

Response to Oral Bacterial Immunization Against Colds

H. C. ALLISBAUGH and L. C. MORGAN
Lilly Research Laboratories, Indianapolis

Introduction

The common cold with its complications is a serious menace to industries, communities, schools, and individuals. Considerable evidence has been advanced within recent years to indicate that a filterable virus is involved in the causation of the disease (1, 2, 3). Protection experiments with the virus have not yet proved practical. Probably only when the virus is associated with or followed by bacterial invasion is there produced that train of symptoms usually recognized as a common cold. For prophylactic procedures one is forced to rely upon the employment of bacterial antigens. Inasmuch as the severe symptoms are probably referable to bacterial invasion, such a course is logical.

A bacterial vaccine for prophylactic use against colds should be a very broad antigen which is capable of being conveniently administered throughout the cold season. Bailey and Shorb (4) placed considerable significance on cultures containing heterophile antigen in producing a non-type-specific immunity against pneumococci. They demonstrated this antigen in pneumococci and were able to protect rabbits against living Type I pneumococci by previously immunizing them with heterophile antigen obtained from sheep red blood cells. They likewise demonstrated the presence of heterophile antigen in organisms, other than pneumococci, that are associated with upper respiratory diseases.

Powell (5) has shown that the heterophile antibodies can readily be produced even when the antigen is administered by the oral route.

Rockwell, VanKirk, and Powell (6, 7) have reported success in prevention of colds with an antigen, administered orally, prepared from organisms associated with upper respiratory diseases and having a high heterophile antigen content. Their work has since been confirmed (8).

Experimental

a. Vaccine Preparation.—Strains of pneumococci, streptococci, *H. influenza* and *N. catarrhalis* were tested for heterophile antigen by immunizing rabbits with heat-killed suspensions and titrating the sera for presence of heterophile antibodies. Only those cultures of demonstrated high heterophile antigen content were selected for preparation of the vaccine employed in this study. Table I shows a typical test for heterophile antigen in the pneumococcus cultures. Only four of the nine strains tested contained sufficient heterophile antigen to be used in the vaccine.

TABLE I.—Test of Pneumococcus Cultures for Heterophile Antigen

Culture		Rabbit	Titer Before Immunization				Titer After Immunization						
			32	64	128	Control	32	62	128	256	512	1024	Control
Park I		198	+++	+	—	—	+++	+++	+++	+++	+++	+++	—
Parker II		178	+	—	—	—	++	+	—	—	—	—	—
Park III		177	+	—	—	—	+++	+	—	—	—	—	—
DR I		176	—	—	—	—	+++	+++	+++	+++	+++	+++	—
Boston I		173	++	+	—	—	+++	+++	+	—	—	—	—
Boston II		171	+	—	—	—	+++	+++	+++	+++	+++	+++	—
Strain V		168	—	—	—	—	+	—	—	—	—	—	—
Strain VIII		167	+	—	—	—	++	+	—	—	—	—	—
Cooper IV		165	—	—	—	—	+++	+++	+++	+++	+++	+++	—

The bacteria used in the vaccine were cultivated on suitable solid media, washed off with physiological saline, heat-killed, and tested for sterility by inoculation on media favorable to the growth of the particular organisms involved. After sedimenting the organisms by centrifugation, they were adsorbed on starch, dried, and filled into capsules. Each lot of filled capsules was tested on rabbits for ability to incite heterophile antibodies and on mice and guinea pigs for safety. Each capsule contained 25 billion pneumococci, 15 billion streptococci, and 5 billion each of *H. influenza* and *N. catarrhalis*.

b. Human Immunization.—This vaccine was administered to 129 individuals, and a group of 129 who were of similar age, working and living under similar conditions, were selected as controls. Treatment consisted of taking one capsule daily for seven days and one or two capsules weekly throughout the duration of the experiment. The capsules were administered with a glass of cold water at least 30 minutes before breakfast. Blood samples were taken from this group before the beginning of the treatment and again on the third to fifth day after the seventh capsule had been taken. The blood sera were tested for heterophile antibodies and streptococcus agglutinins.

