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COMMUNICATIONS

Lack of Adjuvant Effect of $AlPO_4$ on Purified Influenza Virus Hemagglutinins in Man

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It has been shown that adsorption of influenza virus hemagglutinins on $AlPO_4$ enhances their antigenic potency in mice (1). This finding prompted the question whether $AlPO_4$ would serve as an adjuvant and increase the hemagglutination-inhibition (HI) antibody response of man to hemagglutinin (HA) vaccine. Polyvalent HA vaccine was prepared commerically and the antibody response of military recruits to adsorbed and unadsorbed preparations was ascertained. No enhancement of antigenicity by $AlPO_4$ was observed.

MATERIALS AND METHODS

Viruses. The strains used for production of vaccine were distributed by the Division of Biologic Standards, National Institutes of Health. Those employed for measuring antibody were from the files of the Virus Laboratory, Ann Arbor, Michigan.

Vaccines. Polyvalent purified HA concentrates were prepared as previously described (2). These were blended to yield a hemagglutinin vaccine containing 200 chick cell agglutination (CCA) units of A_2/Taiwan/4/64, 100 CCA units each of A_1/AA/1/57 and A_0/PR/8/34, and 300 CCA units of B/Maryland/1/59 per ml. Formalin and Merthiolate were added to yield final concentrations of 1:4000 and 1:10,000, respectively. The adsorbed vaccine contained the same concentration of hemagglutinins and 3.8 mg $AlPO_4$/ml.

Subjects, vaccination and bleeding schedule. Recruits coming on active duty at the Great Lakes Naval Training Center, Great Lakes, Illinois volunteered for the study. They were given 1 ml of either vaccine subcutaneously and bled just before and 2 weeks after vaccination. Forty-eight paired specimens were obtained from men who were given adsorbed vaccine and 47 from those who received unadsorbed vaccine.

HI antibody titration. A standard pattern method using 0.5% chicken erythrocytes was employed (3). The sera were heated at 56°C for 30 min prior to use, except when tested against the A_2 strain, in which case trypsin and KIO_4 were employed for inactivation.

RESULTS AND DISCUSSION

The results are summarized in Table I. The geometric mean prevaccination antibody titers of the two groups as measured with each antigen were remarkably similar, indicating successful randomization of members in each group with respect to their prior antigenic experince. Hence, the postvaccination antibody titers can be used as a valid index of the antigenic potency of the two preparations under test. The frequencies of antibody increase and the antibody levels achieved after administration of unadsorbed or adsorbed vaccine indicated that both preparations were antigenically potent. The minor differences in response to the two vaccines are not considered to be significant in studies involving multiple comparisons with groups of this size. The findings demonstrate that $AlPO_4$ fails to exert an adjuvant effect on HA vaccines given to adult human subjects.

The divergent effects of $AlPO_4$ on antibody response to HA vaccines observed in mice and men are unexplained. In the two studies, different

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TABLE I

HI antibody response to unadsorbed and to $AlPO_4$ adsorbed polyvalent influenza hemagglutinin vaccine

Vaccine	Serum Specimen	A/PR/8/34		A_1/AA/1/57		A_2/Taiwan/4/64		B/Md/1/59	
		Geo. mean titer[a]	S. D.	Geo. mean titer	S. D.	Geo. mean titer	S. D.	Geo. mean titer	S. D.
HA unadsorbed	Prevac.	3.6	1.98	5.7	1.03	3.8	2.18	7.0	1.34
	Postvac.	7.3	1.63	8.8	1.03	8.5	1.43	9.1	1.01
		47/47[b]		47/47		46/47		40/47	
HA with $AlPO_4$	Prevac.	3.3	2.16	5.0	1.62	3.7	1.81	6.6	1.22
	Postvac.	7.1	1.70	8.2	1.67	8.7	1.29	9.5	1.28
		48/48		47/48		48/48		44/48	

[a] Expressed as log to the base 2.

[b] Proportion showing twofold rise or greater.

doses of vaccine of different composition were given by different routes to subjects of different species. Moreover, the human subjects were conditioned by prior infection to undergo a "booster" response to either vaccine. Systematic studies of the effect of the variables mentioned have been initiated.

It is not yet known whether $AlPO_4$ will function as an adjuvant for HA vaccines given to antigenically inexperienced infants or young children. However, the present findings do not justify the use of a mineral carrier in HA vaccines intended for general application.

SUMMARY

$AlPO_4$ failed to enhance the antigenicity of purified influenza hemagglutinin vaccines given to adult human subjects.

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