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Commentary
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Laminitis: Two Steps Strategy to Control the Digit Vasomotor Dysfunction

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Commentary

Laminitis is an important affecting ungulates foot disease because of its severely debilitating, painful and potentially career-ending and life-threatening progress [1,2]. In cattle-farming, moreover it causes heavy economic losses related to decreased milk production, weight loss, culling, decreased reproductive performances and treatment costs [3].

Laminitis is the symptomatic manifestation of multi-factorial systemic disease that affects the general condition of the animal [4-6] and the possible mechanisms, as well as the potential triggering factors that may contribute to the tissue damage and development of the clinical signs at this anatomical site are numerous and interrelated [7,8].

Whatever the mechanisms for what it take place, a number of evidences reveal that impaired local perfusion occurs in the distal digit during acute/sub-acute stage of laminitis [9-11]. The perturbations in the digital circulation play a crucial role in causing damage to the soft tissues of the hoof by impairing nutrient blood flow through the laminar and solar corium with consequent necrosis of the horn-producing cells and disruption of the hoof-bone attachment apparatus.

So, the questions that arise is: how is the vascular disturbance initiate? It is indeed likely that advances in laminitis therapies will be enforced once the links between the multi-factorial events involved in the pathogenesis of the disease and the initiation of digit vascular homeostasis perturbation are delineate.

The factors triggering the local circulatory disturbances are still poorly defined. Based on the frequent association of both equine and bovine laminitis with inappropriate feeding management, it has been suggested that biologically active substances are produced and absorbed from the alimentary tract when gastrointestinal disturbances occur due to overeating of high-energy rations [4,12,13]. Such substances, likely including endotoxin and dietary amines, would alter tone, permeability and/or integrity of digital vessels either *per se* or by modifying the local levels and/or actions of many endogenous mediators of neuronal and humoral origin. Such mediators are endowed with vasoactive, pro-inflammatory pro-thrombotic and/or cytotoxic properties and may represent the triggering factors leading to imbalance of the finely tuned homeostatic network in the digital vasculature [4,10].

The occurrence of endothelial damage and/or dysfunction has also been suggested as an initiating factor of impaired foot vascular function in equine and bovine laminitis [4-6,14-16].

Data from laboratory animal models, moreover, suggest that when the vascular endothelium is compromised, the underlying smooth muscle acquires time-dependently the ability to change its reactivity to vasoactive stimuli [17,18].

Therefore, in order to effectively manage the tissue damage induced by the impaired digital perfusion, it is important to identify the mechanisms responsible not just for the initiation but also for the maintenance of such vascular events.

Recently we have observed that the removal of endothelium do not produce short term effects on the reactivity of bovine digital vein to 5-HT but smooth muscle hyper-reactivity to contractile stimulus was recorded as a reaction to a chronic lack of endothelial compensatory function [19]. It is apparent therefore that, regardless of the initiating mechanisms, a fundamental and progressive change in the smooth muscle control of vascular function develops in endothelial damaged veins that give rise to a persistent increase of venous tone. This may help to explain the recurrent failure in laminitis therapies due to the persistence of progressive worsening of the vascular dysfunctions despite the initial insult may be resolved. As over-activation of the RhoA/ROCK pathway and

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production of reactive oxygen species could account for the longer-term changes recorded in the smooth muscle reactivity [19], these biochemical mechanisms are potential targets for controlling the progressive vasocontractile dysfunction of digital veins in animals affected with laminitis.

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