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PREVENTION OF INFLUENZA AND OTHER RESPIRATORY DISEASES (U)

ANNUAL PROGRESS REPORT

BY

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3. Type 7 adenovirus, though repeatedly introduced to the Base by incoming troops, failed to cause a significant amount of illness in the student

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4. Influenza A_2 and B, though present over a long period in the Denver area, failed to cause a significant illness in the student population which had received standard military vaccine.
5. Coronavirus infections were demonstrated with considerable frequency during the early part of the 1970-71 respiratory disease season. Mycoplasma infections were very infrequent.

SUMMARY

1. The rates of febrile upper respiratory infection in students at Lowry Air Force Base were the lowest observed to date.

2. Illness due to Type 4 adenovirus was eliminated by the use of oral live vaccine.

3. Type 7 adenovirus, though repeatedly introduced to the Base by incoming troops, failed to cause a significant amount of illness in the student squadrons which had received Type 4 vaccine.

4. Influenza A_2 and B, though present over a long period in the Denver area, failed to cause significant illness in the student population which had received standard military vaccine.

5. Coronavirus infections were demonstrated with considerable frequency during the early part of the 1970-71 respiratory disease season. Mycoplasma infections were very infrequent.

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PURPOSE:

A. General Aim

The studies carried out during the winter of 1970-71 were designed to define the role of the various agents which are responsible for acute respiratory illness among Air Force personnel at Lowry Air Force Base and to evaluate means for their prevention.

B. Specific Aims

1. Adenovirus Disease

Adenovirus infections have consistently been shown to be the largest single cause of respiratory illness at Lowry Air Force Base in recent years. The proportion of febrile illness due to adenoviruses has ranged from 35 to 50 per cent. Furthermore, adenovirus illness tends to be more severe than that due to the other viral illnesses which have been present and consequently has caused more disability. Earlier studies have shown that adenovirus Type 4 illness can be readily controlled by the use of oral live vaccine of the type now widely used in the Army, but this has not been utilized to date by the Air Force except in experimental field trials.

For ten years or more, the annual epidemics of adenovirus diseases at Lowry Air Force Base have been due to Type 4 and only sporadic cases of Type 7 and even less frequently of Type 3 have been observed. The effectiveness of the oral Type 4 vaccine hardly needs further documentation since there have been many studies in the military populations which have shown its high effectiveness. The one question which still requires study is whether the widespread use of Type 4 vaccine in recruit populations facilitates the spread of Type 7 infections and leads to the replacement of Type 4 epidemics by outbreaks due to Type 7 and consequently has less than the expected effect in reducing overall illness rates.

For these reasons [illegible] deemed appropriate to administer oral Type 4 vaccine to all students on the base and to all incoming students at such a time as the incidence of adenovirus illness appeared to be reaching significant levels. The intent was to confirm the effectiveness of the Type 4 vaccine in eliminating Type 4 illness than to follow the population in order to determine whether Type 7 infections occurred in significant numbers. In the event that a Type 7 outbreak followed, plans were made to procure and administer oral Type 7 vaccine to the affected population.

2. Influenza

Polyvalent aqueous influenza vaccine had been administered to

all students at Lackland Air Force Base shortly after their induction into the Air Force and prior to their arrival at Lowry Air Force Base. For this reason it was impossible to conduct a controlled study to determine the effectiveness of the vaccine in preventing illness. The situation, however, did provide an opportunity to evaluate the antibody levels to the virus strains contained in the vaccine which was in use in military personnel during the past winter season. Since earlier studies had concentrated on the antibody response to experimental vaccines, usually prepared with adjuvant, this information was of considerable value. It was also considered important to determine the extent of influenza illness due to either A2 or B infections in this totally vaccinated population. Both types of virus were present in the Denver area during the study period and presumably provided opportunities for the exposure of the military personnel.

