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1. The antibody response of recruits of the standard trivalent vaccine was excellent to all 3 components, A/Sichuan/88, A/Taiwan/86, and B/Victoria/87.

2. Between the 2nd of January and the end of February there were concurrent outbreaks of influenza A/H1N1, and influenza B with peaks during the 3rd and 4th weeks of January.

3. The attack rates of influenza A/H1N1 for the whole base were 0.6%, and influenza B was 0.3%. The lowest attack rates were observed in Air Force Students who had been 100% vaccinated. The highest rate was seen in permanent party from the Army, Navy or Marine units (1.8%).

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Abstract (continued)

4. The attack rate of A/H1N1 in Air Force permanent party who had not been vaccinated during the fall of 1988 was considerably higher (2.2%) than the rate in those who had been vaccinated (0.6%), suggesting a vaccine efficacy of 72%. The comparable figure for influenza B was 82%. In other words, unvaccinated persons were 3 times as likely to become ill with influenza A/H1N1, and 5 times as likely to become ill with influenza B.

5. The protective HI antibody titer for influenza B was 32.

6. With influenza A/H1N1 the great majority of cases occurred in persons with titers of $\leq$16. However, there were 3 vaccinated, and 3 unvaccinated persons who had titers 32, and 2 vaccinated persons with titers $\geq$64.

7. The highest attack rates of A/H1N1 were in persons between 26 and 35 years of age.

8. The HI test was the most sensitive test for diagnosis of influenza. Viruses were isolated from 59% of patients who had serologic influenza A/H1N1, and from 61% of those with influenza B.

9. The total number of "positive" cultures for group A beta-hemolytic streptococci was 18 in the permanent party, and 13 in the students, for a total of 31 cultures. No rheumatic fever has been found.

10. The febrile URI rates were the lowest of any since the study had begun at Lowry Air Force Base in 1952. The highest rate observed in any week in the students was 2.6/thousand/week, and in permanent party 4.7/thousand/week.

11. No adenovirus was found even though vaccination was discontinued in recruits 2 years ago.

12. Vaccine efficacy in the student population has been excellent when the coverage was 100%, and 90% or more of the students had post-vaccination titers of $\geq$32. During this winter there were only 6 cases of influenza A/H1N1, and 6 of influenza B in the student population, none of A/H3N2.

13. More data are needed on how large the "most susceptible" portion of the population can be before vaccine efficacy is seriously impaired.

14. Data on cellular immunity are needed, particularly in the permanent party personnel.

FOREWORD

For the protection of human subjects, the investigators(s) have adhered to policies of applicable Federal Law 45CFR46.

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CONTENTS

INTRODUCTION

The 1988-1989 season differed sharply from that of the previous year with all 3 types of influenza virus present. An outbreak of influenza A/H1N1 and influenza B began during the week following the Christmas break in contrast to last year when the influenza A/H3N2 outbreak occurred during November and December. The outbreak continued until the last week of February, a total of 9 weeks. The situation was somewhat similar to that in 1983-1984 when the 2 same viruses were present and the attack rate in the student population was negligible.

ANTIBODY RESPONSE TO VACCINATION. Table 1.

The HI antibody response to vaccination of 100 recruits who had been bled before and after vaccination at Lackland Air Force Base soon after arrival there was late due to delays in obtaining clearance from the Air Force. Prevaccination sera were collected on the 10th of January. It is possible that some influenza occurred before the second bleeding. The trivalent vaccine which contained 15 μg each of the hemagglutin of A/Sichuan, A/Taiwan/86, and B/Victoria/87 produced an excellent response.

1) A/Sichuan (H3N2).

Before vaccination 81% had titers $\leq$8, the most susceptible range. After vaccination only 5% had titers $\leq$8, and 93% had titers $\geq$32, the "protective" range.

2) A/Taiwan (H1N1).

Before vaccination 63% had titers $\leq$8. After vaccination only 3% had titers $\leq$8, and 93% had titers $\geq$32.

3) B/Victoria.

Before vaccination 88% had titers $\leq$8. After vaccination this % was reduced to only 5%, and 92% had titers $\geq$32. This response was far better than that observed in recent years.

When it was learned that the vaccine would not be given at Lackland until December, arrangements were made to obtain blood from a number of students, and permanent party who came into the clinic for reasons other than respiratory illnesses. No prevaccination sera were available from either the students or permanent party. In Table 2 the distribution of titers of 24 students whom had been vaccinated more than 1 month earlier showed some loss of titers when compared to those of the Lackland recruits. The A/Sichuan titers were quite similar to the latter, but the A/Taiwan and B/Victoria titers showed some drop off, with 88% of persons having titers of $\geq$32 for A/Taiwan and only 76% for B/Victoria.

The results of tests of 33 permanent party are shown in Table 3. All had been vaccinated during the latter part of October. The titers against A/Sichuan were satisfactory with 93% of persons having titers $\geq$32. With A/Taiwan 84% of persons had titers $\geq$32. However, with B/Victoria only 69% had titers of 32.

INFLUENZA OUTBREAK

Surveillance was begun during the week of October 24th and continued through the end of May 1989. During the period before the Christmas break rates of febrile respiratory disease were extremely low. No influenza was detected during this period. Immediately after the Christmas break, however, during the week beginning January 2nd, a case of influenza B was detected in a member of the permanent party, and another case in the following week. At that time influenza A/H1N1 was also detected. Both viruses continued to cause increasing numbers of cases, with a peak during the week of January 23rd. Cases caused by both viruses continued to occur over a 9 week period at relatively low rates.

