Immunization Against Swine Influenza in the Yale University Community

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Nineteen percent of the approximately 30,000 members of the Yale community aged 18 through 59 received swine influenza monovalent vaccine (A/New Jersey/1976) during the three days of a mass immunization program in Nov. 1976. Based on 1508 card questionnaires received, 71.2 percent of the vaccine recipients experienced a sore arm, 23.4 percent headache, 13.4 percent chilliness, and 9.7 percent feverishness or fever. The sore arm was judged as severe in 5.9 percent as was the headache in 4.2 percent. Other reactions were regarded as severe in less than 2 percent. All reactions were reported more commonly by women than men and all decreased with age.

Serologic tests carried out at the start of the immunization period revealed that influenza A/New Jersey/1976 antibody was absent from 78.6 percent of the recipients; almost all persons under 25 lacked this antibody. A significant antibody rise occurred in 78.3 percent of those receiving a single dose of monovalent vaccine. Somewhat better antibody responses occurred in 36–59 year olds than in those age 17–25 (84.9 vs 75.5 percent); the geometric mean antibody titer was also much higher (1:136.8 vs 1:31.2). However, the presence of pre-existing homologous antibody did not significantly improve the antibody response to the vaccine. Cross-reacting antibody rises to A/Victoria/1975 were found in 16.2 percent of the recipients of monovalent vaccine.

The isolation of an influenza strain in recruits at Fort Dix, New Jersey in January, 1976 [1] that bore surface markers similar to the great pandemic strain of 1918 was deemed of much importance for several reasons. First, the 1918 outbreak was one of the most severe affecting mankind with an estimated death toll of some 20 million persons worldwide and over 1/2 million in the United States [2]. The death rate was especially high in young adults. The morbidity from the disease was about 500 million cases—over 1/2 the world's population fell ill. While it was not possible to measure whether the New Jersey isolate would have the same pathogenicity and virulence as the 1918 strain, the identity of the specific hemagglutinin and neuraminidase suggested this potential. Second, while swine influenza virus has produced illness in pigs since 1918 with occasional sporadic human cases, the Fort Dix outbreak was the first recognized example of person-to-person spread, involving some 500 persons. Whether this was due to the acquisition of a new spreading potential, or simply represented the enhanced transmission of a strain of low virulence in the closed environment of recruit training was a highly important but unanswerable question. Third, there appeared to be sufficient time to prepare and administer a swine flu vaccine before the next winter season. On the advice of the
Influenza Advisory Committee to the Public Health Service the Director of the Center for Disease Control proposed that a nationwide program for all ages be instituted. The scientific, political, and financial bases for this decision and the problems encountered in its implementation are, and will continue to be, a matter of vigorous debate. (See Osborn, J., ed., Influenza in American 1918–1976, N.Y., Prodist, 1976, and the Nov.–Dec. 1977 issue of the Yale J. Biol. & Med.)

In response to this directive the members of the Yale University Health Plan and of the New Haven community were offered the swine flu vaccine in a mass immunization program. Information describing the vaccine and an informed consent card were given to each individual. The vaccine was administered over a 3 day period in the Yale Gymnasium using jet injection guns. Since data on the vaccine was limited to field trials carried out largely in young adults the current investigation was initiated to determine the acceptance rate, the reaction rate and the immunological response in a broad age group.

MATERIALS AND METHODS

The Population: The Yale University Health Plan offered the Swine Influenza Immunization Program to the entire Yale University Community of about 30,000 persons. The Yale Health Plan itself enrolls about 20,000 of these, including students, faculty, employees, and their families.

The Vaccine: A whole monovalent vaccine prepared by Merrell-National Laboratories containing 200 chicken cell agglutinating (CCA) units of the A / New Jersey 1976 strain of influenza vaccine was used in adults, ages 18–59. A bivalent vaccine also manufactured by Merrell-National Laboratories containing 200 CCA units of the same swine influenza strain and 200 CCA units of A2 / Victoria / 1975 strain was given to persons 60 years old and over and to high risk groups, such as persons with chronic cardiac or pulmonary diseases. The monovalent vaccine was given by jet gun in the Yale University Gymnasium and the bivalent by needle and syringe. A single 0.5 ml dose of each was given subcutaneously in the arm.

