Guidelines for the Control of Equine Viral Infections

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VIRUSES are unique because they contain only one type of nucleic acid whereas all other forms of life contain two. The type of nucleic acid is the cornerstone of virus taxonomy; it may be either deoxyribonucleic acid or ribonucleic acid. Viruses, thereafter, are further differentiated by physical and morphological features.

DNA Viruses

DNA viruses fall into five groups (Table I). At least twelve viruses affecting horses are DNA viruses; one or perhaps two are Papovaviruses, namely, equine papilloma and equine sarcoid; at least one is an Adenovirus (Mayr, Pette and Pape, 1966), seven are Herpesviruses and perhaps three are Poxviruses, horse pox, grease and papular dermatitis. Horse pox characterised by the development of typical pocks on the lips and oral mucosa and grease characterised by dermatitis of the pasterns and heels may be different clinical manifestations of infection by the same virus (Andrewes and Pereira, 1967). Papular dermatitis, on the other hand, is unlikely to be a variant of horse pox (McIntyre, 1949).

The seven Herpesviruses are equine herpes 1 (Plummer and Waterson, 1963) commonly called equine rhinopneumonitis virus and often implicated in upper respiratory tract infections and abortions, herpes 2

TABLE I
DNA VIRUSES INFECTING HORSES

Group	Virus
Picodnavirus	—
Papovavirus	Equine papilloma
Adenovirus	Equine adeno
Herpesvirus	Herpes 1
	Herpes 2
	CEO
	Herpes 3
	Cytomegalovirus
	Australian coital exanthema
	Iowa leukocyte
Poxvirus	Horse pox
	Grease
	Papular dermatitis?

Paper presented at the general meeting of the British Equine Veterinary Association, Edinburgh, 1970.

TABLE II
RNA VIRUSES ISOLATED FROM HORSES
OR EQUINE TISSUES

Group	Virus
Picornavirus	Rhino 1
	Rhino 2
	Aborted foal
Reovirus	African horse sickness
Myxovirus	Influenza A
	Influenza C
Paramyxovirus	Parainfluenza-3
Rhabdovirus	Rabies
	Vesicular stomatitis
	Ditchfield's
Coronavirus	Eastern encephalitis
Arbovirus	Western encephalitis
	Venezuelan encephalitis
	West Nile
	Japanese B encephalitis
	Murray Valley encephalitis
	Equine infectious anaemia
	Infectious arteritis
Oncornavirus	
Ungrouped	

(Plummer and Waterson, 1963) isolated from the respiratory tract of a colt with rhinitis, CEO virus (Kono and Kobazashi, 1964) isolated in Japan spontaneously from cultures of equine kidney and bone marrow cells, herpes 3 (Karpas, 1966) isolated from the kidneys of an apparently healthy foal, equine cytomegalovirus (Hsiung, Fischman, Fong and Green, 1969) isolated from spontaneously degenerating equine kidney cell cultures after prolonged cultivation, Australian coital exanthema virus (Pascoe, Spradbrow and Bagust, 1969) isolated from lesions on a stallion, and Iowa leukocyte virus (Kemeny and Pearson, 1970) isolated from the leukocytes of 71 out of 80 apparently normal Iowa horses. The antigenic relationships of the Iowa leukocyte virus to the other equine herpesviruses has yet to be established.

RNA Viruses

RNA viruses have either cubic, helical or unknown symmetries. There are two groups of cubic RNA viruses, Picornavirus and Reovirus, four groups of