In students, in whom the vaccination coverage was 100%, a total of 6 cases of A/H1N1, and 6 of influenza B were detected. In the permanent party the number of cases detected was considerably larger, with 39 cases of influenza A, and 16 of influenza B being confirmed. These data are shown in Table 4, and Figure 1.

A word of explanation is necessary about the figures presented on the number of cases in the permanent party since these are different from those used in several of the subsequent tables. While the followup of the students was 100%, in the permanent party during the epidemic period the followup was only about 75%. This was due to 2 factors. First, it has always been more difficult to get complete followup on the permanent party. Second, during the height of the epidemic Mrs. Viola De Tuerk, the secretary who has been running the office at Lowry Air Force Base since 1952, became ill with influenza for the first time during her 37 years in that position. For about a week there was a gap in our coverage. However, at least half of the persons reporting with febrile URIs were seen, and specimens were collected. The percentage of positives for each week was extrapolated to the total number seen during that week. The data presented in Table 4, and Figure 1 represent an estimate of the true number of cases of influenza A/H1N1 from 39-49 and influenza B from 23 to 26.

It was impossible to distinguish on clinical grounds between influenza A(H1N1), and influenza B. Both caused relatively mild illnesses. The temperatures of the patients at the time when they reported to the clinic were low. In the permanent party, 40% patients with either virus had temperatures below 100, and 2/3 had temperatures of 101 (Table 5). Only between 13% and 16% had temperatures of 102 (Table 5 and 6). In the student population the number of cases was very small (Table 6). Tables 5 and 6 also present data on the percent of persons who had positive cultures for group A beta-hemolytic streptococci.

Table 4 also records the number of patients who came to the clinic during that period with respiratory infections with temperatures below 99 . There was an increase in the number of patients coming in without fever which was parallel to the occurrence of influenza. The peak of the outbreak was during the week of January 16th, and the peak of the patients coming in without fever was during the following week. If one estimates the excess number of clinic visits during this period by comparing the number during the 3 highest weeks before the epidemic, plus the 3 highest weeks after the epidemic with the number during the 6 highest weeks of the outbreak, it appears that the excess

was slightly more than 200. This was at a time when there were 69 confirmed cases of influenza. The data did not permit a breakdown between students, and permanent party, or between influenza A, and influenza B. Nonetheless, it appears that a significant number of afebrile cases were probably caused by influenza. A similar situation has been observed in the past when either of these 2 viruses has been present.

A single isolate of influenza A/H3N2 was made from a patient with onset of disease on 1/17/89. The paired sera on this patient showed an increase of titer in A/Shanghai HI test from 8 to 32. The CF titers for influenza A were 16 in both specimens. At that time a small number of cases of influenza caused by that virus had occurred at the Veterans Administration Hospital nursing home unit, and at the National Jewish Hospital of Denver. The A/H3N2 virus was introduced, and did not spread. This was consistent with the high level of immunity which had been produced by vaccination.

ATTACK RATES OF INFLUENZA A/H1N1, AND INFLUENZA B

There has been considerable change in the operation at Lowry Air Force Base since the last Annual Report. The greatest change has been in the size of the student population in the Air Force. Data on the number of persons in each unit were assembled on the middle of each month. Those on which the following figures are based were made on the basis of the January 15th count.

The Air Force student population has decreased considerably compared to prior years, and during January 1989 the number was approximately 1397. In addition to the Air Force students there were approximately 493 students from the other 3 services, namely Army, Navy, and Marines, who came to Lowry Air Force Base for a variety of training courses. The Air Force students without exception have been vaccinated at Lackland Air Force Base. The vaccination status of the other students was impossible to determine with precision. An estimate of 75% coverage was based on the proportion of vaccinated and unvaccinated persons who came to the clinic for diseases other than influenza.

The Air Force permanent party numbered 4008. In contrast to previous years, when we were uncertain how many of them had been vaccinated, during the current year the figure of 91% vaccination coverage was documented in 2 ways; first, by a report from the vaccination unit on the Base, and second, by counting the number of permanent party who came into the clinic with disease other than influenza, and stated that they had not been vaccinated. The 2 figures tallied closely. Shot records were checked when available.

The attack rates of influenza A/H1N1 in different groups are shown in Table 7. Thirty-nine cases were confirmed among 6120 persons on the whole base i.e. students plus permanent party, a rate of 0.6%. If we accepted the estimate of 50 cases, as noted in the previous section, the rate would be 0.8%. In the table the Air Force personnel is separated from the personnel of other services because the vaccination status of the Air Force personnel was known while it could not be determined with certainty in personnel from other services. It appeared that the Air Force students had the lowest rates of illness. The highest rates were observed in the permanent party from other services. Furthermore, the number of these cases was very small, and the differences were not significant. It is remarkable that only 3 cases were

found among 1397 the Air Force students even though the virus was present on the base for a period of 9 weeks.

Attack rates of influenza B are shown in the same format (Table 8). The attack rate for the whole base was 0.4%. The lowest rates were found in Air Force students, and Air Force permanent party. The personnel from other services showed slightly higher rates with a rate of 1.8% in the permanent party. The rates of influenza B were approximately 1/2 of those observed with A/H1N1. This was surprising in view of the fact that the post-vaccination titers for influenza B were considerably lower than those for A/H1N1.

