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Hong Kong influenza in the Royal Air Force 1968–70

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SUMMARY

A prospective serological and clinical study of the epidemics due to the A2/Hong Kong/68 influenza virus was made during the winters 1968–9 and 1969–70 in volunteer subjects in the Royal Air Force. In October 1968 nearly all subjects had haemagglutination inhibiting (HI) antibody to the A2/Singapore/57 virus and more than half had antibody to strains more recently prevalent in Britain. The proportion with HI antibody to A2/Hong Kong/68 increased from 31 % in October 1968 (most at low titres) to 44 % after the first epidemic and 72 % after the second (most at high titres). Serological infection rates were much lower in those who had detectable antibody at the beginning of each winter than in those who did not. Respiratory illnesses coupled with serological evidence of influenza infection during the winter were rare in persons with an initial titre of HI antibody of 1/40 or more. Infection in the first winter conferred complete protection against infection, with or without illness, in the second. In both epidemics about half those with serological evidence of infection had no reported illness.

INTRODUCTION

Epidemics caused by the influenza A2 virus have occurred in Britain during most winters since the subtype first appeared in 1957. Meanwhile, the antigenic composition of the virus has gradually drifted from the original, with alterations being detected in relatively small stages over the years.

Then, in the summer of 1968, a new variant which was substantially different from all previous variants appeared in Hong Kong and caused extensive outbreaks in the Far East (Cockburn, Delon & Ferreira, 1969). This virus had an antigenically distinct haemagglutinin but its neuraminidase component was later shown to be similar to that of the earlier A2 strains (Coleman *et al.* 1968). The magnitude of the change in haemagglutinin, however, was such that antibody acquired by exposure to earlier variants was expected to confer little protection and widespread epidemics were forecast in all parts of the world, including Britain. This

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situation afforded an opportunity to study prospectively the spread of a new antigenic variant and the illnesses it caused in relation to serological measures of immunity and other factors thought to affect susceptibility to influenza virus infection and consequent illness. With the collaboration of the Royal Air Force Medical Service, an investigation was organized therefore to study the expected epidemic in the winter of 1968–9. In the event, no major epidemic occurred that winter. However, the following year, in 1969–70, there was a severe, explosive outbreak of influenza in all parts of the country. So it was decided to extend the study for a further year. Preliminary results have already been reported (Miller, Pereira & Clarke, 1971) and this paper gives the detailed findings.

MATERIALS AND METHODS

General plan

In the autumn of 1968 volunteers were recruited from among personnel in 13 R.A.F. stations in various parts of England and Wales. Blood specimens were obtained from the volunteers at that time and again in the spring of 1969. Any acute respiratory illness they reported in the intervening winter was investigated virologically and a clinical report was completed. All stations also kept records of every acute respiratory illness, in both volunteers and other personnel, which resulted in their absence from work.

After the unexpectedly severe epidemic in 1969–70 arrangements were made to extend the study by collecting a third blood specimen from all volunteers who could be contacted in the spring and summer of 1970, and to make a retrospective enquiry into any illness experienced in the previous winter.

Field methods

At the start of the study in October 1968, each station was visited by a doctor from the Epidemiological Research Laboratory, Colindale, who, with the help of the Station Medical Officer, enrolled the volunteers. A specimen of venous blood (5–10 ml.) was taken from each volunteer and a Personal Record Card was completed. This card recorded the following information: name of station, volunteer's name, rank, place of residence (i.e. billets, mess, married quarters), age and sex, blood group and influenza vaccination history (obtained from service or other medical documents), and current smoking habits with details of amount and type of tobacco smoked.

During the ensuing winter, when a volunteer reported to the Station Medical Officer with an acute respiratory or non-specific febrile illness, a nose and throat swab and acute and convalescent sera were obtained if possible. For each such illness a detailed clinical record was also completed and the date and diagnosis were entered on the Personal Record Card.