TABLE III
RNA VIRUSES INCRIMINATED SEROLOGICALLY
AS INFECTING HORSES

Group	Virus
Myxovirus	Influenza B
Paramyxovirus	Parainfluenza-1
	Parainfluenza-2
Rhabdovirus	Cocal
Arbovirus	Aura
	Sagiyama
	Una
	Absettarov
	Ilheus
	St. Louis encephalitis
	Wesselsbron
	Cache Valley
	Calovo
	Germiston
	Kairi
	Maguari
	Bwamba
	Pongola
	Tahyna
	Trivittatus
	Bimiti
	Kemerovo
	Kowanyama
	Nyamanini
	Tacaiuma

helical RNA viruses, Myxovirus, Rhabdovirus, Paramyxovirus and Coronavirus, and two groups with unknown symmetries, Arbovirus and Oncornavirus (Tables II and III). Three Picornaviruses infect horses, namely rhino 1 (Plummer, 1962), rhino 2 (Ditchfield and Macpherson, 1965) and aborted foal virus (Bohm, 1964). African horse sickness virus is believed now to be a Reovirus (Ozawa, 1968). Three Myxoviruses, influenza A (Heller, Espmark and Viriden, 1956), influenza B (Ditchfield, Macpherson and Zbitnew, 1965), and influenza C (Ditchfield *et al.*, 1965) and three Rhabdoviruses, rabies, vesicular stomatitis and cocal viruses, infect horses. Serological evidence (Ditchfield *et al.*, 1965) incriminates parainfluenza-1 and parainfluenza-2 viruses belonging to the Paramyxovirus group.

In addition, parainfluenza-3 virus has been isolated from horses with upper respiratory tract infections (Ditchfield, Zbitnew and Macpherson, 1963). There is possibly one Coronavirus infecting horses; Ditchfield (1969) isolated a virus from a Thoroughbred with undifferentiated respiratory disease and found that it possessed a morphology similar to that of infectious bronchitis virus of poultry, the type-virus of the Coronavirus group.

There are more than 200 arboviruses and at least 27 infect horses. Equine infectious anaemia virus probably belongs to the Oncornavirus group, i.e. the RNA tumour viruses. Infectious arteritis virus (Doll, Bryons, McCollum and Crow, 1957), on the other hand, is known to be a RNA virus but it is as yet ungrouped. Recent electron microscopic studies revealed a morphology like that of the arboviruses (Breese and McCollum, 1969).

Unclassified Viruses

Three diseases of horses, Borna disease (Zwick and Witte, 1929), Near East equine encephalomyelitis (Daubney and Mahlau, 1957) and Nigerian horse staggers (Porterfield, Hill and Morris, 1958) are caused by viruses as yet unclassified and it is possible that the three diseases are caused by the same virus. Finally, there are at least three other alleged viral diseases, serum hepatitis (Theiler, 1919), grass sickness (Obel, 1955) and virus diarrhoea (Rooney, 1969).

Disease Syndromes

In summary, 58 viruses are known to infect horses and every year more are added to the list. At least 28 of the 58 viruses induce clinical disease; the other 30 are incriminated only by the detection of specific antibodies in horse sera. The differential diagnostic problems posed by this array of viruses are formidable and highlight the need for more laboratories and more virologists. Diagnosis is further confounded by the fact that eleven of the viruses provoke respiratory symptoms and eleven cause encephalitis (Table IV). In addition, equine herpes 1 and equine arteritis viruses induce abortion; equine arteritis virus is also associated with pinkeye; herpes 1 and Australian coital exanthema viruses cause venereal lesions; pox, grease, papular dermatitis and vesicular stomatitis viruses cause skin and mucosal lesions; equine infectious anaemia virus induces progressive weakness and anaemia; and African horse sickness virus produces oedema subcutaneously as well as in the lungs.

TRANSMISSION

A key factor in controlling infectious disease is a knowledge of the modes of transmission. In general, viruses are transmitted either by arthropod vectors or by contact between sick and healthy animals. None of the DNA viruses affecting horses is transmitted by vectors, eight are contagions and four are transmitted by modes as yet unknown. In contrast, 31 RNA viruses are transmitted by vectors and 12 by contact. Two of the three unclassified viruses, Near East equine encephalomyelitis virus and Nigerian horse virus, are transmitted by arthropods. Daubney (1967) has suggested that Borna disease virus is also arthropod-borne.

