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SHORT COMMUNICATION

PROPHYLACTIC EFFECT OF INFLUENZA SUBUNIT (HA) VACCINE
IN EPIDEMIC YEAR 1972-1973

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In the epidemic year 1972-1973, influenza HA vaccine became officially available in Japan.

For several years, the Research Council on Influenza Vaccine (President: Dr. H. Fukumi, NIH of Japan) have carried out extensive tests on new types of influenza vaccines. They concluded that HA vaccine produces a satisfactory antibody response in man with few side reactions after vaccination (The 11th Congress on Influenza Vaccine, Tokyo, Dec. 12, 1972). Similar reports were presented by others (Ruben and Jackson, 1972). It has been reported that antibodies to purified influenza virus hemagglutinin can neutralize the virus (Schild, 1970).

The best way to evaluate the effectiveness of vaccination is to carry out field trials during epidemics. But, so far, insufficient information has been obtained in field trials on the effectiveness of HA vaccine (Eickhoff, 1971; Gill et al., 1971). During the epidemic year 1972-1973, an outbreak of influenza occurred in Osaka so that we had the opportunity to check the efficacy of vaccination with influenza HA vaccine on school-age children, who are the most susceptible to influenza (Stuart-Harris, 1970).

From January to February 1973, we isolated A type influenza viruses from 30 persons, and

found that all strains were Hong Kong type viruses. In an elementary school with 897 children in Matsubara City, Osaka, there was also an outbreak of influenza after the winter vacation (Dec. 25-Jan. 7) and three classes had to close for 3 to 5 days to reduce further dissemination of the disease. The disease was identified by isolating influenza virus from 3 school children and 3 persons in the families of these children and by serological procedures. The antigenic characteristics of the isolated viruses were determined by the hemagglutination-inhibition test using rabbit antisera and by the patients' convalescent sera (Tables 1 and 2).

The HA vaccine used during this epidemic year in Japan contained A/Fukuoka/1/70 (H3N2), A/Chiba/5/71 (H3N2) and B/Osaka/2/70, and the concentrations of the antigens were 150, 150 and 300 CCA equivalents/ml, respectively. The subunits were separated with ether. School children at the elementary school in Matsubara were immunized by two subcutaneous injections of 0.3 ml of HA vaccine (The Chemo-Sero-Therapeutic Research Institute, Kumamoto) on Nov. 11 and Nov. 21, respectively. The vaccination rate was as shown in Table 3. The proportions of vaccinated and unvaccinated children were

similar so that we could estimate the effect of immunization by comparison of the two groups.

We compared data on absence rates during January and February 1973 of the children who were vaccinated twice and not at all (Fig. 1). In this Figure, only absence due to symptoms, such as fever, headache, cough or general fatigue is scored. During this period there were also outbreaks of chickenpox and tonsilitis at the school, but absence due to the latter was not scored, although absence due to the common cold was.

TABLE 1. *Antigenicity of newly isolated influenza virus^a*

Virus	Rabbit antiserum	
	A/Aichi/2/68	A/Fukuoka/1/70
A/Aichi/2/68	2,048	1,024
A/Fukuoka/1/70	2,048	1,024
A/Chiba/5/71	1,024	256
A/Osaka/2/73	512	512

^a Chorioallantoic fluid of fertile eggs infected with virus was used as antigen. Rabbit antiserum was treated with RDE and heated at 56 C for 30 min. A/Osaka/2/73 was chosen as a representative of current strains in this table. The results of antigenic analyses of all newly isolated viruses were quite similar. Numbers indicate reciprocals of the highest dilutions causing inhibition of hemagglutination.

The peak of the epidemic of influenza at this school was between Jan. 19 and Jan. 27, and during this period the absence-rate of the non-vaccinated group was approximately twice that of the vaccinated group. The average durations of absence from school were 2.23, 2.04 and 1.71 days, respectively for the non-immunized, once immunized and twice immunized groups. This result is similar to that with inactivated whole virus vaccine (Nakamura and Okuno, 1966).

