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PREVENTION OF INFLUENZA AND OTHER RESPIRATORY DISEASES (U)

ANNUAL PROGRESS REPORT

BY

Gordon Meiklejohn, M.D. and
Theodore C. Eickhoff, M.D.

August, 1975
(For the period 1 June 1974 to 31 May 1975)

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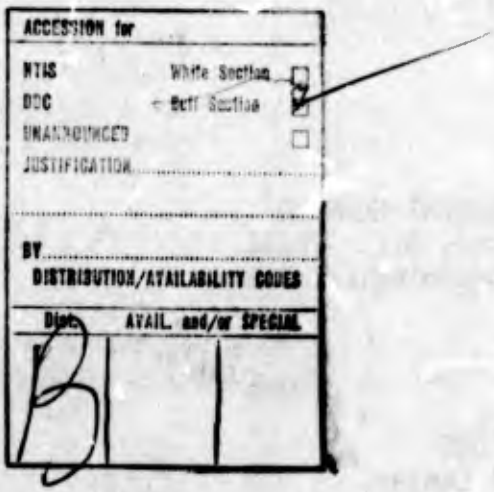
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INTRODUCTION

In the past several years, influenza A strains have continued their slow antigenic drift. The introduction of the A/England/42/72 (H3N2) strain in 1972 was followed a year later by the introduction of the A/Port Chalmers/1/73 (H3N2) strain, a strain which differed somewhat both in the hemagglutinin and neuraminidase antigens. A major antigenic change in influenza B virus occurred during the 1972-73 season with the introduction of the B/Hong Kong/72 strain, which circulated widely in the United States that year causing focal outbreaks of typical influenza. There is, of course, no way to predict with certainty the occurrence of influenza in either military or civilian populations, but past experience suggested that it was not unreasonable to anticipate the occurrence of influenza A, and perhaps B as well during the 1974-75 season.

Recombinant neuramindiase-specific influenza vaccines have been investigated extensively in animal models, and to a lesser extent, in humans. A major field trial of efficacy in a military population had not been carried out. The theoretical basis for the use of such a vaccine is as follows: Anti-neuraminidase antibody is known to modify the clinical expression of influenza in animals, and limited data suggest that this may also hold for man. Anti-neuraminidase antibody does not prevent infection by influenza virus in a host lacking antibody to the hemagglutinin, but does modify infection if it occurs, so as to produce asymptomatic or only mildly symptomatic infection. The natural infection results in the development of antibody to the viral hemagglutinin. The net result is that a more durable, and possibly broader immunity may be produced by the modified natural infection than would otherwise be produced by inactivated vaccines containing the hemagglutinin antigen which prevents natural infection.

Thus, it appeared that recombinant, neuraminidase-specific influenza vaccines were ready for major field trials in military populations. It was felt to be very important to assess the efficacy of such a preparation in comparison to the standard bivalent military influenza vaccines in order to assess the possible superiority of the recombinant vaccine.

The primary purpose of this investigation was to determine the protective efficacy of a recombinant neuraminidase-specific influenza A vaccine in a military population. A second objective was the continuing assessment of effectiveness of standard military bivalent influenza vaccines in the event of an outbreak of either influenza A or influenza B.

The vaccine considered most suitable was prepared by Dr. Edwin Kilbourne, Department of Microbiology, Mount Sinai School of Medicine, New York, New York. The strain used in the vaccine is the X-42 strain, being a recombinant strain containing the hemagglutinin of A/Equine/1/Prague/56, and the neuraminidase of A/Port Chalmers/1/73 (H3N2). Its antigenic composition is thus H eq.1 N2). Preliminary data received from Dr. Kilbourne indicated that the X-42 vaccine was satisfactorily immunogenic in a group of 10 volunteers, and appeared not to cause local or systemic reactions with unusual frequency or severity.

METHODS

Vaccines Used

Three vaccines were used in the field trial. The first vaccine was the X-42 recombinant neuraminidase-specific vaccine (H eq.1 N2) the IND of which is held by the National Institute of Allergy and Infectious Disease, NIH. The vaccine was prepared on contract from NIAID by Merrell-National Laboratories, Lot No. 1926.

The second vaccine used was a monovalent preparation containing 500 CCA units of B/Hong Kong/5/72 vaccine, kindly made available by Dr. Frank Brandon, Parke, Davis and Company, Detroit, Michigan (Lot No. 9036190).