Copies of each station's weekly sickness returns (Stats. 58), which show details of all personnel absent from duty because of sickness for more than 48 hr., were sent to the Epidemiological Research Laboratory. From these returns weekly acute respiratory illness rates on each station were calculated.

Table 1. *The study population*

Blood specimens obtained	Total no. of persons	Illness records incomplete		Vaccinated		Total persons records complete and not vaccinated
		1968/9	1969/70	1968/9	1969/70	
1 and 2	912	18	—	119	—	775
2 and 3	560	—	19	—	62	479
1, 2 and 3	560	30		102		428

Stations were visited again in the early summer of 1969 and a second serum specimen was obtained from all volunteers who were still available. At the time of this visit a note was made of whether the volunteer had received influenza vaccine during the winter. Also, the survey records of illnesses were checked for discrepancies against each individual's service medical records and the Stats. 58. Few discrepancies were found, indicating that records were usually accurately maintained. If a volunteer was posted to another station in Britain during the winter, the Medical Officer at the new station was asked to continue the record of illnesses and, at the end of the winter, to take a second blood specimen and report whether or not the volunteer had been vaccinated against influenza. Volunteers who were posted abroad were not followed-up.

In the summer of 1970 an attempt was made to trace all volunteers from whom a second specimen of blood had been obtained the previous summer. This time those who had been posted abroad were included, but not those who had left the R.A.F. A third specimen of blood was taken from all those traced and the following details were entered on special record cards: the volunteer's account of his smoking habits immediately before the 1969–70 epidemic; whether or not he had received influenza vaccine since the second specimen of blood was taken; and all respiratory illnesses experienced in the interval which were recorded in the service medical records (i.e. illnesses for which the Medical Officer had been consulted). There was no means of checking the completeness of the records obtained, but cross-checks applied in the previous winter gave reason for confidence that omissions were likely to have been few.

Volunteer population

A total of 1183 volunteers, ranging from 30 to 136 on different stations, were recruited initially. Their average age was 29 years, with a range of from 17 to 57 years: 60% of them were under 30 years of age and 89% were male.

Subsequently, for a variety of reasons, many of the original volunteers were lost to the study; some because later specimens of blood were not obtained, some because they received influenza vaccine, and some because their illness records were not complete. The numbers whose records could be analysed, therefore, were depleted in successive stages of the study (Table 1). Of the original 1183 volunteers, 912 gave a second specimen of blood at the end of the first winter; but illness histories were incomplete for 18 of them and another 119 had received influenza vaccine during that winter. This left 775 volunteers for study during the winter

1968–9. A third specimen of blood was obtained from 560 of the 775; illness histories in the second winter were incomplete for 19 of these persons, and 62 received vaccine during that winter, leaving 479 for whom results could be analysed. Only 428 (36%) of the original 1183 volunteers gave three specimens of blood, had complete illness records throughout both winters and received no vaccine in either winter.

This lapse rate is high. However, we were unable to demonstrate any important differences between the base population and the residual group in respect of the distribution of the initial antibody titres, illness rates or other possibly significant variables about which we had information.

Laboratory methods

Routine blood specimens were transported by hand, or if this was not possible, by post, to the Virus Reference Laboratory, where the serum was separated and tested for haemagglutination inhibiting (HI) antibody by the methods described by Pereira, Pereira & Law (1964).

The initial sera, taken in October 1968, were examined on receipt for HI antibody to the A2/Singapore/57 virus and then stored at $-30°$ C. On receipt of the second sera, in the summer of 1969, the paired specimens were tested together for the presence of HI antibody to the Hong Kong variant of the A2 influenza virus, after which they were stored again at $-30°$ C. The third serum, taken in the summer of 1970, was tested for HI antibody in parallel with the first serum and, if a rise in antibody between the first and second sera had been detected, the third was also tested with the second serum. The initial sera from a selected group of volunteers (for convenience restricted to those from whom three specimens had been obtained) were also tested for HI antibody to A2/England/68 and A2/Tokyo/67 viruses which had been prevalent in the U.K. immediately before the Hong Kong/68 variant appeared and which carried the same neuraminidase as the A2/Hong Kong/68 virus.

