did have a significant HI antibody rise to A2/Hong Kong. These could not be used to determine the rate of influenza A disease because the HI test is useless in determining infection in the A vaccinees. Occasionally a child with a history of illness had CF antibody titre rises to both A and B antigens. Almost always a diagnosis of causal type could be made as one antigen showed much greater antibody response (usually against the antigen not in the vaccine received).

The tabulation above shows the efficacy of the 400-CCA-unit dose of B vaccine, calculated by the same method, to be 16%. The B vaccinees receiving the 100-CCA-unit dose had the same attack rate of B disease as the A vaccinees in the same schools, suggesting no protective effect by this measure.

These calculations of vaccine effectiveness are based on the assumptions that the CF tests for A and B had similar sensitivity and that the occasional vaccine-induced, low-titre CF responses were infrequently accompanied by spurious influenza-like illness. The latter occurrence would tend to decrease the calculated effectiveness of the vaccines. We do not believe that any great confidence can be placed in the exact percentage efficacy calculated for the vaccines from these relatively small numbers.

Conclusion

In the absence of adequate controls, it was not possible to determine the effect of influenza vaccine in schoolchildren or on disease in their families and communities. However, we do believe that this study showed that the influenza B vaccine employed produced unacceptable reactions in children and was less effective in preventing disease than the A2/Hong Kong-strain vaccine.

A Field Evaluation of Inactivated, Zonal-centrifuged Influenza Vaccines in Children in Chapel Hill, North Carolina, 1968–69 *

by W. Paul Glezen, Frank A. Loda & Floyd W. Denny

A field evaluation of inactivated, zonal-centrifuged influenza vaccines, administered parenterally to children, was performed in Chapel Hill, North Carolina, during the 1968–69 respiratory disease season. The objectives of the study were to test the acceptance, antigenicity and efficacy of a single dose of vaccine in children of different age-groups and to explore the feasibility of mass immunization of schoolchildren to provide an epidemiological barrier to the spread of influenza in the community. The only junior high school in Chapel Hill was chosen as the primary target for this effort because it included the age-group which usually has the highest morbidity rate during influenza epidemics (Table 1). Other populations included a small group of infants, a day-care nursery for 3–5-year-old children, the first grade at one elementary school, university students and adult teachers, and day-care nursery and laboratory personnel. Voluntary participation was invited with the understanding that influenza vaccines would be given under a double-blind system and that paired blood specimens would be obtained. The vaccines employed were monovalent vaccines to influenza viruses A2/Hong Kong/68 (800 CCA units/ml) and B/Massachusetts/66 (800 CCA units/ml) and a bivalent vaccine including influenza A2 and B strains (2400 CCA units/ml). Venous blood samples were obtained at the time the vaccines were administered (in mid-November) and approximately 21 days later. A third blood sample was obtained from the public-school children and university students early in March after natural infections with influenza virus A2/Hong Kong had ceased to occur. Respiratory disease surveillance was maintained for each group during the influenza A2/Hong Kong outbreak.

Febrile reactions to the vaccines were common in young children (Table 2) but were more frequent among children who received vaccines including the

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TABLE 1

AGE DISTRIBUTION OF PERSONS IN STUDY OF INACTIVATED, ZONAL-CENTRIFUGED INFLUENZA VACCINES, CHAPEL HILL, 1968–69

Age-group	No. of persons in each vaccine group			Total
	A2/Hong Kong/68	Other [a]	No vaccine	
Infants (<2 years)	12	11	39	62
Pre-school (3–5 years)	23	24	10	57
First grade (6 years)	26	27	60	113
Junior high school	486	178	576	1 240
College students	75	75	3	153
Adults	200	—	51	251
Total	822	315	739	1 876

[a] Monovalent B/Mass./66 or bivalent A2/Taiwan/64, A2/Japan/170/62 and B/Mass./66.

TABLE 2

FREQUENCY OF FEBRILE REACTIONS TO INACTIVATED, ZONAL-CENTRIFUGED INFLUENZA VACCINES, CHAPEL HILL, 1968–69

Age-group	Dose (ml)	Influenza vaccine type					
		A2/Hong Kong/68			Monovalent B or bivalent		
		No. reporting	Febrile		No. reporting	Febrile	
			No.	%		No.	%
Infants (<2 years)	0.2	10	3	30	9	7	78
First grade	0.5	24	2	8	22	12	54
Junior high school	0.5	384	17	4	123	6	5
Adults [a]	0.5	58	3	5	58	3	5

[a] Received injections of monovalent A2/Hong Kong/68 and bivalent influenza vaccines simultaneously.

influenza B antigen than among those who received the monovalent influenza A2/Hong Kong antigen. Reactions were not frequent in junior-high-school students and there was no difference between the 2 vaccines.

Haemagglutination-inhibition (HI) antibody titres to influenza A2/Hong Kong antigen were determined for all sera collected (Table 3). Only 3% of vaccine study subjects had HI antibody titres of 1 : 16 or greater before the vaccines were administered. Approximately 85% of persons who received the A2/Hong Kong vaccine developed a significant antibody response within 21 days and the median titre was 1 : 32. There was little difference in the antibody response among the different age-groups except for the first-grade students, who had a geometric mean titre of 1 : 87. It is suspected that some of these students encountered natural infection prior to the time that the second blood sample was obtained. Antibody responses to natural infections were considerably higher than those to the vaccine. In a group of 30 university students hospitalized with influenza virus infection, the geometric mean titre was 1 : 254.

