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Influenza	Vaccine	A/USSR/90/77	B/Hong Kong/72
Hemagglutinin	Adenovirus	A/Brazil/78	B/Singapore/222/79
Neuraminidase	Respiratory tract	A/Calif/78	B/Denver/1/79
Field trial	A/Texas/76	A/Denver/9284/79	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)
1) During the 1978-9 season H1N1 influenza was present on the base for 16 weeks, but incidence remained very low in the vaccinated population. The peak incidence of febrile respiratory disease in students was 7.2/1000/week.
2) Cases of influenza occurred almost entirely in persons with H.I. antibody titers for A/Brazil/78 of less than 8.
3) Military formula vaccine produced a moderately good antibody response in seronegative persons and a marked response in seropositive persons. → next page
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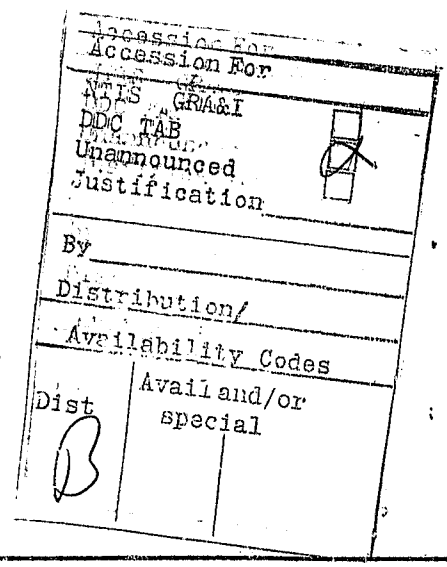
Summary (continued)

4) The 1978-9 strains such as A/Brazil/78 or A/Denver/78 showed only slight antigenic drift from A/USSR/90. Strain A/Fukushima/78 showed a considerably greater antigenic drift.
5) The first injections of vaccine evoked an excellent response to A/Texas/77, a satisfactory response to B/Hong Kong/72 and a fair response to A/Brazil/77.
6) The second injection of vaccine caused insignificant changes in titer for A/Texas/77 and B/Hong Kong/72, but a substantial increase in titers for A/Brazil/78, notably in persons whose titers remained low after the first injection.
7) Antibody levels for A/Brazil/75 in civilians suggested that more than 60% of young adults had experienced infection by the spring of 1979. In younger persons the percentages of persons with antibody were lower.
8) Antibody levels for B/Hong Kong/72 were low in air force students before vaccination in 1973 and 1974 and continue to be low in civilians of comparable age.
9) Following vaccination antibody titers of $\geq$ 16 were found in 91% of students and titers of $\geq$ 32 in 75%.
10) The 1979 influenza B strain, B/Singapore/222/79 showed considerable antigenic drift from B/Hong Kong/72 and antibody titers to the new strain was less satisfactory. Approximately 70% of persons had titers of $\geq$ 16 and 50% titers of $\geq$ 32. A change in vaccine strain from B/Hong Kong/72 to B/Singapore/79 was indicated.
11) An influenza B outbreak occurred in the Denver area in December, 1979, and January, 1980, caused by a strain like B/Singapore/79. A scattering of cases occurred at Lowry AFB, but the incidence of febrile respiratory disease has at no time exceeded 5.3/1000/week.
12) Other respiratory diseases caused little illness during the 1979-80 season. A few cases of adeno virus disease were detected, all in persons who had not received vaccine. Streptococcal infections accounted for about 15% of febrile U.R.I. A few viruses with the characteristics of echoviruses were isolated. Rubella and rubeola were not a problem.



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PREVENTION OF INFLUENZA AND OTHER RESPIRATORY DISEASES (U)

ANNUAL PROGRESS REPORT

BY

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Steven R. Mostow, M.D.

February, 1980
(For the period 1 February 1979 to 30 January 1980)

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CONTENTS

I. Completion of Analysis of 1978-9 H1N1 Outbreak

A. Overall incidence of febrile respiratory disease and of influenza

When last year's annual report was prepared in January, 1979, the second outbreak of H1N1 influenza at Lowry AFB had just passed its peak and data were incomplete. In Table 1 the overall incidence of febrile respiratory disease during the 1978-9 season is shown. Incidence remained low throughout the season, reaching at the highest point only 7.2/1000/week in students and 10.2/1000/week in the permanent party.

In the column on the right the number of confirmed cases of influenza is shown. The 91 confirmed cases were concentrated in January, with a small number of cases spread over the 16-week period from 13 November to 26 February. If the January base population is taken as the average for the whole season the attack rate for the whole base was 1.1%. This contrasts sharply with rates observed during the 1977-8 epidemic when a minimum of 30% of the students reported with influenza and the peak weekly rate reached almost 200/1000/week. The reasons for this difference and the role which vaccination played are considered in the following sections.

B. Attack rates in students and permanent party

In the 1978-9 epidemic the attack rate had been far lower in the permanent party than in students. In 1978-9, however, the rate in students (0.8%) was lower in the permanent party (1.4%). Thirty-one cases were detected in students and 60 cases in permanent party. Of these 60, 54 occurred in persons 25 years old or younger and only 6 cases in persons 26 or older. It was, unfortunately, impossible to obtain a breakdown of the age distribution which would have provided a denominator for an accurate estimation of rates in the younger and older segments of the permanent party. The latter comprise a major segment of the permanent party and within this group the rate was obviously very low.

