

THE VIBRIOCIDAL ANTIBODY TITER AS A MEASURE  
OF IMMUNITY TO CHOLERA IN MAN

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The Cholera vaccine field trials have confirmed the important role of immunity in man to susceptibility to cholera. Since the adaptation of the vibriocidal antibody titration to a microtechnique by Benenson in 1965, we have conducted extensive serological surveys to evaluate the relationship of the level of vibriocidal antibody to immunity to cholera.

A serological survey in September, 1965, in the Matlab vaccine trial area revealed a rise in the vibriocidal titer with increasing age which correlated with the fall in the cholera case rate with age. An analysis of the 179 cholera cases occurring in this population over the subsequent 9 months revealed that cholera was selectively occurring in individuals with low vibriocidal titers. Among adults, the population survey indicated that only 13% had titers of less than 1:20, however, 33% of the cholera admissions had titers of less than 1:20. By comparing the distribution of the admission antibody titers of the cholera cases to the distribution of titers in the population survey, we estimated that the case rate fell 50% with each doubling of the vibriocidal titer.

During the 1965-66 cholera season in Dacca, we followed family contacts of cholera cases by collecting an initial serological specimen and daily rectal swab cultures for 10 days to relate the subsequent infection rate in these contacts to their level of vibriocidal antibody titer at the time of exposure. The results, summarized in Table 1, indicate that there was a progressive fall in the cholera infection rate (with or without diarrhea) with increasing levels of vibriocidal antibody titer.

TABLE 1 - Cholera Infection Rates Among Family Contacts of Cholera Cases by Initial Vibriocidal Antibody Titer

Initial Vibrio- cidal Titer	Total Contacts	Vibrio cholera present		Total %
		Diarrhea %	Asymptomatic %	
< 20	190	14.7	12.6	27.4
20	65	6.2	7.7	13.8
40	65	6.2	7.7	13.8
80	42	2.4	4.8	7.1
→ 160	59	1.7	1.7	3.4
Total	421	9.0	8.8	17.8

The 1966 vaccine field trial in Matlab utilized a standard U.S. commercial vaccine in a 1 and 2 injection schedule with a diphtheria-tetanus toxoid control. Serological surveys were made prior to, as well as 3 and 6 months after immunization. Also all cholera cases were studied serologically. Table 2 gives the distribution of the population by antibody titer based on the survey 3 months after injection, as well as the distribution by admission antibody titer of the cholera cases that occurred from 1 to 5 months after injection. This indicates that the case rates fall progressively with higher levels of vibriocidal antibody, approximating again a 50% reduction for every doubling of the vibriocidal titer.

TABLE 2 - Cholera Case Rates in the 1966 Vaccine Trial Population by Level of Vibriocidal Antibody

Vibriocidal Titer	Population	Cases	Rate per 1000
< 20	5427	21	3.87
20	4771	10	2.10
40	8253	8	0.97
80	9636	8	0.83
160	6000	2	0.33
320	3113	1	0.32
→ 640	2662	0	0.00
Total	39862	50	1.25

This relationship of case rate to vibriocidal antibody titer was utilized to predict vaccine effectiveness. Table 3 summarizes the geometric mean vibriocidal titers for each of the 3 vaccine groups 3 months after injection, and the predicted vaccine effectiveness, calculated assuming a 50% reduction in case rate for each doubling of the titer.

TABLE 3 - Geometric Mean Vibriocidal Titer by Vaccine Group, and Predicted Vaccine Effectiveness

<u>Vaccine Group</u>	<u>Number Surveyed</u>	<u>Geometric Mean Titer</u>	<u>Predicted Effectiveness</u>
Control	194	1:29	- - - -
1 dose	200	1:75	60%
2 doses	395	1:84	67%

Table 4 gives the observed case rates in each of the vaccine groups and the observed vaccine effectiveness during the 1 to 5 month period following injection.

TABLE 4 - Cholera Case Rates by Vaccine Group, and Observed Vaccine Effectiveness

<u>Vaccine Group</u>	<u>Population</u>	<u>Cases</u>	<u>Rate per 1000</u>	<u>Effectiveness</u>
Control	9923	31	3.12	- - -
1 dose	10020	14	1.40	55%
2 doses	19919	20	1.00	68%

There is good agreement between the observed and predicted vaccine effectiveness. A retrospective examination of the 1965 serological survey conducted in the 1963 and 1964 vaccine field trial populations where a high potency vaccine and a purified Ogawa antigen were utilized revealed the same relationship between vaccine efficacy, and the vibriocidal titer produced by the vaccine.

All of these studies indicate that there is a consistent relationship between the vibriocidal antibody titer and susceptibility to cholera. The cholera case rate in a population falls by 50% with every doubling of the vibriocidal titer. This relationship has been consistent whether the vibriocidal antibody has been acquired by natural infection or by a variety of cholera vaccines.

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