The repeatability of antibody estimations was tested on a sample of specimens. No significant differences were found on repeated tests in the distribution of antibody titres between specimens or in the frequency of significant ($\geqslant$ fourfold) increases in titre.

The paired sera taken from volunteers when they became ill in the winter 1968–9 were sent to the nearest Public Health Laboratory for influenza complement-fixing antibody estimations (Bradstreet & Taylor, 1962). Swabs from the nose and throat were broken off into bottles containing a virus transport medium, placed on melting water ice and sent the same day to the laboratory, where they were examined for influenza virus by standard virus isolation procedures (Medical Research Council, 1965); all strains were sent to the Virus Reference Laboratory for further characterization.

Table 2. *Relation between diagnosis and laboratory results*

	Influenza	URTI	MRTI	LRTI	Total
Positive laboratory results*	14	6	1	1	22
Negative laboratory results	63	88	15	10	176
Total	77	94	16	11	198

* Influenza A virus isolated, or fourfold or greater increase in complement-fixing antibody titre.

RESULTS

The incidence of acute respiratory illnesses in the survey stations

The total population of the 13 R.A.F. stations which participated in the study was 14,710 in October 1968; the numbers on individual stations at this time ranged from 500 to 2900, though the figures varied during the study because of the movement of personnel. For this reason sickness rates have been calculated by taking man-weeks at risk as the denominator. The mean respiratory illness rates during the winter 1968–9 ranged from 2 to 5 per 1000 man-weeks in different stations. There were three peaks in the rates – in November, early January and the end of February; these peaks corresponded with those shown in the national morbidity statistics (Miller *et al.* 1971). The peak incidence of illnesses diagnosed clinically as influenza occurred at the same times as the peak incidence of other respiratory disease.

In the winter of 1969–70, when information was obtained restrospectively, records were received from only seven stations and for only part of the period in question. However, such records as were available confirmed that in these stations there was a large-scale influenza epidemic during December and January, which coincided with the national epidemic.

Illness rates in volunteers

The general pattern of illness during the two epidemics in volunteers was similar to that in all personnel on the same stations. During the first winter 38% of the volunteers observed had at least one respiratory illness; the rate for upper respiratory tract (URT) illnesses was 26%, for influenza 12% and for lower respiratory tract (LRT) illnesses 5%. In the second winter 41% had a respiratory illness; 28% had URT illnesses, 17% had influenza, and 8% LRT illnesses. Thus the attack rates for URT illnesses were similar in the two winters, whereas, those for influenza and LRT illnesses were proportionately considerably higher in the second winter than in the first.

In 1968–9 illnesses were investigated in the laboratory by examination of nose and throat swabs for virus and/or paired sera taken at the time of illness for a four fold or greater increase in titre of complement-fixing antibody. Table 2 shows the relation between the clinical diagnosis and laboratory results. Only 14 (7%) of the 198 illnesses investigated were diagnosed clinically as influenza and confirmed as such in the laboratory. These 14 comprised 64% of the 22 with positive laboratory results, but only 18% of the 77 illnesses called influenza.

Table 3. *Percentage distribution of HI antibody titres to four strains of A2 influenza virus in October* 1968

	Antibody titre					Total persons	
	< 1/10 %	1/10 %	1/20 %	1/40 %	⩾ 1/80 %	No.	%
A2/Singapore/57	10	5	9	17	58	559*	100
A2/Tokyo/67	40	16	14	15	16	554†	100
A2/England/68	46	13	16	12	13	554†	100
A2/Hong Kong/68	69	12	13	4	2	560	100

* Excludes one person whose A2/Singapore/57 antibody titre was not estimated.
† Excludes six persons whose A2/Tokyo/67 and A2/England/68 antibody titre was not estimated.

