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Formation of Agglutinins in Response to Routine Inoculation of Typhoid Vaccine.*

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The universality of inoculation of typhoid vaccine has rendered the Widal reaction perhaps even more unreliable for diagnosis than it has been in the past. For this reason a further study of the agglutinin response to typhoid vaccine would be of value in helping to interpret this diagnostic test.

Broesamlen[1] states that 74% of 482 healthy persons whom he followed showed positive agglutination after typhoid vaccine, and that 41% were still positive at the end of 2 years. Fennel[2] studied 30 individuals and came to the conclusion that previous vaccination repressed agglutination formation and that there was no relation between the local and systemic reaction and the agglutinin formation. It is interesting to note that the present study fails to confirm the conclusions of either of these workers.

Opportunity was afforded by the routine inoculation of the class in bacteriology against typhoid fever to study the formation of agglutinins in a group of 95 healthy young adults.

Samples of blood were taken from each student 10 days before inoculation and tested by macroscopic methods for the presence of agglutinins. A group of 25 were again tested just after the second inoculation. The final tests were performed on blood taken 10 days to 2 weeks after the third dose of vaccine. A history was obtained from each student as to whether he had had typhoid fever, previous vaccinations, and as to the type and severity of reaction to the inoculations. The data collected in this way were carefully analyzed statistically and the following conclusions seem to be warranted:

1. Agglutinins are developed more universally by those who have had typhoid (100%), or previous vaccination (83%) than by those who have had neither (45%).

2. Agglutinins are developed in higher titer by those who have had typhoid (1/242), or previous vaccination (1/163) than by those who have had neither (1/74).

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* Credit should be given to two students of the class, H. A. King, Jr., and D. A. Savant, who performed a large part of the routine work.

[1] Broesamlen, *Deutsches Arch. f. Klin. Med.*, 1918, cxxix, 208.

[2] Fennel, E. A., *J. Am. Med. Assn.*, 1918, lxx, 1915.

3. Agglutinins from previous vaccinations persisted in titer high enough for diagnosis (1/40) in only 21% at the end of one year, and in only 12% at the end of 2 years.

4. There is some correlation, but not marked, between the severity of reaction to inoculation and the titer developed. (Correlation coefficient is $+0.393 \pm 0.058$.)

5. There is no significant correlation between the number of previous vaccinations and the titer developed. (Correlation coefficient is $+0.154 \pm 0.092$.)

6. There is no significant correlation between the time elapsed since the last vaccination and the titer developed. (Correlation coefficient is -0.105 ± 0.093.)

7. There was a steady rise in agglutinin titer in the group of 25 on whom 3 sets of tests were performed. (Typhoid group 1/3, 1/73, 1/276; previously vaccinated group 1/28, 1/59, 1/270; unvaccinated group 1/0, 1/50, 1/62.)

Further study of this group is contemplated. Parallel agglutination and complement fixation tests are to be run at the end of 3 months from inoculation.

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I. Relation of Bile Salts, Cholesterin, Sodium Citrate and Sodium Bicarbonate to Toxicity of Pneumococcus.

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Experiments were performed to determine certain facts relative to the action of sodium citrate, sodium bicarbonate, and some of the constituents of the bile, namely cholesterin and sodium taurocholate, on the toxicity of the pneumococcus. These substances were used separately and in combinations and were injected intraperitoneally into the white mouse. In all, approximately 75 such mice were employed. It is thought by some that bile salts increase the toxicity of the pneumococcus and that cholesterin acts as a buffer reducing this toxicity. The results obtained by various workers[1,2,3,4]

[1] Rosenow, E. C., *J. Inf. Dis.*, 1911, ix, 190.

[2] Cole, Rufus, *J. Exp. Med.*, 1912, xvi, 664.

[3] Horrall, O. H., and Carlson, A. J., *Am. J. Physiol.*, 1928, lxxxv, 59.

[4] Ravdin, I. S., Morrison, M. E., and Smyth, C. M., *Ann. Surg.*, 1929, lxxxix, 871.