TABLE IV
THE COMMON DISEASE SYNDROMES
INDUCED BY EQUINE VIRUSES

Respiratory Disease	Encephalitis
Adeno	Rabies
Herpes 1	E.E.E.
Herpes 2	W.E.E.
Rhino 1	V.E.E.
Rhino 2	W.N.
A.H.S.	Jap. B
Influenza A	M.V.E.
Influenza C	Borna
Parainfluenza-3	N.E.E.E.
Corona	Nigerian staggers
Arteritis	Serum hepatitis

The geographical distribution of equine viruses is closely correlated with the mode of transmission. The vector-transmitted viruses have a restricted global distribution (Table V) whereas the contagions are widely distributed (Table VI).

VACCINATION

Vector-transmitted Viruses

With the possible exception of African horse sickness, infections of horses by vector-transmitted viruses are accidental and play no role in the natural life cycles of the viruses concerned. Cases are sporadic. Eradication is impossible. One is limited, therefore, to prophylactic vaccination as being the only practical control measure. Eleven of the thirty-four known vector-transmitted viruses cause disease and vaccines have been developed against six of them (Table VII). There is also a vaccine for vesicular stomatitis but it has not been used to protect horses (Corrêa, 1964). Similarly Japanese B encephalitis vaccine and Wesselsbron vaccine have not been used to protect horses (Kodama, Sasaki and Inoue, 1968; Neitz, 1966).

TABLE V
LOCI OF EQUINE VECTOR-TRANSMITTED
VIRUS DISEASES

	Africa	Asia	Austral- asia	Europe	North Amer- ica	South Amer- ica
A.H.S.	+					
V.S.					+	+
E.E.E.					+	+
W.E.E.					+	+
V.E.E.					+	+
West Nile	+	+		+		
Jap. B		+				
M.V.E.		+	+			
Borna				+		
N.E.E.E.	+	+				
Nigerian	+					

Viral Contagions

Unlike the diseases transmitted by vectors, the contagions are open to attack on several fronts—segregation, deliberate exposure, vaccination, therapy. Nevertheless the favoured technique is vaccination. Seventeen of the twenty known viral contagions of horses cause disease and vaccines have been developed against five of them (Table VIII). In addition, parainfluenza-3 vaccines have been developed for use in humans and cattle (Potash, Tytell, Sweet, Machlowitz, Stokes, Weibel, Woodhour and Hilleman, 1966; Byrne, Abinanti and Huebner, 1961).

Efficacies of Vaccines

How efficient are the vaccines? In 1947 Francis published a classification of human viral infections based on the duration of the infection in the host and the durability of the immunity induced. He recognised four groups; the first were diseases in which the virus persisted and immunity did not; the second were diseases in which the infection was transient and immunity was persistent; the third were the diseases in which both

TABLE VI
LOCI OF EQUINE VIRAL CONTAGIONS

	Africa	Asia	Austral- asia	Europe	North Amer- ica	South Amer- ica
Papilloma	+	+	+	+	+	+
Adeno		+		+	+	
Herpes	+	+	+	+	+	+
Pox	+	+		+	+	
P.D.			+		+	
Rhino	+			+	+	
Influenza	+	+	+	+	+	+
Rabies	+	+		+	+	+
Parainfluenza				+	+	
Corona					+	
E.I.A.	+	+	+	+	+	+
Arteritis	+	+	+	+	+	+

infection and immunity were transient; and the fourth were the diseases in which both the infection and the immunity persisted.

The Francis classification furnishes a guide as to whether or not vaccines are feasible and whether or not they can be expected to be efficient. Diseases falling into the first group will never be controlled by vaccines. In contrast, diseases falling into the other three groups are amenable to control by vaccination but the only efficient vaccines as measured by the durability of the immunity induced are those developed against the diseases classified in the second group.