3. Surveillance of Other Respiratory Diseases

In past studies there has always been a sizeable segment of acute respiratory disease which could not be classified with respect to etiology. The common identified causes have been adenovirus infections, streptococcal infections, rubella and influenza. During the current studies, routine tests of all serum pairs for mycoplasma and coronavirus infections were also conducted in order to determine what role these agents play as causes of illness at Lowry Air Force Base.

METHODS

A. Study Population

Five student squadrons were selected for detailed surveillance. The squadrons were picked because they had the longest training cycles. There was, nonetheless, considerable turnover of population during the period of observation and considerable variability even within squadrons in the length of time men remained on the base. At the time when the study was begun, the combined population of the squadrons was approximately 1937; it fluctuated thereafter between that figure and a figure slightly in excess of 1818. The men in the squadrons had been inducted at Lackland Air Force Base and had spent approximately one month there prior to their arrival at Lowry.

In addition, during January 1971, after it became apparent that illness rates were disproportionately high in the single receiving squadron, the men in this squadron were followed in a somewhat different manner. These men remained in a receiving squadron following arrival from Lackland for a period of one or two weeks. They were then assigned to the regular student squadrons. The number of men in this unit varied between 251 and 436.

2. Surveillance

1. Clinical: All men reporting to the Dispensary with symptoms of respiratory disease and a temperature of more than 99° were screened at the desk maintained by the Commission and, if they fell within the study groups, clinical data were obtained, serum specimens were taken at the time and arrangements made for a convalescent blood to be collected three weeks later. Throat cultures for bacteria were done routinely and throat washings were collected for viral isolations on a selected basis.

The men in the receiving squadron were treated somewhat differently in that clinical data and specimen for virologic study were collected only from those men whose oral temperature exceeded 101°. This difference in procedure stemmed from the fact that the rapid turnover within this unit made it virtually impossible to maintain the thorough follow-up which was possible with the organized student squadrons. It seemed, however, worthwhile, in order to identify the obviously large number of cases of illness in this group and to obtain a sample of the types of disease which were being introduced to the base each week from Lackland Air Force Base.

2. Serologic: Adenovirus complement fixation tests were performed as a screening procedure on all serum pairs. These were performed with an antigen prepared from Type 4 virus grown in Hela cells using an overnight fixation technique which has been described in earlier reports. Neutralization tests for Types of 4 and 7 were subsequently run in Hela cell tissue culture on those serum pairs which had shown a fourfold or greater rise in complement fixing antibody.

Serum pairs were also tested by complement fixation against influenza A and B antigens. The influenza A antigen consisted of allantoic fluid of chick embryos infected with the A2/Aichi/68 (Hong Kong) strain and the influenza B strain was B/Mass/68. All serum pairs which showed a fourfold or greater increase in the antibody titer by complement fixation were also tested in hemagglutination inhibition tests using the same strains.

Mycoplasma complement fixation tests were done using antigen prepared locally from organisms grown on glass. Tests for coronaviruses were initially done by complement-fixation tests and subsequently most serum pairs which had shown a fourfold or greater rise were checked by hemagglutination inhibition tests. Two strains were used. Strain OC 38 was grown in suckling mouse brain and strain 229E in tissue culture. Rubella tests were done using a hemagglutination inhibition technique. Streptococcal infections were diagnosed on the basis of a throat culture which showed beta hemolytic streptococci.

3. Virus Isolations: Throat washings were collected in broth from a sample of patients, usually those with oral temperatures of 101°

swabs. These were either inoculated directly into tissue culture or eggs after addition of appropriate antibiotics or frozen at minus 56°. For adenovirus isolations Hep 2 cells were used and proved to be highly satisfactory. Initial plans to use human embryonic kidney tissue culture as well were as a result abandoned since the medium appeared to have little advantage in terms of sensitivity and the cost was considerably greater. Influenza virus isolations were attempted in the amniotic sack of 10- to 11-day-old chick embryos and in human embryonic kidney tissue culture which were then incubated between 32° and 33° C.

