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Antigenicity of Adenovirus Type 4 Soluble Antigens in Man

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Adult volunteers immunized with soluble antigens derived from adenovirus type 1 suspensions had markedly fewer responses to infectious virus challenge than did control subjects (Kasel et al., Proc. Soc. Exptl. Biol. Med. **117**:186, 1964). A study was therefore undertaken to determine the antigenic potency in man of a preparation containing soluble antigens of type 4 virus. This communication describes the antibody responses of 13 antibody-negative (<1:4) adult male volunteers to adenovirus type 4 soluble antigens as measured by serum-neutralization tests.

A preparation containing both the type-specific and group-specific soluble antigens was employed in this study; these antigens respectively correspond to the C and A (E and L) antigens described by Klemperer and Pereira (Virology **9**:536, 1959) and Wilcox and Ginsberg (Proc. Natl. Acad. Sci. U.S. **47**:512, 1959). A nonprototype strain of type 4 virus (received through the courtesy of Robert Chanock, National Institutes of Health, Bethesda, Md.) was employed to prepare stock virus suspensions. The material used to obtain soluble antigens was the 19th and 20th WI-38 passage harvest fluids. Procedures for the preparation, assay, and safety-testing of the soluble antigens were similar to those previously described by Wilcox and Ginsberg and by Kasel et al., except that the fraction containing the bulk of both antigens was rechromatographed a single time. Extensive tissue culture tests indicated the absence of infectious type 4 adenovirus and adventitious agents. The final preparation had less than 100 μg of protein per ml, and had complement-fixing antigen titers of 1:64 (group-specific) and 1:16 (type-specific). Volunteer selection, clinical procedures, and laboratory methodology were as described by Kasel et al. Volunteers were given intramuscular injections of the antigen preparation on days 1 and 7; five received a total of 3 ml, and the others, 2 ml.

There was no local reaction to immunization, and there were no changes in tests of hematologic, renal, or hepatic function. Virus isolation studies of throat and rectal specimens, obtained twice weekly for 1 month, were all negative for infectious virus.

The distribution of neutralizing-antibody titers with sera obtained from volunteers 28 days after the first administration of the antigen preparation is shown in Table 1. Eleven of 13 individuals (83%) became seropositive. It should be noted that the postimmunization antibody titers in those individuals who developed neutralizing antibody compared favorably to antibody titers achieved in volunteers fed infectious adenovirus type 4 by enteric-coated capsules (Couch et al., Am. Rev. Respirat. Diseases Part 2 **88**:394, 1963).

TABLE 1. *Distribution of neutralizing-antibody titers in antibody-negative volunteers 28 days after immunization with an adenovirus type 4 soluble-antigen preparation*

No. of volunteers	No. of volunteers with indicated titer of neutralizing antibody				
	<4	4	8	16	≥32
13	2	4	4	1	2*

* Titers in these individuals were ≥1:256 and ≥1:8,192.

These results reveal the capacity of soluble antigens of type 4 adenovirus to induce neutralizing antibody in adult volunteers. It is also possible that preparations with increased protein (antigen) concentration may increase the rate and degree of seroconversion.