

## Laminitis

**A**t the 2004 American College of Veterinary Internal Medicine (ACVIM) Medical Forum, Dr Jim Belknap discussed the latest thinking about cause and treatment of laminitis. He said that the pathophysiology behind equine laminitis is one of the most controversial topics in equine medicine. Given that the treatment modalities for laminitis are based on purported pathophysiologic mechanisms, laminitis therapy is also extremely controversial. His presentation was organized by the main theories addressing laminitis and the treatments proposed to address those theories.

### ALTERED DIGITAL BLOOD FLOW DUE TO VASCULAR TONE

A general conclusion from the studies supporting ischemia is that a decrease in laminar blood flow occurs in the developmental stages of laminitis owing most likely to venoconstriction and capillary collapse from increased interstitial pressure. Conflicting reports are present, using hoof wall temperature as an indicator of laminar blood flow, with 1 investigator reporting decreased temperature (and therefore blood flow) in the prodromal stage, whereas another investigator reports increased hoof wall temperature. The latter investigator proposes that the increase in hoof wall temperature is indicative of excessive blood flow to the laminae in the developmental stage of laminitis. However, a caveat using hoof wall temperature as an indicator of blood flow is that hoof wall temperature is likely to reflect the degree of shunting through the high concentration of arteriovenous anastomoses present in the laminar circulation, which may actually lead to decreased laminar capillary perfusion. The majority of treatments based on vasoactive mechanisms, including vasodilators and hemorrhheologic agents, have experienced an initial peak in their clinical use followed by a decreased enthusiasm by practitioners regarding their clinical efficacy over time.

### ALTERED DIGITAL BLOOD FLOW DUE TO THROMBUS FORMATION

Thrombi have been identified in vessels of laminitic digits in both experimental models and clinical cases of laminitis, and radioisotope-labeled platelets have been used to demonstrate localization of platelets and platelet-neutrophil complexes to the digital microvasculature in the laminitic horse. Although heparin (the main drug used in laminitis therapy to address thrombosis) was demonstrated to decrease the incidence of laminitis when given before carbohydrate overload, 2 clinical studies addressing heparin treatment as a preventive of laminitis in small intestinal colic cases reported conflicting results.

### INFLAMMATION AS A CAUSE OF LAMINITIS

Nonsteroidal anti-inflammatory drugs, the family of drugs that has best endured the test of time in the treatment of the clinical case of laminitis, also has the strongest experimental data to support its use. A recent report from Dr Belknap's laboratory demonstrated a 30-fold and 160-fold increase, respectively, in IL-1 $\epsilon$  and IL-6 gene expression in the laminae in the developmental stage of laminitis. He has also recently found a marked increase in gene expression of (cyclo-oxygenase enzyme) COX-2 in the laminae at the same early time point, with no change in COX-1 levels. Laminitis most commonly occurs secondary to diseases associated with endotoxemia, including gram-negative sepsis and acute abdomens. The main treatments used to directly address circulating endotoxin have been 1) commercial endotoxin antiserum, which has conflicting reports in the horse regarding efficacy to treat endotoxemia; and 2) polymyxin B, which has experimental support for treating endotoxemia but limited reported effects in experimental laminitis.

### BREAKDOWN OF THE BASEMENT MEMBRANE IN THE DIGITAL LAMINAE

The breakdown of the basement membrane underlying the epidermal cells of the secondary epidermal laminae has recently been well demonstrated using histologic and histochemical techniques in laminitic digits and coincides with upregulation and activation of matrix metal-

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loproteases such as MMP-2 and MMP-9. Like many treatments for laminitis, deep digital flexor tenotomy (DDFT) has appeared to enjoy something of a roller coaster in popularity in the last 15 years. Whereas 2 retrospective clinical studies of DDFT for chronic cases have reported long-term survival rates from 59% to 85%, a study of DDFT involving mainly acute cases reported disappointing results, with over 50% of the animals being euthanized within 1 month of surgery and no horses returning to any athletic performance.

A great deal of the advancement made in shoeing laminitis cases has come from Gene Ovniczek, who has combined 3 principles into his shoeing technique: 1) bringing the breakover farther back to decrease dorsal hoof wall stress; 2) markedly raising the heel to decrease tension on P3 by the DDFT; and—possibly most important—3) supporting P3 through application of a resilient substance to the entire caudal two thirds of the ground surface of the foot (vs solely applying frog pressure, as used in previous methods such as application of heart bar shoes or lily pads).