J. Vaccines

The influenza vaccine which had been given to the men at Lackland Air Force Base was standard military issue aqueous vaccine prepared in the allantoic fluid of chick embryos and inactivated by formaldehyde. The vaccine contained a total unit age of 1000 CCA units which was split between influenza A_2/Aichi/68, 600 units and influenza B 400 CCA units B/Mass 66).

The adenovirus vaccine consisted of a new lot of material (Lot #16CI-[illegible]), prepared by Wyeth from Type 4 virus grown in human embryonic kidney. The lyophilized virus was compressed into a pill and then covered with an enteric coating. The titer of virus in the vaccine was estimated to be about 5.5 tissue culture infectious doses per pill.

Adenovirus vaccine was withheld until approximately the middle of January when it became obvious that the incidence of febrile pharyngitis was rising rapidly. Vaccine became available at this time and was administered to all the student squadrons on the base between the 18th and 26th of January 1971. Beginning on 1 February, the receiving squadron was vaccinated and thereafter vaccine was administered each day to those men who had arrived in the receiving squadron from Lackland. Administration of vaccine was continued until 1 June 1971. By that time, a total of 6,630 men had received vaccine.

L. Observations in the Civilian Population

As in former years, serum specimens were collected from all medical students at the time of Fall registration and also from a large number of other Medical Center personnel. Serum specimens were collected from the majority of this group again in the Spring in order to estimate the incidence of infection during the winter season. In addition, serum pairs were collected from a number of children in affiliated institutions who were already enrolled in other studies of viral respiratory disease. Hospitalized patients with illness suggestive of influenza were studied by serologic tests and virus isolation attempts.

RESULTS

I Pattern of Upper Respiratory Infections

Upper respiratory illness followed a pattern quite different from that observed in recent years. While the incidence of illness followed its usual low level prior to the Christmas break, following the return of men from their Christmas holiday there was a sharp and early rise in incidence. This contrasted sharply with the previous year when incidence rates did not begin to increase greatly until the first week of March. (Table 1)

Adenovirus illnesses for the first time in several years were present in significant numbers before the Christmas holiday and then began to increase sharply during the month of January. It was for this reason that basewide immunization with live oral adenovirus type 4 vaccine was carried out and the subsequent pattern was undoubtedly greatly influenced by this action. (Table 2) During the months of February, March, April and May, the incidence of respiratory disease among the student population as a whole followed a relatively flat line which was considerably lower than that observed in earlier years. The highest rate for any week was in the first week of March when the rate reached 32/1000 men/week. At no other time was the rate in excess of 30/1000/week. This contrasted with the prior year when rates remained above 30/1000/week over a ten week span and reached a peak of 54/1000/week.

II. Effectiveness of Adenovirus Type 4 Vaccine

The setting in which the vaccine was used and evaluated was somewhat unusual and deserves explanation. As noted earlier, adenovirus infections had been occurring soon after the start of the observation period in November and had begun to increase in number early in January. In view of the experience of earlier years, when it had repeatedly been noted that adenovirus infections caused from one third to up to three quarters of all the febrile illness in the student population, a decision was made to give vaccine to all the men in the student squadrons at one time and to follow this by administration of vaccine to all incoming men as soon as possible after their arrival at the Base. Type 4 vaccine was used because all available evidence suggested that Type 4 was the prevalent type. While neutralization tests were not done on serum pairs from all men who became ill before the administration of the vaccine, 12 of 12 individuals tested showed increases in neutralizing antibody for Type 4, and no increases in antibody to Type 7 were observed.

Type 7 infections began to be detected during the period following the administration of vaccine and continued at a low level throughout the remainder of the study. The most interesting observation was that, following the administration of the Type 4 vaccine, adenovirus illness ceased to be a significant problem in the student squadrons while at the

same time adenovirus illness continued to occur at a high rate in the man coming into the receiving squadron from Lackland Air Force Base, particularly during the first two weeks following arrival at Lowry. These men were introducing both Type 4 and Type 7 infections but neither type appeared to spread in the student squadrons even though they were constantly taking in men from the receiving squadron.