Questionnaire: A short anonymous questionnaire was prepared on a postcard to be returned by Campus (free) mail which requested information on the occurrence and severity of reactions within 48 hours of receiving the influenza vaccine. The reactions itemized were fever (feverishness), headache, chilliness, muscle aches, and sore arm. A space was left to record other reactions. The age and sex of the respondent was requested. The cards were distributed randomly to 2,000 persons.

Serological studies: An initial serum sample was obtained on the day of immunization from 387 volunteers of all ages (16–70). A follow-up sample was successfully obtained 3 to 4 weeks later from 269 of the same persons (71.5 percent): 222 of these had received monovalent and 47 bivalent vaccine. The hemagglutination-inhibition titers to A / New Jersey / 1976, A2 / Victoria / 1975, and B / Hong Kong / 1972 were measured on microtiter plates after treatment of the serum with receptor destroying enzyme. The methods employed were those recommended by the Center for Disease Control. The diluents were added and the dilutions were made using automated equipment (Cooke Engineering Co.). Positive and negative controls were included in each test. All questionable results were repeated. The geometric mean antibody titer was based on sera with a titer of 1:10 or higher.

RESULTS

Vaccine Acceptance

The immunization program was offered on November 10, 11 and 12th, 1976 in the
Payne-Whitney Gymnasium of Yale University to some 30,000 persons in the Yale community. Special risk, pediatric, and athletic groups were immunized separately during November in the outpatient clinic of the Yale Health Service. In all, 5674 doses of monovalent and 1763 of bivalent vaccine were given. The 7437 persons receiving vaccine represents 25 percent of the Yale community. Based on the age distribution of persons enrolled in the Yale Health Plan, about 19 percent were immunized with monovalent vaccine in the 18 through 59 age group during the 3 day period.

Reactions to Vaccine

Seventy-seven percent (1540) of 2,000 questionnaire cards distributed were returned. An analysis was made of 1508 of these on which the appropriate items had been filled out; this represented 757 females and 751 males. The overall reactions are tabulated by sex in Table 1. Seventy-one percent of recipients reported soreness of the arm at the site of the jet injection of monovalent vaccine but only 5.9 percent classified this as severe. Sore arms were reported by 81 percent of females and 57.2 percent of males. Headache and muscle aches were recorded with about equal frequency in both sexes (22 to 24 percent), but were rarely judged as severe. Chilliness was reported by 8.9 percent of males and 17.9 percent of females; less than 2 percent of either sex felt it was severe. The occurrence of fever or feverishness was noted on 9.7 percent of the cards, 6.8 percent by males, and 11.0 percent by females; only 0.2 percent felt it was more than of slight degree. Other symptoms mentioned as present included fatigue in 5.1 percent, nausea in 3.1 percent, and itching in 1.1 percent (Table 2).

Analysis of the questionnaire results by age and sex is given in Fig. 1. In general, all reactions decreased with increasing age and all were more common in females than in

| Reaction      | Percent Reporting Reaction | Male | Total |
|---------------|-----------------------------|------|-------|
|               | Female                      |      |       |
| Fever         | Slight (<100°F)             | 9.8  | 6.0   | 7.9  |
|               | Moderate (100-100.9°F)      | 0.8  | 0.8   | 1.6  |
|               | Severe (103°F)              | 0.4  | 0     | 0.2  |
|               |                             | 11.0 | 6.8   | 9.7  |
| Headache      | Moderate                    | 21.4 | 16.9  | 19.2 |
|               | Severe                      | 4.2  | 0     | 4.2  |
|               |                             | 25.6 | 16.9  | 23.4 |
| Chilliness    | Moderate                    | 16.1 | 8.1   | 12.1 |
|               | Severe                      | 1.8  | 0.8   | 1.3  |
|               |                             | 17.9 | 8.9   | 13.4 |
| Muscle Aches  | Moderate                    | 25.3 | 16.4  | 20.8 |
|               | Severe                      | 2.8  | 0.7   | 1.8  |
|               |                             | 28.1 | 17.1  | 22.6 |
| Sore Arm      | Moderate                    | 70.6 | 55.9  | 65.3 |
|               | Severe                      | 10.4 | 1.3   | 5.9  |
|               |                             | 81.0 | 57.2  | 71.2 |
TABLE 2
Other Symptoms Mentioned

| Symptom    | Number | % of Total |
|------------|--------|------------|
| Fatigue    |        |            |
| F          | 44     | 5.8        |
| M          | 33     | 4.4        |
|            | 77     | 5.1        |
| Nausea     |        |            |
| F          | 35     | 4.6        |
| M          | 11     | 1.5        |
|            | 46     | 3.1        |
| Itching    |        |            |
| F          | 9      | 1.2        |
| M          | 8      | 1.1        |
|            | 17     | 1.1        |