THE NEED FOR ANNUAL REVACCINATION

In the past we have repeatedly observed that the rates of influenza in people who have been vaccinated in the Fall have been lower than in persons who have not received vaccine during that season. The number of cases in unvaccinated persons has always been small, and in addition, we have been unable to get a solid denominator for the vaccination coverage in the permanent party. During this past winter there were enough cases of influenza A/H1N1 to make an estimate of the vaccine effectiveness, and enough influenza B to suggest a trend. We define a nonvaccinated person as one who had not received vaccine in the fall of 1988, or who had not been vaccinated after June 1988. Most of the individuals classified as not vaccinated had received none the year before, and in some instances, not for as many as 5 years or more. Data showing the need for annual vaccination against influenza A/H1N1 are presented in Table 9. In the Air Force permanent party the rate was 0.7% in vaccinated persons, and 2.2% in unvaccinated persons. These figures suggest vaccination efficacy of 68% for Air Force permanent party more than 3 to 1. This is similar to the results which we have obtained in the past, and indicates that individuals who were vaccinated fared better during this period of 9 weeks when influenza A/H1N1 was on the base, providing an opportunity for exposure to this virus.

Similar data on influenza B are shown in Table 10. The number of cases of influenza B was only about half that of influenza A. Their numbers were small. The estimated vaccine efficacy however, was 82% more than 5 to 1.

The rates in students are too small to warrant any estimate of vaccination efficacy.

The data in these 2 tables suggest that there is a definite value in annual revaccination. We have hoped to find a way to eliminate the necessity of such a procedure, but it appears that with present aqueous vaccines it is necessary to insist on annual revaccination if influenza rates are to be held to a reasonable level.

PROTECTIVE ANTIBODY LEVELS

It has long been recognized that there is an inverse relationship between HI antibody titer and the frequency of clinical illness. This relationship is not clearly shown when the test antigens are not those that cause the outbreak of influenza, and particularly when ether-treated antigens have been used in HI tests. It is shown most clearly when a strain from the outbreak is used in

the HI test, and the virus is a whole virus of sufficient avidity. Inhibitors sometimes have caused difficulty in the past.

In previous reports we have estimated the attack rates at various titers in the student population, since we have had available baseline data on approximately 100 recruits who have been bled at Lackland before and after vaccination. In the permanent party with no denominator it has been impossible to determine accurate rates. This year, because the vaccination coverage was known, it was possible to estimate the number of individuals with each titer.

With A/H1N1 (Table 11), the number of cases (28) was sufficient to provide data of reasonable significance. The attack rates were higher in persons with titers $\leq$32. However, as in the past, 8 cases occurred in individuals with titers $\geq$32. The specificity of these high titers is open to question. In the past we have shown by mouse neutralization tests that these persons lacked neutralizing antibody.

When the 16 cases of influenza B were analyzed in the same manner there was a sharp cutoff at a titer of 32 (Table 11). The attack rate was 0.7% in vaccinated persons with $\leq$16. No cases were detected in persons with titers of $\geq$32. In unvaccinated persons no cases were found in individuals with titers >16.

AGE DISTRIBUTION OF CASES OF INFLUENZA

We have been interested in the age distribution of cases of influenza particularly since 1977. At that time A/H1N1 strains reappeared. It was observed that individuals who were more than 23-24 years of age had high levels of immunity to the H1N1 virus. It appeared that persons born before 1954 or 1955 had acquired a lasting immunity to the H1N1 virus. This immunity appeared to be mainly cellular since it was found at that time that a large number of these individuals remained well, even though they had no measurable HI antibody to the H1N1 viruses. Ten years have past since that observation was first made, and the "age cutoff" now appears to be about 40 years of age.

In Table 12, the age distribution of cases of influenza A/H1N1 and influenza B are shown. Only cases in the Air Force permanent party are shown because the age distribution in the other services was unknown. The number of cases of influenza B was so small (12) that the distribution is almost meaningless. Over half of the cases occurred in people over 31 years of age. The distribution of A/H1N1 Air Force cases shows the largest number occurring in individuals between 26 and 35. Above that age cases became uncommon, and no cases were found in the 352 individuals who were more than 40 years of age.

Influenza A strains of the H3N2 subtype have now been prevalent since 1968, so that individuals born between 1968 (21 years ago) and 1977 had their primary influenza infections with that particular virus subtype. It would be of considerable interest in the future to see whether they have acquired a lasting immunity to these H3N2 viruses. Since 1977 when A/H1N1 subtype reappeared, primary infection may have been caused by either one of the two influenza A subtypes. In the future it will be interesting to determine whether lasting immunity is obtained against one or another subtype of influenza A.

COMPARISON OF TEMPERATURES OF PATIENTS WITH INFLUENZA A (H1N1), INFLUENZA B STREPTOCOCCAL INFECTION AND FEBRILE URs OF UNKNOWN ETIOLOGY

For a long time we had the impression that influenza outbreaks could be recognized in the clinic because patients would appear and feel much sicker than they would with most other URI diseases. Temperatures about 101 would become more common. Most earlier impressions were based on outbreaks of influenza A/H3N2. Our impression holds up pretty well for that virus.

In earlier studies when there was a hospital at Lowry Air Force Base, patients were usually admitted to the hospital when they had temperatures which exceeded 100°F. High attack rates were observed at that level. Obviously we missed many cases of influenza which had lower temperatures. At the present time we followup all patients who come to the clinic with URIs and oral temperatures ≥99°F.

