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Horserace Betting Levy Board research funding 1998 – 2010

Equine influenza

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The 'flu': How has HBLB funding helped challenge this persistent threat?

Introduction

Equine influenza is a major cause of respiratory disease in the horse and, despite the availability of vaccines, continues to cause problems around the world for the thoroughbred industry.

In the UK, vaccination has been mandatory for racehorses since 1981, following the serious large-scale outbreak in 1979. Although, this policy has not eradicated 'flu from our racehorse population altogether, it has been successful in minimising the potentially devastating effects of the disease.

Since 1981, no race days have had to be cancelled due to major flu outbreaks and the disease now occurs in isolated small outbreaks rather than the catastrophic nationwide problems that have been documented in the past.

However, the flu virus is remarkably adaptable and can rapidly develop the ability to overcome protective vaccines. Constant and on-going vigilance is essential if we are to keep the threat of equine flu at bay.

Equine Influenza Surveillance Programme

The HBLB-funded Equine Influenza Surveillance Programme

Flu viruses have incredible ability to change their structure and in doing so, they render vaccines ineffective. Consequently, on-going monitoring of strain patterns is essential to ensure that vaccines are modified to be effective against the prevalent flu strains. This monitoring work is undertaken in an on-going flu surveillance programme at the Animal Health Trust (AHT), supported by HBLB funding.

This research team works closely with vets in practice, other scientists internationally and the pharmaceutical industry to ensure that vaccines are as effective as possible.

How do equine influenza viruses overcome vaccines?

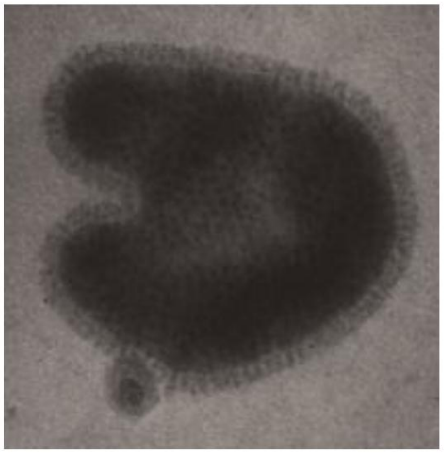
Equine influenza virus undergoes variation through a process known as antigenic drift. The proteins on the surface of the virus particles gradually mutate, which is how they avoid recognition by the host immune system and it also allows the viruses to change their binding specificity facilitating the cross species transmission events seen with other influenza A viruses, such as swine flu.

Influenza viruses can be divided into subtypes, based on proteins that are located on their surface: one of the most important is haemagglutinin (HA). The HA protein is responsible for the binding of virus particles to the surface of cells and cell membranes.

It is also a major target for the antibody response. Antibodies to HA will protect horses against influenza viruses of a similar antigenic type and is therefore an important component of vaccines.

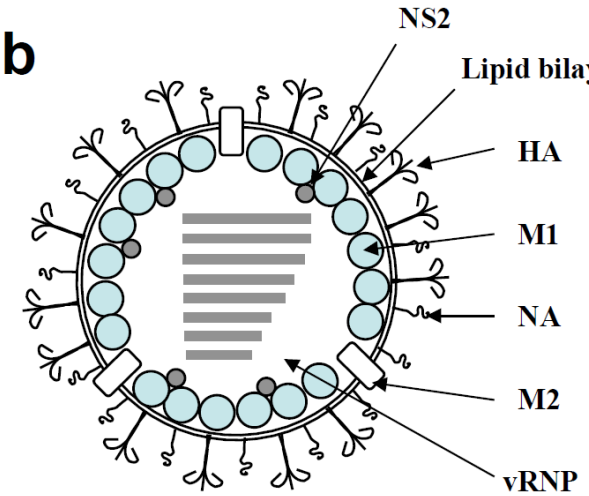
Changes in the HA proteins can lead to vaccine breakdown. In an attempt to ensure that vaccines remain up to date, several countries participate in surveillance schemes to collect data about viruses that are currently circulating. Viruses are isolated from nasal swabs taken from affected horses, they are then characterised at genetic and antigenic levels.

a



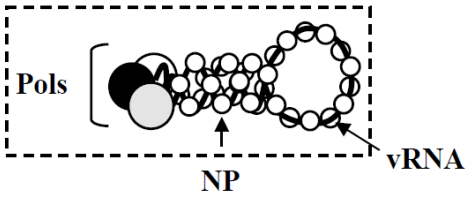
Courtesy of Ray Wright, Animal Health Trust, UK

b



HA: haemagglutinin
M1: matrix protein
M2: tetrameric ion channel
NA: neuraminidase
NS2: non structural protein 2
NP: nucleoprotein
NS1: non structural protein 1
Pols: polymerase (PA, PB1, PB2)
vRNA: virus RNA
vRNP: viral ribonucleoprotein

c



Kindly provided by Dr. Romain Paillot, Animal Health Trust, UK

Figure 1 Electron micrograph of EIV (a) and a cartoon showing the structure of the influenza A virus (b). It has a segmented RNA genome consisting of 8 segments which are coated in protein (c).

Equine influenza lineages

The HBLB has contributed to the funding of work that showed that the Equine influenza viruses diverged into two distinct lineages, the European and American, in the late 1980s. Viruses from the two lineages were sufficiently different that a horse that had been vaccinated with a virus from the American lineage would not be well protected against a virus from the European lineage. More recently, the American lineage has evolved into two further sublineages, Florida sublineage Clade 1 and Clade 2.