# Female 55 187 184 83 63 40 38 50 47 10 757
# Male 64 196 181 91 45 42 31 39 46 16 751

FIG. 1a,b. Frequency of fever (upper panel) and headache (lower panel) according to age and sex.
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**CHILLINESS**

**MUSCLE ACHES**

FIG. 1c,d. Frequency of chilliness (upper panel) and muscle aches (lower panel) by age and sex.

males at any age. The decrease with increasing age was most marked for the symptoms of sore arm (Fig. 1e) and muscle aches (Fig. 1d). However, males in the 15–19 age group complained less commonly of sore arm and of muscle aches than males in the 20–24 bracket; this was not observed in females. An interesting and unexplained phenomenon was the occurrence of a sharp peak in the complaint of headaches starting in 30–34 year old females which increased from 20 percent to 40 percent at age 40–44 (Fig. 1b). Since the questionnaire cards were returned anonymously, it was not possible to correlate the occurrence of the reactions with the presence or absence of pre-existing antibody to swine influenza. However, the overall results for antibody tests given in the next section is consistent with the view that vaccine reactions were less common in persons with pre-existing antibody.

The occurrence of one or more reactions in the same person was analyzed by sex and is shown in Table 3. The percent of females reporting one or more reactions was consistently higher than in males and increased with the number of reactions. For
example, 26.6 percent of females reported 3 or more reactions vs. 16.4 percent in males and twice as many females as males reported 5 or more reactions.

**Pre-existing Antibody**

Hemagglutinin-inhibition (HI) antibody to A/New Jersey/1976, A/Victoria/1975 and B/Hong Kong/1972 antigens was measured in the sera of 271 persons on the day that swine influenza vaccine was administered to determine pre-existing antibody titers.

The percent of sera lacking antibody to various antigens at the lowest dilution tested (1:10) is shown by age groups in Table 4. Antibody to the A/NJ/76 swine flu antigen was absent in 99.1 percent of persons tested under age 25 (mostly age 18–25) but gradually appeared with increasing age so that 55 percent lacked antibody age 36–59 and none of the 9 sera age 60 or over lacked antibody. In the 18 through 59 target age group for the swine flu vaccine 84.3 percent lacked antibody to this virus. Antibody to the A/Victoria/75 strain was absent in 56 percent of the 271 sera tested, more often so in the older age groups. Antibody to the B/Hong Kong/72 virus was absent in 57.6 percent of the total group and about equally in age groups up through 59.

**Humoral Antibody Responses**

Paired sera taken at the time of immunization and 3–4 weeks later from 222

![Graph showing frequency of sore arm by age and sex.](image)

**FIG. 1e.** Frequency of sore arm by age and sex.
TABLE 4
Percent Lacking HI Antibody at ≤1:10 to A/New Jersey/76, A/Vict/75, and B/Hong Kong/72 Influenza Antigens in Pre-Immunization Sera

| Age   | Sex | No. Tested | A/NJ/76 % | A/Vict/75 % | B/HK/72 % |
|-------|-----|------------|-----------|-------------|-----------|
| 18-25 | F   | 46         | 100       | 32.6        | 63.0      |
|       | M   | 70         | 98.5      | 45.7        | 52.8      |
|       |     | 116        | 99.1      | 40.5        | 56.9      |
| 26-35 | F   | 44         | 95.4      | 68.1        | 63.6      |
|       | M   | 33         | 78.8      | 63.6        | 54.5      |
|       |     | 77         | 88.3      | 66.2        | 59.7      |
| 36-59 | F   | 39         | 64.1      | 74.3        | 51.3      |
|       | M   | 30         | 43.3      | 66.6        | 56.7      |
|       |     | 69         | 55.0      | 71.0        | 53.6      |
| ≥60   | F   | 5          | 0         | 40          | 60.0      |
|       | M   | 4          | 0         | 75          | 100       |
|       |     | 9          | 0         | 77.7        | 77.7      |
| Totals| F   | 134        | 84.3      | 56.7        | 59.7      |
|       | M   | 137        | 78.8      | 55.4        | 55.4      |
|       |     | 271        | 78.6      | 56.0        | 57.6      |