Our notions about the height of temperatures have been modified considerably during recent outbreaks of influenza caused by either A/H1N1 or influenza B viruses. In Tables 5 and 6 the temperatures at the time the patients reported to the clinic are shown for both students and permanent party for 4 diseases; namely, influenza A/H1N1, influenza B, streptococcal pharyngitis, and unclassified respiratory diseases. The important observation is that only about 1/3 of the patients with either confirmed A/H1N1 or influenza B had temperatures ≥101. About 40% had temperatures between 99 and 100. We noted earlier in this report the increase in the number of clinic visits for non-febrile URIs during the influenza epidemic. These presumably represented, in large part, patients with influenza whose temperatures were normal at the time they came to the clinic.

The patients with febrile URIs of unknown etiology had the lowest range of temperatures with 71% of permanent party and 80% of students having temperatures ≤101.

COMPARISON OF DIAGNOSTIC TESTS FOR INFLUENZA

The simultaneous occurrence of influenza A/H1N1 and influenza B applied another opportunity to compare the usefulness of 3 procedures, namely, virus isolation, CF tests, and HI tests for the diagnosis of influenza. In the past we have often encountered difficulty in isolating H1N1 virus from serologically confirmed cases, and have had some difficulty also in isolating influenza B. Therefore, it was of interest to have another opportunity to check on the results of these 3 procedures.

The results are shown in Table 13. With A/H1N1 virus isolation was accomplished in 20/34 (59%) of patients. The CF test was positive in 28/34 (82%). The HI tests with A/Taiwan antigen was positive in 31/34 patients (91 %).

With influenza B the results were quite similar. Virus isolation was more accomplished in 14/23 patients (61%). CF tests were positive 22/23 (96%), and the HI tests with B/Victoria were positive 23/23 (100%). These results are consistent with those we observed in the past in that there has been a relatively low virus recovery rate. The proportion of positives with

CF and HI tests vary greatly from year to year, and probably reflect changes in the virus. We have no idea what this means in terms of virulence, infectivity or other properties.

STREPTOCOCCAL INFECTION

Streptococcal infection has been of interest and concern since World War II. In the first year of our influenza study at Lowry Air Force Base in 1952 there were 120 diagnosed cases of rheumatic fever. This complication gradually faded away to virtually none for at least the last 16 years. During World War II, this area, the Rocky Mountain area, was considered to be endemic for rheumatic fever, and Dr. Rammelkamp's group for this reason was located in Cheyenne, where they played an essential role in streptococcal research.

The decision to locate the Air Force Academy in Colorado was questioned by the Commission on Streptococcal Diseases. During its first 3 years, when the Air Force Academy was located at Lowry Air Force Base, it was housed in quarters especially designed to minimize contact between individual students. There was no problem with rheumatic fever at that time at Lowry Air Force Base, and to my knowledge the Academy has not had any serious problem since that time.

During the past 2 years, rheumatic fever outbreaks have occurred in small numbers, in many parts of the country, including Utah.

The clinic at Lowry Air Force Base has been on the alert for streptococcal infection, and especially for rheumatic fever. Mr. James, a former Master Sergeant has been in charge for many years of the microbiology laboratory in the clinic. Throat cultures are done virtually on all patients with febrile URIs. A year ago he noticed strains of beta-hemolytic streptococci with mucoid characteristics. Eight strains were sent to Dr. Kaplan in Minneapolis. These were identified as type M18, the same type associated with numerous cases of rheumatic fever in Utah.

Mr. James has left now, but the cultures continue to be done routinely. The number of patients with febrile URIs who had positive cultures with beta-hemolytic streptococci is shown in Table 4. It is noteworthy that the number of positives was never very large; at the most 4 per week. There were 13 positive cultures in students and 18 in permanent party. No cases of rheumatic fever have been detected to date.

It is of interest that students arriving from Lackland Air Force Base in the Fall of 1988 had all received an injection of bicillin as prophylaxis against streptococcal infection. The situation at the present time does not seem alarming, but it should be followed closely in view of the possible resurgence of streptococci with rheumatogenic potential.

ETIOLOGY OF FEBRILE URI-1988-1989

The number of patients with febrile URIs was lower during the past season than any season since this study started at Lowry Air Force Base. During a period of 30 weeks only 162 of the permanent party, and 75 students were seen in the clinic (Table 4).

The highest rate observed in any week in students was 2.6/thousand/week, and in permanent party 4.7/thousand/week.

Patients with positive cultures for beta-hemolytic streptococci outnumbered the cases with influenza B, but were fewer than cases of influenza A (Table 14). No case of adenovirus was detected. This is particularly interesting because adenovirus vaccination was discontinued 2 years ago at Lackland Air Force Base, and no outbreak of either type 4, or type 7, which in the past were prevalent in this population, has been observed. The only sign of adenovirus infection was the detection of 3 persons with CF titers of 16, and 1 person with a titer of 32 in both acute and convalescent sera, indicating a recent infection with an adenovirus. We have very rarely encountered titers this high in persons who have received oral adenovirus vaccine.