C. Attack rates in relation to H1N1 antibody levels

The lack of an unvaccinated control group makes it impossible, as in most recent field trials, to obtain an accurate assessment of vaccine effectiveness. Indirect evidence can be obtained by determining antibody response following vaccination and by observing attack rates in persons with different antibody levels. Such an analysis involves several asymptions as is based on extrapolation from small numbers. With these reservations, the analysis provides interesting data and suggests a relatively high degree of vaccine effectiveness.

The data on which this assessment is based are presented in Tables 2 and 3. In Table 2 H.I. antibody levels are shown before and after vaccination in tests with A/USSR/92/77 ether-split antigen and with A/Brazil/78 antigen. With the former titers were higher and "antibody" was often found in persons who had never been infected with H1N1 virus, suggesting that the test was non-specific. With A/Brazil/78 antigen titers were lower. As will be noted later, many persons with confirmed H1N1 infections failed to show any increase in antibody in tests with A/Brazil/78 antigen. Tests with this antigen were insensitive. Antibody titers

at any level, including titers of only 8, appeared to indicate prior contact with H1N1 virus, either through infection or vaccination. It seemed more meaningful to use the data obtained with A/Brazil/78 in the following analysis because the outbreak was caused by virus strains of the 1978 type.

In Table 3 attack rates are presented which are extrapolations of the observed results of H.I. tests with post-vaccination sera of the whole student population and the estimated 60% of the permanent party which was believed to be 25 years old or less. The attack rate for persons with titers of < 8 was 7.0%. For those with titers of 8 or 16 the attack rate was 0.4% and for those with titers of $\geq$ 32 was only 0.08%. Credit for this large difference (100-fold between the < 8 and $\geq$ 32 categories) cannot be attributed solely to the vaccine, for one half or more of this population had been infected during the epidemic of the previous year and was presumably immune even before vaccination. Even so, it is reasonable to conclude that the antibody evoked by vaccination contributed substantially to the protection of the remaining half which had not yet been infected.

D. Cases in unvaccinated persons

Fifteen of the 91 cases (11.5%) which were detected occurred in persons who had not received H1N1 vaccine. All personnel were supposed to have received this vaccine, but it appeared that approximately 10% did not receive H1N1 vaccine. Many of those who were missed were older members of the permanent party who were presumably already immune. Fourteen of the 15, unvaccinated persons who were ill with influenza had titers of < 8 in their acute sera.

E. Comment on antibody levels and susceptibility to influenza

The relationship between H.I. antibody titer and susceptibility to clinical influenza has long been of interest to this laboratory. The currently accepted "protective" level, advanced by the C.D.C., is a titer of 40. In our laboratory this would correspond to a titer of 32, but in point of fact, most persons with titers of 16 have escaped illness, and clinical influenza has been very rare in persons with titers above that level. In H1N1 infections the low avidity of the antigens such as A/Brazil/78 causes the "protective" level to drop even further to an H.I. antibody level of only 8. Other more sensitive methods of measuring neutralizing antibody might show that antibody is present in sera of persons with H.I. titers 8 or even less than 8.

F. Diagnostic methods for H1N1 influenza

A diagnosis of influenza A was made in 91 cases on the basis of virus isolation and/or a $\geq$ 4-fold rise in C.F. antibody or H.I. antibody to one or more H1N1 strains. The ratios and percent of positivity of these methods were as follows:

Virus isolation (RMK)	49/91	53.8%
C.F. (H1N1)	65/81	80.2%
H.I. A/USSR/92/77	59/81	72.8%
A/USSR/90/77	49/81	60.4%
A/Brazil/78	44/80	55.0%
A/Denver/1/78	49/78	62.8%
A/California/78	37/61	60.6%
A/Fukushima/78	16/43	37.2%

II. Comparison of H1N1 Strains

The first wave of H1N1, which caused a large outbreak at Lowry AFB early in 1978, was caused by viruses resembling A/USSR/90/77 (or A/USSR/92/77). Following this outbreak influenza activity rapidly died down and none was found during the summer or early fall. Outbreaks did occur in the Southern Hemisphere and from one of these strain A/Brazil/11/78 was isolated and has been generally accepted as the prototype strain for the 1978-9 winter outbreaks. A similar strain, A/Denver/9284/78 (or A/Denver/1/78), isolated at Lowry AFB, served as the representative local viral strain. The Brazil and Denver strains showed in tests with ferret antisera some drift away from A/USSR/90/77. Finally, late in 1978 the strain A/Fukushima/101/78 was isolated in Japan and showed even further antigenic drift.

The following section presents data comparing antibody levels of persons with influenza and vaccinated persons in tests with the 5 influenza strains noted above. The goal of these studies was to determine the extent to which antigenic drift affected antibody response and vaccine effectiveness. Technical problems, centering around lack of avidity of newly isolated strains, were encountered and have not been completely resolved.

A. Antibody levels following infection in 1978 and in 1979

In tests with 5 antigens the convalescent H.I. antibody levels of unvaccinated persons infected in 1978 with A/USSR/90/77 (Table 4) are compared with those of unvaccinated persons infected in 1979 with A/Brazil/78 (Table 5). A/Brazil/78 is used as a generic term which includes A/Denver/1/78.