persons receiving monovalent A/New Jersey/1976 vaccine and from 47 persons receiving bivalent (A/New Jersey/1976 and A/Victoria/1975, containing 200 CCA units of each vaccine) vaccine were tested simultaneously for antibody responses by the HI test. Table 5 gives the detailed results: 78.3 percent of persons receiving monovalent swine flu vaccine showed a four-fold or greater rise in antibody titer to the vaccine strain. The response rate increased with age, rising from 75 percent in the 18–25 age group to 85 percent in the 36–59 year old group. No significant difference in antibody responses was seen between 190 persons without pre-existing swine flu antibody and 32 persons with pre-existing antibody. Four-fold or greater rises to A/Victoria/1975 antigen were found in 16.3 percent of persons receiving only monovalent A2/NJ/1976 vaccine virus, presumably due to antigenic cross-reactions. Sera from 2 persons showed a rise to B/Hong Kong/1972 antigen, possibly representing early examples of the B/Hong Kong outbreak which followed shortly thereafter. The response to the bivalent vaccine in the 47 persons tested was poor: only 51 percent showed a significant rise to A/New Jersey/1976 antigen and 25.5 percent to A/Victoria/1975 antigen both of which were present in the vaccine.

An analysis of responses to monovalent vaccine by sex and prior antibody status is presented in Table 6. No consistent differences in response rate to the vaccine virus were seen in the presence or absence of pre-existing antibody. However, 21 percent of males showed a rise to A/Victoria/1975 antigen which was not included in the vaccine as compared with only 7.8 percent of the females; the greater response rate in males was higher whether pre-existing antibody to A/Victoria/75 was present or not. Males may have received an A/Victoria vaccine while in military service and this response may represent a cross reaction "booster" effect.

An analysis of vaccine responses by geometric mean antibody titer (GMT) pre and post immunization is summarized in Table 7. The results paralleled those measured
TABLE 5
Percent Showing Four-fold or Greater Antibody Responses to Monovalent and Bivalent Vaccine According to Pre-Vaccine Antibody Status against the Test Antigen

| Vaccine               | Pre-Vaccine Titer* | Age  | No. with four-fold rise | A/New Jersey/1976 | A/Victoria/1975 |
|-----------------------|--------------------|------|-------------------------|-------------------|------------------|
| Monovalent (A/NJ/76)  |                    |      |                         |                   |                  |
| 18-25                 |                    | <10  | 103                     | 74.7              | 38               |
|                       |                    | ≥10  | 104                     | 75.0              | 66               |
| 26-35                 |                    | <10  | 56                      | 80.3              | 41               |
|                       |                    | ≥10  | 9                       | 66.6              | 24               |
| 36-59                 |                    | <10  | 31                      | 90.3              | 41               |
|                       |                    | ≥10  | 22                      | 77.2              | 12               |
| 65                    |                    |      | 65                      | 78.5              | 65               |
| Total                 | <10                |      | 190                     | 78.9              | 120              |
|                       | ≥10                |      | 222                     | 78.3              | 222              |
| Bivalent (A/NJ/76 + A/Vict/75) |                | <10  | 30                      | 56.6              | 22               |
| 16-35                 |                    | ≥10  | 8                       | 50.0              | 16               |
| >60                   |                    | <10  | 0                       | 0                 | 6                |
|                       |                    | ≥10  | 9                       | 33.3              | 3                |
| Total                 | <10                |      | 30                      | 56.6              | 28               |
|                       | ≥10                |      | 17                      | 41.1              | 19               |

*To test antigen

TABLE 6
H.I. Antibody Responses to Monovalent A/NJ/76 Vaccine by Sex

| Vaccine Given | Sex | Pre-existing Antibody* | No. Tested | Percent with Four-fold Response |        | A/NJ/76 | A/Vict/75 |
|---------------|-----|------------------------|------------|---------------------------------|--------|---------|-----------|
| Mono-Valent   | F   | <10                    | 91         | 79.1                            | 8.9    |
|               |     | ≥10                    | 12         | 83.3                            | 6.3    |
|               |     |                        | 103        | 79.6                            | 7.8    |
| M             |     | <10                    | 99         | 78.7                            | 26.5   |
|               |     | ≥10                    | 20         | 70.0                            | 14.5   |
|               |     |                        | 119        | 77.2                            | 21.0   |

