Focus Article: Protection against Equine Influenza in 2012: a view from a practitioner’s perspective

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Although we encounter other serious equine infectious diseases more frequently than influenza, the disastrous spread of infection in largely unvaccinated horses in South Africa and Australia in recent years served as a reminder of why effective vaccination programmes are so important to maintain in the UK. Few infectious diseases spread as rapidly as influenza and although fatalities are rare they certainly occur in addition to necessarily prolonged convalescence which all translate into a highly unpleasant illness and severe disruption of equestrian activities. Our dual responsibilities as practitioners are firstly, to provide our clients with the most effective available vaccines, and secondly, to collect diagnostic samples from clinical cases so that we maintain awareness of currently circulating influenza strains that we should be targeting with vaccine products. It is fair to say that greater efforts could and should be made in both of these areas.

Current threat from specific influenza strains

The Sentinel Practice Scheme

A prerequisite for formulation of effective vaccines is knowledge of the currently circulating equine influenza virus strains and subtypes. This is greatly facilitated by the Sentinel Practice Scheme\(^1\) developed and run by the Animal Health Trust and funded by the Horserace Betting Levy Board. Registration is easily achieved online and participating practices are supplied with nasopharyngeal swabs and virus transport medium, and are asked to submit swabs taken from horses suspected of having influenza for testing at no cost to the owner. When influenza virus is detected, attempts are then made to grow the virus for precise characterisation of the virus strain. This information is vital for the Expert Surveillance Panel of the World Organisation for Animal Health (OIE) who then provide independent expert evidence-based advice on recommended vaccine strain updates. The veterinarians in the field, who submit samples via this free scheme, play a crucial role in surveillance of equine influenza and, ultimately, in ensuring that available vaccines contain the most appropriate strains. However, many of us would frequently not submit swabs from coughing horses, especially if disease is clinically mild and it is highly likely that many more outbreaks of equine influenza occur than are diagnosed. Greater awareness and participation in the Sentinel Practice Scheme should be encouraged to improve the accuracy of our awareness of the current threat.

Virus strain evolution

Since the original identification of H7N7 equine influenza in 1956 (Prague ’56) and H3N8 in 1963 (Miami ’63), continual evolution and extinctions have occurred (Figure 1). No threat has arisen in the UK from H7N7 strains for over 30 years, leaving sole focus now on H3N8 strains. In the late 1980’s notable divergence of H3N8 strains occurred into so-called “American” and “European” strains although the latter have not been isolated in the UK since 2005 (Aboyne ’05) and are no longer considered a threat, leaving sole focus now on H3N8-American strains. Further divergence of H3N8-American strains also occurred to produce so called “Kentucky” and “Florida” strains with the former predominating through the 1990’s (e.g. Newmarket/1/’93, Kentucky ’98) and the latter predominating since the turn of the 21st century. No H3N8-American-Kentucky strains have been isolated in the UK.
since 2006 (Cheshire '06) and are no longer considered a threat, leaving sole focus now on H3N8-American-Florida strains. The pattern of divergence continued in Florida strains which divided into clades 1 and 2 and both clades continue to present a current threat to horses in the UK to date, although there has been a gradual change in emphasis from Florida clade 1 strains (e.g. South Africa/4/'03, Ohio ’03) to Florida clade 2 strains (e.g. Richmond/1/’07) as the major threat in the UK. Indeed, all isolates identified in UK since May 2010 have been H3N8-American-Florida-clade 2 strains although the continued predominance of Florida clade 1 strains in USA is one reason why we cannot yet discount these latter strains as a current threat2.

Figure 1: Evolution of equine influenza from 1956 to 2012. Note that H7N7, H3N8-European and H3N8-American-Kentucky strains are no longer circulating and are not deemed to pose a threat to horses in the UK. Only H3N8-American-Florida strains (clade 1 and, more especially, clade 2) represent a current threat.

