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EPIDEMIOLOGICAL SURVEILLANCE OF INFLUENZA AND OTHER  
RESPIRATORY DISEASES IN MILITARY PERSONNEL

PREVENTION OF INFLUENZA AND OTHER RESPIRATORY DISEASES -  
LABORATORY STUDIES

ANNUAL REPORT

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1. Influenza A of the H3N2 subtype was prevalent in early November 1987 until mid March 1988.					
2. The virus A/Colorado/1/87 showed considerable antigenic drift from the A/Leningrad which had been incorporated into the 1987 vaccine and was closely related to A/Sichuan/87, next year's vaccine strain.					
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## Abstract (continued)

3. Antibody response of recruits vaccinated at Lackland Air Force Base with vaccine containing A/Lenigrad/86, A/Taiwan/86 and B/Ann Arbor/86 was excellent. Recruits also responded well to the heterologous strains A/Colorado and A/Sichuan.
4. No cases of influenza were detected among 177 students who reported to the clinic with febrile URIs. Only 10 cases were detected in 176 members of the permanent party seen in the clinic. These 10 cases were spread over a period of 17 weeks from 7 November to 14 March.
5. H3N2 influenza virus strains isolated during the winter of 1987-88 differed somewhat from earlier strains. They were isolated with more difficulty in monkey kidney tissue and many strains hemagglutinated chicken red cells either poorly or not at all.
6. During the six seasons since 1977 when influenza A H3N2 has been in the Denver area in the student population of (2800-3200) at Lowry Air Base in no year have more than four cases been confirmed, suggesting that the vaccine has been highly effective.
7. Influenza B was not detected until May 1988 when three cases occurred. There was no upswing in number of clinic visits and virus did not appear to spread.
8. The paired sera collected from recruits in 1986 who had received vaccine containing A/Mississippi/85 when tested with the new virus A/Sichuan proved useful in showing the need for a change in vaccine composition. The human data are probably more valid than those obtained with ferret sera.
9. Parainfluenza I infections occurred in considerable numbers - 19 cases were diagnosed in students and 2 in members of the permanent party.
10. No cases of adenovirus disease were detected, but the elevated CF titers of 8 persons suggested that they had recently been infected by adenovirus. The Air Force decided to discontinue adenovirus vaccine in May of 1988.
11. Streptococcal infections occurred at a rate like that seen in most past years with no outbreaks of any size, but need to be watched carefully. Acute Rheumatic Fever has not reappeared to date.

FOREWORD

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## INTRODUCTION

→ During the 1987-88 season the influenza virus again proved its unpredictable character. The dominant virus was an H3N2 subtype of influenza A. The season was unique in that the virus appeared remarkably early, in early November, and continued to cause sharp outbreaks in some segments of the civilian community well into March 1988. The virus showed considerable antigenic drift away from A/Leningrad/87 and furthermore behaved quite differently when grown in tissue culture or chick embryo. Despite the antigenic drift, the antibody response to the 1987 strains following vaccination with A/Leningrad/86 vaccine was remarkably good in recruits and somewhat less effective in previously vaccinated individuals in the permanent party. No cases of influenza were detected in students throughout the winter season and only 10 occurred in members of the permanent party. These 10 cases were spread over a period of 17 weeks and no more than three in any single week. Also of considerable interest was the demonstration of 21 cases of parainfluenza I infection, of which 19 occurred in students and two in permanent party members. Influenza B did not appear until May when three cases were detected.

## Antibody Response Following Vaccination

The vaccine (Parke Davis ether split vaccine) contained 15 ug each of A/Leningrad/86, A/Taiwan/86 and B/Ann Arbor/86. At Lackland Air Force Base where the vaccine was administered, some delay was encountered in receiving clearance. As a result, prevaccination sera were not collected until the first week of December and the post-vaccination titers until January 4, 1988. It was known that influenza A (H3N2) was occurring in many parts of the country at that time and it is possible that some individuals included in the vaccine study at Lackland actually were infected during the period between the two bleedings. These titers are shown in Table 1.