PREDICTABILITY OF VACCINE EFFECTIVENESS

Predictability of vaccine effectiveness was discussed in the last report covering the period from 1982-1988, which faced the risky business of trying to predict whether or not vaccine was effective. We did this because we had data over the 6 year period which showed that influenza had been held to very low rates in the student population, and the vaccine had also done very well in the permanent party. It seemed appropriate to try to define the levels of antibody following vaccination which would provide a high level of protection. We concentrated on the attack rates of the student population because they were 100% covered by vaccination; whereas, in the permanent party, vaccination coverage was uncertain until 2 years ago.

We stated at that time that if the vaccination coverage was 100%, and the HI antibody titers of over 90% of the students have titers of $\geq$32, unless there was major antigenic drift or shift, there should be high level of protection. This has been observed repeatedly with A/H3N2 viruses, and in the more distant past, with influenza B viruses. With the A/H1N1 virus we needed more data. Furthermore, during the past decade when influenza B virus was prevalent, the B vaccine did not do as well as the A/H3N2 vaccine.

The point was made in last year's report that the most susceptible segment of the group would be the individuals with titers $\leq$8, while those with titers of $\geq$32 should be protected. Those with titers of $\geq$32 would show lower rates than those with titers 16, but there would be a number of cases in the population with high titers.

During this season evidence was obtained with each of the 3 prevalent types of influenza virus; namely, the 2 subtypes of influenza A and influenza B. The response of students vaccinated at Lackland was extraordinarily good. The tests were on 100 pairs of serum before and 1 month after vaccination (Table 1). Before vaccination, HI titers of most of the recruits were low to all 3 viruses. After vaccination 92% or 93% of students had titers $\geq$32. More than 90% of the recruits had titer rises of 4-fold or more. On the basis of these responses there was reason to predict that there would be excellent protection against A/H3N2, and this appeared to be the case when an A/H3N2 virus was isolated from a member of the permanent party. There were no secondary cases. If this was a herald case, it was one that carried no message.

The outbreak of both influenza A/H1N1, and B provided an unique opportunity to verify these predictions. The cases which occurred were very few in number, both in the Air Force, and non-Air Force permanent party personnel. It was estimated that there were only 50 cases of influenza A on the base, and 26 cases of influenza B, rates of 0.7% , and 0.3% respectively. The Air Force students fared somewhat better with the rates of 0.2% of A/H1N1, and 0.3% of influenza B respectively.

In the absence of appropriate controls, it is difficult to guess how much of the vaccine contributed to the low attack rates. The only partial control was a group of permanent party, numbering 362, who had escaped vaccination during the fall of 1988. The attack rates in the people who did not receive vaccination at that time were considerably higher than in the group which was vaccinated. This indicates that annual revaccination of the current type of aqueous vaccine is necessary to maintain low rates of illness.

The impact of antigenic drift is uncertain. However, we reported long ago, at the end of the H1N1 period in 1957, when a very different virus appeared (A/Denver/57), that vaccine prepared from an earlier H1N1 virus (A/Ann Arbor/56) provided protection of 84%, the highest we have seen in this country with an aqueous vaccine. The difference between A/Denver/57, and A/Ann Arbor/56, from which the vaccine was prepared, was greater than the difference between A/Taiwan, and A/Chile H1N1 virus which circulated in the past decade. Thus, we can still expect protection.

One must assume that when there is antigenic shift a new vaccine must be prepared. This has occurred only at intervals of 10 years or more.

Finally, a word should be said about the selection of strains for vaccine production. All the strains are not equal in terms of their capacity to produce an homologous, or heterologous antibody response. It was disturbing in the early part of the 1980's to observe a poor response to the B component to the vaccine. The new B/Victoria strain seems to be far more satisfactory than those used earlier during this period.

It is clear that, if the criteria listed above are met, vaccination will provide a high level of protection. What is not well defined yet, is how low antibody levels can be, and still provide satisfactory protection. It is questionable whether the antibody titers 6 months after vaccination in the permanent party will remain sufficiently high to provide protection 6 months or more later. In the past we have observed good protection up to 4 or 5 months, even though the antibody levels are falling.

To get more information on the actual decline of antibody levels we collected serum in November and December from 33 permanent party members who came into the clinic with complaints other than febrile URIs, and from 24 persons during April, and May when there was no influenza present. We had similar data on 24 students who were bled in November or December, and on 18 students who were bled in April or May.

The distribution of HI titers in the permanent party and students is presented in Table 15.

In the permanent party it was obvious that the situation soon after vaccination was satisfactory with both the A/Sichuan, and A/Taiwan viruses. With influenza B virus, the situation was not as good. There was a somewhat surprising decline in the number of individuals with high titers for A/Sichuan, after 6 or 7 months. There was a similar decline for B/Victoria. The titers against the A/Taiwan showed relatively little change, reflecting the fact that this virus had been widely prevalent during the intervening period.

In the student population, the post-vaccination titers taken in January tended to be even higher than they were with the permanent party (Table 15). The percent of individuals with titers in the "most susceptible" range (≤ 8) had increased in the post-vaccination sera for A/Sichuan from 0%-28%; for A/Taiwan from 4%-6%; for B/Victoria from 8%-50%. At the other end of the scale in the "protective" category, the percent with titers ≥ 32 for A/Sichuan was down from 96% to 72%, A/H1N1 from 88% to 78%, and B/Victoria from 75% to 28%.

A/H3N2 reached Lowry Air Force Base in January, but there was no evidence of influenza spreading through the population. If this virus had appeared in April or May at the time when HI titers had fallen sharply, the outcome might well have been different.

