LAMINITIS LATEST

Equine Science Update

Report by Mark Andrews.

At the recent meeting of the British Equine Veterinary Association in London, Dr Chris Pollitt, from the Australian Equine Laminitis Research Unit, explained his current understanding of the changes that occur in the foot of a horse with laminitis. " Laminitis is the failure of the attachment between the hoof and the distal phalanx. We now see it as a dynamic molecular process, superimposed on normal biology. Many of its features are normal processes appearing at the wrong time or in the wrong place."

The discovery that fructans can be used experimentally to induce laminitis has allowed him to examine the changes that occur in the foot in the early stages of the disease. "Alimentary overload with oligo-fructan is a valid experimental model for inducing acute laminitis." He points out that using oligo-fructan

(OF) to induce laminitis in experimental horses has advantages over the previously used method of giving a large dose of starch. OF given at 10mg/kg predictably causes laminitis every time. But the signs are less severe than with the starch model and none of the animals have to be killed.

The epidermal basal cells, which produce the inter-tubular horn of the hoof wall, lie on the basement membrane, a tough connective tissue sheet. They are firmly attached to it by discs called hemidesmosomes. As the hoof wall grows down, the hemidesmosomes release and then reattach to allow the basal cells and the secondary epidermal lamellae to slide over the basement membrane. Pollitt has shown that the matrix metalloproteinase enzymes (MMP 2 and MMP 9) break down the connections between the basement membrane and the lamellar epidermal cells. Normally this process

is kept in check by tissue inhibitors of metalloproteinases (TIMPs). He believes that uncontrolled, excessive activation of the MMP enzymes is responsible for the changes that occur in the early stages of laminitis.

Tests in the laboratory demonstrated that it is virtually impossible to pull the lamellae apart in sections of healthy hoof. "Seven or eight individual lamellae can withstand a kilo of force trying to separate the laminae" he explains." The fibres attaching the hoof to the bone are more likely to tear than are the lamellae to separate. In contrast, when the sections have been treated to activate the MMP-2 enzymes the lamellae separate easily."

An extract of Streptococcus bovis, the bacteria that multiply dramatically in the large intestine in response to fructan, has a similar effect. However, Pollitt has not yet been able to prove that toxins released by the bacteria actually reach the laminae to be able to have their effect. "We`ve never been able to show any bacterial product at the lamellar zone so far."

Using isolated sections of hoof (" explants"), he has shown that when the MMP-2 enzyme is activated it breaks down the connections between the basement membrane and the lamellar epidermal cells. If the explants are deprived of glucose the basal cell nuclei and the internal cell skeleton are lost. These two findings offer an explanation for naturally occurring cases of laminitis. Laminitis may result when activation of the MMPs occurs (as in grain or grass overload) or when glucose uptake by the lamellar basal cells is compromised (for example in Cushing's syndrome).

The effect of fructans appears to be dose dependent. That is, as the amount of fructans given increases so does the number of hemidesmosomes lost and hence the severity of the laminitis.

Further studies have shown that the MMP-2 enzymes are concentrated in the basal cells adjacent to the basement membrane. \ldblquote Increased MMP2 activity is seen in hoof tissues at an early stage in the development of laminitis. "We can now analyse lamellar MMP2 activity in real time to assess the progress of laminitis. We can use this technique both to diagnose laminitis in the early stages and to test preventive strategies" he said.

He points out that these changes appear before the horses show any clinical signs of laminitis. "So any attempts to prevent the clinical signs of laminitis developing must be carried out early."

One treatment that Pollitt has shown to be effective in preventing laminitis is cryotherapy, using iced water. He induced laminitis by giving 10g/kg of OF. One foot of each horse was placed in a boot containing a 50/50 mixture of water and ice cubes. Measurement of the temperature in the foot showed that the ice boot cooled the foot to 5o C. It was kept in place for 48 hours. Pollitt reports that there were no adverse effects of the prolonged period of low temperature. In fact the horses preferred to stand on the foot in the ice boot. "It is important that the ice water comes up to just below the knee. If only the foot is cooled laminitis still occurs."

"We don't yet know how long this protective effect would last. But horses with toxic colitis (which often causes laminitis) have been treated successfully with an ice-water bath. The clinicians involved believe that it has prevented laminitis."