Table 3 summarizes the data on Types 4 and 7 infections in three periods, namely, before vaccination, during the vaccination period and following the vaccination of the bulk of the population. Before vaccination adenovirus infections represented 32% (28 of 88) of all febrile illness and all men tested appeared to have had Type 4 infections. During the three weeks following the initiation of vaccination it was impossible to separate the men who were ill with Type 4 adenovirus infection from those who developed a serologic response due to vaccination. A large number of men (23) fell into this category. The Type 7 infections obviously could be separated by neutralization test, and these have been listed in the table. It is noteworthy that Type 7 infections occurred in numbers equal to Type 4 during the period from 18 January to 7 February. Thereafter, from the 8th of February until the 31st of May, adenovirus infections for the first time since 1960 played a relatively negligible role in the overall respiratory disease picture. A few cases of Type 4 illness occurred in men who had been inadvertently missed by the vaccination program but only one case was detected in a man who had been vaccinated more than 2 weeks previously. Type 7 adenovirus failed to cause a significant amount of disease among the population at risk. At the highest only four men per week among the 1500 to 1800 men in student squadrons were ill with Type 7 infections. In total only 23 Type 7 infections occurred in these squadrons, an illness rate of between 1.3% and 1.5%.

The Type 4 vaccine appeared to be more effective than that used during the prior year. Data provided by the manufacturer and by Colonel Edward Buescher had suggested that the titer of the vaccine was considerably higher. The continuing occurrence of infection made it impossible to obtain a precise measurement of antibody response but in a number of men who acquired Type 7 infections soon after administration of vaccine, it was noted the Type 4 antibody response frequently reached levels which had not been observed with earlier vaccines.

Certain observations in the receiving squadron were of special interest. Attention was drawn to this squadron when it became obvious that illness rates were extremely high in men within a few days after their arrival from Lackland. The nature of the training program and the limitations of staff made it impossible to follow this group with the same thoroughness used in the established student squadrons. However, men who reported with temperatures of 101° F (rather than 99° as in the study squadrons) were bled and in many instances throat washings were collected. In Table 4 the results of these studies are shown. In 85%

of the men the illnesses were caused by adenoviruses, pointing up the fact that the problem created by adenovirus infections far exceeded that caused by all other viral or bacterial agents. During this particular period adenovirus Type 7 infections appeared to be somewhat more frequent than adenovirus Type 4 infections.

The puzzling question of why adenovirus Type 7 did not spread more widely in the student squadrons could not be completely answered. In an attempt to obtain some measure of the susceptibility of the population, neutralization tests were done on three groups of men who reported with illness which was not due to adenovirus. One group was bled before the Christmas break, another during January and another late in the study during May. In the group bled before Christmas (Table 5) only 18% had Type 7 neutralizing antibody in a dilution of 1 to 2. In the mid portion of the study this percentage had risen to 38% and by May 56% of the men had antibody. There was no way of determining whether this antibody had been acquired during the outbreak which must have been occurring at Lackland Air Force Base or following arrival at Lowry. The interesting fact, however, is that the established squadrons which contained large numbers of men followed over a long period of time Type 7 failed to produce a large amount of illness.

The suggestion that the administration of Type 4 vaccine might facilitate the spread of Type 7 is not supported by these observations. Other types of adenovirus did not appear in significant numbers. During the whole season only three men were detected who had significant increases in complement fixing antibody titer who could not be identified by neutralization test being due to either Type 4 or Type 7.

The data obtained from virus isolation attempts corroborated the serologic information. (Table 6) The throat washings were collected subsequent to the administration of vaccine during the period when both Type 4 and Type 7 were prevalent. Throat washings were tested in a HeLa cell line which appeared to be highly susceptible to both Type 4 or 7 adenovirus strains. Viruses were isolated from 89% of the 40 patients who had shown significant rises in complement fixing antibody titer. All of these men had temperatures over 101° at the time when the specimen was collected. Of the 32 virus strains isolated 16 were Type 4 and 16 Type 7. From throat washings of six individuals who had failed to show any rise in complement fixing antibody titer no adenovirus strains were isolated.