Only 4% of 349 junior-high-school students who received the influenza A2/Hong Kong vaccine had

TABLE 3

HI ANTIBODY RESPONSE TO SINGLE DOSE OF INACTIVATED MONOVALENT VACCINE TO INFLUENZA VIRUS A2/Hong Kong/68, CHAPEL HILL, 1968–69

Population		Dose (ml)	Percentage with antibody response	Geometric mean titre
Age-group	No.			
Infants (<2 years)	8	0.2	100	1 : 23
Pre-school (3-5 years)	18	0.25	83	1 : 30
First grade	18	0.5	100	1 : 87
Junior high school	349	0.5	85	1 : 42
Young adults	75	0.5 [a]	83	1 : 27

[a] A small number received 1.0 ml or 0.75 ml.

an antibody response between the 2nd and 3rd serum samples, when influenza virus A2/Hong Kong was prevalent in the community. In contrast 27% (32 of 121) of students who received the bivalent vaccine had an antibody rise suggesting natural infection during the same interval.

Of the 1240 students in the junior high school, 40% received 1 injection of the monovalent vaccine to influenza virus A2/Hong Kong. To see whether immunization of this proportion of the school population would have any effect on total absenteeism during the period when influenza virus A2/Hong Kong was prevalent in the community, the daily rate of absence in the junior high school was compared with that for the senior high school (see accompanying figure). There was no difference in absence rates for the 2 schools. It should be noted that the daily rate for the junior high school never exceeded 10%, which is probably below the threshold for true epidemic occurrence of influenza.

The frequencies of febrile respiratory illnesses for each vaccine group in pre-school and school-aged children were very similar (Table 4). Questionnaires sent to the university students in the vaccine study revealed equal illness rates for the 2 vaccine groups. Influenza virus A2/Hong Kong was isolated from 20 schoolchildren who were ill during the epidemic but the isolations were equally distributed among the vaccine groups.

Other concurrent studies of influenza virus infections in children with lower respiratory tract illnesses showed interesting patterns (Table 5). A sharp outbreak of influenza B virus infections in March 1969 provided an opportunity to compare the clinical manifestations of influenza B infections with those produced by the A2/Hong Kong virus.

DAILY ABSENCE RATE FOR JUNIOR HIGH SCHOOL (40% VACCINATED) COMPARED WITH SENIOR HIGH SCHOOL DURING EPIDEMIC OF A2/HONG KONG INFLUENZA, CHAPEL HILL, 1968–69

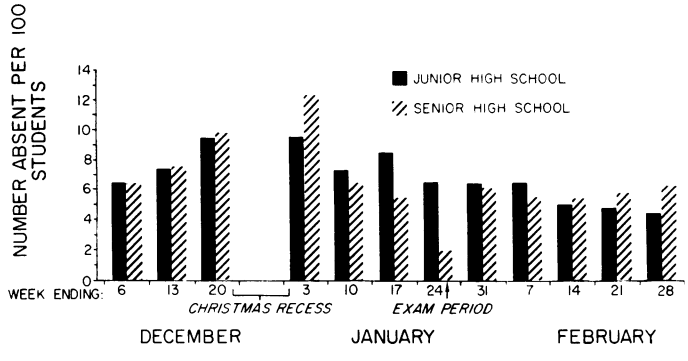

TABLE 4

FREQUENCY OF FEBRILE RESPIRATORY ILLNESSES AMONG CHILDREN IN INFLUENZA VACCINE STUDY, CHAPEL HILL, DECEMBER 1968–FEBRUARY 1969

Vaccine	No. of children	Children ill	
		No.	%
A2/Hong Kong/68	494	76	15
Other [a]	211	30	14
None	593	108	18

[a] Monovalent B/Mass./66 or bivalent.

TABLE 5

ASSOCIATION OF 2 INFLUENZA VIRUSES WITH LOWER RESPIRATORY TRACT ILLNESSES IN CHILDREN, CHAPEL HILL, 1968–69

Clinical diagnosis	No. of isolations	
	A2/Hong Kong/68	B
Croup	11	1
Tracheobronchitis	8	20
Bronchiolitis	4	0
Pneumonia	1	3
Total	24	24

TABLE 6

NUMBER OF ISOLATIONS OF 2 INFLUENZA VIRUSES FROM CHILDREN WITH LOWER RESPIRATORY TRACT ILLNESSES, CHAPEL HILL, 1968–69

Age (years)	A2/Hong Kong/68	B
<2	14	0
2–5	5	8
6–8	3	9
9–11	1	3
⩾12	1	4
Total	24	24

A large proportion of A2/Hong Kong infections were detected in children with croup while influenza B was seen almost solely in children with tracheobronchitis. The contrast is sharpened when the ages of these children are compared (Table 6). Over half of the influenza A2/Hong Kong isolates were from infants under 2 years of age while most of the influenza B infections occurred in school-aged children.

In summary, the zonal-centrifuged vaccines appeared safe and acceptable for children but there was little evidence in this study that 1 injection of the recommended dose for age provided sufficient antigen stimulus for protection.

Immunoglobulins in External Secretions

by HOWARD C. GOODMAN [a]

The presence of antibodies in stools (copro-antibodies) reported in the early 1920s led to a series of investigations of antibodies associated with mucous membranes (reviewed by Pierce [b]). The present renewed interest in these antibodies as a specialized system of defence for mucous surfaces dates from the observations in 1962 by Tomasi and his co-workers that IgA is the predominant immunoglobulin in secretions of the parotid and salivary glands and in colostrum, tears, bile, and gastrointestinal secretions. Others demonstrated IgA in nasal secretions and tracheobronchial washings and subsequently there has been a series of investigations of the immunoglobulins in nasal secretions and of the antibody activities associated with them. " Secretory " IgA is an 11S molecule which is a dimer plus an additional polypeptide chain (" secretory component "). Tomasi & Bienen-

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