- (1) The homologous response to the A/Leningrad titer was remarkably good with 99% of recruits obtaining titers of  $\geq 32$ , and 97% showing increases in titer  $\geq 4X$ .
- (2) In tests with the heterologous Colorado strain, A/Colorado/1/87, the titers were clearly somewhat lower than those observed with A/Leningrad strain. 89% of persons had titers of  $\geq 32$  and 91% had increases in antibody titer  $\geq 4X$ .
- (3) In tests with A/Sichuan/87, 90% of persons had titers  $\geq 32$  and 92% had increases  $\geq 4X$ .

(4) In tests with A/Taiwan/86 H1N1, 97% had titers  $\geq 32$  and 95% of individuals had increases in titer  $\geq 4X$ .

(5) With B/Ann Arbor/86 following vaccination 92% had titers  $\geq 32$  and 86% had titer increases  $\geq 4X$ .

#### The Occurrence of Influenza A and B, and Parainfluenza I

Table 2 presents by weeks from 19 October 1987 to 2 May 1988 the number of patients who came to the clinic with URI symptoms without fever, and with fever. The level of 99°F was selected to define fever on the basis of past experience, which showed that many cases of influenza had temperatures between 99° and 100°. The three groupings under febrile URI list the total number of clinic visits and the number of confirmed cases of influenza A or B or Parainfluenza I. Data on the students and permanent party are recorded separately.

Influenza A, which had been present in the civilian community since early November, did not appear on the Base until the week of 7 December. Sporadic cases on the Base occurred until the week of 14 March. The largest number seen in any week was only three cases. All were in the permanent party, and not a single case was detected in students at the time. Influenza B was not detected until the week of 1 May. Two other cases were found in the following week.

Parainfluenza I was first detected during the week of 26 October. This virus produced a different hemadsorption pattern. They could not be typed with any of the A or B antisera. They were transferred to the University Hospital Virus Diagnostic Laboratory where they were identified by FA antibody as parainfluenza I viruses. Parainfluenza I antigen was purchased for CF tests and this virus was included along with influenza A and B and adenoviruses in tests of all serum pairs. It should be noted that the convalescent sera were tested only up to a dilution of 32 due to the cost of this antigen.

A majority of cases of parainfluenza I occurred early in the season before the end of November. Nineteen were students between the ages of 19 and 21, and only two were detected in the permanent party, both age 25.

#### Laboratory Results in Influenza A Cases

In Table 3, the results of laboratory procedures on the 10 confirmed cases of influenza are shown. It is noteworthy that

virus was isolated from only one of these 10 patients. All but one showed a significant rise in CF antibody titer. The acute titers of many of these individuals were high to A/Leningrad, ranging from 8 up to 512. However, they were uniformly much lower in tests with A/Colorado. With the exception of the single individual with a titer of 32 against A/Colorado, all had titers of 16 or less. A/Sichuan titers were slightly lower. Eight of the 10 had titers  $\leq 8$ . Though the number of cases is very small, results are similar to those observed in other outbreaks of H3N2 influenza A in which the "protective titer" appears to be  $\geq 32$  against the homologous virus.

#### Comments on the Behavior of the 1987-88 H3N2 Influenza A Strain

Only a single virus was isolated from the 10 patients at Lowry Air Force Base. Our laboratory received more than 50 isolates of H3N2 viruses during the past season. These came from the Diagnostic Laboratory at the University Hospital, from other hospitals in the Denver area, and from elsewhere in the state of Colorado. It is noteworthy that a number of the strains hemagglutinated chicken cells only in very low titer or not at all. On the other hand, there were a number of strains which hemagglutinated guinea pig red cells at higher titers than chicken red blood cells. (Table 4)

#### Review of Past Experience with the H3N2 Virus Vaccine (Table 5)

When the A/Hong Kong/68 virus was first introduced into the Lowry population, an explosive outbreak followed and 157 cases were confirmed. There were considerably more cases than our laboratory was able to handle. A similar situation occurred in 1972-73 when the A/England/72 virus appeared and again caused an explosive outbreak. Subsequently, vaccine appeared to reduce the incidence in students very markedly, and since 1977, even though the virus had been present during six seasons, the number of cases at no time exceeded four. In this past year the number was zero. It appears that this is the most effective component of the tri-valent vaccine. There have been numerous cases of both influenza B and influenza A H1N1 within the past four seasons with more than 100 cases of these occurring in the Base population. If this peculiar virus somehow ceased its continuing drift, it would appear that influenza H3N2 in this population would be well under control.

