The Equine Influenza Expert Surveillance Panel

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The Equine Influenza surveillance panel was created in order to improve the efficacy of equine influenza vaccines by ensuring that vaccines contain epidemiologically relevant strains. The catalyst for this initiative was the 1979 epidemic of A/equine 2 (H3N8) virus which seriously affected racing in the UK and Europe. At the time it was not known whether the failure of vaccines in the face of the epidemic was a result of inadequate potency, inappropriate vaccination schedules or antigenic drift from the original prototype strain A/equine /Miami/63 included in vaccines.

Funded by the Horserace Betting Levy Board a collaboration to improve equine influenza surveillance was set up between the Royal Veterinary College and two WHO laboratories, the National Institute of Medical Research and the National Institute of Biological Standardisation and Control, the former being the WHO World Reference Laboratory for Influenza and the latter the WHO Reference Laboratory for Influenza Vaccine standards.

The conclusion and recommendations of the first meeting held in 1983 highlighted the need for a much higher level of surveillance and virus collection and characterization, modernization of methods of vaccine standardization and the development of a challenge system in horse so that vaccines could be tested in the target species. It was agreed that there was a strong case for modelling the standardization of vaccines and surveillance systems for equine influenza on those already in place for human influenza. However at that time the numbers of viruses available for characterization were woefully inadequate as a basis for any conclusions on relevant strains for vaccines. As a result the choice of strains for updating vaccines following the 1979 outbreak was largely based on geographic and market considerations with American manufacturers opting for an American virus A/equine /Kentucky /81 and European manufacturers in general opting for European strains such as Fontainebleau/79 , Brentwood/79 and Borlange/79.

As a result of the introduction of mandatory vaccination in 1981 for racing thoroughbreds by the Jockey Clubs of the tripartite countries (England, Ireland and France) together with some other European countries, the racing industry of the UK committed to a long term program to monitor vaccine efficacy used in the mandatory vaccination program and to conduct ongoing surveillance of equine influenza. It was recognized that before a formal vaccine strain selection process could be introduced a much greater level of surveillance was required on a worldwide basis. The OIE designated three laboratories in Germany, England and USA (Kentucky) who had the remit to improve the level of surveillance, virus collection and characterization.

It was almost 10 years before it was agreed that the numbers of viruses being examined was sufficient to provide a meaningful basis for vaccine strain selection but at the second meeting of WHO and OIE experts which was held following the 1989 epidemic of influenza, it was recommended that an Expert Surveillance

Panel should be set up which included 3 WHO reference laboratories, 3 OIE reference laboratories and a Scandinavian laboratory which was very active in equine influenza surveillance.

It has become apparent that antigenic drift in equids is slower than in humans and that equine serum is more cross-reactive than ferret serum used for characterisation.

The challenge for the Expert Surveillance panel is to identify the point at which the majority of isolates have undergone significant antigenic drift such that a strain change is called for. They have been assisted in this task with the application of antigenic cartography, a visual means by which the progress and direction of antigenic change can be followed. Decisions to recommend an update are only made when all criteria are met i.e. differentiation of viruses using HI and ferret sera, infection in fully vaccinated horses in the field and when available lack of protection in experimental challenge studies.

The first formal recommendation to update strains was made in 1993 and referred to the need to replace strains from 1979-1981 with viruses isolated in 1989. Subsequently with the discovery that the H3N8 lineage had diverged into two sublineages designated European and American, a recommendation was made that vaccines should contain representative of both lineages represented by Suffolk/89 and Newmarket/2/93 as European lineage viruses and Newmarket/1/93 and Kentucky 1994 as American lineage viruses. It was not until 2004 that the panel recommended that a further update was necessary for the American lineage viruses and that the 1993/1994 viruses should be replaced by viruses antigenically similar to South Africa/2003. This decision was based on field infections in vaccinated horses and antigenic differences determined in HI tests using ferret sera.

In spite of the fact that there are licensing regulations in place to facilitate the speedy updating of strains (EMEA Guidelines), vaccine manufacturers have been slow to follow recommendation preferring to promote the cross protection remaining even though protection is not optimal with outdated strains. It was only in the latter half of 2008 an update vaccine became available in USA and in mid 2009 in Europe. Many of the market leaders did not adopt the recommendations when first published, claiming that without provision of extraneous agent tested seed viruses the updating process was more onerous than that expected of human influenza manufacturers. This in fact is a misconception as the panel only recommends that vaccine viruses selected should be antigenically indistinguishable from the recommended strain thus allowing manufacturers to select regional isolates and those with the most advantageous growth characteristics. This is in line with the human influenza system.

The key point to appreciate is that while outdated vaccine will still provide a measure of immunity, a mismatch of strains generates a situation where vaccine provide quite reasonable clinical protection such that the disease is mild and short lived, but that these infected animals shed large amounts of virus and fuel spread of infection. International travel of horses for racing relies on vaccination to control infection and the equine industry has stated that it requires products which minimize virus excretion. Thus there are significant benefits to using the best quality vaccines containing up to date strains.

The recent epidemic of equine influenza in Australia highlights the huge economic consequences of major epidemics and underlines the importance of supporting schemes which contribute to better vaccines through appropriate selection of strains and monitoring that products meet the potency standards laid down by OIE.

The current surveillance data shows that Florida sublineage viruses from clades 1 and 2 are circulating in the Europe and are causing sporadic disease mainly in unvaccinated horse populations. Antigenically there were no major differences between the currently circulating strains and those characterised previously using ferret antisera from 2005 to 2007, suggesting limited antigenic drift has occurred. In the USA two characterised isolates belonged to the Florida sublineage clade 1 as was the case in 2006-2007 and were antigenically similar to the previous isolates. There was no evidence of Florida clade 2 viruses circulating in North America. Interestingly the viruses circulating in Mongolia, India and China have been classified as Florida sublineage clade 2 viruses similar genetically to those circulating in Europe.