*To the antigen used in the test
TABLE 7
Geometric Mean Antibody Titer (GMT) Before and After A/NJ/76 Vaccine

| Vaccine      | Age       | No. | State | A/NJ  | A/Vict.| B/HK |
|--------------|-----------|-----|-------|-------|--------|------|
| Monovalent   | 18-25     | 103 | Pre   | 5.0   | 10.5   | 8.3  |
|              |           |     | Post  | 31.2  | 18.0   | 9.3  |
|              | 26-35     | 65  | Pre   | 5.6   | 7.2    | 8.3  |
|              |           |     | Post  | 50.6  | 10.5   | 9.8  |
|              | 35-59     | 53  | Pre   | 8.5   | 6.2    | 7.2  |
|              |           |     | Post  | 136.8 | 8.3    | 8.4  |
| Bivalent     | ≥60       | 9   | Pre   | 45.6  | 7.9    | 5.8  |
|              |           |     | Post  | 100.8 | 15.9   | 8.5  |
| High Risk**  | 38        |     | Pre   | 6.7   | 7.3    | 6.4  |
|              |           |     | Post  | 31.6  | 14.4   | 7.1  |

*For the purposes of calculation of the GMT a titer of 1:5 was assigned to sera with a titer <1:10.
**High risk included persons with chronic pulmonary, cardiac, and metabolic disease.

by four-fold antibody increases: the highest post-immunization titers were attained in the older age group. In the ≤25 year old age group receiving monovalent vaccine the average GMT never reached the 1:40 titer above which re-infection is rare [3]. Cross-reacting antibody increases to A/Vict/72 antigen occurred with increasing age. The GMT response to A2/New Jersey/1976 was satisfactory in 9 persons over 60 receiving it but poor in 38 special risk persons under age 60. A poor response in both age groups was also seen to the A2/Victoria/1975 antigen contained in the bivalent vaccine. Little increase in GMT to B/Hong Kong occurred after monovalent or bivalent vaccine since it was not included in either preparation.

The percent of persons attaining the presumably protective titer of ≥1:40 post-vaccination varied with age (Table 8). The ≥1:40 titer was achieved in 51.9 percent of

TABLE 8
Percent at ≥1:40 H.I. Titer for A/NJ/76 Pre and Post Monovalent or Bivalent Vaccine

| Vaccine      | Age Group | Vaccine Status | No. Tested | Percent at ≥1:40 to A/NJ/76 |
|--------------|-----------|----------------|------------|----------------------------|
| Monovalent   | 18-25     | Pre            | 104        | 0                          |
|              |           | Post           | 104        | 51.9                       |
|              | 26-35     | Pre            | 65         | 0                          |
|              |           | Post           | 65         | 63.1                       |
|              | 36-59     | Pre            | 53         | 7.5                        |
|              |           | Post           | 53         | 90.6                       |
| Total        |           | Pre            | 222        | 1.8                        |
|              |           | Post           | 222        | 64.4                       |
| Bivalent     | 16-59     | Pre            | 38         | 5.2                        |
|              |           | Post           | 38         | 44.7                       |
|              | 60+       | Pre            | 9          | 66.6                       |
|              |           | Post           | 9          | 100.0                      |
| Total        |           | Pre            | 47         | 17.0                       |
|              |           | Post           | 47         | 55.3                       |
the 25 age group, in 63.1 percent of the 26–35 year old age group, and in 90.6 percent of the 36–59 year old age group after one injection of A/NJ/76 monovalent vaccine. Overall 64.4 percent of the titers were at this level or higher. A poor response was seen in the 38 persons in the high risk group, age 16–59, that received bivalent vaccine—only 44.7 percent reached a level of 1:40.

DISCUSSION

Approximately 19 percent of the 30,000 persons age 15 to 60 in the Yale community, received monovalent A/New Jersey/1976 vaccine by jet injection on the 3 days of the mass immunization program; an additional 1674 doses of bivalent vaccine were given to high risk groups. Influenza assessment data from the National Influenza Center at CDC indicate that by Feb. 2, 1977, 56.52 percent of persons 18 years and over in Connecticut had been immunized, much above the national average of 31.63 percent [4]. The reason for the lower response rate in the Yale community is not clear. Some persons may have received vaccine after the mass campaign was over or through other health services. While one might anticipate a higher level of health consciousness in a University community, skepticism as to the possibility of an outbreak or as to the effectiveness of the vaccine may also be higher in a University community than the average Connecticut community.