When sera were tested with A/USSR/92/77 (P.D.) little difference was found between sera collected in the 2 years. With A/USSR/90/77 titers were slightly lower in persons infected with A/Brazil/78 than in those infected with A/USSR/90/77. Results with A/Brazil/78 and A/Denver/1/78 were almost interchangeable. With 1978 sera they closely resembled those with A/USSR/90/77, but with 1979 sera titers with these two strains were somewhat higher than with A/USSR/90/77. It is worthy of note that a large population of persons (from 30% to 50%) had titers of 8 or < 8 in their convalescent sera and relatively few had titers of 256 or higher, a point which emphasizes the low avidity of all these strains.

Titers obtained with A/Fukushima/78 were low, reflecting the wide antigenic variation, and suggesting that many individuals who had H1N1 infections with the earlier H1N1 strains might be susceptible to infection with A/Fukushima/78.

B. Antibody levels for different H1N1 strains following vaccination

When serum pairs from 67 vaccinated students were tested with A/USSR/92/77 antigen the response appeared to be good (Table 3). Ninety-two percent had titers of $\geq$ 32. However, with that antigen presumably non-specific titers of 8 had been frequently seen in sera collected before H1N1 appeared and occasionally titers of 16 or higher had been observed. When this group of persons was divided into: 1) those with titers of 8 or less who had probably escaped infection in 1978 and, 2) those with titers of $\geq$ 16, who had probably been infected in 1978, one interesting difference was observed. Those in the former group respond for the most part with titers in the range from 32 to 128. The latter responded far more biskly and, with a single experience had titers between 128 and 1024.

Fifty-two of the same serum pairs were tested with A/Brazil/78. Titers for the whole group were considerably lower in the pre-vaccination sera. The post-vaccination titers of 32% were < 8. As in the A/USSR/92/78 tests the poor responses were in the group who presumably were not previously infected. The previously infected persons showed a surprisingly sharp response, particularly in view of the low titers observed in the convalescent titers of patients when this antigen was used.

In Tables 6 and 7 the post-vaccination titers against 5 H1N1 strains are shown in relatively small groups of persons who were seronegative or seropositive at the time of vaccination. With all strains titers are far higher in the seropositive persons. Titers are highest with A/USSR/92/77. The titers with A/USSR/90/77 are essentially the same as with A/Brazil/78 and A/Denver/78. The titers for A/Fukushima/78 were extremely low in the seronegative group, but the response in the seropositive persons fell only slightly short of those observed with the other strains.

Table 8 presents another view of what happens with a second exposure to a new H1N1 antigen. Instead of a sequence of infection followed by vaccination the data presented here represent a group who had been vaccinated and subsequently infected by H1N1 virus. Antibody titers were considerably higher than those seen in infected persons who had not received vaccine. With the exception of A/Fukushima/77 all persons had titers of $\geq$ 16 and from 85% to 100% had titers $\geq$ 64. Titers were slightly lower than those seen in persons who were vaccinated following infection.

The appearance of strain A/Fukushima/77 caused considerable concern since the degree of antigenic drift appeared to be sufficiently great that A/USSR/90/77 or A/Brazil/78 vaccine or even prior infection with either of these strains might not provide protection. Table 9 presents A/Fukushima/78 antibody titers in persons with different types of H1N1

experience. The convalescent sera of persons infected in 1978 or 1979 showed, in most persons, only low or absent H.I. titers. On the other hand 75% of vaccinated persons who had influenza in 1979 had titers of $\geq$ 16 (group 5). Even higher titers were observed in persons who had been infected and later vaccinated (group 4). All had titers of $\geq$ 16 and 95% had titers of $\geq$ 64.

These observations reemphasize the importance of more than a single stimulation by a new influenza antigen in evoking a high and hopefully "protective" antibody response. Infection alone or single injections of vaccine are generally inadequate. A second injection of vaccine produces little change in titer except in those who have responded poorly to the first. In the poor responders it uniformly evokes a good response. Vaccinated persons who get influenza have a greater antibody response than those who have not been vaccinated. The highest and broadest response is seen in persons who had had influenza and are then vaccinated.

These are now new observations. They are, in fact, so old that in some quarters they are not known or may even have been forgotten. Very similar data gathered during the 1957 Asian influenza pandemic were presented in the 1957-8 annual report to the Commission on Influenza, AFEB (Table 10).

III. Antibody Levels in Air Force Students in Fall of 1979

A. Vaccine administration during summer and fall of 1979

During the summer and early fall of 1979 all recruits at Lackland Air Force Base received whole virus vaccine prepared by Connaught Laboratories containing 20 µg each of A/Texas/1/77, A/USSR/90/77 and B/Hong Kong/2/72. From 9 October onward the vaccine was changed to a Connaught Laboratories whole virus vaccine containing 7 µg each of A/Texas/77, B/Hong Kong/12 and A/Brazil/78. Thereafter students received 2 injections of this vaccine, one on the 4th and another on the 29th day of their training periods.

Students who had departed for Lackland before the new program was begun were given the 7 µg vaccine at Lowry AFB during the first half of November. Paired sera were obtained from 100 of these students before and 3 weeks after the second injection of vaccine was given. The data shown in the following section were obtained from this group of students.

B. Antibody levels before second injection of vaccine

Seventy-five serum pairs from these students were tested with the antigens shown in Table 11. In the prevaccination sera (i.e., after their first injection of vaccine) titers against A/Texas/77 were very high, with 93% having titers of $\geq$ 32. Titers with B/Hong Kong/92 were lower, with 75% having titers of $\geq$ 32 and with very few persons in the highest titer range. With A/Brazil/78 73% had titers of $\geq$ 32 and 47% had titers of $\geq$ 256. Titers with A/Fukushima/78 were lower. Only 57% had titers of $\geq$ 32.