INFLUENZA

Standard military aqueous vaccine had been given to all men during the latter part of their basic training at Lackland Air Force Base. As a result, it was impossible to measure antibody response before and after vaccination. In order to obtain some estimate of the antibody levels of the student population the sera of 50 men who became ill with non-

influenzal disease during November - December of 1970 were tested in H.I. tests against A_2/Aichi and B/Mass/66 antigens. It appeared that the response to the vaccine was good (Table 7), since only 8% of the men had titers of less than 1:8 and only six per cent had titers of 1:8; the remainder had titers between 1:16 and 1:256.

Both Influenza A_2 (Hong Kong) and Influenza B were present in the Denver area throughout most of the winter season. In contrast to the initial wave of Hong Kong Influenza in 1968, the outbreak followed an indolent course with no sharp peak, but was readily recognizable due to appearance of characteristic cases of influenza and a rise in the incidence of bacterial pneumonia. The student population at Lowry Air Force Base, however, escaped almost entirely during the whole season. In the study population only four cases of Influenza A_2 and only three of Influenza B were detected. The former occurred between January and March and the latter scattered over the whole period of the study with the latest case occurring on the 25th of May.

On the other hand, studies in the civilian population revealed a very different picture. When medical students and laboratory personnel at the University of Colorado Medical Center were tested (Table 8) 52% had Influenza A_2 H.I. titers of less than 1:8, 3% had titers of 1:8 with the remainder having titers 1:16 or higher; titers for Influenza B were also low. This was, for practical purposes, an unvaccinated population and the relatively high proportion of individuals without H.I. antibody corroborated last year's experience which showed a quite similar distribution. One hundred of these individuals were bled again in May or June 1971 (Table 9). Thirteen of the 52 individuals who had titers of less than 1:8 in the fall of 1970 had shown rises in titer to between 1:16 and 1:256 in the spring of 1971. An additional four individuals who had pre-existing antibody titer, also showed fourfold or greater increases in titer. There was no adequate documentation of illness during this period. It is clear, however, that the overall infection rate in this group was at least 17%, and that among individuals who lacked H.I. antibody, the seroconversion rate was 25%.

The same pattern has been repeatedly observed in recent years, namely of outbreaks in the civilian community and introduction of influenza onto the base but with failure of the virus to spread or cause epidemics in a totally vaccinated population. In the years before vaccine was used, the reverse situation obtained, and the military population experienced sharper outbreaks than the civilian. The vaccine which the airmen had received appeared to be of relatively good potency and the infecting strain was very similar to that contained in the vaccine. The illness rate of Influenza A_2, of approximately 0.25%, was remarkably low and suggests that it would be difficult to obtain a vaccine of higher effectiveness in this setting.

The incidence of Influenza B was also very low but is difficult to

estimate vaccine effectiveness of Influenza B because the amount of illness in the adult population in the Denver region was insignificant. None of the Medical Center personnel seroconverted during the period of observation. Fairly sharp outbreaks were noted in scattered childhood population as in the past.

Tests with Recombinant Viruses

Through the courtesy of Dr. Ed Kilbourne, two recombinant Influenza A strains, namely X-15 and Hke, were obtained in order to test the H.I. antibody response of certain population groups from whom serum samples from previous studies were available. These represented three types of individuals. The first were men who had received adjuvant vaccine in 1968 prepared from the A_2 strain, Ann Arbor/67. These men had not had prior experience with Hong Kong type virus. The second group was comprised of men who had received this vaccine and had then become ill with infections due to the Hong Kong virus. The third group was composed of men who had had A_2 Influenza in 1967. Results of H.I. tests with these serum pairs are presented in Table 10 which shows the proportion and percentage of men in each group who were found to have fourfold or greater increases in antibody titer with the antigens used in the test.