The fact that a population with a uniformly high HI antibody titer will be well protected has been repeatedly demonstrated (Table 16). We do not know whether a fall in HI antibody titers implies a decline in vaccine efficacy or why individuals in the "most susceptible" range do not become ill. The effect of vaccine in enhancing cellular immunity needs further study.

Figure 1

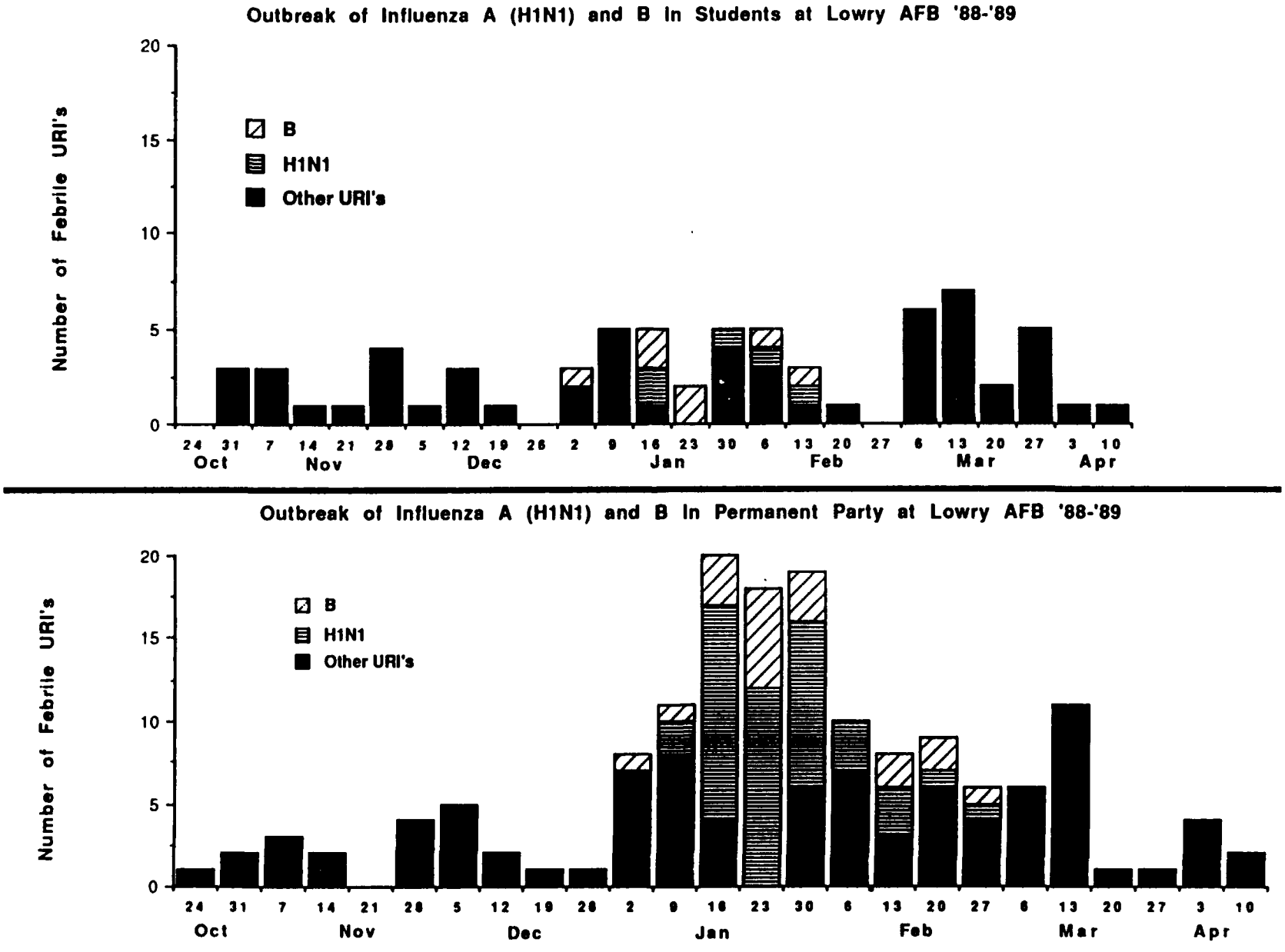
Outbreak of Influenza A (H1N1) and B In Students at Lowry AFB '88-'89
Number of Febrile URI's
B
H1N1
Other URI's
0
5
10
15
20
24 31 7 14 21 28 5 12 19 26 2 9 16 23 30 6 13 20 27 6 13 20 27 3 10
Oct Nov Dec Jan Feb Mar Apr
Outbreak of Influenza A (H1N1) and B In Permanent Party at Lowry AFB '88-'89
Number of Febrile URI's
B
H1N1
Other URI's
0
5
10
15
20
24 31 7 14 21 28 5 12 19 26 2 9 16 23 30 6 13 20 27 6 13 20 27 3 10
Oct Nov Dec Jan Feb Mar Apr

Table 1

Antibody response of 100 recruits who received vaccine containing 15 ug each of A/Sichuan/87, A/Taiwan/86, B/Victoria/87 at Lackland Air Force Base.