C. Antibody levels following second injection of vaccine

In the post-vaccination sera essentially no change was seen with A/Texas/77 or B/Hong Kong/72. However, with both H1N1 strains there was a marked increase in titer for both the H1N1 strains. With A/Brazil/78 the percent with titers $\geq$ 32 rose to 99 and with A/Fukushima/78 to 80%. With the former 33% showed $\geq$ 4-fold increases in titer and with the latter 23%.

D. Which persons benefitted from second injection of vaccine

The data presented in Table 12 show that the proportion of persons with 4-fold or greater increases in titer for A/Brazil/11/78 was directly related to the antibody titer before the second injection of vaccine. Thus, all persons with titers of 8 or less showed > 4-fold response. Decreasing proportions showed 4-fold increases as titer levels rose and no individuals with titers of 256 or more showed 4-fold antibody rises.

The most plausible explanation for the different behavior with the H1N1 strain is that either infection or the first injection of vaccine had served as an adequate priming dose, but had not elicited a "maximal" response. In contrast, all or almost all, persons had been infected once or more than once by H3N2 or influenza B viruses, and the first injection of vaccine had evoked the maximal response possible for the amount of antigen which was given.

This pattern of response has been repeatedly observed in the past and has led to the generalization that a second injection of aqueous vaccine contributes little to protection. These findings re-emphasize the difference in response of persons who are vaccinated with strains which have long been prevalent, such as H3N2 (since 1968) or influenza B (which has shown only gradual drift) and in those who encounter for the first time a new influenza family such as H1N1.

V. H1N1 Antibody Levels in Civilians in the Denver Area

During the H1N1 epidemic of 1978-9 cases of Reye's Syndrome began to appear in unexpected numbers and a study was organized under the coordination of Dr. Neil Halsey at Denver Childrens' Hospital, Colorado General Hospital and Fitzsimons Army Hospital. Sixteen children were admitted with Reye's Syndrome and in 12 of these diagnostic increases in H1N1 antibody were demonstrated. H1N1 strains were isolated from 2 patients. In others sera collected late in the course had titers comparable with recent infection. While occasional cases of influenza A, along with many other agents, have previously been followed by Reye's Syndrome, the results of this study provide the most convincing evidence to date that influenza A, like influenza B, can serve as the initiating event in Reye's Syndrome.

In order to obtain an estimate of the number of cases of H1N1 influenza which occurred during this epidemic a large number of civilian sera were screened for H1N1 antibody before, during and after the epidemic. The sera came from 2 sources, the Denver Childrens' Hospital and the Colorado State Health Department Laboratories. Results with 4 H1N1 antigens are presented in Tables 13, 14, 15, and 16.

Most cases of influenza occurred during the period from mid-December 1979 to the end of January, 1980. Thus antibody in sera collected earlier in 1978 probably had been acquired during the epidemic of the previous winter. Sera after February, 1979, represented to combined effect of the two epidemics. Those collected January, 1979, may represent persons infected either in 1978 or 1979.

If it is assumed that in tests with A/USSR/92/77 a titer of $\geq$ 16 indicates prior infection (Table 13) certain trends are apparent. In hospital patients bled between February and May, 1979, highest percentages of persons with titers were seen in teenagers, with decreasing percentages in younger individuals. These percentages are considerably higher than those seen in the State laboratory sera for comparably aged persons collected in October, 1978 and higher than those in similar persons bled in May, 1979. The data suggest that at least 40% of this age group were infected during the first H1N1 wave and another 20% during the second wave. In view of the insensitivity of tests with these antigens with sera from confirmed cases of influenza, the true figure was probably higher. Air Force personnel, who had been vaccinated and had in many instances been infected had a far higher rate (90%) of persons positive at this titer.

The same trends are seen in tests with A/USSR/90/77 (Table 14). With this less sensitive antigen a titer of 8 roughly matches a titer of 16 with A/USSR/92/77. One additional group, bled in January, 1979, was tested with this and with the A/Brazil/78 and A/Fukushima/78 antigens. The results suggest that a substantial number of infections occurred in the childhood group during the period between the January and later bloods. This is more apparent in tests with A/Brazil/78 (Table 15), which was the epidemic strain, than with A/USSR/90/77. The distribution of titers for A/Fukushima/78 (Table 16) was far lower and suggests that even after two epidemics this population might have proved vulnerable to a Fukushima wave if this strain had been introduced and had possessed those characteristics which make it possible for an epidemic strain to spread.

V. Observations on Influenza B Antigen Levels

During the summer month influenza A activity around the world remained a relatively low level. Meanwhile outbreaks of influenza B occurred and virus strains which were isolated showed considerable antigenic drift from B/Hong Kong/72. This provided reason for concern that the current vaccine, which contained B/Hong Kong/72 as the influenza B component, might fail to provide protection in the event of an epidemic. For this reason data for previous years were researched and a sample of this year's vaccines was tested for antibody against the new influenza B strain, B/Singapore/222/79 which had been provided by CDC as a prototype of the new variants.

A. Antibody levels in unvaccinated young adults

For many years antibody levels against B/Hong Kong/72 have been low in the young adult population even though outbreaks of influenza B have occurred on at least two occasions, in 1974 and 1976. Table 17 shows antibody levels of air force students before vaccination in 1973 and 1974. Only 25% had titers of $\geq$ 32. In a sample of civilians in the same age range in 1978 and 1979 the percent with titers of $\geq$ 32 was even lower, 8% in 1978 and 6% in 1979.