In tests with A_2/AA/67 the great majority of men who had either A_2 illness or adjuvant vaccine showed increases in the titer. A smaller proportion of those who had Hong Kong influenza showed significant rises. In tests with the A_2/Aichi/68 strain only 42% of the vaccinees and 32% of the cases of A_2/67 influenza showed significant rises, but 94% of those men who had Hong Kong Influenza showed significant increases in titer. In tests with the X-15 strain, which lacks the Hong Kong hemagglutinin but has the Hong Kong type neuraminidase, no significant rises in antibody titer were demonstrated.

In tests with strain Hke, the results were somewhat surprising. Many individuals who had received A_2/67 vaccine showed fourfold increases in titer (56%). This suggested considerable crossing between the hemagglutinin of the earlier A_2 strains and the Hong Kong strain, and was consistent with results of tests with the A_2/67 strain. Cases of A_2/67 influenza due to the same virus type as that from which the vaccine had been prepared, on the other hand, showed significant increase in titer and only 5% of individuals. The explanation for this difference is not clear. Individuals who had been previously vaccinated and acquired Hong Kong infections uniformly showed fourfold increases in titer with the Hke strain.

These results are somewhat puzzling if one accepts the hypothesis that the earlier A_2 strains share a common neuraminidase with Hong Kong strains but have completely different hemagglutinins. The data suggest that there is considerable overlap between the hemagglutinins. Steps are underway to measure the neuraminidase antibody by direct assay and

enzyme activity, but these tests have not yet reached the point which warrants reporting.

Other Respiratory Diseases

Other respiratory diseases occurred throughout the winter at relatively low rates with no sharp epidemic peaks. A summary of the etiologic diagnosis on all illnesses during this period is presented in Table 11. Streptococcal infections followed adenovirus infections in frequency and were scattered throughout the whole winter period. Rubella occurred in its characteristic spring-time epidemic as a disease characterized by rash and adenopathy and was identified only because base medical officers wished to be sure that they were dealing with rubella rather than some enterovirus. All men with rubella-like rashes were shown to have H.I. rises in tests with rubella antigens. Mycoplasma infections were identified in only five individuals among more than 450 serum pairs tested with sensitive complement-fixing antigen. None of these five men was seriously ill with pneumonia.

The results of tests for coronaviruses were of particular interest. Antigens from strains 0039 and 229E were provided through the courtesy of Dr. Kenneth McIntosh. Sera were tested initially by complement-fixation and, in 15 instances in which fourfold or greater rises were obtained, were then run in H.I. tests (Table 12). The magnitude of the antibody increases were frequently only fourfold, but there was remarkably good correlation between the results of the two tests. A surprising number of individuals who showed antibody rises had concurrent infections with other agents, most frequently adenoviruses. In those instances where only corona-antibody rises were demonstrated the illnesses tended to be mild and most frequently were described as a febrile pharyngitis. The majority of the cases occurred early in the season prior to the Christmas break. The two infections attributable to strain 229E occurred at the very end of the study period. In an effort to detect coronavirus infections during the spring in a group of 70 men who reported with respiratory illness but had no fever, in other words, men with illness of minimal severity, tests disclosed only two cases of coronavirus infection, both due to strain 229E.

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Week Beginning	1969-70 No. of U.R.I.	1969-70 Rate/ 1000/Wk.	1970-71 No. of U.R.I.	1970-71 Rate/ 1000/Wk.
[illegible] December	[illegible]	11.8	30	7.8
[illegible]	[illegible]2	10.5	26	6.8
[illegible]	[illegible]	2.0	10	2.6
[illegible]	20	5.0	29	7.6
[illegible] January	23	5.8	45	11.8
[illegible]	[illegible]6	11.5	54	14.2
[illegible]	[illegible]3	10.8	82*	21.6
[illegible]	[illegible]3	10.8	109	28.7
[illegible] February	[illegible]	7.8	99	26.1
[illegible]	[illegible]	16.8	83	21.8
[illegible]	[illegible]	15.0	92	24.2
[illegible]	66	16.5	106	27.9
[illegible] March	[illegible]41	35.3	120	31.6
[illegible]	152	38.0	108	28.4
[illegible]	150	37.8	102	26.8
[illegible]	156	39.0	109	28.7
[illegible]	[illegible]48	37.0	85	22.4
[illegible] April	[illegible]17	54.3	104	27.4
[illegible]	166	41.0	110	28.9
[illegible]	[illegible]46	36.5	84	22.1
[illegible]	129*	32.3	100	26.3
[illegible] May	[illegible]39	34.8	110	28.9
[illegible]	124	31.0	84	22.1
[illegible]	117	29.3	97	25.5
[illegible]25	58	14.5	80	21.1
[illegible] June	[illegible]8	12.0	53	13.9
[illegible]	43	10.8	59	15.5
	2430		2170	

