Section of Comparative Medicine

President Olga Uvarov MRCVS

Meeting February 21 1968

Antigenic Variations in Influenza Viruses [*Abridged*]

Dr H G Pereira
(*World Influenza Centre, National Institute for Medical Research, Mill Hill, London*)

Antigenic Variation in Influenza Viruses in Man and Animals

Of the 3 types A, B and C into which influenza viruses are divided, only the first has been shown unequivocally to cause natural infections in hosts other than man. Type A viruses isolated from man, pigs, horses and birds are indistinguishable in all their basic characters such as morphology, chemical composition and mechanism of replication. Their internal nucleoprotein component is antigenically identical. They all interact genetically with each other and hybrids of any two strains can be obtained by suitable manipulations.

This concept of the unity of influenza A viruses is relatively recent. Although close relationship between porcine and human strains was accepted very soon after the discovery of influenza viruses, there has been a tendency to consider avian and equine strains as standing apart even after their identification as influenza A viruses had been established by the demonstration of the type-specific nucleoprotein antigen. This tendency has been reversed by accumulated evidence on the close genetic and antigenic relationships between all influenza A viruses.

A classification of influenza A viruses according to natural hosts and antigenic structure is shown in Table 1. Antigenic subtypes can only be clearly distinguished among human and equine strains. Antigenic variants showing varying degrees of cross-reactivity can be distinguished within human or equine subtypes and within porcine and avian strains.

Recent interest in the study of avian influenza viruses has resulted in the description of numerous isolates which could be arbitrarily classified into 6 antigenic groups (Pereira *et al.* 1966). Representative strains of each of these groups are shown in Table 2. All but one out of a total of 44 strains received for study at the World Influenza Centre could be allocated to one or another of the six antigenic groups. Their distribution according to natural hosts is shown in Table 3. The majority of strains belong to Group 2 and originate from Pavia and surrounding districts in Northern Italy (Pereira *et al.* 1968). Other strains were from several countries in Europe, Africa and North America. With the single exception of the isolate from terns in South Africa, all strains were derived from birds bred in captivity.

Table 1
Classification of influenza A viruses

Natural host	*Subtype*	*Antigenic variants*
Human	A0, A1, A2	Several in each subtype
Porcine	–	At least 3
Equine	Eq 1, Eq 2	At least 2 within Eq 2
Avian	–	At least 6

Table 2
Antigenic groups of avian influenza A viruses

Antigenic group	*Representative strains*
1	FPV, T/England/63
2	Virus N, Quail/Italy/1117/65
3	Duck/England/56
4	Duck/Czech./56, Duck/Eng./62
5	Ch/Scotland/59, Tern/S.A./61
6	T/Canada/63, T/Mass./65

Table 3
Distribution of avian influenza A strains investigated at the World Influenza Centre, according to natural host and antigenic group

Host	No. of strains	Antigenic grouping 1	2	3	4	5	6	–
Chicken	5	1	3	–	–	1	–	–
Duck	10	–	7	1	2	–	–	–
Turkey	16	1	7	–	–	2	5	1
Quail	10	–	10	–	–	–	–	–
Pheasant	2	–	2	–	–	–	–	–
Tern	1	–	–	–	–	1	–	–
Total	44	2	29	1	2	4	5	1

Table 4
Antigenically related influenza A viruses of human and animal sources

(1) Eq 1/Prague/56, FPV, Turkey/England/63

(2) Eq 2/Miami/63, Quail/Italy/1117/65, Pheasant/Italy/647/66, Duck/England/62, Turkey/Canada/63

(3) A2/Singapore/1/57, T/Mass./65

(4) Chicken/Scotland/59, Swine/S15/30

antigenic component shared by human A2 and avian influenza strains is represented mainly if not wholly by the viral neuraminidase. This finding is illustrated in Table 5 where it is seen that, with the particular sera used in this test, cross-reactions between the two viruses are detected by strain-specific complement fixation and by neuraminidase-inhibition but not by hæmagglutination-inhibition. Of particular interest is the fact that an antiserum prepared against highly purified A2 neuraminidase fails to inhibit the hæmagglutinin of either virus but reacts with both in complement fixation and neuraminidase-inhibition tests.

A comparison of the avian strain turkey/Massachusetts/65 with successive antigenic variants of human A2 subtype is shown in Table 6, where it is seen that the avian strain is clearly related to early but not to late A2 antigenic variants. It is tempting to speculate from this result that the A2 strain may have originated from

Table 5
Comparison of strains turkey/Massachusetts/65 and A2/Singapore/1/57 by hæmagglutination-inhibition, strain-specific complement fixation and neuraminidase-inhibition

Strain	Antiserum T/Mass./65 HI	CF	NI	A2/Sing./57 HI	CF	NI	A2/Neuraminidase HI	CF	NI
T/Mass./65	*480*	*960*	*820*	<10	160	680	<10	640	800
A2/Sing./57	<10	160	800	*640*	*1,280*	*950*	<10	480	1,200

Figures represent reciprocals of 50% serum endpoints

Table 6
Comparison of avian and human A2 strains by strain-specific complement fixation

Antigen	Anti-V sera T/Mass./65	A2/Sing./57	A2/Eng./61	A2/Ned./63	A2/Eng./64
T/Mass./65	*480*	480	160	<10	<10
A2/Sing./57	160	*1,280*	80	60	30
A2/Eng./61	160	640	*320*	40	40
A2/Ned./63	<10	240	60	*960*	240
A2/Eng./64	15	40	30	480	*480*

Figures represent reciprocals of serum dilutions showing 50% complement fixation in the presence of optional antigen dilutions

A recent comparison of influenza A viruses of human and animal origins revealed antigenic relationships between a number of strains derived from different hosts. Table 4 shows four antigenically related groups, each including strains of mammalian and avian origins. Of particular interest was the cross-reaction observed between human A2/Singapore/1/57 and the avian strain turkey/Massachusetts/65. This cross-reaction was detected most clearly by strain-specific complement fixation (Pereira *et al.* 1967). Subsequent studies (Webster & Pereira 1968) revealed that the an avian strain and subsequently drifted away from it when exposed to immunological selection in human populations.

REFERENCES

Pereira H G, Lang G, Olesink O M, Snoeyenbos G H, Roberts D H & Easterday B C (1966) *Bull. Wld Hlth Org.* 35, 799

Pereira H G, Rinaldi A & Nardelli L (1968) *Bull. Wld Hlth Org.* 37, 553

Pereira H G, Tumova B & Webster R G (1967) *Nature (Lond.)* 215, 982

Webster R G & Pereira H G (1968) *J. gen. Virol.* 3, 201