

Antigenicity of Typhoid Vaccine Prepared from Cultures Grown at 30° C

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We have had occasion to prepare typhoid vaccine from cultures grown at 30° C (lot B-5512A), and compare this with similar vaccine prepared from cultures grown at 37° C (lot B-5512B). The standard cultures used were Rawlings (No. 222) and Panama 58 (No. 228), and each lot of vaccine comprised 50 per cent of No. 222 and 50 per cent of No. 228. With the exception of use of 30° C incubation in the preparation of lot B-5512A, both vaccines were prepared as recommended for distribution for human use by the National Institute of Health.

Antigenicity of vaccines B-5512A and B-5512B was first tested by one dose immunization of rabbits (each animal receiving 2.5 billion organisms subcutaneously), and eight days later measuring the agglutinin titer of these rabbits. Table 1 shows the results of these tests conducted in the 55° C water bath. Stronger agglutinins were incited by vaccine prepared from cultures grown at 30° C than from cultures grown at 37° C.

These tests were then amplified to include the usual comparisons made in the 37° C water bath with serum from rabbits treated with National Institute of Health control vaccine. The results are shown in Table 2, and it appears that both experimental vaccines were fully equal in agglutinin production to the control vaccine, and both would have been deemed satisfactorily antigenic for human use (1). None of the rabbits used in these tests showed any agglutinins in a titer of 1-10 for either strain of typhoid bacilli before immunization.

Two groups of 20 mice each were then immunized with weekly subcutaneous doses of vaccines B-5512A and B-5512B; the first dose was 50 million, and second and third doses each were 100 million bacilli. This is equivalent to one-tenth of a human immunization. One week after the third dose of vaccine, subdivisions of these groups, along with a normal control group of mice, received decimal dilutions of pooled No. 222 and No. 228 living cultures in mucin as an immunity test (2). The results are shown in Table 3. It is observed that typhoid vaccine lot B-5512A prepared from cultures grown at 30° C produces definitely better active immunity against infection than regular typhoid vaccine lot B-5512B prepared from cultures grown at 37° C. For more exact end points of active immunity it is obvious that much larger groups of mice would be necessary.

Conclusions

The results of tests for agglutinin production in rabbits and active immunity in mice indicate that typhoid vaccine prepared from cultures grown at 30° C is better than similar vaccine prepared from cultures grown at 37° C in the regular way.

TABLE I.—Comparative Agglutination Tests of Sera of Rabbits Treated with Vaccine Prepared from Cultures Grown at 30° and 37° Centigrade Respectively

Vaccine Used	Resultant Rabbit Serum	Typhoid Agglutino- gen	Serum Dilutions					0			
			1-320	1-640	1-1280	1-2560	1-5120				
B-5512A (30° C)	6959	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	—	—	—
	6960	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	+	—	—
	6961	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	+	+	—
B-5512B (37° C)	6962	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	+	+	—
	6963	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	+	+	—
	6964	222	+	+	+	+	+	+	+	+	—
		228	+	+	+	+	+	+	+	+	—

Above readings made after incubation in 55° C. water bath one hour and standing overnight in icebox.

TABLE II.—Comparison of Agglutinin Production Using National Institute of Health Control Typhoid Vaccine as a Standard

Vaccine Used	Resultant Rabbit Serum	Typhoid Agglutino- gen	Serum Dilutions							
			1-20	1-40	1-80	1-160	1-320	0		
B-5512A (30° C)	6960	222	+	+	+	+	+	+	+	+
		228	+	+	+	+	+	+	+	+
		222	+	+	+	+	+	+	+	+
		228	+	+	+	+	+	+	+	+
6962	222	+	+	+	+	+	+	+	+	
	228	+	+	+	+	+	+	+	+	
B-5512B (37° C)	6963	222	+	+	+	+	+	+	+	+
		228	+	+	+	+	+	+	+	+
6964	222	+	+	+	+	+	+	+	+	
	228	+	+	+	+	+	+	+	+	
6265	222	+	+	+	+	+	+	+	+	
	228	+	+	+	+	+	+	+	+	
National Institute of Health	6266	222	+	+	+	+	+	+	+	+
		228	+	+	+	+	+	+	+	+
Lot 130	6267	222	+	+	+	+	+	+	+	+
		228	+	+	+	+	+	+	+	+

Above readings made after incubation in 37° C. water bath one hour and standing overnight in icebox. There was insufficient serum from rabbit 6959 shown in Table 1 to use in this test.

TABLE III.—Tests of Active Immunity of Typhoid Vaccines in Mice

Dose of pooled typhoid cultures 222 and 228 in mucin	Mice which received vaccine B-5512A	Mice which received vaccine B-5512B	Normal mice
10 ⁻² cc.	D D D	D D D	D D D
10 ⁻³	S S D	D D D	D D D
10 ⁻⁴	S D D	D D D	D D D
10 ⁻⁵	S S S	S S D	S D D
10 ⁻⁶	S S S	S S D	S D D
10 ⁻⁷	S S S	S S D	S D D
10 ⁻⁸	S S	S D	S S D

S indicates survival of a mouse for 7 days.

D indicates death of a mouse within 7 days.

Bibliography

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