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THE EQUINE INFLUENZA SURVEILLANCE PROGRAMME

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Il n'y a pas de procédure formelle de sélection des souches de vaccin de la grippe équine et les vaccins sont préparés à partir de souches prototypes anciennes. On a montré que la dérive antigénique des virus A/équin 2 affectait l'efficacité des vaccins aussi bien dans les études de terrain qu'expérimentales. Un effort international a permis d'augmenter le nombre de virus de la grippe équine isolés et caractérisés et a fourni la base pour un examen formel de la pertinence des souches de virus utilisées dans les vaccins. Un comité d'experts examine chaque année les données épidémiologiques ou l'efficacité des vaccins, la caractérisation antigénique et génétique des virus du monde entier soumis aux laboratoires de l'Office International des Epizooties et de l'Organisation Mondiale de la Santé. Des recommandations sont publiées tous les ans dans le Bulletin de l'OIE. Les autorités européennes délivrant les autorisations de mise sur le marché ont réagi en développant une procédure d'autorisation rapide pour les vaccins de la grippe équine quand ceux-ci ont besoin d'être remis au goût du jour.

A partir de l'observation que depuis 1987, la seule lignée des virus A/équin 2 a divergé en 2 sous-lignées correspondant aux virus de type américain et européen, le comité d'experts a recommandé que les vaccins contiennent 2 virus A/équin 2 correspondants aux virus Kentucky/94 (type américain) et Newmarket/2/93 (type européen). Etant donné la preuve sérologique que les virus A/équin 1 continuent à circuler même s'ils n'ont pas été isolés au cours des 10 dernières années, un virus A/équin 1 tel que Prague/56 (H7N7) devrait aussi être intégré dans les vaccins.

Equine influenza is caused by two virus subtypes, A/equine 1 (H7N7) and A/equine 2 (H3N8), and has a worldwide distribution with the exception of Australasia. During the last 10 years there have been very few confirmed outbreaks caused by A/equine 1 viruses, but repeated epidemics of influenza caused by A/equine 2 viruses have occurred, affecting both vaccinated and unvaccinated horses around the world.

Inactivated influenza vaccines containing representatives of both subtypes are used in many countries, particularly for vaccination of competition animals. Historically there has been no formal review of antigenic drift and its effect on vaccine efficacy, and many vaccines retained the original prototype viruses A/equine/2/ Miami/63 (H3N8) and A/equine/1/Prague/56 (H7N7) for twenty years or more.

During 1979-1981 a widespread epidemic of influenza A/equine 2 affected vaccinated and unvaccinated horses in Europe and America. As a result of antigenic and genetic analysis of viruses arising during the outbreak and comparison with earlier isolates, it was concluded that antigenic drift had occurred among A/equine 2 viruses which was likely to have compromised vaccine efficacy and inclusion of recent strains in vaccines was recommended. Additionally, it was noted that antigenic variants co-circulated and that more surveillance and virus characterisation was required in order to select the most prevalent viruses for inclusion in vaccines (Hinshaw et al 1983). Vaccine manufacturers responded by including Fontainebleau/79 like viruses, or Kentucky/81 like viruses in vaccines either in addition to or replacing the prototype H3N8 virus Miami/63.

During the 1989 epidemic of influenza A/equine 2 which occurred in Europe, well vaccinated horses with high levels of vaccinal antibody succumbed to infection and disease providing evidence that vaccine induced antibody was failing to protect against infection with the strains of influenza circulating at that time. Experimental studies in ponies provided supporting evidence that vaccines containing early strains were less effective in suppressing virus excretion than vaccines containing modern viruses antigenically homologous with the infecting virus. In response to these findings some vaccine manufacturers updated their vaccines with recent isolates of H3N8 viruses eg Suffolk/89, Borlange/91. At the time these viruses were selected it was not known whether they were representative of the most prevalent antigenic types circulating although this information was accumulated retrospectively.

The need to increase surveillance and virus characterisation in order to select appropriate vaccine strains was further emphasised at a meeting held in 1992 to discuss Newly Emerging Strains Of Equine Influenza. Subsequently there has been a concerted and coordinated effort to isolate more viruses from outbreaks around the world (Mumford and Wood 1993) and to characterise them antigenically and genetically in order to monitor the continuing epidemiological relevance of strains included in vaccines.

Progress in surveillance and vaccine strain selection was reviewed at a meeting of WHO/OIE experts held in 1995 on Progress in Surveillance of Equine Influenza and Application to Vaccine Strain Selection. The group concluded that since 1992 surveillance had improved especially in Europe and America and surveillance and reporting had been initiated in East Asia, Africa and South America. More viruses were available for

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characterisation and genetic analysis of a large number of viruses by the OIE Influenza Reference Laboratories in Newmarket and Kentucky has revealed that the single evolutionary lineage of A/equine 2 viruses has diverged into two groups since 1987, one circulating mainly in Europe and the other mainly in the Americas (Daly et al 1995).

An extensive panel of post infection ferret sera have been used to analyse the antigenic character of a large number of recent isolates and were able to differentiate between American- and European-like viruses. However a small number of isolates particularly from Eastern Europe and Italy were not identical antigenically to the majority of isolates from other countries in Europe.

The significance of the antigenic diversity between the two sub-lineages was tested in limited studies in horses which showed that a vaccine containing an American-like virus is less effective against challenge with a European-like virus than a vaccine based on an antigenically homologous European-like virus, particularly with regard to suppression of virus excretion.

Formal reporting of antigenic and genetic drift has been instituted on an annual basis through publication in the OIE Bulletin of recommendations made by the Expert Surveillance Panel which includes representatives from WHO and OIE influenza reference laboratories. To date decisions have been based on review of antigenic analysis using post-infection ferret sera, genetic analysis, ie sequencing of the HA gene, epidemiological surveillance of vaccine efficacy and some vaccination and challenge data from studies in horses.

Following the 1995 meeting the Expert Surveillance Panel recommended that vaccines should contain two A/equine/2 viruses, one representative of American-like (eg Kentucky/94 or Newmarket/1/93) and the other representative of European-like viruses (eg Suffolk/89 or Newmarket/2/93). In 1996 and 1997 the Expert Surveillance Panel have reviewed available data and concluded that there has been no indication that further changes are necessary.

The means by which recommendations for new strains can be implemented rapidly and efficiently is now under review. A rapid licensing system for influenza vaccines containing updated strains is being developed in Europe on the basis that accurate standardisation of in vitro vaccine potency tests will allow a reduction in animal testing of the final product, such that delays in new products reaching the market can be avoided.

Freeze dried post-infection equine antisera to A/equine/2 American-like and European-like viruses have been prepared and are currently being evaluated in an International Collaborative study. These reagents will be used to standardise the sensitivity of serological tests used to measure the antibody responses to vaccines in horses and small animals. Antigens and antisera are also being prepared to provide reagents for the Single Radial Diffusion test to be used as an in process potency test for vaccines. Once the reagents and rapid licensing system are in place it will be possible for vaccine manufacturers to response speedily to recommendations to update vaccine strains arising from the data collected by the Expert Surveillance Panel.

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