UK vaccine products – what we have versus what we would like

Vaccine virus strains
Antigenic similarity between currently circulating strains and strains included in vaccine products is a vital contributor to vaccine efficacy. The OIE Expert Surveillance Panel3 meet annually to consider evidence of current international threat from equine influenza and recommend strains that should be incorporated into commercial vaccine products. Although strains continually evolve and present a moving target for vaccine manufacturers to follow, in this Olympic year where so many Brits have risen to the challenge the UK vaccine industry would not be deserving of a medal for their efforts and achievements! With relevance to current strains there have been 2 important update recommendations by the OIE Expert Surveillance Panel in recent years. Firstly, in 2004 following a major influenza outbreak in South Africa and vaccine breakdown in the UK, the panel recommended update of influenza vaccines to contain a Florida clade 1 virus similar to South Africa/4/’03 or Ohio ‘03. To date, 8 years on from that recommendation, 3 of the 4
UK equine influenza vaccines still have not complied (Duvaxyn IE plus, Equilis prequenza and Equip F), with only Proteq-flu containing the OIE recommended strain (Ohio ‘03). Secondly, in 2010 following recognition of increasing activity attributable to Florida clade 2 viruses, the panel updated their recommendation to include representatives of both Florida clade 1 (South Africa ‘03-like or Ohio ‘03-like) and Florida clade 2 viruses (Richmond ‘07-like). This recommendation was reconfirmed in 2011 and 20123. Two years on from the 2010 recommendation no current UK vaccine product yet fully complies, although assurance of active research and forthcoming development of strain updates has been made unofficially by some manufacturers. Figure 2 details the content of UK licensed equine influenza vaccines4 and shows only 1 out of 11 included influenza strains to be compliant with current OIE Expert Surveillance Panel recommendations.

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<thead>
<tr>
<th>H3N8 Equi 2</th>
<th>H7N7 Equi 1</th>
<th>Vaccine format</th>
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<td>European</td>
<td>American</td>
<td>Kentucky</td>
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<td>2012 OIE Recommendation</td>
<td>-</td>
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<tr>
<td>Duvaxyn IE plus (Elanco)</td>
<td>Prague ’56</td>
<td>Suffolk ’89</td>
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<tr>
<td>Equilis prequenza (MSD)</td>
<td>Prague ’56</td>
<td>Nwmkt/2 ’93</td>
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<td>Equip F (Pfizer)</td>
<td>Nwmkt ’77</td>
<td>Borlange ’91</td>
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<td>Proteq-flu (Merial)</td>
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<td>Nwmkt/2 ’93</td>
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**Figure 2:** Currently available equine influenza vaccine products in UK4 compared with 2012 recommendation from OIE Expert Surveillance Panel3. Only Proteq-flu contains a recommended strain (Ohio ‘03) and none are fully compliant with current recommendations.

**Vaccine technology**

In addition to strain selection, vaccine products also differ with respect to the means by which the influenza antigen is presented to the horse’s immune system. Mimicking of natural virus infection and simulation of naturally occurring immunity represents the “holy grail” for vaccine technology. Given that equine influenza is primarily a local infection of the respiratory epithelium, effective clinical protection and elimination of viral shedding is likely to be best achieved via opsonisation of virus by mucosal antibody (mainly IgE) and, probably more importantly, by targeting of virus-infected respiratory cells by cytotoxic T lymphocytes (cell-mediated immunity, CMI) (Paillot et al 2006). Although, under limited circumstances, systemic IgG concentrations may correlate with clinical protection, there is less obvious direct benefit of a strong systemic IgG response given the non-viraemic nature of equine influenza infection. The most basic means of antigen presentation comprises killed virus combined with an immunostimulant adjuvant such as carbopol (e.g. Duvaxyn IE Plus). Although likely to provoke a strong systemic IgG response via the “exogenous pathway” (Gildea et al 2011), the ability of such vaccines to produce effective mucosal IgE and CMI responses is dubious (Paillot et al 2006). The desirable stimulation of CMI depends on the “endogenous pathway” which is classically stimulated by virus antigen that is synthesised within respiratory epithelial cells as seen in natural infection. The live canary-pox vector technology seen in Proteq-flu is the only UK vaccine product that truly achieves intracellular antigen synthesis although there is evidence that the immune-stimulating complex (ISCOM) technology seen in Equilis Prequenza and Equip F also stimulates CMI (Paillot et al 2006, 2008; Paillot & Prowse 2012).
The sorry state of current affairs