B. Antibody levels following vaccination

Table 18 presents the distribution of H.I. antibody titers for B/Hong Kong/72 following vaccination of air force students during the period from 1973 to 1979. Until 1974 vaccination was done at Lowry AFB and both pre- and post-vaccination sera were tested. After 1975, personnel were vaccinated during basic training at Lackland AFB and only post-vaccination sera were available. This explains the fact that data relating to the proportion of persons who showed $\geq$ 4 X rises in titer are presented only for the earlier period.

The early tests encountered problems with inhibitors and low avidity. The avidity problem was lessened or eliminated by continuing egg passage or by the use of tissue culture fluid as antigen. All tests shown here were done with allantoic fluid antigen from passages at or beyond the 22nd egg passage.

The earliest test, which compared 250, 500 and 1000 CCA doses, showed some improvement of response with increased amount of antigen. In most subsequent years the vaccine potency was 500 CCA and the response appeared to be satisfactory, whether whole or split virus vaccine was used and without regard to manufacturer. The 250 CCA Wyeth vaccine used in 1978 appeared to produce a comparable response. Only the 20 µg Connaught vaccine used in 1979 appeared to be somewhat inferior. There has been no opportunity to evaluate 7 µg vaccine.

C. In Table 19 results of tests with 4 influenza B antigens with sera from 50 students before and after receiving a second injection of vaccine which contained 7 µg of B/Hong Kong/72 hemagglutinin. The two B/Singapore/79 and the B/Denver/1/79 antigens were used in order to find the one which would be least affected by low avidity. In particular, the B/Denver/1/79 strain was used because it had been isolated in tissue culture rather than in chick embryos. In 1974 it had been shown here that second passage tissue culture virus was satisfactory as an antigen in H.I. tests in contrast to egg-passed virus; which did not become satisfactory as an antigen until the 15th to 22nd passage.

The response to the earlier injection of vaccine, as noted earlier, had been moderately good when tested with B/Hong Kong/72. With all three of the 1979 influenza B antigens the response was less satisfactory. It was best when B/Denver/1/79 was used, but even with this antigen the percent of persons with titers $\geq$ 32 was only 46% in the first serum and 50% in the second. These titers were considerably lower than those observed with B/Hong Kong/72. While low avidity may, in part, account for this difference, there appears to have been antigenic drift of sufficient degree to warrant a change of sufficient magnitude to warrant a change in vaccine composition for the coming year.

VI. Influenza B Outbreak, 1979-80

A. Occurrence of cases

The first evidence of influenza B in the Denver area was on 5 November, 1979, at Lowry AFB. Two other cases followed these on the 15th and 26th

of November. All were confirmed by C.F. antibody rises of 16-fold or more. In no instance was a virus isolated or an H.I. antibody were detected using B/Hong Kong/72 as antigen. No cases were detected during December, but after the Christmas break cases began to occur and 5 virus strains were identified between the 8th and 21st of January. The overall incidence of febrile respiratory disease remained low throughout this period.

In the civilian community the first case of influenza had its onset on 15 November in a small mountain town 30 miles southwest of Denver. A sharp school outbreak was reported from that community. The first large outbreak reported in Denver occurred at National Jewish Hospital where a large population of children and staff were ill during the 2 weeks preceding the Christmas holiday. A single influenza B strain was isolated. Convalescent sera collected in January suggested that more than one half of patients and staff had been infected recently with influenza B. C.F. antibody titers were 32 or higher in 44 of 79 persons (56%), in contrast to only 12% of persons in screening tests of the population before the outbreak. A virus strain was isolated from a fatal case early in January. Throughout January cases continued to occur both in children and adults, but explosive outbreaks in school populations were uncommon. This was surprising in view of the relatively low levels of B/Hong Kong/72 antibody in the civilian population.

B. Nature of 1979-80 influenza B strains

Information obtained from C.D.C. indicated that the 1979 influenza B strains showed considerable antigenic drift from B/Hong Kong/72, and strain B/Singapore/222/79 was forwarded to our laboratory. The results presented in Table 19 indicate that the 1979 Denver strain was similar to A/Singapore/222/79.

C. Problems with serodiagnosis

Relatively few sera have been tested to date, but it is already obvious that the 1979 strains used so far often fail to demonstrate antibody in H.I. tests with convalescent sera even when virus has been isolated from the patient and a significant rise in C.F. antibody has been demonstrated. This is true with either B/Hong Kong/72 or B/79 antigens. The former might be explained by antigenic drift, but the latter is presumably due to low avidity, and means should be found to increase avidity or for other tests to be developed to demonstrate increases in neutralizing antibody.

VII. Other Febrile Respiratory Diseases

As in 1978-79 the 1979-80 season has been one of extremely low incidence of febrile respiratory diseases. This is shown in Table 20. In both student and permanent party populations rates have remained below 4/1000/week except during the middle of January when rates peaked at 5.3 in students and 4.9 in permanent party. It is noteworthy that scattered cases of influenza B occurred throughout this period, but no epidemic developed. This is the third occasion since 1974 that a similar situation has been observed, i.e., influenza B outbreaks in the surrounding community but virtually none in the vaccinated base personnel. Without the protection provided by vaccination sharp outbreaks would have been expected on this base.