The third vaccine was standard military bivalent vaccine, containing 700 CCA units of A/Port Chalmers/1/73 (H3N2) as the A component and 500 CCA units of B/Hong Kong/5/72 as the B component. This vaccine was made available through standard military channels, as Lot No. 145401, prepared by Wyeth Laboratories, Inc., Marietta, Pennsylvania.

All vaccines were administered by jet guns, kindly made available by Dr. Thomas Vernon, State Epidemiologist, Colorado State Department of Health.

Experimental Subjects

All experimental subjects were members of the student population at Lowry Air Force Base, an Air Force facility located three miles from the University of Colorado Medical Center. The procedures used conformed to the regulations contained in AFR-169-8, Paragraph 1B (4) governing the use of vaccines. Approval was requested and received from the Army Investigational Drug Review Board, the Department of Preventive Medicine, United States Air Force, and the Human Research Committee, University of Colorado School of Medicine. Written informed consent was obtained from all participants who received investigational vaccines. A copy of the consent form is appended.

Study Design and Plan of Investigation

It had been anticipated that approximately 4000 men would be available in student squadrons at Lowry Air Force Base on November 1, 1975, who had not received influenza vaccine following induction into the Air Force. The men would be requested to enroll in a field trial on a voluntary basis, and would so indicate with appropriate informed consent. Those who volunteered would then be randomized on the basis of the terminal digit of their social security number into three groups of approximately equal size, one of which would receive standard bivalent influenza vaccine, the second to receive the X-42 recombinant neuraminidase-specific influenza A vaccine, and the third to receive monovalent vaccine containing 500 CCA units of B/Hong Kong/72. In this way, without having a true placebo control group, it would have been possible to utilize as controls the two groups of men who received monovalent vaccines. If influenza B had occurred, those who received the X-42 vaccine would serve as a control; if influenza A had occurred, those who received monovalent B vaccine would serve as a control.

Due to a variety of administrative delays, final approvals to proceed with the study were not received until early December, 1974, and actual

administration of vaccine took place on Monday through Thursday, 9-12 December 1974. It rapidly became apparent that the pool of unvaccinated men had been seriously eroded in the six weeks that had elapsed since 1 November 1974, and that a substantial number of students had already received the standard military bivalent influenza vaccine, either at Lackland Air Force Base, or as part of the influenza vaccination programs carried out for permanent party at Lowry Air Force Base.

Further technical problems became apparent during the initial phase of vaccine administration, in that there was inadequate opportunity to explain the proposed study to the students, particularly in the context of long lines of students and the necessity for rapid processing. Accordingly, the protocol was modified so that volunteers were randomized into two groups to receive the X-42 neuraminidase-specific recombinant vaccine, and the monovalent B/Hong Kong vaccine; non-volunteers were given the standard military bivalent vaccine. This procedure was to remain in effect until approximately 1000 men each had been recruited into the two monovalent vaccine groups, at which time further volunteers would be given standard military bivalent vaccine to reach a total of 1000 men in each of the three groups.

Because of the delay in initiation of the program and consequent diminution in the number of unvaccinated men, and the inability to fully explain the nature and conduct of the field trial, only 599 students volunteered to participate. The final distribution of vaccines administered was as follows: X-42 vaccine - 281 students; monovalent B vaccine - 318 students; standard military bivalent vaccine - 1495 students.

In order to evaluate the immunogenicity of the vaccines administered, 101 students in the X-42 vaccine group, 89 students in the monovalent B vaccine group, and 7 students in the standard bivalent vaccine group were bled just prior to vaccine administration and again two weeks later.

Thereafter, all students reporting to the base dispensary with respiratory symptoms and oral temperatures of 99°F or higher were asked to report to the influenza office. There, a brief notation was made of date of onset and clinical symptoms. Men were asked to volunteer to submit throat washings, collected in broth. They were further asked to volunteer to provide an acute serum specimen and if they were willing to do so, arrangements were further made for a second specimen to be collected three weeks later. During the 1974-1975 season, surveillance was maintained on a total of 158 students who were referred to the influenza office as a result of symptoms referable to the respiratory tract and oral temperatures of 99°F or higher. Throat washings were obtained from all of these students, and acute and convalescent serum specimens were obtained from 46 students who volunteered to provide them.