## Influenza B

Influenza B was not detected on the Base until May 1988 when three cases occurred in the period of two weeks. There was no evidence of any widespread illness in either students or permanent party and it was assumed that these were sporadic cases of the type which occur throughout the year. The viruses have been sent to the CDC for testing to see whether there is any further antigenic drift away from the B/Ann Arbor/86. As in the past, this virus caused some concern in view of the very low levels of B antibody in large segments of the permanent party.

## Criteria for Changing Vaccine Strains

The control of influenza A H3N2 outbreaks at Lowry Air Force Base has been accompanied by numerous changes in the vaccine strain in order to accommodate antigenic drift. The criteria which determine need for such a change are by no means clear, and have been based in the past in large part on differences in HI titers observed in ferrets immunized with the earlier and the more recently isolated viruses. Some human data have been available. These have also been taken into consideration.

We are in the fortunate position of having large numbers of pre- and post-vaccination sera of recruits who have been vaccinated during the previous years. Recruits are ideal for this purpose since they have all been primed by prior infection and received influenza vaccine for the first time. Their response is far better than that in permanent party who have been previously vaccinated. Last fall when vaccine containing A/Leningrad/86 rather than A/Mississippi/85 was distributed, it was possible to test the response of recruits to A/Sichuan/87. 90% of recruits responded with titers  $>32$ , suggesting that they would be well protected. This proved to be the case.

We have recently retested 25 serum pairs of recruits who had received A/Mississippi vaccine a year ago against the homologous virus, and also against A/Leningrad and A/Sichuan. The homologous response to A/Miss/85 was again excellent with 100% of individuals responding with titers  $>32$ . 92% actually had titers of  $>128$ . With A/Leningrad, 84% of individuals had post-vaccination titers of  $>32$ . When the same serum were tested with A/Sichuan/87, titers were considerably lower. No one had a titer  $>32$  before vaccination, and only 60% had titers  $>32$  after vaccination. This provided clear warning that the vaccine strain was due for a change. What we can see here is that, while the Leningrad

vaccine in recruits evoked a good response to the A/Sichuan virus (single drift), and obviously protected well, the A/Miss vaccine did not promise very good protection against A/Sichuan (double drift). If there is antigenic drift of the same order next year, A/Sichuan virus should do as well as the A/Leningrad did during this past season.

We are more comfortable with these data obtained with human sera than we are with those obtained with ferret sera alone. I will plan to conduct tests each year as soon as the candidate virus strains become available.

### Parainfluenza I Infections

Soon after operations began in October 1987, we began to isolate a hemadsorbing agent which did not behave like influenza and which turned out to be parainfluenza I. We tested all paired sera from patients throughout the winter by complement fixation tests with commercially purchased parainfluenza I antigen. Virus strains were isolated from 12 of the 21 confirmed cases. The CF tests should be read with the knowledge that the highest dilution was 32 in order to conserve antigen, which proved to be quite costly. All but one of the 21 patients exhibited a fourfold or greater rise in titer.

The clinical diagnoses recorded on these patients by various health personnel were "URI," "pharyngitis," "viral infection" and "flu-like illness." The temperatures of most patients were between 99° and 100°. The one patient who had a temperature of 101.5° had a concurrent infection with a group A beta hemolytic streptococcus.

We had not been aware of this virus being so prevalent in the military population in the past. It appears to affect predominantly young people, since 19 of the cases were in recruits under 21 years of age, and the two cases in permanent party were in individuals 25 years old. We have in the past had similar flurries due to coronaviruses, enteroviruses and parainfluenza III infections. We did not test this year for RSV virus.

### Adenovirus Disease

No cases of adenovirus disease were detected during the 1987-88 season. However, the presence of adenovirus was evident

because of the finding that six individuals had CF titers of 32, and two had titers of 64. Titers of this order were not observed in our experience following vaccination, and imply infection in the recent past.

