Protection against Hong Kong Influenza by Adjuvant Vaccine containing A2/Ann Arbor/67

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An unique opportunity occurred in November 1968 to observe the effect of Hong Kong influenza on a student population at Lowry Air Force Base, Denver, Colorado; the personnel there had very recently been immunized with experimental mineral-oil adjuvant vaccines containing A2/Ann Arbor/67 as the A2 antigen. It will be seen from the following tabulation of the composition of these vaccines that both the bivalent and the polyvalent preparations contained 100 CCA units of A2/Ann Arbor/67:

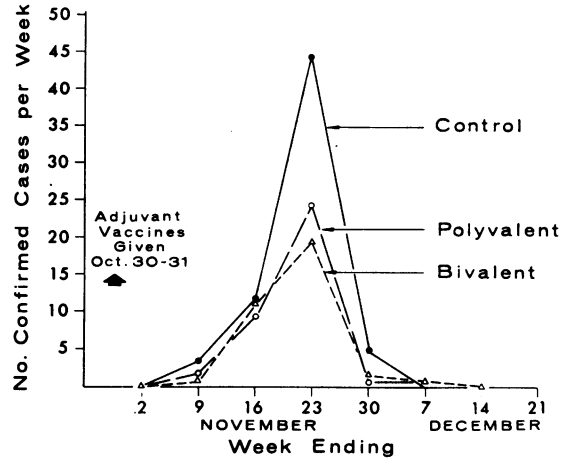
Preparation	*CCA units*
Bivalent vaccine	
A2/AA/67	100
B/Mass./66	100
Polyvalent vaccine	
A2/AA/67	100
A/Swine/31	100
A/PR/8/34	50
B/Lee/40	50
B/Mass./66	50
Control: saline	

These vaccines and a saline control were administered to groups of approximately 1200 students each on 30 and 31 October 1968.

As shown in the accompanying figure, confirmed cases of Hong Kong influenza began to occur within a week after administration of the vaccines, reaching a peak 3 weeks later. Since a vaccine effect, if present, might be reasonably expected not to become apparent until approximately 2 weeks after vaccine administration, only cases that occurred after 16 November were considered in evaluating vaccine effect. From the figure, it is apparent that the number of confirmed cases of Hong Kong influenza was greater in the control population than in either vaccine group.

A summary of the haemagglutination-inhibition (HI) antibody response to the A2/Ann Arbor/67 antigen, as determined on sera drawn before and 6 weeks after vaccination, is shown in the upper part of Table 1. Note that an excellent response was

EPIDEMIC CURVES OF CONFIRMED CASES OF INFLUENZA AMONG ADJUVANT VACCINE STUDY GROUPS, LOWRY AIR FORCE BASE, 1968



obtained. Over 90% of students immunized demonstrated a 4-fold or greater HI antibody response. Mean titre rises in the 2 vaccine groups were 7.7-fold and 10.8-fold.

The lower part of Table 1 shows the HI antibody responses to the A2/Hong Kong/68 antigen, carried out on the same pre- and post-vaccine sera. The proportion of students showing a 4-fold or greater HI antibody response to the A2/Hong Kong/68 antigen was remarkably uniform in all 3 groups, approximately 41%. Note, however, that over half the students in the control population showed no response at all, and only a small proportion showed 2-fold or 4-fold titre rises. The majority of those who responded at all responded with 8-fold or greater titre rises. In contrast, a larger proportion of students who received the bivalent or polyvalent vaccines showed minimal titre rises of 2-fold to 4-fold. This suggests that the majority of students with infection responded with an 8-fold or greater titre rise, and the increased proportion of 2-fold and 4-fold titre rises noted in the vaccine groups may therefore represent in part a vaccine response, rather than a response to illness.

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TABLE 1

SUMMARY OF HI ANTIBODY RESPONSE TO A2/Ann Arbor/67 AND A2/Hong Kong/68 6 WEEKS AFTER VACCINATION

Vaccine	Percentage of men with indicated titre rise					Percentage with ⩾4-fold rise	Mean [a] rise (x-fold)
	Nil	2-fold	4-fold	8-fold	⩾16-fold		
				A2/Ann Arbor/68			
B	2.6	6.6	21.1	40.8	28.9	90.8	7.7
Polyvalent	1.3	1.3	8.9	30.4	58.2	97.5	10.8
Control	60.3	17.9	10.3	6.4	5.1	21.8	3.9
				A2/Hong Kong/68			
B	35.5	23.7	11.8	10.5	18.4	40.8	5.2
Polyvalent	29.1	29.1	19.0	10.1	12.7	41.8	4.3
Control	52.6	6.4	2.6	20.5	17.9	41.0	8.3

[a] Of men who had any titre rise.

TABLE 2

ANALYSIS OF CONFIRMED CASES OF INFLUENZA IN THE ADJUVANT VACCINE STUDY POPULATION, NOVEMBER–DECEMBER 1968

	Vaccine group		
	Bivalent	Polyvalent	Control
No. of men	1 197	1 151	1 231
Seen in dispensary with febrile respiratory disease, Nov.–Dec. 1968	46 (3.8%)	53 (4.6%)	80 (6.5%)
No. of men with ⩾ 4-fold HI or CF rise to A2/Hong Kong/68	35 (2.9%)	36 (3.1%)	64 (5.2%)
Before 16 Nov.	13 (1.1%)	10 (0.9%)	15 (1.2%)
After 16 Nov.	22 (1.8%)	26 (2.2%)	49 (4.0%)
Reduction in seropositives after 16 Nov.	54%	43%	–

An analysis of the illness experience in the 3 study groups is shown in Table 2. A remarkably small proportion of students in the control group, 6.5%, were seen in the base dispensary with febrile respiratory disease during November and December 1968. This figure is all the more remarkable in view of the 41% seroconversion rate in the control group. An even smaller proportion of students in the bivalent and polyvalent vaccine groups, 3.8% and 4.6% respectively, came to the dispensary with febrile respiratory disease during the same period. Confining further analysis to students with serological confirmation of Hong Kong influenza with onset after 16 November, 4.0% of students in the control group were found to have Hong Kong influenza, as compared with 1.8% and 2.2% of students who received bivalent and polyvalent vaccines, respectively. Based on a ratio of observed to expected numbers of cases, the rate of confirmed Hong Kong influenza was reduced 54% in the group that received bivalent vaccine and 43% in those who received polyvalent vaccine.

Because of the remarkably small numbers of men who reported to the dispensary with febrile respiratory disease during the epidemic period, these results must be interpreted with caution. The data do suggest, however, that the mineral-oil adjuvant vaccines containing 100 CCA units of A2/Ann Arbor/67 antigen conferred definite, albeit modest, protection against illness caused by the Hong Kong variant.