The throat washings were collected in beef-heart extract broth, which were initially stored in the freezer compartment of the refrigerator at Lowry Air Force Base dispensary at approximately -5°C, and transferred 1 to 3 days later to the University where they were tested either immediately or following further storage at -20°C and were later tested in Rhesus monkey kidney tissue culture and in chick embryos in order to detect the presence of influenza virus.

Serum pairs were tested by complement fixation tests for influenza A and B, by hemagglutination inhibition tests using influenza strains A/Port Chalmers/1/73, A/Scotland/840/74, A/South Australian/54/74, and influenza B strain B/Hong Kong/5/72. Neuraminidase inhibition tests were carried out using the X-42 strain.

RESULTS

Antibody Response to Vaccination

X-42 Vaccine. Pre- and post-antibody titers of 50 men who had received the X-42 vaccine were measured in HI tests against strains Port Chalmers/73, Scotland/74, and X-42 and in neuraminidase inhibition tests against strain X-42. Results are presented in Table 1.

Since the strain from which the vaccine was prepared presumably had the hemagglutinin of influenza A/Equine/1 and the neuraminidase of Port Chalmers/73, it was anticipated that there would be some increase in HI antibody against the X-42 strain and none in tests with either Port Chalmers/73 or Scotland/74. This, however, was not the case. In only 12% of individuals were there HI antibody responses against the X-42 strain and most of these were of low order. Tests with the strain H/Equine/1 from which the hemagglutinin was derived also rarely showed significant rises in antibody titers. On the other hand, a larger proportion of the men showed antibody rises in tests using Port Chalmers and Scotland antigens, particularly with the former. While the proportion showing increases in antibody titer is only 28% of the total, when the results were analyzed with respect to their prevaccination antibody titers (Table 2), it was found that approximately 60% of the men who had titers of 8 or less than 8 showed a fourfold or greater response in tests with Port Chalmers/73 antigen. This is the type of response which was seen in the past with low potency influenza vaccines.

These findings were disconcerting since it is obvious that, if a significant outbreak of influenza had occurred and protection attributable to the vaccine had been demonstrated, it would have been impossible to determine whether this was due to the increase in neuraminidase antibody or to the increase in HI antibody. These data are being transmitted to Dr. Kilbourne for explanation. It should be noted that he had previously been aware of the fact that when X-42 vaccine was tested in humans, some individuals had shown increases in antibody titer to Port Chalmers/74 type strains.

The neuraminidase antibody titer increases which are also shown in Table 1 were remarkably large and uniform. While almost half of the individuals had titers of 32 or less before vaccination, only a single individual showed a titer of less than 128 following vaccination and a large proportion showed inhibition at the final dilution tested, namely 4096. A large number of sera from vaccinated individuals and from cases of influenza have now been tested in this laboratory and these are the highest titers which have been observed. Because the technique is different and more complicated than well standardized tests such as HI or CF tests, many tests were repeated and efforts were made to check them in other ways.

In Table 3, the HI results already presented in Table 1 are again shown in comparison with the results which were obtained in men who had received monovalent influenza B vaccine and who consequently should not have shown

any increase in titer of NI antibody. In these tests, sera from both vaccine groups were interspersed so as to obtain a side by side comparison. The distribution of pre-vaccination of NI antibody titers is remarkably similar in the two groups. The marked increase in antibody titers among recipients of the X-42 vaccine has been noted above. Comparable increases were not observed in men who received the influenza B vaccine. While there were three individuals among the 50 who showed fourfold increases in titer, these were fourfold only and were balanced by two individuals who showed fourfold drops in titer. These data suggest that the results presented above are based on a specific, measurable antibody.

Bivalent Vaccine. Commercial bivalent vaccine of a potency similar to that used by the Armed Services during the 1974-75 winter was tested in civilians rather than in military personnel since there were insufficient numbers of serum pairs available from the latter. The civilians were technicians in medical school laboratories or at the adjoining Blood Bank, or students in the School of Medical Technology. This group apparently had had less recent exposure to the influenza A viruses than the recruits at Lowry Air Force Base. The serum pairs were tested against four influenza A strains and against B/Hong Kong/72. Results are presented in Table 4.