Nine cases of adenovirus disease have been detected to date. All occurred in personnel who had passed through Lackland AFB during the period when no vaccine was being given. Virus strains with the characteristics of echovirus were isolated before Christmas. There were forwarded to C.D.C. for typing, but no reply has yet been received. Group A beta-hemolytic streptocci have been cultured from the throats of approximately 15% of patients with febrile U.R.I. Rubella and rubeola seem to have disappeared since screening and vaccination programs were introduced at Lackland AFB.

Week of	Number of Cases/1000/week in Students	Permanent Party	Number of Cases of HlNl Influenza
1 Nov.	6.8	1.1	-
6 Nov.	3.5	2.0	-
13 Nov.	4.8	3.2	2
20 Nov.	5.2	3.2	1
27 Nov.	2.6	4.8	-
4 Dec.	3.2	1.8	-
11 Dec.	2.6	5.2	1
18 Dec.	2.6	3.4	1
25 Dec.	-	-	-
1 Jan.	3.2	3.6	15
8 Jan.	7.2	5.9	29
15 Jan.	6.2	8.8	32
22 Jan.	7.2	10.2	13
29 Jan.	3.5	2.0	1
5 Feb.	2.9	3.8	2
12 Feb.	3.5	3.6	1
19 Feb.	4.2	4.5	-
26 Feb.	1.9	2.7	1
5 Mar.	2.9	3.4	-
12 Mar.	3.5	1.8	-
19 Mar.	1.6	1.6	-
26 Mar.	1.6	1.4	-
2 Apr.	3.5	3.2	-
9 Apr.	2.9	1.8	-
16 Apr.	1.6	1.1	-
23 Apr.	1.9	1.4	-
30 Apr.	0.3	1.4	-
7 May	2.9	1.8	-
15 May	3.2	1.8	

TABLE 1. Incidence of febrile respiratory disease in students and permanent party and number of confirmed cases of HlNl influenza during winter season of 1978-9.

Tested with A/USSR/92/77		Percent of persons with titers of <8	8	16	32	64	128	256	512	1024	% with titer ≥ 32
All persons (67)	Pre-	48	8	11	22	8	3	2	2	0	
	Post-	0	5	3	14	8	24	17	16	15	92
Persons with titer ≤8* (32)	Pre-	100	--	--	--	--	--	--	--	--	
	Post-	0	6	6	25	16	25	3	13	6	88
Persons with titer ≥16* (30)	Pre-	0	0	23	47	17	7	3	3	0	
	Post-	0	0	0	3	0	24	24	24	28	100

Tested with A/Brazil/78		Percent of persons with titers of <8	8	16	32	64	128	256	512	1024	% with titer ≥ 32
All persons (52)	Pre-	69	15	10	4	2	--	--	--	--	
	Post-	13	19	11	9	8	10	13	8	11	
Persons with titers ≤8* (31)	Pre-	100	--	--	--	--	--	--	--	--	
	Post-	22	32	1°	10	10	6	--	--	--	
Persons with titers ≥16* (21)	Pre-	24	38	24	9	5	--	--	--	--	
	Post-	--	--	--	--	5	14	33	19	28	

*Titer in test with A/USSR/92/77

Table 2. Distribution of HI antibody titers for A/USSR/92/77 (PD antigen) and A/Brazil/78 of students at Lowry AFB before and 3 weeks after receiving trivalent influenza vaccine containing 20 µg of A/USSR/90 (CL).

Titer	% of Persons With Titer of	Estimated No. of Persons	Observed No. of Cases	Attack Rate (%)
< 8	13	825	58	7.0
8	19	1205	5	0.4
16	11	698	3	0.4
≥ 32	57	3618	3	0.08
		6346*	69	1.1

*Based on whole student population plus the 60% of the permanent party which was 25 years old or younger.

Table 3. Estimated attack rate of H1N1 influenza among persons with different H.I. antibody titers for A/Brazil/78.

Test Antigen	Percent with titer of <8-8	16-32	64-128	256-512	>1024	% ≥16	% ≥64
A/USSR/92/77 (P.D.)	5	25	55	15	--	95	70
A/USSR/90/77	35	30	35	--	--	65	35
A/Brazil/11/78	40	25	30	5	--	60	35
A/Den/9284/78	35	25	30	10	--	65	40
A/Fukushima/103/78	75	15	5	5	--	25	10

TABLE 4. H1 antibody titers following infection in 1978 in 20 unvaccinated persons in tests with 5 H1N1 strains (Group 1).

Test Antigen	Percent with titer of <8-8	16-32	64-128	256-512	>1024	% ≥16	% ≥64
A/USSR/92/77 (P.D.)	--	50	43	7	--	100	50
A/USSR/90/77	50	35	14	--	--	49	14
A/Brazil/11/78	35	29	21	14	--	65	25
A/Den/9284/78	43	28	14	14	--	57	28
A/Fukushima/103/78	86	--	--	7*	7*	(14)	(14)

*Age 27 and 28. All others were 25 or younger.

TABLE 5. H1 antibody titers following infection in 1979 in 14 unvaccinated persons in tests with 5 H1N1 antigens (Group 2).

Test Antigen	Percent with titer of					%	%
	<8-8	16-32	64-128	256-512	>1024	>16	>64
A/USSR/92/77 (P.D.)	10	60	15	15	--	90	30
A/USSR/90/77	30	30	25	15	--	70	40
A/Brazil/11/78	40	20	40	--	--	60	40
A/Den/9284/78	35	30	25	10	--	65	35
A/Fukushima/103/78	75	20	5	--	--	25	5

TABLE 6. Hl antibody titers following vaccination with 20 µg of A/USSR/90/77 in 20 seronegative persons in 1978 (Group 3).