*Type 4 adenovirus vaccine administered

Table 1. Incidence of Febrile Respiratory Disease in the Whole Student Population during the Seasons 1969-70 and 1970-71

Adenovirus Infections

Week Beginning	Type 4 Not Vacc.	Type 4 Vacc. <2 wks.	Type 4 Vacc. >2 wks.	Type 4 Not Typed	Type 7	Other U.R.I.	Total U.R.I.
[illegible] Nov.				1		6	7
[illegible]				3		7	10
[illegible]	1			2		12	15
[illegible] Dec.	1			2		10	13
[illegible]	3					4	7
[illegible]	2						2
[illegible]				2		5	7
[illegible] Jan.	1			2		8	11
[illegible]	[illegible]			4		8	16
[illegible]	2	2		2		3	9
[illegible]	1	12		4	4	7	28
[illegible] Feb.	2			1	1	6	10
[illegible]	1	1		1	1	7	11
[illegible]	1				3	6	10
[illegible]		2			4	6	12
[illegible] Mar.	2	1	1		4	6	14
[illegible]				1		11	12
[illegible]					1	8	9
[illegible]					1	6	7
[illegible]	1				2	12	15
5 Apr.						7	7
12						13	13
[illegible]						5	5
[illegible]		1				4	5
[illegible] May	1	1			1	7	10
[illegible]		2				8	10
[illegible]						10	10
[illegible]		1			1	7	9
[illegible]						2	2
[illegible] June	23	23	1	25	23	201	296

Table 2. Number of Cases of Adenovirus and Other Febrile Upper Respiratory Infections in Five Student Squadrons. (Population Varied from 1537 to 1818 Men)

	Adenovirus Illness					
	Type 4 **	Untyped	Type 7	Other U.R.I.	Total U.R.I.	Per Cent Adenovirus
Before Vaccination 2 Nov. to 17 Jan. (11 weeks)	14	16	0	63	95	32
Vaccination Period 18 Jan. to 7 Feb. (3 weeks)	4	6	6	0	36	44
After Vaccination * 8 Feb. to 31 May (17 weeks)	6 ***	1	17	118	142	17

* During this period only newly arrived men in receiving squadron were vaccinated.

** 23 cases with adenovirus CF and Type 4 neutralizing antibody rises not included in this group.

*** Includes one man who had Type 4 illness more than 2 weeks after vaccination.

Table 3. Number and proportion of cases of Adenovirus and other Febrile Upper Respiratory Infections in five student squadrons before vaccination was begun during major vaccination period and following vaccination period.

Number of Illnesses Caused by		Unknown Agent	Percent Caused by Adenovirus
Adenovirus			
Type 4	9	-	
Type 7	15	-	
Not Tested	10	-	
Total	34	6	85

Table 4. Results of Tests for Adenovirus Infection in 40 Men in Receiving Squadron who Reported to Dispensary with Temperature of 101°F or Higher

Period When Sera Collected	Antibody Percent/ Number Tested	Percent With Type 7 Antibody
20 Nov. to 18 Dec.		18
15 Jan. to 4 March		38
7 May to 26 May	28/50	56

Table 5. Percent of Men with Type 7 Neutralizing Antibody During Early, Middle, and Late Phases of Study.

