Mechanisms for development of laminitis

Until laminitis can be reliably induced in a natural pasture with measured changes of trigger substances in both grass and horses, I will consider all mechanisms for pasture laminitis theoretical.

Researchers in cattle laminitis are looking at the same factors as the equine researchers.
[Boosman abstract] Hopefully we can work together to solve this problem.

Insulin Resistance or Hyperinsulinemia

This has always been of special interest to me, as the only medical diagnosis as to why my horses have reoccurring laminitis is that they are insulin resistant. Their insulin levels while they were laminitic were 4-7 times higher than normal, and even when sound, my half Connemara's insulin is 2-4 times normal levels on 2 hours per day of grazing green grass. Insulin resistance is being linked to horses with chronic laminitis more and more frequently as more vets learn about this new diagnostic test for predisposition. The theory was first proposed by Field and Jeffcott (1989) when they showed that fat ponies and horses that had previously suffered from laminitis were far more intolerant to oral glucose loading than normal horses or ponies.

Several authors have suggested the concept of 'the Thrifty gene' operates in horses as well as in humans. (Frederick, 2002) This is similar to the reasoning as to why Native Americans are prone to Type 2 diabetes. Because they have been genetically selected to thrive on a low carbohydrate diet, their metabolisms are just not equipped to handle too much sugar. Where human diabetes manifests as a lack of insulin and high blood sugar, IR horses have high levels of insulin, but frequently normal glucose levels. IR is more like the 'pre-diabetic' syndrome in humans. Because glucose cannot get into the cells, the feedback loop kicks in to produce more and more insulin. When these 'thrifty' individuals eat sugar, their bodies over react, creating hyperinsulinaemia, or high insulin.

While insulin resistance is associated with laminitis, previously researchers could only speculate on the causative factor. Insulin resistance was once thought to cause starvation of laminar tissues, although that theory has now been disproved. There are many theories about how insulin resistance may cause inflammation, or disruption of normal blood flow. Johnson on Metabolic Syndrome. pdf Some thought it was inflammatory substances created as a consequence of obesity. I've often thought the link between obesity and chronic laminitis has been over stated. When I called my state's veterinary teaching hospital, a veterinarian on staff started chewing me out for allowing my horses to become fat, without ever seeing them. My horses are NOT fat, although they continue to be in a state of compensated insulin resistance even with all their ribs showing.

New research at U of Queensland, has finally found a causative agent; insulin. Asplin Abstract Laminitis was induced in healthy, lean, young ponies by prolonged (up to 72 hours) administration of insulin via euglycemic clamp. This procedure maintains blood glucose at a set level, eliminating involvement of glucose toxicity. Prior to the study, all ponies' insulin levels were in normal range. One pony reacted to the clamp procedure as being insulin resistant; another was more insulin sensitive than normal. In addition to clinical observation of lameness, examination of hoof tissues after euthanasia confirmed laminitis in all four feet. There was no evidence of gastrointestinal involvement. As the ponies were not obese, this also eliminates implication of inflammatory factors by fat tissue.

Genetic prediposition for laminitis has been demonstrated in Welsh ponies . These genetic tendancies probably exist in other breeds as well. Blood tests for insulin, glucose and triglycerides can identify horses at risk, and predict those individuals that need special management to prevent laminitis.Trieber Abstract

Carbohydrate Overload

The most well known cause of laminitis is carbohydrate overload. This is your typical 'grain room break-in' or fructan fermentation scenario. If more carbohydrate is present than the small intestine can digest, it overflows into the cecum, or 'hindgut' where fermentation of fiber by microorganisms takes place. Because each type of carbohydrate and fiber has specific microorganisms involved in fermentation, overflow of starch or fructan may cause a sudden change in the population dynamics of the gut microbes. Lactic acid bacteria (LAB), that prefer starch or fructan, have a population explosion. There is some disagreement as to which mechanism is responsible for causing the laminitis. It is probable that several mechanisms are involved. The increase in lactic acid formed by the fermentation by LAB causes a massive die off the microbes that were there before. Some used to think this caused endo-toxemia from the massive die off of bacteria and subsequent absorption of the by products from their breakdown. However, researchers have found that administration of endotoxins alone do NOT induce laminitis. Other pathogenic bacteria, such as Streptococcus bovis have been implicated, for which starch and fructan are preferred substrates. (Milinovich abstract)

The fructan connection

K. Hinckley (1996) first postulated the fructan theory. A. Longland (animal scientist) teamed up with A. Cairns (plant physiologist) to add a possible explanation to this theory. Much of their data is based on Water Soluble Carbs, which includes both sugar and fructan. Some is from grass grown near the Artic circle. The work conducted in England is all based on perennial ryegrass, which does have higher fructan levels than other species. C. Pollitt has induced laminitis experimentally by feeding boluses containing large amounts of inulin by stomach tube. Inulin is the type of fructan extracted from chicory roots. Grass fructan is not commercially available. The theory suggests that fermentation of fructan can cause the same cascade of events in the hind gut that occurs when horses binge on grain.. It involves drastic changes in the populations of hind gut microbes, accompanied by acidity which damages the lining of the intestine, allowing 'trigger factors' to enter the blood stream. I have a problem with the fructan-gut damage theory, because it's impossible for a horse to ingest as much fructan in full day of grazing worse case scenario for grass fructan concentration as the amount necessary to induce laminitis in a clinical setting .

A study by Bailey has shown that short chain fructan causes a rise in insulin levels in ponies that are predisposed to lamintits. If fructan causes a rise in insulin, then all NSC, not just sugar and starch, needs to be minimized in horse with insulin resistance.

If your horse presented with laminitis accompanied by colic and diarreah, the 'gut trigger' theory should be considered. When I've asked around, grass founder accompanied by colic seems quite rare. I believe that most cases of laminitis are caused by excess sugars and fructans that trigger overproduction of insulin.

Vasoactive Amines

Researchers at the Royal Veterinary College in London have found amine compounds in the hind gut of horses on grass that could trigger vascular changes that occur at the onset of laminitis. (Bailey, Elliott 1998, 2002) Theses are some of the same substances that cause migraine headaches in people who are sensitive to red wine and aged cheese. Blood veins respond differently than arteries.

Bibliography

Bailey, Elliott, 5-hydroxytryptamine in equine plasma constricts digital blood vessels in vitro: implications for the pathogenesis of acute laminitis, 1998, Equine Vet J, 30: 124-130

Bailey, Rycroft, Elliott, Production of amines in equine cecal contents in an in vitro model of carbohydrate overload. J. Anim Sci 2002. 80: 2656-2662

Field, Jeffcott, Equine Laminitis—another hypothesis for pathogenesis. Med Hypotheses, 1989 Nov;30 (3) 203-10

Frederick, 2002 Founder! - Hope for Refractory Laminitis, http://www.whpublishing.com/store/products.html

Hinckley, Henderson, (1996) The epidemiology of equine laminitis in the UK
Proceedings of the 35th congress of the British Equine Veterinary Association, Warwick. Pg.62

Muller, Lier, Fermentation of fructans by epiphytic lactic acid bacteria J. App. Bacter. 1994, 76: 406-411

Suzuki and Chatterton, Science and Technology of Fructans, 1993, CRC Press, Boca Raton, FL