c. Serological Study.—The results of the heterophile antibody titrations are given in Table II. Analysis of this table shows that 37.5% of

TABLE II.—Heterophile Antibody Titration on 112 Individuals

Before Immunization						
Titer	0 to 40	40	80	160	320	640
Individuals	42	32	20	7	9	2

After Immunization						
Titer	0 to 40	40	80	160	320	640
Individuals	12	15	29	35	15	6

this group had a titer of less than forty, and 16.1% had a titer of one hundred and sixty or above before treatment. After treatment 10.7% had a titer less than 40, and 50% had a titer of 160 or over.

Tables III and IV show the results of the streptococcus agglutinations. The tests shown in Table III were made using a mixture of two *Strepto-*

coccus viridans cultures as the antigen. Before immunization 90% of the group had a titer of less than 40, and 10% had a titer of 40; while after treatment 27.5% had a titer of less than 40, and 65% had a titer of 80 or more. The tests shown in Table IV were made using the three

TABLE III.—*Streptococcus* Agglutination on 40 Individuals Using Two Cultures of *Streptococcus Viridans*

Before Immunization					
Titer	0 to 40	40	80	160	320
Individuals	36	4	0	0	0

After Immunization					
Titer	0 to 40	40	80	160	320
Individuals	11	3	18	8	1

TABLE IV.—*Streptococcus* Agglutination Tests on 45 Individuals Using Each Type Separately (Hemolytic, Viridans, and Indifferent)

Before Immunization						
Titer	0 to 40	40	80	160	320	
Hemolytic	27	12	3	3	0	
Viridans	34	7	2	2	0	
Indifferent	23	15	4	3	0	

After Immunization						
Titer	0 to 40	40	80	160	320	640
Hemolytic	18	3	4	8	9	3
Viridans	6	5	18	11	5	0
Indifferent	3	2	6	6	13	15

types of streptococci separately. Before immunization the percentage of the group having a titer of 160 or over was 7.5% for hemolytic, 5.0% for viridans, and 7.5% for indifferent. After treatment the percentage having the same titer was 50% for hemolytic, 40% for viridans, and

85% for indifferent. The sera of all individuals in this group agglutinated some type of streptococci after treatment.

d. **Clinical Study.**—The control and experimental groups were observed for colds from November 10, 1935, until March 10, 1936. In evaluating the data obtained, it was necessary to divide the individuals into groups on the basis of the number of capsules they had taken since a considerable number failed to follow the treatment during the whole period. Table V shows that, although a large number of individuals failed to continue the treatment, the number of colds experienced by the

TABLE V.—Clinical Study
November 10, 1935 to March 10, 1936
129 patients—129 controls

Experimental Group				
Number of Capsules Taken	Patients	Colds	Days Duration	Colds per Person
1-10	35	32	507	.94
11-20	59	49	398	.83
21-30	17	13	63	.76
30 or more	18	5	90	.28
Totals	129	99	1058	.70

Control Group				
Patients	Colds	Days Duration	Colds per Person	Percent Reduction
35	41	444	1.17	19.6
59	62	671	1.14	27.2
17	24	248	1.41	46.1
18	22	166	1.22	77.7
129	148	1529	1.24	33.1

experimental groups was 33.1% less than that by the controls. The minimum reduction was 19.6% and the maximum 77.7%.

Summary

This paper presents additional evidence that a vaccine, prepared from bacteria associated with upper respiratory diseases and having a high heterophile antigen content, is of value in preventing colds. Such a vaccine, administered orally, causes a rapid increase in heterophile antibodies and also streptococcus agglutinins.

The results of the clinical study indicate that those individuals who rigidly followed the treatment according to directions were benefited more by the vaccine than those who were prone to be somewhat lax.

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