The HBLB-supported surveillance programme has isolated both Florida clade 1 and 2 viruses from the UK in 2007 to 2010. Both of these virus groups are in circulation in other parts of the world and have caused large outbreaks of equine influenza in Australia, Japan, Mongolia and India.

Due to the global transport of horses, equine influenza virus in one continent is a risk to horses in other areas of the world. The outbreaks in Australia and Japan were caused by viruses similar to those circulating in the USA in previous years.

How can vaccines be kept up-to-date and effective?

The HBLB has funded the development of tests to show whether a virus has mutated significantly compared to other strains or not. This assay is used to characterise the viruses isolated in the field and compare them with a panel of reference strains including those used in vaccines.

It has also championed the technique of antigenic cartography that was first used for human influenza to help visualise the antigenic relationship between virus strains and is now applied to equine influenza virus data obtained through the surveillance programme.

The greater the antigenic distance between viruses isolated in the field and the strains used in vaccines, the greater the chance that there will be a breakdown in protection offered by those vaccines so this work serves as an early warning system for potential vaccine failure.

How is equine influenza surveillance achieved in UK?

Along with the introduction of mandatory vaccination for racing thoroughbreds in 1981, the racing industry of the UK committed to a long-term programme to monitor vaccine efficacy and to conduct ongoing surveillance of equine influenza virus.

Surveillance is also carried out in other countries, but generally remains poorly funded. Within the UK this work is funded by the HBLB and is carried out by the AHT, an OIE reference laboratory for equine influenza virus.

Nasal swabs are collected by equine practitioners from horses suspected of influenza and are sent to the AHT for diagnostic screening. Virus is isolated from positive samples and characterised as described above.

A sentinel practice scheme has been established, through which diagnostic testing can be carried out free of charge. Currently there are 55 equine practitioners registered for this scheme, each participant receives a sampling pack plus regular newsletters.

There is also a dedicated website with further information about outbreaks and characterisation of viruses - www.equiflunet.org.uk

The vaccine strain selection process can only work if there are viruses to review. The UK and Ireland have the most comprehensive surveillance systems in place, in other countries it has proven difficult to obtain funding for this type of research.

Why is flu vaccination mandatory in racehorses?

The short answer is because it does what the racing industry wants it to; that is, since the introduction of the mandatory flu vaccination policy, there have been no race meetings cancelled due to flu.

Although horses still can and do get flu, vaccinated horses generally suffer less severe disease than those that are not vaccinated.

Mandatory vaccination was introduced by the Jockey Club for racing thoroughbreds in 1981, in response to the extensive outbreak of equine influenza in 1979 that caused widespread disruption to the equine industry and this highlights the importance of continually striving to keep the vaccines updated as the flu viruses evolve and circumvent them.

A further outbreak occurred in 1989 in which vaccinated horses were not protected. Since then, three major changes have been recommended to vaccine strains. The first formal recommendation to update strains was made in 1993 and referred to the need to replace out-of-date vaccine strains from 1979-1981 with viruses isolated in 1989.

In the mid 1990s it became clear that equine H3N8 viruses had diverged into 2 sublineages, designated European and American, which were antigenically distinct. In 1995 a recommendation was made that vaccines should contain a representative of both sublineages.

No major breakdowns in vaccination occurred in the UK until 2003, when over 1,000 horses were affected in Newmarket. Later the same year, a huge outbreak occurred in South Africa, where no vaccination programme was in place.

In 2004, a further update was recommended for the American lineage viruses: the 1993/1994 viruses should be replaced by viruses antigenically similar to South Africa/4/2003. This decision was based on field infections in vaccinated horses and antigenic differences determined in the laboratory using ferret sera.

The most recent change in the recommendations were made in early 2010: there is no longer a requirement for the Eurasian lineage virus and the vaccines should contain a representative of both Florida sublineage clades 1 (e.g. South Africa/4/2003, Lincoln/07) and 2 (Richmond/1/2007).

The recent epidemics of Equine influenza in a vaccinated horse population in Japan and a naïve population in Australia demonstrate the huge economic consequences of major outbreaks.

These events highlight the importance of supporting schemes that contribute to better vaccines through appropriate selection of strains and monitoring that products meet the potency standards laid down by the OIE.

The existence of a network of collaborating centres with experts in equine influenza around the world is crucial to provide a global service for management of such outbreaks. The recent pandemic of swine influenza in humans shows how rapidly influenza can spread in a susceptible population. Unlike most other animals, high value competition horses are also transported around the world for events and breeding and are vulnerable to infection unless adequately protected.

Conclusions

Flu is a persistent threat to racing and racehorses. It is a cunning enemy, continually evolving to resist control by vaccination. The HBLB-funded **Equine Influenza Surveillance Programme** contributes the majority of the data available for vaccine strain selection and in doing so helps reduce the impact of equine influenza virus on the UK's horse population for the benefit of the racing industry.

With large epidemics of divergent equine influenza viruses occurring elsewhere in the world and the ability of influenza to cross the species barrier, surveillance has never been so important in order to keep the equine population in the UK as well protected as possible.

The racing industry's on going support of this work is essential to avoid catastrophic flu vaccine breakdown.

To find out more about HBLB's research go to:

- HBLB's Advances in equine veterinary science and practice

  http://onlinelibrary.wiley.com/journal/10.1001/%28ISSN%292042-3306/homepage/hblb_virtual_issue.htm