When one inspects the distribution of pre-vaccination antibody titers, it is apparent that the number of men with low titers was smallest in tests against the England/72 strain, next against Port Chalmers/73, next against Scotland/74, and finally against the South Australia/74 strain. The administration of Port Chalmers/72 vaccine evoked an antibody response against the homologous strain in 76% of the men. In tests with the antecedent England/72 strain, 68% of the men showed a fourfold or greater increase in antibody titer and a similar 68% in tests against the succeeding Scotland/74 strain. The antibody response was lowest against the South Australia/74 strain which evoked an antibody response in only 59% of the men. The levels of antibody titer appeared to be somewhat lower in tests with the Scotland strain and still lower when the South Australia/74 strain was used.

These results were of interest in view of the discussions which occurred last fall regarding the desirability of changing the influenza A component in the vaccine. The proposal was to substitute a bivalent A component containing 350 CCA units of PC and 350 CCA units of Scotland/74 for the present vaccine which contains 700 CCA units of PC.

There was considerable doubt on the part of former members of the Commission that an antigenic change of this small magnitude warranted a change in vaccine composition. The data presented here suggest that the gain from such a change in composition would probably be relatively slight. In support of the change, one notes the percent of men who had titers of 8 or less following vaccination, this figure is only 8% when tested against Port Chalmers/73 and 14% when tested against Scotland/74. Whether this is sufficient to warrant the additional alteration in manufacturing processing is an open question.

The results in tests with B/Hong Kong/72 are presented in the last two lines of the Table 4. A surprising 70% of individuals in this group had titers of 8 or less prior to vaccination. Fifty-one percent showed a fourfold greater increase in titer but a relatively large number, namely

17%, still had titers of 8 or less after vaccination. This response appeared to be somewhat poorer than that observed with vaccines prepared the year before.

In order to determine what type of neuraminidase antibody response would be evoked by commercial vaccine (Fluogen), 24 pairs of sera from this same group were tested using strain X-42 (Table 5). The results of the HI tests resemble those obtained with the larger group of 37 individuals. The NI tests show considerably less antibody response than was observed in military personnel who received the X-42 vaccine. Only 50% of persons showed an increase in titer of fourfold or higher. While most of the persons whose titers were less than 16 showed increases in antibody, the distribution of post-vaccination antibody titers fell for the most part in the range between 128 and 512, a level considerably lower than that which had been observed in recipients of X-42 vaccine. Whether this difference reflects (1) the lower pre-vaccination titers, (2) a special property of X-42 strain or (3) some damage to the neuraminidase component of the vaccine in the process of preparation cannot be defined at this time and probably should be studied further.

BHK-72 Vaccine. The results of HI tests for B/Hong Kong/72 in military personnel who received monovalent B/Hong Kong/72 vaccine (500 CCA units) are shown in Table 6. Pre-vaccination titers were low in more than two-thirds of the group. Response following vaccination was good, with high post-vaccination titers and 83% of persons showing fourfold or greater increases in titer. The results closely match those from the previous year when late egg passage virus was used as antigen. They are considerably better than the influenza B response of civilians who received polyvalent vaccine of the same manufacturer which supposedly contained the same amount of influenza B antigen.

Occurrence of Febrile Respiratory Disease

Observations on the number of men reporting to the dispensary with febrile respiratory disease were begun October 14 and ended on April 14 of 1975. Results are presented in Table 7. Because of the delays noted in an earlier section, vaccine administration was not actually carried out until the week beginning the 9th of December. Two cases of influenza A had already occurred before this time. Influenza cases in very small numbers were detected on the base over a period of 12 weeks ending on the 17th of February. The total number of 18 cases detected is probably somewhat less than the true number since these were diagnoses based on virus isolations and probably did not detect 100% of the cases. In spite of the presence of influenza over this long period, there was no significant rise in number of men reporting with febrile respiratory disease. The highest rate reached was 8.7/1000/week during the week commencing on the 13th of January. For the balance of the period, rates remained below 5.8/1000/week. It was thus apparent that this vaccinated population was relatively insusceptible to clinical influenza and obviously an unfortunate milieu in which to attempt to test vaccine effectiveness in a relatively small number of men. Only two cases of influenza were detected in the experimental group, both in men who had received the B/Hong Kong/72 vaccine. This, however, is obviously not a significant observation.

