An Outbreak of Influenza B at an Indiana Boarding School: Estimate of Vaccine Efficacy

FRANK DeSTEFANO, MD

AN OUTBREAK OF INFLUENZA-LIKE illness occurred in February 1980 at a private boarding school for boys in grades 5–12. The school is in a rural community in northeastern Indiana. From January 24 to 27, the school was closed for semester break, and most of the boys went to their homes throughout the Midwest and other parts of the country. Shortly after the beginning of the winter term, a large number of cadets began reporting to the infirmary with an influenza-like illness. This apparent outbreak of influenza surprised the school physician because most of the boys had received influenza vaccine in the fall. He therefore notified the Indiana State Board of Health, whose staff asked the Immunization Division at the Centers for Disease Control to assist in investigating the outbreak.

For the past several years the school has been vaccinating cadets against influenza in the fall of each year. All students are vaccinated unless their parents request otherwise (a few cadets are vaccinated by their personal physicians). In the fall of 1979 most of the boys had received influenza vaccine (1979–80 formulation, subvirion vaccine in 0.5 ml dosages).

This outbreak provided an opportunity for investigators to study the epidemiology of influenza in a highly vaccinated, healthy, young population and to obtain an estimate of influenza vaccine efficacy.

Tearsheet requests to Frank DeStefano, MD, Family Planning Evaluation Division, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Ga. 30333. At the time of this investigation, Dr. DeStefano was with the Immunization Division of the Centers for Disease Control. Laboratory analyses were performed by the World Health Organization Collaborating Center for Influenza, Centers for Disease Control.

Methods

Questionnaire survey. All the cadets eat at the same time in the school cafeteria. At dinner on February 21, all were asked to complete a questionnaire on influenza-like illness. The investigators, as well as some of the school staff, were present at that time to answer questions and help the boys complete the questionnaires. Ten cadets who were in the infirmary when the questionnaire was administered were interviewed individually the next morning.

Review of infirmary records. We reviewed the infirmary records to obtain the following information:

- the infirmary census for cadets with an upper respiratory infection

(URI) each day from September 1, 1979, to February 20, 1980,
- influenza vaccination histories on all cadets, and
- clinical characteristics of illness for all cadets admitted to the infirmary from January 8 (resumption of classes following the Christmas holidays) to February 21, 1980.

Laboratory specimens. On February 21, combined throat and nasopharyngeal swabs for influenza virus isolation were obtained from 10 cadets in the infirmary who had an influenza-like illness. (Most of those boys had had onset of symptoms more than 3 days before the specimens were collected.) Acute- and convalescent-phase serum specimens for influenza antibody titers were obtained from 24 cadets who had been admitted to the infirmary because of influenza-like illness. The virus isolation (*1*) and influenza antibody measurements (*2*) were performed at the World Health Organization Collaborating Center for Influenza, Centers for Disease Control, Atlanta.

Case definition. A case of influenza was defined according to available clinical descriptions of influenza B infection in the literature (*3*):

- onset on or after January 25, 1980 (1 day after the beginning of semester break),
- maximum temperature $\geq$ 100 F, and
- at least 1 of the following symptoms: cough, sore throat, coryza, chills, myalgia, or headache.

Cadets were assigned to the "non-influenza" category if they reported no symptoms or reported one or more symptoms with date(s) of onset, but their illness did not fit our case definition. An "unknown" category was also established for cadets who reported one or more symptoms but no date(s) of onset.

Results

Laboratory specimens. An influenza B virus was isolated from 1 of the 10 throat and nasopharyngeal specimens. This virus, designated B/Indiana/1/80, were cross-reactive to B/Singapore/79 and B/Buenos Aires/79 (table 1). The virus was less well inhibited than the vaccine reference strain by antiserums to B/Hong Kong/72. Of the 24 acute- and convalescent-phase serum specimens obtained, 5 showed a $\geq$ 4-fold rise in hemagglutination inhibition antibody titers to influenza B. It should be noted, however, that of the 24 acute-phase serum specimens obtained only 4 (16.7 percent) had a titer $\leq$ 10 to B/Hong Kong/72 and 15 (62.5 percent) had a titer $\geq$ 40. It is of interest that the boy from whom the influenza B virus was isolated was the only cadet with an acute-phase titer $<$ 10.

Review of infirmary records. After the semester break there was an increase in the infirmary census because of URI (see chart). In January a daily average of about 1 percent of the cadets were in the infirmary because of URI, whereas after the semester break the average increased to about 3 percent, with a peak of almost 7 percent from February 15–17. The number of new admissions to the infirmary because of URI, both febrile and nonfebrile, also increased after the semester break.

Questionnaire results. Questionnaires were completed and returned by 240 cadets (92 percent of enrollment). Table 2 lists the numbers of cadets according to illness and vaccination categories. Cadets who received only one of the recommended two doses of influenza vaccine and had no record of having received influenza vaccine in 1978 were assigned to a separate vaccination category even though one dose may have been adequate to protect against influenza B infection.