Equine viral diseases occupy every niche of the Francis classification (Table IX). Thus equine infectious anaemia is ranked in the first group, the group of diseases for which vaccines cannot be developed. Equine serum hepatitis, if it is a virus infection, probably also belongs to the first group.

Eleven diseases are assigned to the second group and vaccines developed against these are, or can be expected to be highly efficient inducing long-lasting sterile immunity. The viruses responsible are papilloma, the poxes, rabies and the arboviruses.

Six diseases fall into the third group and vaccines developed against these diseases in general, have proved disappointing. The viruses responsible are characterised by having a multiplicity of serotypes. There are, for

TABLE VII
VACCINES AVAILABLE FOR EQUINE
VECTOR-TRANSMITTED VIRUSES

Virus	Type of Vaccine	Protection (yrs.)
A.H.S.	Killed	< 1
	Live	< 2
E.E.E.	Killed	< 1
W.E.E.	Killed	< 1
	Live	> 1
V.E.E.	Killed	< 1
	Live	> 1
Borna	Killed	?
Nigerian	Live	?

TABLE VIII
VACCINES AVAILABLE FOR EQUINE
VIRAL CONTAGIONS

Virus	Type of Vaccine	Protection (yrs.)
Papilloma	Killed	?
Herpes 1	Killed	< 1
	Live	< 1
Influenza A	Killed	< 1
Rabies	Killed	> 1
	Live	> 2
Arteritis	Live	> 1

example, nine serotypes of African horse sickness virus. Undoubtedly, many of the poor results from vaccination can be attributed to antigenic drift because immunity to the homologous serotype is often of long duration.

Ten diseases are assigned to the fourth group. These are the diseases in which the virus persists. Consequently relapses are common despite the presence of antibodies. Successful vaccination against the members of this group necessitates use of live attenuated viruses and it is, in effect, deliberate infection.

Three of the current vaccines developed against vector-transmitted viruses and three likely to be developed in the future can therefore be classed as excellent. Three current vaccines are poor. Two still to be developed will probably be poor. In contrast, three of the five current vaccines used against equine viral contagions are vaccines of low efficacy and, in the future, it is likely that eleven out of sixteen possible vaccines will be poor products.

TREATMENT

If the forecast that most of the vaccines developed against equine viral contagions will be of low efficacy is correct then other control measures must be exploited. Treatment whether by serotherapy or by chemotherapy of established viral infections is doomed to failure because the virus population curve in the infected animal reaches its peak before the onset of clinical signs.

For example, in horses infected with Eastern equine encephalitis the peak of the virus population curve occurs one day before the onset of fever and five days before the onset of encephalitis (Byrne, French, Yancey, Gochenour, Russell, Ramsburg, Brand, Scheider and Buescher, 1964). Similarly, in horses infected with influenza A/equi/2 virus the peak of the virus population curve coincides with the first wave of the intermittent fever and precedes by many hours the onset of coughing (Blaskovic, Kapitancik, Sabo, Styk, Vrtiak and Kaplan, 1969).

Treatment, therefore, to be successful must be prophylactically administered; it is too late to alter the course of the first clinical case but the disease can be averted in the in-contacts. The common prophylactic treatment is the administration of antiserum. Unfortunately it is expensive and not without dangers, particularly, the risk of transmitting serum hepatitis. Interferon is another possible natural product but it has failed to live up to its initial promise.

Many pharmaceutical houses are synthesising and developing anti-viral drugs but the "breakthrough" has yet to come. Amantadine appears to have a selective action on influenza virus. Methisazone shows promises in protecting smallpox contacts. Iodode-

oxyuridine, likewise, acts against smallpox and human herpes. Others will follow—they will be needed!

SUMMARY

Twelve DNA viruses and forty-three RNA viruses are known to infect horses. In addition, there are three unclassified viruses and, at least, three alleged viruses infecting horses.