There are two other points of some interest. Febrile respiratory disease rates were considerably higher during October and November than later in the season but the cause of these illnesses remains unclear. The rates observed during the balance of the study were the lowest observed yet during studies at Lowry Air Force Base. Adenovirus disease was virtually absent with only two cases detected, both during the month of February. Streptococcal disease was also relatively uncommon and was scattered throughout the winter period of the study.

Relationship Between Neuraminidase-Inhibiting Antibody Titer and Influenzal Illness

Paired sera from 49 patients with confirmed influenza A were tested for NI antibody with X-42 antigen. Twenty-eight were from patients ill in 1972-73 (England/72) and 21 from patients ill in 1973-74 (Port Chalmers/73). Because results were so similar in the two groups, they have been combined for tabulation. In Table 8, the antibody response to infection is compared to that in recipients of X-42 vaccine.

There were several points of interest. In the acute phase sera of the cases, most titers were low, with 71%, 16 or less and 81%, 32 or less. A few individuals, however, had titers between 64 and 256. In contrast, in the pre-vaccination sera of the vaccinated group, titers were scattered over a wide range with 38% having titers of 16 or less; 48%, 32 or less; and 52%, 64 or higher. It appeared, that influenza A cases were concentrated in the group with lower NI titers, but the relationship was less sharp than that observed for HI antibody during previous influenza outbreaks. A rise in antibody was observed in almost all cases and the increase in titer was large. Post-vaccination titers appeared to be even higher than those observed following infection, but this observation must be accepted with caution because the two groups differed in several respects and the NI test as done in this laboratory still needs further standardization.

DISCUSSION

A number of old lessons were relearned and reinforced during the conduct of this year's field trial. First, it is apparent that delay in initiation of the trial much beyond 1 November of any given year may seriously compromise the likelihood of achieving study groups of sufficient size to be meaningful. Ordinarily, influenza vaccine is not given at Lackland Air Force Base during the period 1 June through 30 September. Thus, in any given year, approximately 3000 or more unvaccinated students may be expected to be present at Lowry Air Force Base. Students being fed into Lowry Air Force Base from the recruit training center at Lackland Air Force Base after November 1, however, have already received influenza vaccine. The ideal time to initiate a field trial at Lowry Air Force Base and to begin vaccinating is thus during the first week of November. Delay beyond that time results in dilution of the student population with recruits who have already been vaccinated at Lackland Air Force Base. Further, influenza vaccination programs for the permanent personnel at Lowry Air Force Base are carried during the first two weeks of November, and members of student squadrons are occasionally inadvertently included in these programs.

Second, there was inadequate opportunity in this field trial to explain the true nature and circumstances of the study for which they were being

asked to volunteer. Accordingly, the volunteer "rate" was disappointingly low. This problem has been discussed at some length with Colonel Darius Wells, Commander of the Dispensary at Lowry Air Force Base, who has suggested the use of some of the audiovisual aids at Lowry Air Force Base as a solution. For example, a video tape of approximately 5 minutes duration could be prepared and shown to the students on the day before or the day of a vaccination program involving volunteers, and the nature of the study for which volunteers were being sought could be explained fully. Third, the small number of paired sera obtained from men under surveillance during the respiratory disease season poses problems in future studies. Although virus isolation can be used as a means of detecting cases of influenza, and in some years correlates very well with serologic diagnosis, there is no assurance that this is the case with all influenza viruses. Further, it is clear that most students are unwilling to volunteer to provide serum specimens, particularly when agreement involves not just one, but two serum specimens. When viewed as a problem relating to the health of Air Force students as a group, rather than to the health of any given individual, mandatory serologic surveillance of a representative sample of students with respiratory tract symptomatology becomes a thoroughly justifiable proposal.

SUMMARY

1. A field trial was set up in newly inducted men at Lowry Air Force Base to evaluate the effectiveness of a recombinant vaccine containing the influenza A to neuraminidase and an equine hemagglutinin (X-42). Difficulties in initiating the study and in securing sufficient men due to unanticipated delays lead to a small population and the low incidence of influenza A at the base precluded the obtaining of significant data on protection.

2. The vaccine elicited a striking response to neuraminidase antibody which was quite comparable to that seen in individuals infected with influenza A during the preceding two years.