Table 4. *Relationship between titres of HI antibody to A2/Hong Kong/68 and A2/England/68 in October* 1968

Antibody titre to A2/England/68	Antibody titre to A2/HK/68					Total persons
	<1/10	1/10	1/20	1/40	⩾ 1/80	
< 1/10	**215**	**22**	15	3	0	255
1/10	**49**	**11**	**8**	1	1	70
1/20	50	**15**	**15**	**3**	6	89
1/40	32	9	**15**	**8**	**3**	67
⩾ 1/80	39	10	17	5	**2**	73
Total persons	385	67	70	20	12	554*

* Excludes six persons whose A2/England/68 antibody titre was not estimated.

Antibody distributions

The distribution of titres of antibody in the initial sera against selected variants of the influenza A2 virus are shown for the 560 persons from whom all three specimens were obtained (Table 3). Over 90 % of sera tested contained detectable antibody to the original 'Asian' A2/Singapore/1/57 virus and in the majority titres were high – 75 % being 1/40 or more. Antibody to variants prevalent more recently (A2/Tokyo/67 and A2/England/68) was less frequently present and the proportion of sera with high titres was much less than with the A2/Singapore/1/57 virus.

Antibody to the Hong Kong/68 variant was present in 31 % of specimens but most titres were low, only 6 % being 1/40 or more. It is now thought that these low titres of HI antibody were almost certainly directed, probably by the mechanism of steric hindrance, against the neuraminidase component of the variant, which is similar to that of the previously circulating variants, and not against the haemagglutinin which is antigenically quite distinct from that of earlier variants.

The relation between antibody to the Hong Kong/68 variant and that to the A2 strain prevalent in Britain the previous winter (A2/England/68) is shown in Table 4. The majority (76 %) of the 169 volunteers with detectable antibody to A2/Hong Kong/68 also had antibody to A2/England/68; of the 32 with high titres (⩾ 1/40) to A2/Hong Kong/68, 18 (56 %) had high titres to the earlier strain. In contrast, of the 385 without antibody to the Hong Kong strain a considerably

Table 5. *Percentage distribution of HI antibody titres to A2/HK/68 before and after the winters* 1968–9 *and* 1969–70

	Antibody titre					Total persons	
	< 1/10 %	1/10 %	1/20 %	1/40 %	⩾1/80 %	No.	%
October 1968	69	12	13	4	2	560	100
June 1969	56	11	9	5	19	560	100
June 1970	28	4	8	9	51	560	100

lower proportion (44%) had detectable antibody against A2/England/68 and of these only 71 (18%) had high titres against it. Conversely 40 (16%) of the 255 persons without antibody to A2/England/68 had detectable antibody to the Hong Kong strain and only 3 (1%) had titres ⩾ 1/40.

No relation was found between initial titre of antibody to A2/Hong Kong/68 and age or sex, ABO blood group, current smoking habits or history of influenza vaccination before October 1968. However, the proportion of volunteers who had antibody differed significantly between stations, with a range of from 18 to 58%; these differences corresponded with differences between stations in the proportion of persons with antibody to A2/England/68 and were probably therefore related to whether or not there had been an epidemic of influenza on the station the previous winter.

The proportions of persons with different titres of antibody to A2/Hong Kong/68 before and after the two winters are shown in Table 5. In October 1968, 69% had no detectable antibody and only 6% had titres of 1/40 or more. However, after the first winter the proportion with no antibody had fallen to 56% and after the second winter to only 28%. Meanwhile, the proportion with high antibody titres (⩾ 1/40) increased to 24% after the winter 1968–9 and to 60% after the winter 1969–70.