From these data it is concluded that, at the concentration of virus to which children were exposed in 1973, HA vaccine was effective in prevention of naturally occurring influenza. The date of immunization of the school children was adequate to prevent the disease in January in the sense of an antibody response. The most troublesome problem about influenza vaccine is the antigenic shift and drift

TABLE 3. *Proportion of vaccinated children^a*

	No. of children (%)
Not vaccinated	382 (43)
Vaccinated once	75 (8)
Vaccinated twice	440 (49)
Total	897 (100)

^a Vaccination was done by subcutaneous injection of 0.3 ml of vaccine.

TABLE 2. *HI antibody titers of patients' sera in acute and convalescent stage^a*

Patient	Onset of disease	Serum specimen on	A/Aichi/2/68	A/Fukuoka/1/70	A/Chiba/5/71	A/Osaka/2/73
M.K.	Jan. 15	Jan. 18	64	16	32	<16
		Feb. 1	1,024	1,024	2,048	2,048
Y.A.	Jan. 14	Jan. 18	32	16	<16	<16
		Feb. 1	2,048	1,024	1,024	2,048
K.T.	Jan. 14	Jan. 18	256	64	64	64
		Feb. 1	8,192	2,048	4,096	4,096

^a Sera from patients were treated with RDE and heated at 56 C for 30 min. A/Osaka/2/73 was isolated from M.K.

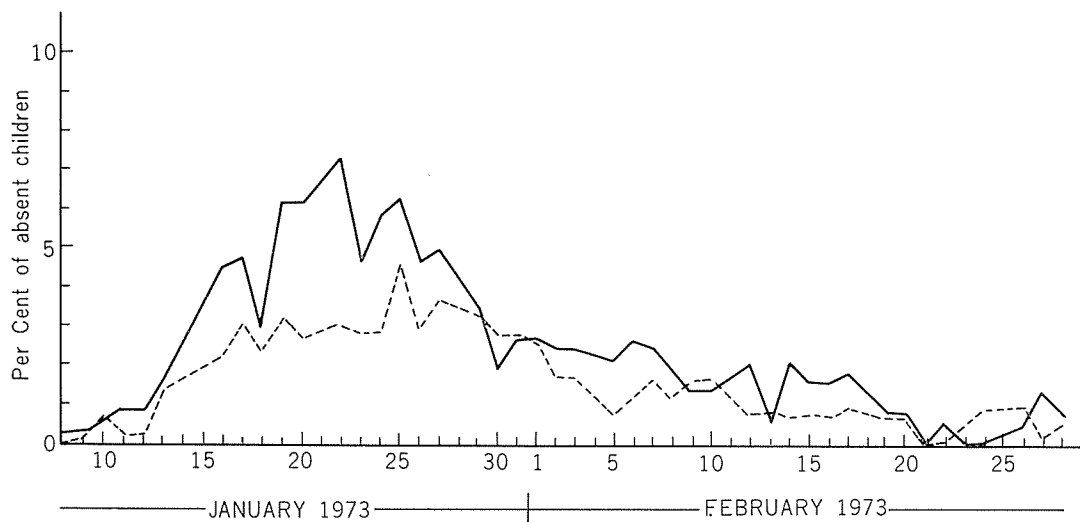


FIGURE 1. Percentages of children absent from school during January and February, 1973. Absence from school was checked daily. —, non-vaccinated group; ----, twice vaccinated group.

of A type viruses. The data in Table 1 show the antigenic relationship between vaccine strains and current strains. Although there is some difference in the antigenicities of these strains, there is also much similarity, judging from results of hemagglutination-inhibition tests.

Possible ways to improve the protective ef-

ficacy of the vaccine are: 1) extension of the period between the first and second immunization, 2) increase in the antigen concentration, since HA vaccine only causes slight side reactions, 3) an additional injection after the second immunization and 4) increase in the vaccination rate.

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