3. The vaccine also elicited an unexpected increase in hemagglutinating inhibiting antibody to the Port Chalmers strain of influenza A. Overall, 23% of the vaccine recipients developed significant rise in HI antibody. Among those with titers of 8 or less than 8, 60% showed increases in antibody.

4. These observations indicated that had influenza occurred, it would have been difficult to assess whether any observed protective effect would have been due to the neuraminidase antibody or to the hemagglutinating inhibiting antibody.

5. Influenza A was present on the base for approximately six weeks, approximately 12 weeks between December and February of 1974-75, but failed to cause a significant amount of disease among Base personnel, virtually all of whom had received regular military vaccine.

6. The incidence of other febrile respiratory disease was the lowest on record. Only two cases of adenovirus infection were documented throughout the season.

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The authors wish to acknowledge the generous assistance of Colonel Darius Wells, Commander of the Dispensary at Lowry Air Force Base, of Mrs. Viola DeTuerk and of other personnel at Lowry Air Force Base. The laboratory assistance of Mrs. Pat Graves and Mrs. Mary Steinbrecher is gratefully acknowledged.

VOLUNTEER AGREEMENT

I, _____, having full capacity to consent do hereby volunteer to participate in a research study entitled: "Evaluation of Influenza Vaccine (A_2/HK/68-B/Mass/71 and B/HK/5/72)" under the direction of Gordon Meiklejohn, M.D.

I have read the explanation of the study on the reverse side of this agreement and have been given an opportunity to ask questions which have been answered to my satisfaction by Gordon Meiklejohn, M.D., Theodore C. Eickhoff, M.D. or E. Dale Everett, M.D.

I further understand that I may at anytime during the course of this study revoke my consent, and withdraw without prejudice; however, I may be required to undergo further examinations if, in the opinion of the attending physician, such examinations are necessary for my health or well-being.

_____

Signature Date

_____

Witness Date

Test	Strain	Serum	Percent with antibody titer of <8	8	16	32	64	128	256	512	1024	2048	4096	% with 4 x rise
H.I.	P.C.	Pre-	24	16	18	8	6	18	4	6	--	--	--	
		Post-	8	6	14	16	16	14	14	8	4	--	--	28
H.I.	Scot.	Pre-	40	10	20	4	8	14	4	--	--	--	--	
		Post-	30	14	12	6	14	12	6	4	2	--	--	18
H.I.	X-42	Pre-	100	--	--	--	--	--	--	--	--	--	--	
		Post-	64	24	4	4	--	2	2	--	--	--	--	12
H.I.	X-42	Pre-	*	26	12	10	20	6	14	4	4	--	4	
		Post-	*	2	--	--	--	10	6	10	16	8	48	86

*Lowest dilution tested was 1:16.

TABLE 1

Comparison of distribution of pre- and post-vaccination antibody titers of 50 persons who received X-42 vaccine in H.I. tests with influenza strains A/Port Chalmers, A/Scotland, and X-42 and N.I. test with strain X-42.

TITER BEFORE VACCINATION	NO. WITH <4 X RISE	NO. WITH >4 X RISE	% WITH 4 X RISE
<8	5	7	58
8	3	5	63
16	8	1	11
32	4	0	0
64	3	0	0
128	8	1	11
256	2	0	0
512	3	0	0
TOTAL	36	14	28

TABLE 2

RESULTS OF H.I. TESTS WITH PORT CHALMERS STRAIN WITH SERA FROM 50 MEN WHO RECEIVED X-42 VACCINE

Vaccine	No. of Persons	Serum	Percent with antibody titers of <16	16	32	64	128	256	512	1024	2048	4096	% with 4 x rise
X-42	50	Pre-	26	12	10	20	6	14	4	4	--	4	
		Post-	2	--	--	--	10	6	10	16	8	48	86
B/HK/72	50	Pre-	24	12	12	20	14	10	4	--	2	2	
		Post-	22	8	12	12	26	8	8	--	--	4	6*

*2 of 50 persons (4%) showed 4 fold decrease in titer.

TABLE 3

Comparison of pre- and post-vaccination N.I. antibody titers of persons who received either X-42 vaccine or influenza B vaccine (control).

