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Relation Between Skin Reactions to Specific Carbohydrate Type I Pneumococcus and Human Blood Groups.

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Tillett and Francis¹ demonstrated the occurrence of a wheal and erythema reaction to the intradermal injection of minute amounts of the homologous type-specific pneumococcus polysaccharide in patients recovering from pneumococcus pneumonia. Subsequent studies by a number of investigators² have, in general, confirmed their findings. These authors showed, furthermore, that positive skin tests of this sort were not restricted to cases immediately or even remotely convalescent from pneumonia, but that an appreciable number of supposedly perfectly healthy individuals also gave positive skin tests. Using the Type I carbohydrate the percentage of positive reactions in normal persons was variously reported from 11.6% to 71%. In our own experience prior to the present series positive tests had been encountered in about 70% of normal cases.³

Recently Witebsky, Neter, and Sobotka⁴ have shown the existence of a close immunological relationship between the Type I Pneumococcus acetyl polysaccharide of Avery and Goebel⁵ and the human blood group specific substance A. These authors pointed out, among other observations, that the iso-agglutination of human blood group A corpuscles could be inhibited by Type I Pneumococcus acetyl polysaccharide. They presented strong evidence by means of this method, and also by employing complement fixation and hemolysis inhibition tests, that the relationship was specifically associated with the acetyl polysaccharide and that it was lost in the deacetylated polysaccharide.

These observations upon the relationship between the blood group specific substance A and the Type I Pneumococcus acetyl polysaccharide led to the present attempt to establish a correlation between

¹ Tillett, W. S., and Francis, T., Jr., *J. Exp. Med.*, 1929, **50**, 687.

² Alston, J. M., Galbraith, G. R., and Stewart, D., *J. Path. and Bact.*, 1930, **33**, 845; Finland, M., and Sutliff, W. D., *J. Exp. Med.*, 1931, **54**, 637; Alston, J. M., and Lowdon, A. S. R., *Brit. J. Exp. Path.*, 1933, **14**, 1.

³ Unpublished data, Wagner, H. C.

⁴ Witebsky, E., Neter, E., and Sobotka, H., *J. Exp. Med.*, 1935, **61**, 703.

⁵ Avery, O. T., and Goebel, W. F., *J. Exp. Med.*, 1933, **58**, 731.

human blood groups and positive skin tests to the Type I acetyl polysaccharide in so-called normal, non-convalescent persons.

The usual method for intradermal tests was employed. In all cases these tests were done using Type I Pneumococcus acetyl polysaccharide,* the deacetylated form of the same preparation and a normal salt solution control. All readings were made in from 15 to 20 minutes from the time of injection, the presence of a wheal and erythema or erythema alone being interpreted as a positive test. The instances, however, in which erythema was encountered without wheal formation were very few. In a few instances the salt solution controls were positive; such cases have been excluded from the series.

Seventy-eight persons were tested, all but 2 were over 16 years of age. Fifty-six cases (71.8% of the entire group) gave positive tests to both forms of carbohydrate. Only 2 reacted to the acetyl polysaccharide but not to its deacetylated derivative. Of the total number reacting to the Type I carbohydrate 28 persons (48.3%) belonged to either blood groups O or B and, therefore, had blood group specific a-agglutinins in their serums; 46 persons (79.3%) belonged to either blood groups O or A and possessed blood group specific b-agglutinins. Twenty persons failed to give tests to either carbohydrate. Of these, 6 were in blood group O, 7 in group A, 4 in group B, and 3 in group AB.

It seems clear that in this series of studies there is no demonstrable relationship between positive intradermal tests to either the acetyl or deacetylated Type I Pneumococcus polysaccharide and the blood group of the individuals tested. Not only is this shown by the appearance of positive tests in cases of each blood group but also by their failure to appear in individuals in each group as well. That the 20 cases which gave negative tests did not do so because of some refractory state is evidenced by the fact that 14 of them were shown to be sensitive to other antigens commonly used for skin tests. The remaining 6 were not so tested. Furthermore, were there any such relationship, as the work of Witebsky suggests there might well be, a wider separation between the positive reactions to the 2 forms of carbohydrate might be expected, sensitivity resulting from pneumococcus infection being shown by positive reactions to both of the antigens and sensitivity due to the blood group specific a-antibodies being shown by positive reactions to the acetyl polysaccharide alone. Such separation was not encountered.

* The Type I Pneumococcus acetyl polysaccharide employed in these experiments was obtained through the courtesy of Dr. Thomas Francis, Jr., of the Hospital of the Rockefeller Institute for Medical Research.

TABLE I.
Analysis of Results on Basis of Blood Groups of 78 Individuals Studied for Skin Sensitivity to Type I Pneumococcus Polysaccharide.

Blood Group	O	A	B	AB	No. of	% of
Serum agglutinins present	a and b	b	a	o	cases	total cases
Positive skin tests to both acetyl and deacetylated polysaccharide	19	25	8	4	56	71.8
Positive skin tests to acetyl polysaccharide only	1	1	0	0	2	2.6
Negative skin tests to both acetyl and deacetylated polysaccharide	6	7	4	3	20	25.6
Distribution of cases among blood groups	26	33	12	7		
Cases having history of pneumonia at some time in the past	4	1	1	0	6	7.7

It is of considerable interest in regard to the mechanism of the positive reactions in question to note that out of repeated attempts to induce passive transfer of skin sensitivity to the Type I Pneumococcus carbohydrate with the serum from 40 of the positively reacting cases, by the Prausnitz-Küstner technique,⁶ only 2 sera were active. In both of these instances the individuals from whom the serum was obtained gave a history of having had pneumonia.

In conclusion it may be stated that in a series of 78 normal individuals tested no correlation could be established between the skin reactivity of these individuals to Type I Pneumococcus specific polysaccharide and their blood groups. It was further shown that sensitivity to the Type I polysaccharide occurring in individuals without previous known pneumococcus infection, could not be transferred passively to the skin of non-sensitive individuals.

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Presence of Antibody in Bile.*

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In the course of an investigation of various factors involved in gallstone formation, studies have been carried out on the presence of antibody in hepatic and gall-bladder bile, when demonstrable amounts of antibody were present in the serum.

⁶ Prausnitz, C., and Küstner, H., *Centralbl. f. Bakteriol.* (Orig.), 1921, **86**, 160.

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