Infection rates

Infection rates have been calculated on the assumption that, after excluding those who had been vaccinated, persons with a fourfold or greater rise in HI antibody to the A2/Hong Kong/68 virus between sera taken before and after either winter were infected with the virus in the relevant interval and those with no such rise were not. The infection rate in persons with antibody titres ⩽ 1/10 before the first winter was about 25%; in the second winter the rate was more than double this figure (Table 6). Persons with higher initial antibody titres showed evidence of infection less often, and in those with antibody titres ⩾ 1/40 infection in either winter was infrequent.

Attention has been directed above to the frequent lack of correspondence between the clinical diagnosis of influenza and laboratory proof of infection at the time of illness. Table 7 shows that in both years only a small minority of persons with serological evidence of infection had an illness diagnosed as influenza, and, conversely, a substantial number were said to have had influenza in whom infection was not substantiated serologically. But during each winter about half of

Table 6. *Infection* rates in relation to initial antibody to influenza A2/Hong Kong/68 virus*

Initial antibody titre	Oct. 1968, no. of persons	Infected* 1968–9		Oct. 1969, no. of persons	Infected* 1969–70	
		No.	%		No.	%
< 1/10	475	121	25	269	155	58
1/10	108	27	25	55	30	55
1/20	113	21	19	41	10	24
1/40	50	5	10	27	3	11
⩾ 1/80	29	2	7	87	1	1
Total	775	176	23	479	199	42

* Fourfold or greater rise in HI antibody to A2/HK/68 in paired sera taken before and after each winter.

Table 7. *Illness rates in persons with and without infection**

Year		All persons		Persons with respiratory illness: Clinical Influenza		Persons with respiratory illness: Other respiratory		Persons without recorded illness	
		No.	%	No.	%	No.	%	No.	%
1968–9	Infected*	176	100	32	18	57	32	87	49
	Not infected*	599	100	48	8	145	24	406	68
1969–70	Infected*	199	100	50	25	47	24	102	51
	Not infected*	280	100	25	9	63	22	192	69

* Fourfold or greater rise in HI antibody to A2/Hong Kong/68 virus in paired sera taken before and after each winter.

those with serological evidence of influenza infection had *no recorded illness*, although it is possible that they had minor illnesses that were not reported.

There is some evidence from Table 7 that the diagnosis of influenza was more accurate in 1969–70 than in 1968–9. In each year just under one-quarter of those *without* evidence of infection experienced a respiratory illness to which a diagnosis other than influenza was attached. A similar proportion of such illnesses was reported in those *with* evidence of infection in 1969–70, but the proportion was higher (32%) in this group in 1968–9, suggesting that in that year it included some cases of influenza. More detailed analysis of the results for 1969–70 supports this suggestion (Table 8). This analysis, which excludes persons with more than one recorded illness during the winter, divides subjects into those who were ill during the height of the epidemic (December 1969 to January 1970) and those who were ill outside this period. The proportion of persons with clinical influenza who had evidence of infection was much higher during than outside the epidemic, and was nearly twice as high as in those with other respiratory diagnoses at any time. In contrast there was little difference in the frequency of infection between those with other diagnoses, either during or outside the epidemic, and those with no recorded respiratory illness.

Table 8. *Infection rates during the* 1969–70 *epidemic*

	Illness during epidemic		Illness outside epidemic		
	Influenza	Other resp.	Influenza	Other resp.	Not ill
Total persons*	44	26	13	58	294
Infected†					
No.	33	10	7	24	102
%	75	38	54	41	35

* Excludes persons with more than one illness.

† Fourfold or greater rise in HI antibody to A2/HK/68 in paired sera taken before and after each winter.