Test Strain	Serum	Percent with antibody titer of <8	8	16	32	64	128	256	512	1024	% with 4 x rise
P.C.	Pre-	51	14	8	8	16	3	--	--	--	
	Post-	--	8	3	6	14	19	16	24	8	76
Eng. A	Pre-	28	22	16	11	8	8	6	--	--	
	Post-	8	3	6	6	14	24	11	14	16	68
Scot.	Pre-	62	11	11	8	6	3	--	--	--	
	Post-	14	3	6	22	16	19	14	8	--	68
So. Aust.	Pre-	73	8	11	8	--	--	--	--	--	
	Post-	27	19	22	19	3	6	3	3	--	59
B/HK/72	Pre-	59	11	16	8	3	3	--	--	--	
	Post-	14	3	19	28	14	14	6	--	3	51

TABLE 4

Distribution of pre- and post-vaccination antibody titers of 37 civilians who received commercial vaccine (Fluogen) in H.I. tests with 4 influenza A strains and 1 influenza B strain.

Test	Strain	Serum	Percent with antibody titer of											% with 4 x rise
			<8	8	16	32	64	128	256	512	1024	2048	4096	
H.I.	P.C.	Pre-	54	17	8	--	17	14	--	--	--	--	--	
		Post-	4	4	4	8	8	17	17	29	8	--	--	79
H.I.	Scot.	Pre-	63	17	13	8	--	--	--	--	--	--	--	
		Post-	17	--	4	29	13	25	8	4	--	--	--	63
N.I.	X-42	Pre-	*	46	17	17	4	--	13	4	--	--	--	
		Post-	*	8	13	17	4	17	21	13	--	--	8	50

*Lowest dilution tested was 1:16.

TABLE 5

Comparison of pre- and post-vaccination antibody titers of 24 civilians who received commercial vaccine in H.I. tests with influenza A strains, Port Chalmers, and Scotland and N.I. tests with strain X-42.

SERUM	PERCENT WITH H.I. TITER OF									% WITH 4 X RISE
	<8	8	16	32	64	128	256	512	1024	
Pre-	67	5	7	9	2	5	2	2	2	
Post-	3	-	2	7	10	24	24	16	14	83

Table 6

Distribution of Pre- and Post-Vaccination
H.I. Antibody Titers for Influenza B/HK/72 of 58 Men
Who Received Monovalent 500 CCA Unit B/HK/72 Vaccine

WEEK OF	TOTAL NO. OF FEBRILE ILLNESSES		NO. OF CASES OF	
	NO. OF CASES	RATE/1000/WK.	INFLUENZA A	STREP. PHAR.
14 Oct.	31	9.9	-	-
21 "	40	12.8	-	-
28 "	29	9.3	-	-
4 Nov.	41	13.3	-	-
11 "	44	14.3	-	-
18 "	40	13.0	-	-
25 "	20	6.5	-	-
2 Dec.	16	5.6	2	2
9 "	4	1.4	-	-
16 "	17	5.9	1	3
23 "	1	0.4	-	-
30 "	0	0.0	-	-
6 Jan.	17	5.3	-	1
13 "	28	8.7	3	6
20 "	9	2.8	2	2
27 "	7	2.2	4	-
3 Feb.	15	5.8	2	1
10 "	15	5.8	3	-
17 "	11	4.3	1	2
24 "	10	3.9	-	1
3 Mar.	12	4.3	-	-
10 "	16	5.7	-	1
17 "	9	3.2	-	-
24 "	9	3.2	-	-
31 "	9	3.2	-	1
7 Apr.	9	3.1	-	1
TOTAL	459		18 (3.9%)	23 (5.0%)

Table 7

Incidence of Febrile Respiratory Disease
For Whole Student Population
During 1974-5 Winter Season

GROUP	SERUM	PERCENT WITH N.I. TITER OF							
		<16	16	32	64	128	256	512	>1024
Cases*	Acute	65	6	10	4	10	2	---	2
	Conv.	---	2	6	2	16	8	6	59
X-42 Vaccine	Pre	26	12	10	20	6	14	4	8
	Post	2	---	---	---	10	6	10	72

*28 cases from 1972-3 (England) and 21 cases from 1973-4 (Port Chalmers) are combined. Results were similar in the two groups.

TABLE 8

COMPARISON OF N.I. ANTIBODY TITER RISES
IN CASES OF INFLUENZA (49) WITH THOSE OBSERVED
IN MEN WHO RECEIVED X-42 VACCINE (50)