Test Antigen		Cumulative % with H.I. titer of									% with
		<8	8	16	32	64	128	256	512	1024	4 x Rise
A/Sichuan/ 87	Pre	67	33	19	7	4	3	1	1	0	
	Post	3	97	95	93	87	79	67	44	27	91
A/Taiwan/ 86	Pre	55	45	37	24	15	10	9	4	2	
	Post	3	97	97	93	90	88	75	55	37	88
B/Victoria/ 87	Pre	75	25	12	7	1	0	0	0	0	
	Post	4	96	95	92	81	61	45	26	15	93

Bled on: 12/16/88, 1/10/89

Table 2

Distribution of HI antibody titers of 24 vaccinated students in December 1988 at Lowry Air Force Base, Denver, Colorado

	Cumulative % with HI titer of								
	<8	8	16	32	64	128	256	512	1024
A/Sichuan/ 2/87 (H3N2)	0	101	101	97	93	76	55	26	13
A/Taiwan/ 1/86 (H1N1)	0	100	96	88	84	71	54	50	25
B/Victoria/ 2/87	8	93	93	76	63	42	21	17	4

Table 3

Distribution of HI antibody titers of 33 vaccinated permanent party in December 1988 at Lowry Air Force Base, Denver, Colorado

	Cumulative % with HI titer of								
	<8	8	16	32	64	128	256	512	1024
A/Sichuan/ 2/87 (H3N2)	0	99	96	93	75	57	36	18	12
A/Taiwan/ 1/86 (H1N1)	3	96	96	84	75	54	33	15	3
B/Victoria/ 2/87	6	93	84	69	45	21	9	3	0

Table 4

Number of Clinic Visits '88-'89

Week of	URI without Fever	URI with Fever of ≥ 99° F											
		Students				Perm. Party				Total			Total
		A	B	Strep	Total	A	B	Strep	Total	A	B	Strep	
10/24	80	-	–	-	-	-	-	-	1	-	-	-	1
10/31	87	-	–	-	3	-	-	-	2	-	-	-	5
11/7	66	-	–	1	3	-	-	-	3	-	-	1	6
11/14	83	-	–	-	1	-	-	-	2	-	-	-	3
11/21	68	-	–	-	1	-	-	-	-	-	-	-	1
11/28	115	-	–	-	4	-	-	1	4	-	-	1	8
12/5	93	-	–	-	1	-	-	1	5	-	-	1	6
12/12	81	-	–	-	3	-	-	1	3	-	-	1	6
12/19	56	-	–	-	1	-	-	1	1	-	-	1	2
12/26	36	-	–	-	-	-	-	1	1	-	-	1	1
1/2	89	-	1	-	3	-	1	3	8	-	2	3	11
1/9	134	-	–	-	5	2	1	3	11	2	1	3	16
1/16	126	3	1	1	5	12	4	-	20	15	5	1	25
1/23	145	-	2	-	2	12	6	-	18	12	8	–	20
1/30	157	1	–	1	5	10*	3	1	19	11*	3	2	24
2/6	134	1	1	-	5	3	-	-	10	4	1	-	15
2/13	121	1	1	-	4	3	2	-	8	4	3	-	12
2/20	87	-	–	1	1	1	2	2	9	1	2	3	10
2/27	106	-	–	-	-	1	1	1	6	1	1	1	6
3/6	90	-	–	-	6	-	-	-	6	-	-	-	12
3/13	107	-	–	3	7	-	-	-	11	-	-	3	18
3/20	107	-	–	1	5	-	-	-	1	-	-	1	6
3/27	103	-	–	1	1	-	-	-	1	-	-	1	2
4/3	102	-	–	-	1	-	-	-	4	-	-	-	5
4/10	104	-	–	-	1	-	-	-	-	-	-	-	1
4/17	95	-	–	2	1	-	-	1	2	-	-	3	3
4/24	98	-	–	-	2	-	-	1	3	-	-	1	5
5/1	70	-	–	2	2	-	-	1	1	-	-	3	3
5/8	64	-	–	-	1	-	-	-	1	-	-	-	2
5/15	83	-	–	-	1	-	-	-	1	-	-	-	2
Total	2887	6	6	13	75	44	20	18	162	50	26	31	237

*=Includes 1 case of Influenza A - H3N2

Table 5

Temperatures of 138 permanent party students who reported to clinic with influenza A or B streptococcal pharyngitis, or unclassified URIs.

Oral Temp.	Influ. A	Influ. B	Strep	Other URIs	Total
	(32)	(16)	(18)	(72)	138
99°-99.9	41%	38%	28%	60%	49%
	66%	69%	56%	77%	71%
100°-100.9	25%	31%	28%	17%	22%
101°-101.9	19%	19%	28%	15%	17%
	35%	32%	45%	23%	29%
102°	16%	13%	17%	8%	12%

( ) = number of persons

Table 6

Temperatures of 70 students who reported to clinic with influenza A or B streptococcal pharyngitis, or unclassified URIs.

