotherapy in human medicine, the Pollitt laboratory established for the first time that horses, unlike humans, could sustain local (digital) hypothermia continuously for at least 48 hours with no adverse clinical effects. In the same year, Pollitt and van Eps also published the first study indicating that cryotherapy of the distal limb decreased the histologic (microscopic) changes to the digital laminae in a carbohydrate overload model of laminitis.

One large advantage in laminitis research is that the veterinary researchers have a tradition of working together on projects, and sharing their data with other groups. As there are only approximately ten laboratories that perform laminitis research throughout the world, we have felt that it is imperative that we work together to have the best chance of moving our understanding (and therefore the treatment) of this disease forward. When I met with Pollitt and van Eps at a laminitis workshop funded by the Dorothy Havemeyer Foundation in the late 2000's, we decided to put our two areas of research together to assess whether cryotherapy would be effective in blocking the severe laminar inflammatory changes that my lab had documented to occur in sepsis related laminitis. The GJCRF funded this collaborative research effort between University of Queensland and Ohio State University. This research, combined with the data our laboratories had already published on cryotherapy and laminar inflammation, was really a turning point as it, for the first time, demonstrated a therapy that was effective at blocking the deleterious inflammatory signaling that likely leads to laminar failure in sepsis-related laminitis. The importance of this GJCRF-funded research is that, although billions of dollars have been spent in hundreds of research laboratories to find an effective therapy for the inflammatory injury that causes organ injury and failure in human sepsis, we have managed to surpass them by first finding an effective treatment for laminar injury in the septic horse. We do have some advantages over our human counterparts- mainly that we are treating a peripheral tissue in which we can use isolated therapy compared to the central tissues such as the lung and liver affected in human sepsis- but it is still a monumental step forward which could not have happened without the concerted effort of funding agencies such as the GJCRF (and their donors) and the research laboratories investigating this crippling disease.

Although we felt that we'd made a great step forward, we had only established that cryotherapy was effective when initiated very early in the process, long before the animals demonstrate clinical signs of laminitis including lameness. As most of us who perform laminitis research are clinician researchers who treat laminitis cases in the clinical aspect of our jobs, we were acutely aware that we had not answered the question of whether cryotherapy would still be effective if initiated at the time the animals exhibit clinical signs of laminitis-related lameness (the time that many veterinarians are called to examine-and treat-a clinical case of laminitis for the first time). Through another GJCRF funded grant, we are in the middle of the project to investigate this question, but have already been able to demonstrate that cryotherapy is incredibly effective at maintaining the laminar structural integrity even when not implemented until the horse exhibits clinical signs of laminitis. These two projects are examples of the GJCRF providing critical funding to bring together researchers from around the world to begin to understand a disease process and establish effective, scientifically tested treatment protocols to limit the numbers of animals, owners, and trainers who have to experience the devastating nature of a disease such as laminitis. Although we are moving more rapidly every day due to the incredible research tools now available to us, cutting edge research tools are very expensive. At a time when many sources of scientific research funding have reached record low levels of funding, the veterinary community depends on funding by research foundations such as the GJCRF if we are going to continue to make progress in treating the disease processes which adversely affect the horse and the entire equine industry.