THE HUMAN ANTIBODY RESPONSE TO SIMULTANEOUS INJECTION OF SIX SPECIFIC POLYSACCHARIDES OF PNEUMOCOCCUS*

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(Received for publication, June 16, 1948)

Previous quantitative studies of the antibody content of the sera of human beings injected with immunizing (1) doses of the specific polysaccharides of pneumococcus have dealt with analyses of sera after injection of two or three (reference 2) and four (reference 3) specific polysaccharides at one time. Since it was feasible for practical purposes to combine into a single solution as many as six polysaccharides of the pneumococcal types most commonly responsible for pneumococcal pneumonias in man, exact knowledge of the antibody response to the injection of so many chemically similar antigens appeared desirable. Data obtained with two different combinations of six polysaccharides are given in the present report.

EXPERIMENTAL

Medical student volunteers, after a preliminary bleeding (subscript 0), were injected subcutaneously with 1 ml. of a solution containing about 0.07 mg. each of six type-specific polysaccharides of pneumococcus. Subjects 201 to 206 received the specific polysaccharides of Types I, II, III, V, VII, VIII pneumococcus, these being the types most common in pneumococcal pneumonia of adults, while Nos. 207 to 212 received Types I, IV, VI, XIV, XVIII, XIX, the types most common in the pneumococcal pneumonias of children. Both antigen solutions were prepared by E. R. Squibb and Sons. Subject J, a woman 63 years of age, received the first solution. Nine months after its injection, sample J_1 was taken, when the antibodies formed were probably no longer at peak levels (2). From the other subjects a bleeding (subscript 1) was taken 6 weeks to 2 months after the injections. Analyses on sera 202_1 and 210_1 could not be completed owing to accidental contamination, and additional samples 202_2 and 210_2 were procured 9.5 and 5.5 months after injection, respectively.

Analyses were carried out according to the method mentioned in reference 4 and described in detail in reference 2. Precautions against bacterial contamination were taken owing to the large number of successive analyses required and the long standing necessary for each analysis. Superscripts after values for antibody nitrogen indicate an unusually large number of absorptions for complete removal of the antibody in question.

* The work reported in this communication was carried out in part under the Harkness Research Fund of the Presbyterian Hospital and was also supported through the Commission on Acute Respiratory Diseases, Army Epidemiological Board, Office of The Surgeon General, United States Army.

DISCUSSION

The analytical values for the type-specific antibody content of the sera of human beings injected subcutaneously with a mixture of six type-specific polysaccharides of pneumococcus resemble those obtained in earlier quantitative micro-

TABLE I

Micrograms Antibody Nitrogen Per 4 Ml. Pre- and Post-Immunization Sera of Subjects Injected with Specific Polysaccharides of Pneumococcus Types I, II, III, V, VII, and VIII, 0.05 to 0.1 Mg. Each

Antibody to	C III	C VI	S I	S II	S III	S V	S VII	S VIII	S XIV
201_0	19	17	0	5	10*, 15	0	0	4, 3	3
201_1		53	31	64	29	21	49[4]	7	
202_0	27	21	0	3	4*, 4	0	0	0, 0	0
202_1		35			(14)‡		15[4]	6	
202_2		40	3, 3	21	1*, 11	0, 0	0	4, 1	
203_0	39	30	0	1	4*, 3	0	1	0, 0	11
203_1		52	33	33	21	107	36[4]	39[8]	
204_0	20	14	0	0	0*, 0	0	0	0, 0	0
204_1		16	3	6	2	4	11[3]	18	
205_0	46		0	0	1*	0	3	6	
205_1		62	15	21	11	1	30[3]	8	
206_0	32		0	0	0*	0	2	3	
206_1		28	8	18	5	0	7[3]	1	
J_0	23		0	0	4*	0	0	0	
J_1	16	15	13	10, 6	12*, 16	0, 8	<31	17	

C III = C-substance derived from Type III pneumococcus, C VI, from Type VI; S I, S II, etc., refer to type-specific polysaccharides.

* After removal of anti-C with C-substance derived from Type III and possibly containing traces of S III.

‡ Last analysis before contamination noted.

analytical studies of the sera of subjects injected with two or three or four of the antigens at a time (2, 3). The total antibody response and the production of antibody to each antigen injected appeared to be as satisfactory as in the subjects treated with smaller numbers of polysaccharides. Variability of response and unequal reactivity of an individual to all of the type-specific polysaccharides in the mixture were encountered as frequently as in the previous series.

In marked contrast to the behavior of the groups previously studied, roughly

one-half of the subjects showed increases in the anti-C content of their sera after the injections. Since almost all of the specific polysaccharides contain C-substance as impurity, it is possible that the intensity of the antigenic stimulus for production of additional amounts of anti-C increases with the number of polysaccharides used, and, hence, the probably greater quantity of C-substance injected. Whether or not all of this or only a portion is antigenic in man is not known.

TABLE II

Micrograms Antibody Nitrogen Per 4 ml. Sera of Subjects Injected with Specific Polysaccharides of Pneumococcus Types I, IV, VI, XIV, XVIII, and XIX, 0.05 to 0.1 Mg. Each

Antibody to.....	C	S I	S III*	S IV	S VI	S XIV	S XVIII	S XIX
207_0	27	0	0	0	0	0	3	0
207_1	26	54		9	2	47	9	6
208_0	6	0	0	0	0	0	5	0
208_1	55[5]	24		16[4]	4	0	52	0
209_0	31	0	0	2	1	4	5	1
209_1	89	24		48[4]	18	56	11	15[3]
210_0	87	0	11	0	0	7	16	0
210_1	158	50		23				
210_2	199	26		21	58[5]	23	35	44[4]
211_0	29	0	1	0	0	4	0	0
211_1	32	5		5	1	9	5	0
212_0	56	4	3	1	1	6	2	0
212_1	57	19		5	8	70	9	14

* S III was not in the mixture injected. Additional data on normals were sought.

Attention is also directed to the relatively large proportion of the subjects whose pre-immunization sera contained measurable quantities of antibodies which precipitate with the specific polysaccharides of Types XIV and XVIII pneumococcus.

SUMMARY

1. The antibody response in human beings after the injection of six type-specific polysaccharides of pneumococcus appears to be roughly of the same magnitude for each type as after the injection of fewer antigens.

2. A larger proportion of increases in anti-C was noted in the present series.

3. Many of the pre-immunization sera tested contained antibodies reactive. with the specific polysaccharides of Types XIV and XVIII pneumococcus.

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