Oral Temp.	Influ. A	Influ. B	Strep	Other URIs	Total
	(6)	(6)	(13)	(45)	70
99°-99.9	50%	50%	46%	51%	50%
	67%	67%	77%	80%	77%
100°-100.9	17%	17%	31%	29%	27%
101°-101.9	33%	16%	15%	13%	16%
	33%	33%	23%	20%	23%
102°	0	17%	8%	7%	7%

( ) = number of persons

Table 7

Attack rates of influenza A/H1N1 in different population groups

Population	No. Persons	No. Cases	Attack Rate %
Air Force	5415	32	0.6
Permanent Party	4008	29	0.7
Students	1397	3	0.2
Other Services	715	7	1.0
Permanent Party	222	4	1.8
Students	493	3	0.6
Whole Base	6120	39	0.6
Permanent Party	4230	33	0.8
Students	1890	6	0.3

Counts include patients with laboratory confirmed influenza

Table 8

Attack rates of influenza B in different population groups

Population	No. Persons	No. Cases	Attack Rate %
Air Force	5415	16	0.3
Permanent Party	4008	12	0.3
Students	1397	4	0.3
Other Services	715	6	0.8
Permanent Party	222	4	1.8
Students	493	2	0.4
Whole Base	6120	22	0.4
Permanent Party	4230	16	0.4
Students	1890	6	0.3

Counts include patients with laboratory confirmed influenza

Table 9

Attack rates of influenza A/H1N1 in vaccinated and unvaccinated permanent party

Population Studied Perm Party	Students	Vacc.	No. cases	No. persons	Attack Rate %	*VE%
AF only	-	+	29	3647	0.7	
	-	0	8	361	2.2	68

*VE = Vaccine efficacy (EST.)

Table 10

Attack rates of influenza B in vaccinated and unvaccinated permanent party

Population Perm Party	Vacc.	No. cases	No. persons	Attack Rate %	*VE%
AF only	+	8	3647	0.2	
	0	4	361	1.1	82

*VE = Vaccine efficacy (EST.)

Table 11

Relationship between acute HI titer and attack rate in Air Force permanent party of influenza A/H1N1 and influenza B at Lowry Air Force Base 1988-89.

A/Taiwan1/86(H1N1

	Vaccinated			Unvaccinated		
Titer	No. Persons	No. Cases	Attack Rate	No. Persons	No. Cases	Attack Rate
≤16	583	15	2.6	58	5	8.6
32	329	3	0.9	32	3	9.3
64	766	1	0.1	76	-	-
128	766	1	0.1	76	-	-
≥256	1203	-	-	119	-	-
Total	3647	20	0.5	361	8	2.2

B/Victoria

	Vaccinated			Unvaccinated		
Titer	No. Persons	No. Cases	Attack Rate	No. Persons	No. Cases	Attack Rate
≤16	1130	8	0.7	293	4	1.4
32	875	-	-	18	-	-
64	875	-	-	50	-	-
128	438	-	-	-	-	-
≥256	329	-	-	-	-	-
Total	3647	8	0.2	361	4	1.1

Table 12

Age distribution in cases of influenza A(H1N1) or influenza B in Air Force permanent party.

Age	Influenza A(H1N1) No. Persons	No. Cases	Attack Rate	Influenza B No. Persons	No. Cases	Attack Rate
18-20	83	0	0	83	1	1.2
21-25	769	4	.7	769	5	0.7
26-30	1182	9	1.0	1182	1	0.8
31-35	817	14	1.3	817	1	0.1
36-40	581	2	.5	581	2	0.3
41-45	255	0	0	255	2	0.8
46-50	72	0	0	72	0	0
≥51	25	0	0	25	0	0

Based on data of February 25, 1989

Table 13

Comparsion of results of virus isolation attempts with results of CF and HI tests using A/Taiwan/86, and B/Victoria/87 antigens

A/H1N1	Isolation	CF Tests	HI Tests A/Taiwan/86
Perm. Party	17/29(59%)	23/29(86%)	28/29(97%)
Students	3/5(60%)	3/5(60%)	3/5(60%)
Total	20/34(59%)	28/34(82%)	31/34(91%)
Influenza B			HI Tests B/Victoria/88
Perm. Party	11/17(65%)	16/17(96%)	17/17(100%)
Students	3/6(50%)	6/6(100%)	6/6(100%)
Total	14/23(61%)	22/23(96%)	23/23(100%)

Table 14

Etiology of Febrile URI - 1988-89

	Number of Cases	% of Cases
Influenza (A/H1N1)	50	21
(H3N2)	1	.4
B	26	11
Streptococcal infection	31	13
Adenovirus	0	0
Unclassified	129	54
Total	237	99.4

Table 15

Decline in HI antibody titer

Virus	No. persons	Time bled	Percent with HI antibody ≤8	16	≥32
Permanent Party					
A/Sichuan	33	Nov-Dec 88	3	3	94
	25	Apr-May 89	64	24	12
A/Taiwan	33	Nov-Dec 88	3	12	85
	25	Apr-May 89	32	16	52
B/Victoria	33	Nov-Dec 88	15	15	70
	25	Apr-May 89	52	32	16
Students					
A/Sichuan	24	Nov-Dec 88	0	4	96
	18	Apr-May 89	30	8	62
A/Taiwan	24	Nov-Dec 88	4	8	88
	18	Apr-May 89	6	17	78
B/Victoria	24	Nov-Dec 88	8	17	75
	18	Apr-May 89	50	22	28

Table 16

Relationship between the pre epidemic titers of Air Force students and number of cases of influenza A/H1N1 and influenza B. The number of cases in permanent party is included to indicate the presence of these viruses which were on the base for a period of 9 weeks.

Vaccine Virus	Challenge Virus	% with HI titer of			No. Student Cases	Attack Rate	No. P.P. Cases
A		≤8	16	≥32			
A/Sichuan	A/Sichuan	5	2	93	0	0	1
A/Taiwan	A/Taiwan	3	4	93	3	0.2	44
B/Victoria	B/Victoria	5	3	92	4	0.3	19

P.P. = Permanent Party