Epidemiologic characteristics of the outbreak. Analysis of cases by grade revealed that the 7th and 8th graders had the highest combined attack rate, 28 percent; the 11th and 12th graders had the lowest attack rate, 10 percent ($P < .05$ by χ^2). The proportion of cadets in each grade who had been vaccinated was not significantly different from the proportions in the other grades. The company-specific attack rate was highest for Com-

Number of students and percentage of school enrollment in infirmary because of upper respiratory infection, Indiana boarding school, January 8–February 20, 1980

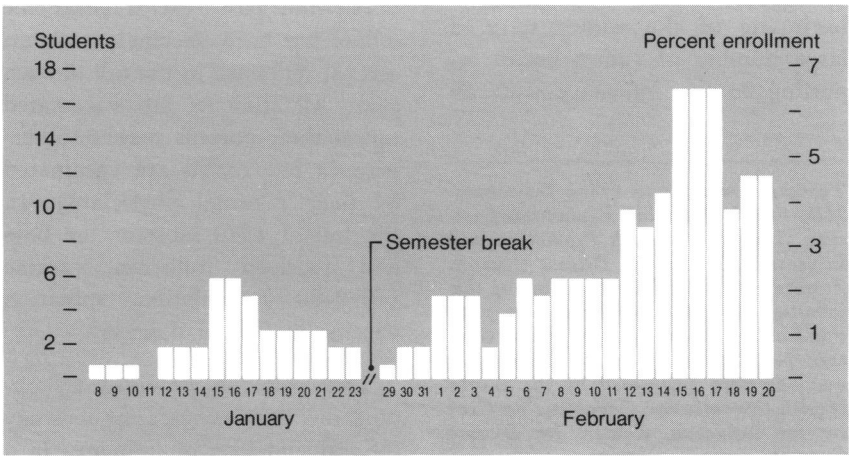

Table 1. Hemagglutination inhibition reactions of influenza B/Indiana/1/80 and other influenza B viruses representative of those circulating in 1979–80

Antigen	Ferret serums			
	B/Hong Kong/5/72	B/Singapore/222/79	B/Illinois/1/79	B/Buenos Aires/37/79
B/Hong Kong/5/72	*160*	320	240	15
B/Singapore/222/79[1]	40	*480*	320	40
B/Illinois/1/79[2]	10	160	*160*	10
B/Buenos Aires/37/79[3]	10	40	40	160
B/Indiana/1/80	40	160	40	160

[1] Variant showing asymmetric antigenic drift from B/Hong Kong/5/72.
[2] Reaction pattern consistent with low avidity variant of B/Singapore/222/79.
[3] Variant showing reciprocal antigenic drift from B/Hong Kong/5/72.

Table 2. Number of students surveyed at Indiana boarding school, by category and influenza vaccination status, January–February 1980

Category	Fully vaccinated	Not vaccinated	One dose of vaccine	Vaccine status unknown
Influenza	21	9	2	0
Noninfluenza	124	14	5	3
Unknown	46	7	5	4
Percent influenza[1]	14	39	29	0

[1] Excludes unknown group.

Table 3. Frequency (percentage) of symptoms in students by illness category, Indiana boarding school, January–February 1980

Symptom	Influenza (N = 32)	Noninfluenza (N = 146)
Cough[1]	91	38
Sore throat[1]	84	30
Runny nose[1]	84	38
Feverish feeling[1]	69	16
Headache[1]	63	28
Chills[1]	44	14
Nausea[2]	41	17
Muscle aches[3]	38	16
Sore, red, or watery eyes[1]	34	8
Abdominal pain[3]	34	16
Diarrhea[3]	25	10
Vomiting[3]	22	7

[1] $P < .001$ by χ^2.
[2] $P < .01$ by χ^2.
[3] $P < .05$ by χ^2.

pany F (23 percent), which included cadets in grades 5–8, but statistically this was not significantly different from the attack rates for any of the 3 other companies (with cadets in grades 9–12), which ranged from 7 to 19 percent.

Table 3 compares the frequency of symptoms by category—influenza and "noninfluenza" (illness not meeting case definition; onset of symptoms, if any, between January 25 and February 21, 1980). Even in the noninfluenza group, after the semester break, 53 percent of the cadets reported onset of at least 1 of the 12 symptoms listed on the questionnaire. Overall, 62 percent of the cadets reported having at least 1 symptom during that time. Cadets who had influenza were absent from school more days than those whose illness was not considered influenza (mean numbers of days were 4.6 and 1.7, respectively).

Vaccine efficacy. When cadets in the "unknown" illness category were excluded, the attack rate (AR) for influenza-like illness was 14 percent for the fully vaccinated cadets and 39 percent for the unvaccinated cadets. The vaccine efficacy ((AR for unvaccinated−AR for vaccinated)÷AR for unvaccinated) was thus 63 percent, with 95 percent confidence limits of 13 to 82 percent. If all the unknowns were assumed to have an influenza illness, the vaccine efficacy would be 40 percent. If all the unknowns were assumed not to have an influenza illness, the vaccine efficacy would be 63 percent.

