Examing the stable door after the horse has bolted: Why is EIA such a challenge?

It is an unfortunate fact that research into a disease is only triggered when outbreaks that have a significant financial impact occur and, as a result, the responses are often frantic and ill thought out. Only then are some of the fundamental issues of the condition brought into public and scientific scrutiny and, all too frequently, we simply close the stable door after the horse has bolted or, more particularly, examine the door to see why the horse has bolted and then close it (Brangan et al., 2008). Such retrospective approaches do little to encourage prospective disease research and surveillance since there is usually ‘panic’, and hasty, irrational, wrong or unjustified decisions are frequently made. It is unwise simply to accept the dogma that is included in textbooks since that is often based on dubious science from ages past. With widespread movement of animals for sport, breeding, leisure or slaughter, it has become increasingly critical that more effort is made to encourage prospective research.

Equine infectious anaemia (EIA) has been recognised and feared in Europe since the middle of the 19th century. The disease is widely distributed worldwide and it remains endemic in some parts of Europe where its geographic proximity to areas where the disease is supposedly not present carries a significant threat. It has very high morbidity and mortality yet remarkably little is known about it. The most important problem with EIA is that no vaccine has proved effective, and even the natural immune processes seem unable to counter its devastating pathological effects. Although in many endemic regions some affected horses seem able to survive for years, the majority succumb. A recent outbreak in Ireland caused severe damage to the equine industry at a time when endemic circumstances were already becoming more difficult. The events associated with this outbreak opened the debate about the published facts on the disease (More et al., 2008). The outbreak probably arose as a result of infection via a plasma transfusion (More et al., 2008) and highlighted the need for proper scrutiny of the use of biological products. The outbreak was however a timely reminder that a casual approach to a dangerous disease can lead to considerable loss.

Where a disease has no known treatment and where the prognosis is extremely poor, there is a marked tendency to forget or disregard it; the fact that many countries have supposedly eliminated EIA whilst others accept its endemicity, has led to an appalling indifference and complacency in disease control. This is unacceptable. There is a clear need for a better understanding of the way the EIA virus evades the immune system so effectively; seroconversion is efficient and forms the basis of serological diagnosis, but the virus survives in spite of it. If the particular mechanisms of immune evasion could be understood the chances of developing genuine preventative measures would improve significantly. It is therefore satisfying that this issue of The Veterinary Journal carries a genuine scientific study that seeks to answer at least some of the unknown questions on the pathophysiology of the disease (Bolfa et al., 2012).

The immune system makes use of the lethal effects of oxidants to overcome pathogens by forcing the production of both reactive oxygen species and reactive nitrogen oxidizing species (Nathan and Shiloh, 2000). Most of these oxygen-derived species are produced at a low level by normal aerobic metabolism and the damage they cause to cells is constantly repaired. However, under the severe levels of oxidative stress that cause necrosis, the damage causes ATP depletion, preventing controlled apoptotic death and causing the cell to break down (Lelli et al., 1998). The system is highly efficient but some lentiviruses in particular seem more than able to overcome the host's immune processes and can induce serious disease even in the face of an active immune system and response; EIA, HIV and Maedi-visna viruses are good examples of this.

In the case of EIA virus, the almost unique way in which the virus evades the immune system's best efforts to overcome it, indicates that it must in some way prevent or impede the natural destructive and protective mechanisms. The pathological effects of the virus however continue without any effective immune responses. It is almost as though the virus is always one step ahead of the host's ability to overcome it and this ultimately results in the demise of the host. Bolfa et al. (2012) have identified possibly significant imbalances between oxidants and antioxidants in EIA virus infected horses. It is interesting that EIA in horses is accepted as a model of lentivirus activity in HIV in humans and the role of oxidative stress in the immune evasion may be a significant aspect of the unique pathogenesis of these conditions. Whether the oxidative imbalances that have been identified provide any immediately useful contribution to the possible treatment of the disease is doubtful but measures that address these may support management methods that could possibly prolong the life of the patient.

It is generally accepted that the pathological processes involved in many disease conditions are a direct result of intracellular oxidative stress representing an imbalance between the production and manifestation of reactive oxygen species in the cell and a biological system's ability to overcome the resulting cellular damage without causing harm to the body. Disturbances in the normal redox state of tissues can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. The recognised responses that arise from oxidative stress form the basis of the pathogenesis if many disease conditions. These include programmed cell death (apoptosis) and even necrosis in the most severe circumstances (Lennon et al., 1991). The natural defences against oxidative stress include the physical barriers that restrict free radicals to their sites of production within cells, enzymes that neutralize dangerous
reactive oxygen species, natural dietary quenchers of free radicals that donate electrons and so restrict the chain reactions early in their course, intracellular mechanisms that repair oxidative damage to DNA, proteins and membranes, and complex stress responses that may culminate in apoptosis if the damage is too great.

Pathology arises when the balance between oxidants and antioxidants is biased towards cell damage and it is this imbalance that Bolfa et al. (2012) have explored. The clinical events associated with EIA have been well described but if solutions are to be found then more fundamental research has to be carried out.

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References