Test Antigen	Percent with titer of					%	%
	<8-8	16-32	64-128	256-512	>1024	>16	>64
A/USSR/92/77 (P.D.)	--	5	57	39	--	100	95
A/USSR/90/77	--	--	20	48	33	100	100
A/Brazil/11/78	--	--	19	52	29	100	100
A/Den/9284/78	--	--	19	48	33	100	100
A/Fukushima/103/78	--	5	57	34	5	95	95

TABLE 7. Hl antibody titers following vaccination with 20 µg of A/USSR/90/77 in 21 seropositive persons, infected in 1978 (Group 4).

Test Antigen	Percent with titer of					%	%
	<8-8	16-32	64-128	256-512	>1024	>16	>64
A/USSR/92/77 (P.D.)	--	--	50	45	5	100	100
A/USSR/90/77	--	15	35	25	25	100	85
A/Brazil/11/78	--	15	35	40	20	100	85
A/Den/9284/78	--	5	25	65	5	100	95
A/Fukushima/103/78	25	30	30	15	--	75	45

TABLE 8. Hl antibody titers following infection in 1979 in 20 persons who had received vaccine containing 20 µg of A/USSR/90/77 late in 1978 (Group 5).

	Group	Percent with titer of <8-8	16-32	64-128	256-412	>1024	% >16	% >64
1.	1978 Cases-unvaccinated	75	15	5	5	--	25	10
2.	1979 Cases-unvaccinated	86	--	--	7*	7*	(14)	(14)
3.	Vaccinated-seronegative	75	20	5	--	--	25	5
4.	Vaccinated-seropositive	--	5	57	34	5	100	95
5.	1979 Cases-vaccinated	25	30	30	15	--	75	45

*Age 27 or 28. All others 25 or younger.

TABLE 9. Comparison of H1 antibody titers following vaccination, infection or combination of infection and vaccination in tests with A/Fukushima/103/78.

	Group	No. of Men	Serum	Percent with titer of <8-8	16-32	64-128	256-512	1024-2048
1.	Infected	118	Conv.*	29	48	24	3	--
2.	Vaccinated X1 200 CCA	95	Post-Vacc.	78	20	2	--	--
3.	Vaccinated X1 400 CCA	20	Post-Vacc.	35	50	15	--	--
4.	Vaccinated X2 200 CCA	40	Post-Vacc.	15	43	40	3	--
5.	Vaccinated 200 CCA then infected	41	Conv.	--	20	39	41	--
6.	Infected, then vaccinated 400 CCA	18	Post-Vacc.	--	11	28	44	17

*All serum pairs showed significant CF antibody rises.

TABLE 10. Comparison of H1 antibody titers following vaccination, infection, or combination of infection and vaccination in test with A/Japan/57 in 1957.

(From Annual Report to Commission on Influenza, AFEB, 1957-58).

TEST STRAIN	SERUM SPECIMEN	CUMULATIVE PERCENT OF PERSONS WITH H.I. TITER MORE THAN 8	16	32	64	128	256	512	1024	% ≥32	% WITH ≥4 X RISE
A/Texas/1/77	Pre-	99	94	93	88	76	56	40	27	93	
	Post	99	96	95	88	76	60	44	28	95	1
A/Brazil/11/78	Pre-	83	78	73	66	61	47	34	25	73	
	Post-	100	100	99	87	80	63	39	32	99	33
A/Fukushima/163/78	Pre-	79	69	57	49	34	22	12	8	57	
	Post-	99	91	80	62	48	30	15	7	80	23
B/Hong Kong/5/72	Pre-	96	91	75	40	25	16	7	4	75	
	Post-	98	95	83	59	29	17	8	3	83	3

Table 11. Distribution of H.I. antibody titers of 75 students before and after second injection of whole virus vaccine which contained 7 µg each of A/Texas/77, A/Brazil/78 and B/Hong Kong/72. The previous vaccine had contained 20 µg of each of the same antigens.

PRE-VACCINATION TITER	NUMBER OF PERSONS	NUMBER WITH ≥4 X RISE	PERCENT WITH ≥4 X RISE
<8 to 8	17	17	100
16 to 32	9	5	56
64 to 128	13	3	23
256 to 1024	36	0	0
TOTAL	75	25	33

Table 12. Relationship between proportion of persons who showed 4-fold or greater increase in H.I. antibody titer for A/Brazil/78 and prevaccination antibody titer following second injection of vaccine.

POPULATION TESTED	AGE RANGE	NO. OF PERSONS	DATE BLED	PERCENT WITH H.I. TITER OF <8	>8	>16	>32
Hospital Patients	0-1	70	Feb.-May 1979	41	59	39	29
	2-11	111		36	65	49	35
	12-18	68		18	82	76	54
State Laboratory Sera	12-25	196	Oct. 1978	38	63	42	23
	12-25	101	May 1979	20	80	61	50
Air Force (Vaccinated)	17-25	61	May 1979	2	98	90	79

Table 13. Comparison of H.I. titers of different population groups in tests with A/USSR/92/77 (P.D.) antigen.

POPULATION TESTED	AGE RANGE	NO. OF PERSONS	DATE BLED	PERCENT WITH H.I. TITERS OF <8	>8	>16	>32
Hospital Patients	0-1	36	Jan. 1979	67	35	19	
	2-11	25		68	32	16	
	12-25	13		38	61	38	
"	0-1	70	Feb.-May 1979	60	40	35	
	2-11	111		50	50	40	
	12-25	79		34	66	41	34
State Laboratory Sera	12-25	101	May 1979	58	42	27	9
Air Force (Vaccinated)	17-25	61	May 1979	20	80	74	64

Table 14. Comparison of H.I. titers of different population groups in tests with A/USSR/90/77.