Result of Serologic Tests	Number Tested	Virus Isolated			% Positive
		Type 4	Type 7	None	
Positive	36	16	16	4	89%
Negative	6	-	-	6	0%

Table 6. Isolation of Adenovirus Strains in Hep 2 Cells from Throat Washings of Men with Pharyngitis and Temperature over 101°F.

	Percent with Titer of						
Test Strain	<8	8	16	32	64	128	≥256
A_2 Aichi/68	8	6	22	24	24	14	2
B Mass/66	4	10	18	36	18	10	4

Table 7. Distribution of H.I. Antibody Titers for A_2/Aichi/68 and B/Mass/66 of 50 Persons who were Ill with Other Diseases During November and December 1970. All had previously received Influenza Vaccine.

	Percent with Titer of						
	<8	8	16	32	64	128	≥256
A_2 Aichi/68	52	3	11	14	15	3	2
B Mass/66	41	13	17	13	9	4	2

Table 8. Distribution of H.I. Antibody Titers for A_2/Aichi/68 and B/Mass/66 of Medical Center Personnel in Fall of 1970. Few had received Vaccine.

Date of Bleeding	Number with Titer of						
	<8	8	16	32	64	128	≥256
September 1970	52	3	11	14	15	3	2
May to July 1971	35*	5	13	15	14	12	6

*13 persons showed titer rises from less than 1:8 to between 1:16 and 1:256, representing a seroconversion rate of 25% in person with titers of <1:8

Table 9. Distribution of H.I. Titers for A_2/Aichi/68 of 100 Medical School Personnel in Fall of 1970 and Summer of 1971.

Classification	A_2/AA/67	A_2/Aichi/68	X-15	Hke
1. Recipients of Adjuvant A_2/AA/67 Vaccine	68/75 (91%)	30/75 (40%)	0/75 (0%)	42/75 (56%)
2. A_2 AA/67 Vaccines who had A_2/HK Influenza	10/17 (59%)	16/17 (94%)	0/17 (0%)	17/17 (100%)
3. Cases of A_2/67 Influenza	19/22 (86%)	7/22 (32%)	0/22 (0%)	1/21 (5%)

Table 10. Proportion of Men with 4-fold or greater rise in H.I. Titer in Test with Standard and Recombinant A_2 Strains.

Etiology	Number of Cases	Percent of Cases
Adenovirus	157	35.0
Coronavirus	20	4.5
Influenza A	7	1.5
Influenza B	4	0.9
Mycoplasma	5	1.1
Rubella	31	7.0
Streptococcus	51	11.4
Unknown	173	38.6

Table 11. Etiology of 448 Cases of Febrile U.R.I. from November 1970 to June 1971.

Patient Number	Onset Date	0038 C.F.	0038 H.I.	229E C.F.
1**	11/17/70	<8/32*	<8/32	<8/<8
2	11 20/70	8/32	8/64	<8/<8
3	11/23/70	8/32	32/128	<8/<8
4	11/25/70	<8/16	<8/32	<8/<8
5	12/1/70	<8/16	8/32	<8/<8
6	12/18/70	<8/32	<8/64	<8/<8
7	12/19/70	<8/64	16/128	<8/<8
8**	12/22/70	<8/16	<8/32	<8/<8
9**	1/6/71	<8/128	16/>512	<8/<8
10**	1/11/71	<8/16	32/64	<8/<8
11	1/12/71	<8/32	32/128	<8/<8
12	1/13/71	<8/16	16/64	<8/<8
13**	1/21/71	8/64	8/32	<8/<8
14	1/27/71	<8/64	16/64	<8/<8
15**	1/29/71	<8/64	16/64	<8/<8
16**	2/8/71	<8/32	-	<8/<8
17	2/23/71	<8/64	-	<8/<8
18	4/16/71	<8/16	-	<8/<8
19	5/3/71	8/8	-	<8/16
20	5/3/71	<8/<8	-	<8/64

* Acute Convalescent

**Concurrent with other infection

Table 12. Results of Serologic Tests for Coronavirus Infections