Discussion

The influenza vaccine for 1979–80 contained 3 antigens: A/Brazil/78 (H1N1), A/Texas/77 (H3N2), and B/Hong Kong/72 (*4*). Influenza activity in the United States began in about early December in 1979: the midwestern States reported some of the most extensive activity during the winter. Most of the viruses isolated were influenza B (*5*). These influenza B viruses showed some antigenic heterogeneity and in general were inhibited less well than the 1972 reference strain by antiserums to the prototype B/Hong Kong/5/72 virus (*6*).

The virus isolated at the military school was also inhibited less well by antiserums to the B/Hong Kong/5/72 virus, but the vaccine did provide a degree of protection that compares favorably with some previous estimates of influenza B vac-

cine efficacy (*7–10*). Indirect evidence for the effectiveness of vaccination at the military school is provided by a comparison with past outbreaks of influenza B infections in unvaccinated populations for which attack rates of 41 to 94 percent were reported for persons 10 to 20 years of age (*7,11,12*). At the military school 86 percent of the boys had been vaccinated, and the overall attack rate was 18 percent. This rate is more than 50 percent lower than attack rates reported for unvaccinated populations and provides support for the estimate of vaccine efficacy of 63 percent.

Thus, although the vaccine was not completely effective, the number of influenza cases that actually occurred at the military school probably was less than half the number that would have occurred if influenza vaccine had not been administered.

References

1. Dowdle, W. A., Kendal, A. P., and Noble, G. R.: Influenza viruses. *In* Diagnostic procedures for viral, rickettsial and chlamydial infections, edited by E. H. Lennette and N. J. Schmidt. American Public Health Association, Washington, D.C., 1979, pp. 585–609.
2. Hierholzer, J. C., and Suggs, M. T.: Standardized viral hemagglutination and hemagglutination-inhibition titer, I & II. Appl Microbiol 18: 816–833 (1969).
3. Douglas, R. G.: Influenza in man. *In* The influenza viruses and influenza, edited by E. D. Kilbourne. Academic Press, New York, 1976, pp. 397–447.
4. Centers for Disease Control: Influenza vaccine. Morbidity Mortality Weekly Rep 28: 231–232, 237–239 (1979).
5. Centers for Disease Control: Influenza—United States. Morbidity Mortality Weekly Rep 28: 602, 620 (1979) and 29: 37–38, 71–72, 83–84, 108, 119–120, 131, 142 (1980).
6. Centers for Disease Control: Antigenic analysis of influenza B viruses. Morbidity Mortality Weekly Rep 29: 57–58 (1980).
7. Clark, P. S., et al.: An influenza B epidemic within a remote Alaska community. JAMA 214: 509–512 (1970).
8. Hall, W. N.: Influenza B and vaccine efficacy in a nursing home [abstract]. *In* Epidemic Intelligence Service 29th annual conference program. Centers for Disease Control, Atlanta, 1980.
9. Brown, P., Gajdusek, D. C., Chen, K. M., and Morris, J. A.: Antigenic response to influenza virus in man. Am J Epidemiol 90: 336–343 (1969).
10. Hoskins, T. W., Davis, J. R., and Smith, A. J.: Influenza at Christ's Hospital: March 1974: Lancet 1: 105–108 (1976).
11. Retallieau, H. F., et al.: The epidemiology of influenza B in a rural setting in 1977. Am J Epidemiol 109: 639–649 (1979).
12. Chin, T. D. Y., et al.: Epidemiologic studies of type B influenza in 1961–62. Am J Public Health 53: 1068–1074 (1963).

SYNOPSIS

DESTEFANO, FRANK (Centers for Disease Control): *An outbreak of influenza B at an Indiana boarding school: estimate of vaccine efficacy. Public Health Reports, Vol. 97, May–June 1982, pp. 269–272.*

During the influenza season of 1979–80, influenza B accounted for most cases of influenza in the United States. The midwestern States experienced widespread influenza B activity beginning in mid-December. From late January to mid-February an outbreak of influenza-like illness occurred at a private boarding school for boys in northeastern Indiana. Most of these boys had been vaccinated against influenza. An influenza B virus was isolated in 1 instance, and 5 of the 24 boys from whom acute- and convalescent-phase serum specimens were obtained showed evidence of influenza B infection.

Through a questionnaire survey, it was determined that 18 percent of the boys had had an influenza-like illness; the attack rate was 39 percent for the unvaccinated and 14 percent for the fully vaccinated. The vaccine efficacy was thus estimated to be 63 percent. As was true of many of the influenza B viruses isolated in the 1979–80 influenza season, the virus isolated at the school demonstrated some variation from the B/Hong Kong/5/72 virus used in the vaccine.