In May 1988 the Air Force discontinued the administration of adenovirus vaccine. We had predicted that about 10 years after the last year when a number of cases had occurred, this decision would be made. The reasoning is simple. If there is no disease, there is no need to vaccinate. The correctness of this decision will be tested, particularly if the Army and Navy continue to vaccinate recruits.

For about 20 years from 1950 to 1970, adenovirus outbreaks caused by types 4 and 7 occurred almost every year at Lowry, and were responsible for URI attack rates of 40-50/1000/week.

We plan to monitor the situation through the summer months through contact with Captain Lindner, who is the Chief of the Medical Services at Lowry Air Force Base Clinic. He will notify me if there is a significant number of cases of unexplained febrile pharyngitis. I will arrange for paired blood specimens to be drawn so that the diagnosis can be ruled in or out. When operations resume in October we will continue to monitor adenoviruses as in the past by doing CF tests on all serum pairs, and will attempt virus isolations.

### Streptococcal Disease

Streptococcal infections aroused considerable interest in the past year because of the reappearance of rheumatic fever in Utah following infections with mucoid strains of type M18. It was fortunate that Mr. James was still in charge of the laboratory. Mr. James had been a Master Sergeant in the Air Force for many years, and since retirement continued on as a consultant. He had isolated eight strains which were identified by Dr. Kaplan in Minneapolis as being type M18. There was a single case of acute rheumatic fever last year in an Air Force person who was admitted to Fitzsimons Army Hospital.

The history of rheumatic fever at Lowry Air Force Base was extremely bad in the 1940s when, along with other Bases in this part of the country, major outbreaks of acute rheumatic fever occurred. During the first year of our studies at Lowry Air Force Base in 1952-53, some 120 cases of acute rheumatic fever were reported at the hospital. In recent years there has been virtually no rheumatic fever.

The number of febrile URIs from which group A beta hemolytic streptococci were isolated is shown in Table 8. The number of isolates was approximately the same as in the past winters, representing roughly 17% of the febrile URIs. There was no particular epidemic peak, and no particular concentration in any specific units. The situation does not appear to be cause for alarm at the present time, but requires careful following.

#### Etiology of Febrile URIs at Lowry Air Force Base (Table 9)

The number of cases of different febrile URIs is shown in students and permanent party and in both combined. Influenza was very low during this past winter and caused about half as many cases of parainfluenza I. Streptococcal diseases accounted for approximately 17% of all patients seen. The largest category by far (73.4%) was of unknown etiology. The total number of patients seen with febrile URIs was smaller than any observed in recent years.

#### Addendum

During the past two years we have been working to computerize the vast amount of serologic data obtained each year. This year the 1987-88 data have been completely transferred to the computer, and it has become much simpler to analyze data. We are planning now to go back on our previous data and enter it into the computer in order to obtain further analysis of the data which go back to 1952-53.

The laboratory was recently visited by Lt. Col. Charles Hoke, Lt. Col. Robert Scott from WRAIR, and Dr. Frank Ennis of the University of Massachusetts. They were most helpful in assessing the effectiveness of the laboratory in the past, and discussing possible activities in the future. Drs. Myron Levin and Brian Lauer participated in these discussions.

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Table 1

Vaccine response in Lackland AFB recruits to 1987-88 influenza vaccine containing 15 ug A/Leningrad/86, A/Taiwan/86 and B/Ann Arbor/86.

Antigen	Cumulative % with titer of:									% 4 fold rises
	<8	8	16	32	64	128	256	512	1024	
<b>A/Leningrad/86 (78)</b>										
Pre	31	69	29	14	5	4	0	0	0	97%
Post	1	99	99	99	96	93	88	76	54	
<b>A/Colorado/87 (78)</b>										
Pre	50	51	16	4	1	0	0	0	0	91%
Post	1	98	95	89	75	56	37	14	8	
<b>A/Sichuan (53)</b>										
Pre	40	61	10	4	2	0	0	0	0	92%
Post	0	100	98	90	64	49	38	17	2	
<b>A/Taiwan/86 (78)</b>										
Pre	54	47	30	17	14	2	1	0	0	95%
Post	0	100	100	97	96	91	78	63	45	
<b>B/Ann Arbor/86 (78)</b>										
Pre	37	62	24	14	4	1	0	0	0	86%
Post	0	100	97	92	79	60	45	19	6	