It is estimated that less than 40% of the horses in the UK are vaccinated against equine influenza and even those that are vaccinated do not receive a Florida clade 2 vaccine strain which represents the major current threat in the UK. Furthermore, in 3 out of 4 instances the vaccine products used do not even comply with OIE expert surveillance panel recommendations from 8 years ago and contain strains 14 to 19 years old as the most up-to-date vaccine components! (Figure 2). Given the current range of outdated vaccine products available, it is unsurprising that vaccine breakdown has been seen during the last year in several countries including USA, France, Germany and UK. This is not a record of which we can be proud and, although vaccine strain selection is the primary responsibility of the four vaccine manufacturers (Elanco Animal Health, Merial Animal Health, MSD Animal Health, Pfizer Animal Health), it is ourselves as veterinary practitioners who choose which products to purchase and supply to our clients and we cannot be absolved of complicity in the currently unacceptable situation. It is inevitable that continued and progressive vaccine breakdown will be seen in the UK until vaccine products are, at last, updated in accordance with OIE Expert Surveillance Panel recommendations. It is evident that most vaccine manufacturers have not taken it upon themselves to voluntarily update their products appropriately. Some have disappointingly placed greater reliance on trying to excuse their inactivity by attempting to convince us of continued efficacy of their outdated products despite independent expert evidence and opinion to the contrary.

The way forward?

Many lessons should have been learned from the dreadful experiences of other nations such as Australia in 2007. It is important to note that the infamous Australian outbreak did not originate through lack of vaccination. Indeed the index cases in Eastern Creek Quarantine Station were fully vaccinated, although not in accordance with OIE Expert Surveillance Panel recommendations current at that time. Had appropriate vaccines been used at the time (3 years after the ESP had recommended them) then this multi-million dollar disaster would not have occurred. It was recommended by the subsequent judicial inquiry that “If there are commercially available vaccines that contain representatives of currently circulating strains, the import conditions should specify that the horses be vaccinated using that vaccine or one of those vaccines”. This statement represents an important landmark whereby regulations not only specify compulsory vaccination but actually stipulate which particular vaccine products should be used. Similar action via regulatory bodies with UK jurisdiction such as the British Horseracing Authority, Fédération Equestre Internationale and Department for the Environment, Food and Rural Affairs could only be in the interests of UK equine health and, no doubt, would finally provoke the vaccine manufacturers into long-overdue action. However, in the current absence of regulatory enforcement in the UK, it is perhaps time for practitioners to exert more influence on the market by choosing vaccine products that are compliant with OIE Expert Surveillance Panel recommendations.

When vaccine breakdown occurs in our clients’ horses, could we honestly claim as a profession to have acted in accordance with best practice and the horses’ best interests to try to avoid the situation?
References, further reading and resources


1Information and registration for the Sentinel Practice Scheme is available at www.aht.org.uk/cms-display/equiflunet_vsent.html.
2Current UK and international equine influenza activity is easily monitored via several updated resources including websites (www.equiflunet.org.uk; www.aht.org.uk/equine_disease.html), text messaging (www.ewagroup.com/merial/alertservice) and twitter (@equiflunet).
4Current details and particulars of equine influenza vaccine products licensed in UK are available online on the websites of the National Office of Animal Health (www.noahcompendium.co.uk), the Veterinary Medicines Directorate (www.vmd.defra.gov.uk) or The European Medicines Agency (www.ema.europa.eu/ema).
5Details of Commissioner’s report on the 2007 Australian Equine Influenza outbreak are available at www.equineinfluenzainquiry.gov.au/