The reaction rates to the monovalent vaccine were much higher than the 2–5 percent level expected on the basis of field trial data [5–8]. Complaints of a sore arm at the site of the jet injection occurred in 71.2 percent of the recipients and 5.9 percent judged the reaction as severe. Headache was complained of in 23.4 percent of the total group, muscle aches in 22.6 percent, chilliness in 13.4 percent, and fever or feverishness in 9.7 percent; these reactions were judged as severe in less than 2 percent except for headache which was reported as severe in 4.2 percent. The frequency, severity, and duration of the reactions to the swine flu vaccine were probably not of sufficient magnitude to deter future use of a similar vaccine should a clear-cut need exist.

All reactions to A/NJ/76 vaccine were reported more commonly by women of all ages than by men. Whether this difference had a biologic basis, such as smaller subject size in relation to dose, or represented a greater subjective perception of discomfort is not known. Certainly the higher frequency of sore arms in women could well reflect a smaller muscle mass.

A decreasing rate of side reactions to the vaccine occurred with increasing age and was observed in both sexes. The presence of pre-existing antibody to the vaccine virus may account for a lower reaction rate, but since the reporting card was submitted anonymously it was not possible to correlate the frequency of side reactions with the presence or absence of antibody. However, it is consistent with the overall age distribution of pre-existing antibody.

Antibody tests on 213 sera obtained at the time of immunization from the 18–59 age group indicated that 78.6 percent lacked A/New Jersey/1976 antibody at a titer of 1:10 or higher, 56.0 percent lacked A/Victoria/1975 antibody, and 57.6 percent lacked B/Hong Kong/1972 antibody. The percent of swine influenza susceptibles varied markedly with age. Antibody was absent in 99.1 percent of the 18–25 year olds, in 88.3 percent of those aged 26–35, and in 55 percent of those 36–59 years old. These figures are generally comparable to those summarized by Hattwick et al. [5] from five community surveys around the country (1961–1976) although the 55 percent susceptibility rate in persons over 30 was greater than in other studies.
The overall antibody response to a single dose of monovalent A/New Jersey/1976 vaccine (Merrell-National, Cincinnati, Ohio) containing 200 CCA units per dose was fairly good: 78.9 percent of the recipients showed a four-fold or greater antibody titer rise to the homologous antigen 3–4 weeks later, the geometric mean antibody titer rose from 1:5.9 to 1:53.1; 64.4 percent of those vaccinated had levels of 1:40 or higher post immunization. Antibody rises occurred more commonly in those age 36–59 (84.9 percent) than in those in the ≤25 age group (75.5 percent). The geometric mean antibody titer after immunization was also much higher in the older (1:136.8) than the younger (1:31.2) group. Despite this, the antibody response rate was similar in 32 persons with pre-existing A/New Jersey/1976 antibody (75.0 percent) as compared with 190 persons lacking this antibody (78.9 percent). While the antigen was not included in the vaccine, antibody rises to A/Victoria/1975 occurred in 16.3 percent recipients of the monovalent A/NJ/76 vaccine presumably as a result of cross-reactions. Only 2 persons showed an antibody increase to B/Hong Kong/1972 antigen which was not included in the vaccine; these 2 may have been early victims of a B/HK outbreak which followed later.

These antibody response rates to the 200 CCA units of Merrell-National monovalent vaccine confirm the results of preliminary field trials [6] although our response rate (75.0 percent) was higher than theirs (49 percent) in persons under 25 years old. As no swine influenza epidemic occurred it was not possible to judge the effectiveness of the vaccine against a natural challenge. However, if an outbreak of swine influenza had occurred late in the fall of 1976 it would have found only 20 percent of the Yale community immunized in the mass campaign. In the 18–25 age group who lacked swine influenza antibody prior to immunization only 52 percent developed a protective level of HI antibody >1:40 from immunization. A booster dose would certainly have been required in this group in the face of an epidemic. In the 26–35 age group the percent with antibody titers at 1:40 or higher rose from none pre-immunization to 63 percent post-immunization; a booster dose might also have been desirable in the face of a large epidemic. In the 35–59 year old age group the pre-immunization antibody prevalence at ≥ 1:40 was 7.5 percent and post-immunization was 90.6 percent. Booster doses would not have been needed in this group. Clearly a virulent influenza strain like that of 1918 could have produced a disastrous epidemic in a population with so many susceptibles remaining in the younger age groups. If such an epidemic had actually occurred it is likely that the mass immunization campaign would have been vigorously pursued and expanded despite the problems of high reaction rates, poor antibody response in the younger age group, and the rare occurrence of the Guillain-Barré syndrome [9].

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