Equine Research News
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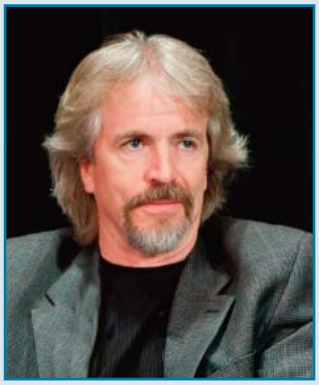
DIGITAL HYPOTHERMIA IN LAMINITIS: TIMING AND SIGNALING

By Jamie Haydon



Dr. James Belknap
DVM, PhD, DACVS
Professor Equine Surgery, The Ohio State University

This interview with Dr. James Belknap covers some of the six projects funded for him and colleagues by Grayson-Jockey Club Research Foundation, keying on promising developments about laminitis from these and other studies. Dr. Belknap was elected to the International Equine Veterinarian Hall of Fame in 2012.

What first sparked your curiosity to explore this area of equine research? Have you studied this area of equine research before?

I have had an interest in studying laminitis for more than 30 years, and have run a laboratory focusing on laminitis pathophysiology and treatment for 21 years. My interest in laminitis was sparked during my large animal internship at University of Georgia, working with Drs. Jim Moore and Doug Allen. Jim was running an impressive research program at that time on equine sepsis; Doug was both active in the research aspect and very active regarding clinical case management of laminitis. I published one retrospective study with Dr. Moore on laminitis that year, then did not return to laminitis research for 10 years.

During that time I completed an equine surgery residency, spent two years in practice, then returned to my alma mater, Colorado State University, for a PhD in cardio-pulmonary physiology. In 1996, when I started my first academic job at Auburn University, I again collaborated with Drs. Moore and Allen on a grant where we first demonstrated inflammatory signaling in a model of sepsis-related laminitis. Since that time, I've been lucky enough to have received approximately 4 million dollars in research funding from multiple agencies---working with many stellar collaborators---to study all types of laminitis.

What was the most significant finding from this research? What, if anything, surprised you about your findings?

The grant, "Hypothermia on inflammatory injury in laminitis," was a collaborative effort between me and Dr. Chris Pollitt and his graduate student, Andrew van Eps, at University of Queensland. We had previously published inflammatory signaling in models of sepsis related laminitis, and they had published that digital hypothermia (immersing the feet in an ice slurry constantly) was protective against lamellar failure in a model of sepsis-related laminitis.

I honestly was pretty cynical about this new therapy and thought that we'd show that it was ineffective in changing the inflammatory signaling occurring in the disease process. The results were some of the most dramatic results I had seen; the hypothermia treatment effectively blocked the expression of a wide range of inflammatory mediators. This was the first work

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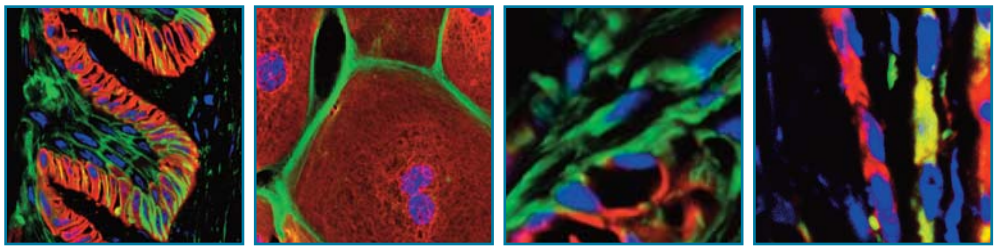
to show that hypothermia was actually changing cellular signaling in the lamellae.



Grayson Funded Laminitis Study Slides Courtesy The Ohio State University

Although that first study demonstrated the efficacy of hypothermia in blocking inflammatory signaling in horses at risk of laminitis, the hypothermia was initiated prior to the onset of disease. We---and veterinarians---were then interested to determine if hypothermia were an effective therapy when not initiated until the horses exhibited signs of lameness.

In the second study funded by Grayson with myself and Dr. van Eps as the main investigators, Digital hypothermia in laminitis: timing and signaling, we determined that hypothermia provides profound protection against lamellar failure even when not initiated until the animal exhibits early clinical signs of laminitis. This study provided the data necessary for a more intensive use of the treatment in the clinical case. Its efficacy has now also been reported in a clinical study of septic horses at risk of laminitis; **the treatment is commonly used throughout the world.**

What did you learn about the research process through your project?

As in many projects, I realized that unexpected results are commonly those that are most important. Another important lesson was the power of collaboration between investigators with different strengths; I have been constantly collaborating with Drs. Van Eps and Pollitt since that first grant. Finally, we learned that well organized, well blinded (i.e., unbiased) investigations can lead to life changing advancements in veterinary medicine using a fraction of the money that has been investigated in the study of human diseases.

How will this research improve equine health and welfare?

Giving Drs. Pollitt and van Eps full credit for the pioneering work with hypothermia, our collaborative effort funded by GJCRF has led to the establishment of the first effective therapy for sepsis-related organ/tissue injury in either humans or horses. Has this research led to additional projects? Yes, we have recently been funded by the GJCRF to assess the efficacy of hypothermia in another type of laminitis, endocrinopathic laminitis. We are also in the midst of a study in which hypothermia was instituted at the time animals exhibit signs of systemic sepsis---the time most veterinarians institute hypothermia as a prophylaxis against sepsis-related laminitis.

In this model, we have shown a much more focused inhibition of signaling than in previous studies, allowing us to focus on these signaling mechanisms in search for therapeutic targets; we have recently found novel signaling related to growth factor signaling that is stimulated in all three types of laminitis, causes the same cellular breakdown of structural integrity in human diseases as occurs in laminitis, and, most importantly, is inhibited by hypothermia. Dr. van Eps and I have recently used these data from our GJCRF-funded studies to submit a USDA grant proposal to test a drug in blocking this signaling, which could lead to the first effective pharmaceutical therapy for laminitis.

Dr. Andrew Van Eps, *BVSc, PhD*
Associate Professor,
University of Pennsylvania SVM

New Junior Membership Program

The Foundation is proud to introduce our new Junior Membership program. The program is aimed at young horse enthusiasts to educate them about horse health in a fun and interactive way.

Admiral is the official ambassador for the program. He was named after Admiral Cary Grayson, for whom the original Grayson Foundation was named in 1940. Admiral Grayson, who assisted the organizers of the Foundation, owned a horse farm in Virginia and a racing stable.

Along with supporting equine research, each member receives a stuffed pony, an annual membership certificate with their pony's name, as well as a breed card with a photo of one of Admiral's equine buddies, such as Secretariat or the Snowman. Their story is on the back of the card. Periodic newsletter, *The Grayson Grazette*, will be emailed to each member and will highlight tips on the care and management of horses and ponies. There will also be fun activity pages, recipes and surprises in store for his fans. Special contest and sharing horse stories are planned for the future. Junior members also will have access to Admiral's email.

To sample our first newsletter please click here.

You can get a printable sign up sheet and more information by clicking here.

You may also sign up online your favorite young horse lover under our Membership page here.