Initial antibody and illness rates

In the first winter, 1968–9, no clear relation could be demonstrated between the subjects' prior antibody titre against influenza A2/Hong Kong/68 virus and their susceptibility to respiratory illnesses, including influenza. However, the next year in 1969–70, there was a progressively lower illness rate with increased antibody titre (Table 9, col. 1). This relation was much stronger and can be seen in both winters if the analysis is restricted to persons with serological evidence of having had influenza infection during the winter (col. 2); the trend was significant in both years (1968–9, $P < 0{\cdot}05$; 1969–70, $P < 0{\cdot}001$). Of those with an antibody titre of 1/40 or more at the beginning of the winter, only three persons in 1968–9 and one person in 1969–70 had a record of respiratory illness accompanied by serological evidence of influenza. In both years non-influenza respiratory illness rates were higher in those with antibody than in those without (col. 3), possibly because the latter group experienced a high rate of infection with influenza virus (col. 2) which either interfered with other viruses or, by causing illness, reduced their chances of exposure to other viruses.

No correlation between the amount of tobacco smoked and respiratory illness rates could be demonstrated, whether there was serological evidence of infection or not, and whether the illness was diagnosed as influenza or not. There were too few attacks of lower respiratory illness for separate analysis.

Infection and illness rates in successive winters

Table 10 shows the relation between infection with or without illness in the first winter and infection with or without illness in the second winter.

There were altogether 158 persons who had one or more respiratory illnesses in 1968–9; 70 (44 %) of them had a respiratory illness the next winter compared with 89 (33 %) of the 270 who had not been ill the first year. Having a respiratory illness in 1968–9, therefore, gave no apparent protection against illness in 1969–70. However, of those who had *serological evidence of influenza infection* in 1968–9, whether or not they also had a reported illness, *none* was again infected in 1969–70. In contrast, of those who were *not infected* in 1968–9, 53 % were infected in 1969–70 and 26 % of them were ill.

Table 9. *Initial antibody and illness rates*

Year	Antibody titre to A2/HK/68 before winter	Persons		Attacks of respiratory illness					
				Total (1)		In persons with infection* (2)		In persons without infection* (3)	
		No.	%	No.	%	No.	%	No.	%
1968–9	< 10	475	100	201	42	72	15	129	27
	10	108	100	42	44	15	14	27	30
	20	113		55		16		39	
	40	50	100	17	37	1	4	16	33
	⩾ 80	29		12		2		10	
Total		775	100	327	42	106	14	221	29
1969–70	< 10	269	100	155	58	105	39	50	19
	10	55	100	21	44	12	18	9	26
	20	41		21		5		16	
	40	27	100	16	39	1	1	15	38
	⩾ 80	87		28		0		28	
Total		479	100	241	50	123	26	118	25

* Fourfold or greater rise in HI antibody to A2/HK/68 in paired sera taken before and after each winter.

Table 10. *Infection and illness rates in successive winters*

1968–9		Total No.	1969–70 Infected* Total No.	%	Infected* Ill No.	%	Not infected* Total No.	%	Not infected* Ill No.	%
Infected*	Ill	36	0	—	—	—	36	100	9	25
	Not ill	48	0	—	—	—	48	100	13	27
	Total	84	0	—	—	—	84	100	22	26
Not infected*	Ill	122	65	53	39	32	57	47	22	18
	Not ill	222	119	54	49	22	103	46	27	12
	Total	344	184	53	88	26	160	47	49	14

* Fourfold or greater rise in HI antibody to A2/HK/68 in paired sera taken before and after each winter.

It may also be noted that of the 122 persons who were ill but not infected in 1969–9, 61 (50 %) were ill again in 1969–70, compared with 76 (34 %) of the 222 who had not been ill the first year. Those who were infected in 1968–9 suffered a higher non-influenza illness rate (26 %) the next year than those who had not been infected (14 %), which partially offset the benefit derived from their immunity to influenza.

DISCUSSION

The unexpected pattern of the epidemics that followed the introduction of the A2/Hong Kong/68 influenza virus into Britain in 1968 and the contrast between its epidemiological behaviour in the winter 1968–9 and that in 1969–70 has been previously described (Miller *et al.* 1971). The introduction of a new antigenic variant into a susceptible population was expected to produce a major epidemic. In the event, although infection was widespread and the cumulative excess morbidity and mortality during the first winter was considerable, the impact of the virus was much less than had been forecast. The next winter, in 1969–70, an explosive epidemic such as had been expected the previous winter, occurred with dramatic effects on morbidity and mortality rates. The results of this serological study amplify the picture of the epidemics obtained from analysis of vital statistics.