Differential diagnosis is difficult. At least twenty-eight of the fifty-eight viruses induce clinical disease but the range of syndromes is limited; eleven provoke respiratory symptoms and eleven cause encephalitis.

Thirty-four equine viruses with a limited geographical distribution are transmitted by arthropod vectors. Twenty viruses are spread by contact and their distribution, in general, is global.

The vector-transmitted virus diseases are best controlled by prophylactic vaccination. The viral contagions are not, in general, well controlled by vaccination and it is likely that prophylactic chemotherapy will become increasingly important in the future.

RÉSUMÉ

On sait que douze virus ADN et quarante trois virus ARN sont responsables d'infections chez le cheval. En outre trois virus non classés et trois autres agents de type viral au moins sont également infectants pour cette espèce.

Le diagnostic différentiel est difficile. Vingt huit au moins des cinquante trois virus provoquent des maladies cliniques mais la gamme des syndromes est restreinte:

Onze virus engendrent des symptômes respiratoires, onze déterminent des encéphalites.

Trente quatre virus dont la distribution géographique est limitée sont transmis par des arthropodes vecteurs.

Vingt virus sont disséminés par contact et leur répartition est en général à l'échelle du globe.

Les maladies provoquées par des virus à propagation vectorielle sont mieux contrôlées par une vaccination préventive.

Les contagions virales ne sont pas, en général, efficacement contrôlées par la vaccination et l'on peut penser que la chimiothérapie préventive de ces affections connaîtra une importance croissante à l'avenir.

TABLE IX
THE FRANCIS CLASSIFICATION APPLIED TO
EQUINE VIRAL DISEASES

Group 1 (+ —)	Group 2 (— +)	Group 3 (— —)	Group 4 (+ +)
E.I.A.	Papilloma ?	A.H.S.	Adeno
	Pox	Influenza A	Herpes 1
	Grease	Influenza C	Herpes 2
	P.D.	V.S.	A.C.E.
	Rabies	Parainfluenza-3	Rhino 1
	E.E.E.	Corona	Rhino 2
	W.E.E.		Arteritis
	V.E.E.		Borna
	W.N.		N.E.E.E.
	Jap. B		Nigerian
	M.V.E.		

ZUSAMMENFASSUNG

Zwölf DNS-Viren und 43 RNS-Viren vermögen das Pferd zu infizieren. Dazu kommen drei unklassierte Viren und zum mindesten drei Erreger, die angeblich Viruscharakter haben.

Die Differentialdiagnose ist schwierig. Mindestens 28 der 58 Viren verursachen klinisch manifeste Krankheiten, aber die Eigenart der Syndrome ist limitiert; elf davon provozieren respiratorische Symptome und elf rufen Enzephalitis hervor.

34 equine Viren benötigen als Vektoren Arthropoden; ihre geographische Ausbreitung ist beschränkt. 20 Viren werden durch Kontakt übertragen; sie werden in der Regel auf der ganzen Welt angetroffen.

Die durch Vektoren übertragenen Viruskrankheiten können am besten durch prophylaktische Impfungen kontrolliert werden. Die übrigen können im allgemeinen durch Impfungen nicht gut kontrolliert werden und es scheint wahrscheinlich, dass die prophylaktische Chemotherapie in Zukunft an Bedeutung gewinnen wird.

SUMARIO

VIRUS EQUINOS Doce DNA virus y cuarenta y tres RNA virus son reconocidos como infectantes al caballo. En adición hay tres no clasificados virus y por lo menos tres tipos de virus muy semejantes que afectan al caballo.

El diagnóstico diferencial es difícil. Aproximadamente 28 de los 58 virus inducen enfermedades clínicas con un espectro de síndromes limitado. 11 provocan síntomas respiratorios y 11 causan encefalitis.