Table 2

## Number of URIs at Lowry AFB 1987-88

Week	Clinic Total	URIs Fever	Febrile URI (99 <sup>o</sup> F)											
			Total				Student				Permanent Party			
			No.	A	B	Para I	No.	A	B	Para I	No.	A	B	Para I
Oct. 19	741	138	17	-	-	-	12	-	-	-	5	-	-	-
26	675	119	19	-	-	2	8	-	-	2	11	-	-	-
Nov. 2	662	172	33	-	-	3	17	-	-	2	16	-	-	1
9	559	124	33	-	-	6	26	-	-	6	7	-	-	-
16	628	167	19	-	-	-	11	-	-	-	8	-	-	-
23	256	59	10	-	-	4	6	-	-	3	4	-	-	1
30	723	165	7	-	-	2	5	-	-	2	2	-	-	-
Dec. 7	575	169	12	1	-	1	4	-	-	-	8	1	-	-
14	664	119	19	-	-	1	9	-	-	1	10	-	-	-
21	215	62	4	2	-	-	1	-	-	-	3	2	-	-
28	152	32	1	-	-	-	-	-	-	-	1	-	-	-
Jan. 4	596	154	8	1	-	-	1	-	-	-	7	1	-	-
11	616	123	14	-	-	2	10	-	-	2	4	-	-	-
18	512	90	6	-	-	-	3	-	-	-	3	-	-	-
25	620	96	10	-	-	-	6	-	-	-	4	-	-	-
Feb. 1	575	117	10	1	-	-	4	-	-	-	6	1	-	-
8	634	115	10	1	-	1	4	-	-	-	6	1	-	-
15	480	101	11	-	-	-	5	-	-	-	6	-	-	-
22	608	106	7	3	-	-	3	-	-	-	4	3	-	-
29	614	96	6	-	-	-	2	-	-	-	4	-	-	-
Mar. 7	696	107	5	-	-	-	3	-	-	1	2	-	-	-
14	569	116	4	1	-	-	1	-	-	-	3	1	-	-
21	655	104	11	-	-	-	7	-	-	-	4	-	-	-
28	456	98	8	-	-	-	5	-	-	-	3	-	-	-

Table 2 (cont.)

Number of URIs at Lowry AFB 1987-88

Week	Clinic Total	URIs Fever	Febrile URI (99 <sup>o</sup> F)											
			Total				Student				Permanent Party			
			No.	A	B	Para I	No.	A	B	Para I	No.	A	B	Para I
Apr. 4	552	103	4	-	-	-	0	-	-	-	4	-	-	-
11	615	116	8	-	-	-	4	-	-	-	4	-	-	-
18	586	124	9	-	-	-	4	-	-	-	5	-	-	-
25	569	111	7	-	-	-	1	-	-	-	6	-	-	-
May 1	540	83	15	-	1	-	3	-	-	-	12	-	1	-
8	583	90	8	-	2	-	3	-	-	-	5	-	2	-
15	528	83	10	-	-	-	6	-	-	-	4	-	-	-
22	438	73	8	-	-	-	3	-	-	-	5	-	-	-
<b>Total</b>			<b>353</b>	<b>10</b>	<b>3</b>	<b>21</b>	<b>177</b>	<b>0</b>	<b>0</b>	<b>19</b>	<b>176</b>	<b>10</b>	<b>3</b>	<b>2</b>

Table 3

Laboratory Results on Confirmed Cases of Influenza A,  
All in Permanent Party

Name	Date of Vacc.	Age	Onset	H.I.			CF A	Virus Isolation
				A/Leningrad	A/Colorado	A/Sichuan		
Tatum	10/87	24	12/7	32/128	16/64	8/64	16/64	+
Ward	10/87	21	12/22	128/512	<8/32	8/32	8/32	-
Smith	12/86	25	12/23	16/128	8/32	16/256	8/64	-
Bell	9/86	39	1/4	64/512	16/256	8/128	8/64	-
Jackson	10/87	43	2/3	8/64	8/32	8/32	8/16	-
Boston	12/87	26	2/12	512/1024	16/128	8/64	8/64	-
Swartz	10/87	24	2/22	32/512	16/64	8/64	8/64	-
McDonnell	10/87	29	2/24	32/128	32/512	16/256	8/32	-
Scott	10/87	30	2/24	16/256	<8/64	<8/16	8/8	-
Koosen	10/87	19	3/14	8/32	16/32	8/32	8/32	-

Table 4

Comparison of influenza isolates in H.A. tests using guinea pig or chicken red blood cells.