At the start of the survey nearly all subjects had antibody to the original A2 virus (A2/Singapore/57), mostly at high titres, and more than half had antibody to recently prevalent variants in Britain. Less than one-third of the volunteers had detectable antibody to the new Hong Kong virus and in those who had it was usually at a low titre. Moreover, such antibody as was present was directed solely against the virus neuraminidase and not the haemagglutinin. It seems highly improbable that this pre-existing antibody was sufficient to have modified the epidemic in 1968–9, particularly since the next year a major epidemic was not averted despite the fact that the proportion of persons with antibody, in many cases at high titres, had increased from 31 to 44 %. By the end of the 1969–70 winter 60 % had antibody titres to the Hong Kong virus of 1/40 or more and for the

next two winters this virus gave relatively little trouble, whether because the proportion of immune persons was sufficient to prevent the spread of infection or for some other reason cannot be determined.

The extent to which antibody to one influenza virus variant protects against infection with succeeding variants and the significance of antibody in measuring protection against illness are important questions. The results of this study provide some information on these points. Infection (i.e. a fourfold or greater increase in antibody titre during a winter period) was observed much less often in those with high initial antibody titres than in those with low titres and was rare if the initial titre was 1/40 or more. Such protection against infection is useful only in so far as it equates with protection against illness. In the first winter no relation between antibody titres and the frequency of (total) respiratory illnesses was found, and in the second winter the reduction in illness rates in those with high titres was slight. However, if the analysis is restricted to those who showed evidence of influenza virus infection, the relation was pronounced in both winters, particularly the second, and statistically highly significant, even though some of the recorded illnesses may not have been influenza. A titre of 1/40 seemed to be the critical level at or above which illness coupled with evidence of influenza virus infection was rare. This finding is particularly important in relation to the results in the first winter since it implies that protection against illness was conferred by anti-neuraminidase antibody. These results indicate, therefore, that the presence of antibody can confer a measure of protection against illness that increases with higher titres. But proved infection with Hong Kong virus in the first winter appeared to confer absolute protection against infection with or without illness in the next winter. In contrast more than one-half of those who were not infected in the first winter were infected during the second, and one-quarter of them were ill.

The serological infection rate in the volunteers was nearly twice as high in the second winter as in the first, but the difference in respiratory illness rates was considerably less, even for illnesses diagnosed as influenza. The clinical diagnosis of influenza is notoriously difficult and the extent of diagnostic inaccuracy was illustrated by results from illnesses investigated in the first winter. There was some evidence, however, that when the epidemic was at its height during the second winter diagnostic accuracy was greater than at other times.

Our findings also suggest that symptomless infection is frequent since, in both winters about half the subjects who had evidence of infection had no recorded illness. It is possible that some illnesses were not recorded and others were too minor to call for medical attention, but it seems likely that many were symptomless. This finding is similar to that in the 1957 epidemics in Tecumseh (Hennessy *et al.* 1964).

The choice of servicemen for this study had disadvantages since their mode of life is not entirely representative of that of the majority of people in this country. Their opportunities for contact with one another, even in those who live outside the camp, are probably greater than in, for example, a group of factory workers who less often share leisure facilities. To offset this there are many advantages in the uniform and comprehensive medical facilities that are available for recording

illnesses and collecting appropriate blood samples. However, while it must be accepted that our results may not accurately reflect the situation in the population as a whole, the pattern of the epidemics in the Royal Air Force stations where the studies were carried out appears to have been similar to the experience of the rest of the population and the distribution of antibody in our subjects was similar to that observed in other population groups over the same period (Miller *et al.* 1971).

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