Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Guest Editorial

Canine infectious respiratory disease: Tackling the unknown unknowns

When the then US Secretary of Defence Donald Rumsfeld made his famous and rather unjustly mocked 2002 NATO speech about the 'known knowns, known unknowns and unknown unknowns' in matters of national security[1] he hit on an important truth about veterinary research, namely, it is only in hindsight that we realise how long we have not known something about animal disease. That truth is illustrated by the article by Dr. Tara Anderson of the University of Florida and her colleagues published in this issue of *The Veterinary Journal* (Anderson et al., 2012). The study describes how retrospective serological analysis demonstrates that host-adapted H3N8 canine influenza was circulating in greyhounds in North America at least as early as 1999. This is an important observation as previous understanding was that this novel disease first occurred in the USA in 2004, since when it has circulated widely in greyhounds and other dogs and is now considered endemic in several States.

Molecular and epidemiological data indicate that the virus we now recognise as H3N8 canine influenza was first established in dogs by cross-species transmission of H3N8 equine influenza (Crawford et al., 2005). This cross-species transmission from horses to dogs has been recognised in the UK (Daly et al., 2008) and Australia (Kirkland et al., 2010) as well as in the USA. However it is only in the USA that the infection has become endemic in dogs. The mode of transmission between the two species is not proven but aerosol infection from horses with the respiratory infection seems most likely although the coincidence of the UK reports of disease in English foxhounds traditionally fed in hunt kennels on raw horse meat means that oral infection cannot be ruled out in some cases.

Whatever the route it is clear that the cross-species transmission is facilitated by the presence of common sialic acid receptors (the binding sites for influenza virus) in both horses and dogs (Daly et al., 2008). In both species the clinical disease is a relatively short period of tracheobronchitis associated with a dry hacking cough and a marked reduction in exercise tolerance, and it is because of the latter clinical sign that the infection assumes such significance in athletic animals such as the racing greyhound and racing Thoroughbred (Daly et al., 2011). Complications of infection in both species include more severe disease in young or immunocompromised animals, particularly where secondary infection supervenes. It is unusual for the influenza virus to spread beyond the respiratory tract although there are occasional reports of influenza viral encephalitis in horses (as seen in some children infected with human influenza virus strains) (Daly et al., 2006). That complication has not been recognised to date in dogs infected with canine influenza.

The retrospective study reported by Anderson et al. (2012) was reliant on access to serum samples that had been collected for a variety of different reasons, including heartworm surveillance and blood banking. In these times of increasing financial pressure on diagnostic facilities this emphasizes the importance of retaining well catalogued serum collections for retrospective analysis. Access to that material also necessitates informed client consent and maintenance of client confidentiality. Of equal importance to the retention of serum samples for future research applications is the retention of paraffin blocks from biopsy and post mortem examinations. It is salutary to remember that important insights into the great 'Spanish' influenza pandemic of the early part of the last century, including the role of secondary bacterial infection, were made possible through access to tissues stored from patients who died almost a century ago (Taubenberg and Kash, 2011). In addition to proper cataloguing of stored serum and tissue samples, appropriate storage is also essential; for example, unexpected fungal contamination was recently reported to have put at risk the paraffin block collection at one of the German veterinary schools (Müller et al., 2011).

The fact that canine influenza was circulating in greyhounds for at least 5 years before the novel disease syndrome was recognised by US veterinarians highlights how important it is that specialist clinicians and diagnosticians dealing with cases of canine infectious respiratory disease are ever vigilant for new pathogenic agents or changes in the outcome of known infections. Two other examples of breakthroughs in our understanding of canine infectious respiratory tract disease (CIRD) in recent years are the recognition of a hitherto unknown canine respiratory coronavirus and the observation of unusually severe disease caused by *Streptococcus equi* subsp. *zooepidemicus*, a pathogen previously thought to be relatively trivial in dogs.

In 2003, a group working at the University of London's Royal Veterinary College (RVC) discovered a novel group 2 coronavirus that was associated with outbreaks of canine respiratory disease at a large rehoming kennel in central London (Erles et al., 2003). In the following years much research ensued to elaborate the role of this virus in the CIRD complex. Although the virus appears to cause only relatively mild upper respiratory disease, it is highly contagious and spreads rapidly through a population, potentially predisposing to more serious respiratory infections (Erles and Brownlie, 2008). Of interest here are the possible origins of the virus which is most closely homologous to human coronavirus OC43 and bovine coronavirus (BCoV). Retrospective studies have shown that CRCoV was around as early as 1996 in Canada (Ellis et al., 2005) and, based on sequence identity across the genome, the virus was probably transmitted to dogs from cattle (Erles et al., 2007). Indeed, it seems that the closer one

[1] See: http://www.nato.int/docu/speech/2002/s020606g.htm.

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looks into the fascinating world of infectious respiratory disease the more unknowns are uncovered which may have eluded us for many years.

Whilst working on the intricacies of CRCoV pathogenesis, the same group at RVC began to receive calls from the rehoming kennel to say that the outbreaks of respiratory disease had taken a turn for the worse and now they had cases where one day the dog was apparently healthy, the next it was dead. What followed was both troubling and challenging as the bacterium *Streptococcus zooepidemicus* emerged as the culprit. The bacterium had, perhaps over a short period of time, developed the ability to cause severe, acute and often fatal haemorrhagic pneumonia in dogs (Priestnall et al., 2010). The disease syndrome was similar to toxic shock-like syndrome in humans and there was a pressing need to identify the bacterial or host factors responsible for the sudden increase in pathogenicity of this agent (Priestnall and Erles, 2011). Work still continues but this reminds us that it is not just the unknowns that we should be concerned about but that the re-emergence of what we consider to be the 'knowns' is an ever present risk.

The paper by Anderson et al. (2012) illustrates one advance in our understanding of a rapidly evolving canine disease syndrome. Doubtless coming years will bring equally exciting breakthroughs.

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