34 virus equinos con limitación en su distribución geográfica son transmitidos por vectores artrópodos. Veinte virus son diseminados por contacto y su distribución en general es global. Es controlada la enfermedad de estos vectores por medio de vacunación. Los contagios del virus no son bien controlados por lo general mediante vacunación y solo una terapia profiláctica que havenido tomando auge en el futuro.

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DISCUSSION

M. A. P. Simons (Epsom) opened the discussion and congratulated Dr. Scott on his review of the equine viruses. The urgency of a better knowledge of virus diseases had been underlined at the recent International Conference in Paris. He asked Dr. Scott if viruses were associated with labial and oral lesions and with grease and mud fever, and he described a case of papular dermatitis in a 2-year-old Thoroughbred and wondered if this might be a viral condition. Mr. Simons said that since many viruses known to infect horses did not occur normally in the British Isles veterinary sanitary regulations were of the first importance and proper inspection by trained eyes was necessary. Air transport was, of course, the hazard. Was the use of insecticidal sprays of any value? On another aspect of epidemic control what proportion of a susceptible population was it necessary to vaccinate to halt the spread of infection? What veterinary laboratories were currently investigating virus diseases?

Dr. G. R. Scott replied that papular dermatitis was a contagion of probably world-wide distribution. The value of insecticidal spraying to limit the spread of arbo-viruses was considerably aided by the inability of most arbo-viruses to flourish for any length of time outside their endemic home area. On control by vaccination it was generally accepted that vaccination of 70 per cent of a population was adequate to abort an epidemic. On the other hand there was a recent hypothesis that vaccination of only 10 per cent was adequate to prevent measles spreading. Current work on equine viruses was being carried out by Robert Burrows at Pirbright, influenza was under study at Cambridge and pox infections were under investigation at Liverpool.

Dr. J. R. Campbell (Glasgow) asked for how long prophylactic treatment should be given to prevent outbreaks of virus infection.

Dr. Scott replied that drugs might well be used in a closed community where animals could be segregated and movement stopped. Drugs could be used prophylactically over a short period for a non-persistent virus. Persistent viruses should be dealt with by infecting horses with live attenuated virus vaccines before they were required to hunt or race.

G. N. Sutherland (York) enquired if an alteration of serotype would affect the value of this year's 'flu vaccine.

Dr. Scott agreed that it would and added that infection in an immunised animal was a good way to produce a new serotype.

I. M. Seckington (Oakham) said that, given a serotype and its vaccine, if the one changed then the other must be changed. He asked why hunters acquired a better immunity than Thoroughbreds.

Dr. Scott replying, did not agree that this was so. He was aware that young animals reacted more severely than older ones.

P. S. Hastie (Buckingham) asked what were the signs shown by the Thoroughbreds in which vaccination was unsatisfactory.

I. M. Seckington said that while stables of hunters vaccinated had remained completely resistant, horses in racing stables had gone down with influenza after vaccination.

Dr. G. R. Scott attributed this to different viruses. They were impossible to distinguish clinically.

R. E. McGrath (Paisley) commented that nowadays most hunters were Thoroughbreds.

M. A. P. Simons pointed out the value of taking a series of blood samples at 21 day intervals to check the identity of viruses. Mr. Burrows at Pirbright was willing to accept and report on them. Serum only should be sent without the blood cellular element.

L. B. Jeffcott (Newmarket) confirmed this, saying that virus abortion was likely to occur in animals that had not, as youngsters, mixed with older animals.

N. W. Keith (Kelso) asked if vaccination against papillomatosis was to be recommended.

Dr. G. R. Scott said that it was not a commercial proposition but it had been used specifically for single cases, allegedly successfully.

Brigadier J. H. Wilkins (Droitwich) asked what was the maximum cover that could be given to horses against virus infections.

Dr. G. R. Scott advised periodic influenza vaccination and said that live vaccine against rhinopneumonitis and equine arteritis had been effective in producing lifelong immunity in the U.S.A. but there was some doubt if the use of such live vaccines was legal in the British Isles.