POPULATION TESTED	AGE RANGE	NO. OF PERSONS	DATE BLED	PERCENT WITH H.I. TITER OF <8	>8	>16	>32
Hospital Patients	0-1	36	Jan. 1979	81	19	8	6
	2-11	25		76	24	8	4
	12-25	13		62	38	23	0
"	0-1	70	Feb.-May	68	36	30	17
	2-11	111	1979	59	41	29	20
	12-18	68		46	54	41	25
State Laboratory Sera	12-25	101	May 1979	58	42	23	12
Air Force (Vaccinated)	17-25	61	May 1979	20	80	77	67

Table 15. Comparison of H.I. antibody titers of different population groups in tests with A/Brazil/78.

POPULATION TESTED	AGE RANGE	NO. OF PERSONS	DATE BLED	PERCENT WITH H.I. TITER OF <8	>8	>16	>32
Hospital Patients	0-1	36	Jan. 1979	67	33	14	8
	2-11	26		88	12	8	4
	12-25	13		62	39	8	0
"	0-1	70	Feb.-May	67	21	11	11
	2-11	111	1979	77	23	16	4
	12-25	79		71	29	18	4
State Laboratory Sera	12-25	101	May 1979	77	23	9	5
Air Force	17-25	61	May 1979	28	72	66	44

Table 16. Comparison of H.I. titers of different population groups in tests with A/Fukushima/78.

YEAR	POPULATION GROUP	NO. OF PERSONS	PERCENT OF PERSONS WITH H.I. TITER OF < 8	> 8	> 16	> 32	> 64	> 128	> 256	> 512	> 1024
1973	Air Force	80	61	38	35	25	13	8	3	2	1
1974	Air Force	58	67	33	28	24	13	11	6	4	2
1978	Civilian	114	64	11	11	8	4	2	-	1	-
1979	Civilian	121	66	12	12	6	1	2	1	-	-

Table 17. H.I. antibody titers for B/Hong Kong/72 of unvaccinated persons in age range 17 to 23 in period from 1973 to 1979.

YEAR	VACCINE MADE BY	POTENCY	NO. OF PERSONS	CUMULATIVE PERCENT OF PERSONS WITH TITER MORE THAN 8	16	32	64	128	256	512	1024	% WITH ≥4 RISE
1973	M.S.D.	250*	73	89	81	69	47	26	18	8	4	52
		500	80	92	89	76	60	43	25	15	6	66
		1000	73	90	87	79	69	54	31	19	8	78
	M.S.D.	500	35	100	97	90	84	74	59	42	31	91
	P.D.	500	37	89	86	84	73	51	35	32	16	70
1974	Wy.	500	58	97	97	95	88	78	59	30	14	83
1975	Wy.	500	74	99	98	87	71	56	37	22	8	**
1977	Wy.	500	50	98	92	88	80	58	38	18	8	**
1978	Conn.	20 µg	67	99	94	78	63	46	27	14	10	**
1979	Conn.	20 µg	75	96	91	75	40	25	16	7	4	**

* C.C.A.

** Vaccinated before arrival at Lowry AFB. No prevaccination serum available.

Table 18. Post-vaccination H.I. antibody titers for B/Hong Kong/72 of students who received military formula influenza vaccines between 1973 and 1979. All tests were done with antigens from egg passages 22 or later.

Test Strain	Serum Specimen	Percent of persons with H.I. titers more than 8	16	32	64	128	256	512	1024	% With 4X Rise
B/Hong Kong/5/72	Pre-	94	90	74	44	24	12	6	-	
	Post-	94	92	84	56	28	12	6	-	2
B/Singapore/222/79 E 9	Pre-	76	56	36	26	14	4	-	-	
	Post-	82	68	46	30	12	4	-	-	6
B/Singapore/222/79 E 8 MK1	Pre-	70	52	26	16	6	-	-	-	
	Post-	72	58	30	22	6	-	-	-	2
B/Denver/1/79 MK2	Pre-	76	64	46	18	14	2	-	-	
	Post-	80	72	50	32	10	4	2	-	0

Table 19. Comparison of results of H.I. tests with B/Hong Kong/5/72 and three different passage lines of B/Singapore/222/78. Sera were collected from 50 persons before and after second injection of vaccine which contained 7 µg of B/Hong Kong/5/72.

WEEK OF	NO. OF CASES/1000/WEEK IN STUDENTS	PERMANENT PARTY	NO. OF CASES OF INFLUENZA B
5 Nov.	3.8	3.7	-
12 Nov.	2.6	2.1	1
19 Nov.	0.2	0.2	1
26 Nov.	1.7	1.3	-
3 Dec.	2.7	2.9	
10 Dec.	2.5	2.1	-
17 Dec.	0.4	1.9	-
23 Dec.	0.4	0.9	-
31 Dec.	1.1	2.4	-
7 Jan.	2.9	4.0	2
14 Jan.	3.9	4.9	2
21 Jan.	5.3	2.7	4
28 Jan.	3.9	2.7	1

Table 10. Incidence of febrile respiratory disease in students and permanent party and number of confirmed cases of influenza B from 1 November 1979 to 4 February 1980.