<u>H.A. Titer</u>	<u>No. of Isolates</u>
Guinea pig > chicken	12
Guinea pig = chicken	18
Guinea pig < chicken	12

Table 5

Number of Confirmed Cases of Influenza A/H3N2  
In Students\* By Years

1968-9	157**
1972-3	258**
1973-4	22
1974-5	9
1975-6	28
1976-7	55
1977-8	4
1980-1	1
1982-3	1
1984-5	4
1985-6	2
1987-8	0

\*Student population varied between 2800 and 3200.

\*\*Number of cases was so large, no attempt was made to confirm diagnosis in all cases.

Table 6

Laboratory Results on Confirmed Cases of Parainfluenza I

<u>Name</u>	<u>Age</u>	<u>Onset</u>	<u>CF Para I</u>	<u>Culture - Confirmed by FA</u>	
<u>Students</u>					
1. Moran	18	10/27	<8/32	-	
2. Hetz	20	10/28	<8/16	-	
3. Hrycyszyn	18	11/2	<8/16	+	
4. Morton	21	11/2	<8/16	-	
5. Cohen	18	11/12		+	TW only
6. Copeland	18	11/12	<8/ 8	+	
7. Fox	18	11/12	<8/32	+	
8. Cannington	18	11/13	8/32	+	
9. Dyer	18	11/13	<8/16	+	
10. Gore	18	11/13	<8/32	+	
11. Natto	18	11/23	<8/32	-	
12. Monday	22	11/24	<8/16	+	
13. Kinney	20	11/27	<8/16	-	
14. Sons	19	11/30	<8/16	+	
15. Atavich	19	12/3	<8/16	+	
16. Farinas	19	12/18	8/32	+	
17. Copeland	20	1/14	<8/32	-	
18. Hook	18	1/14	<8/32	-	
19. O'Hare	20	2/8	8/32	-	
<u>Permanent Party</u>					
1. Speight	25	11/2	<8/16	-	
2. Matthews	25	11/24	8/32	+	

Table 7

Vaccine response of 25 Lackland AFB recruits to 1986-87 influenza vaccine containing 15 ug A/Mississippi/85. in tests with current and projected vaccine strains.

<u>Antigen</u>	Cumulative % with titer of:									% $\geq$ 4 fold rises
	<8	8	16	32	64	128	256	512	1024	
<b>A/Mississippi/85</b>										
Pre	40	60	44	28	16	16	8	-	-	
Post	-	100	100	100	100	92	88	72	40	96%
<b>A/Leningrad/86</b>										
Pre	60	40	16	8	-	-	-	-	-	
Post	-	100	84	84	72	36	24	16	8	80%
<b>A/Sichuan/87</b>										
Pre	88	12	-	-	-	-	-	-	-	
Post	12	88	76	56	32	8	-	-	-	72%

Table 8

Group A Beta Hemolytic Streptococcal Infections  
 Number of Positive Cultures

<u>Month</u>	<u>Students</u>	<u>Permanent Party</u>
October	5	1
November	13	6
December	3	3
January	8	1
February	1	4
March	2	1
April	1	4
May	4	2
Total	<u>37/2800</u> 1.3%	<u>22/5200</u> 0.4%

Table 9

Etiology of Febrile URIs - 1987-88				
Number of Cases				
	Student	Permanent Party	Combined	%
Influenza A	0	10	10	2.8
Influenza B	0	3	3	0.8
Parainfluenza I	19	2	21	5.9
Strep. Pharyng.	37	22	59	16.7
Adenovirus	0	0	0	0
Chlamydia TWAR	0	0	0	0
Unknown	<u>121</u>	<u>139</u>	<u>260</u>	73.4
	177	176	353	