AGGLUTININ PRODUCTION: TOTAL AMOUNT INJECTED VARIED, DOSAGE AND FREQUENCY OF INJECTIONS CONSTANT.

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It is a general proposition that when certain foreign substances (immunogens) are injected into animals, specific immune bodies are built up.

The resulting antibodies depend upon the nature of the foreign element inoculated. Thus, if bacterial toxins, snake venoms or ferments are introduced in the animal body antitoxins, antivenoms or antiferments result. Likewise, if soluble substances such as blood sera or egg white are inoculated, precipitins are elaborated by the cells of the animal. While if organized cells such as bacterial or red blood cells are injected, agglutinins and lysins may be set forth.

These specific antibodies as well as others undoubtedly play an important rôle in protecting the individual against various toxic substances. So that by this mechanism highly poisonous toxins are rendered harmless by their corresponding antitoxin. Likewise, an individual may be guarded against invasion of pathogenic organisms such as the typhoid bacillus by the elaboration of or the increase of substances which are detrimental to them.

Since this paper deals with agglutinins the discussion will be confined to them. The phenomenon of agglutinins may be defined as the clumping together of cells of plant and animal origin,—organized substances such as bacteria (vegetable), trypanosomes and red blood cells (animal) in suspension.

Agglutinins are the names given to these antibodies which are responsible for the above phenomenon.

Charrin and Roger[1] in 1891 first noticed the characteristic growth of an organism when cultivated in immune serum. Metchnikoff[2] made a similar observation. Gruber and Durham[3] thoroughly studied the agglutination phenomenon and along with Bordet[4] were the first to reveal the fact that agglutinins had an independent specific action of their own. Widal[5] showed the practical use of agglutinins in diagnosing typhoid fever.

The demonstration of the presence of agglutinins may be carried out both microscopically and macroscopically. In this work the latter method was resorted to because of its accurateness and simplicity of its manipulation.

[1] Compt. Rend. Soc. de Biol., 1889, 667.

[2] Ann. d.l' Inst. Pasteur, 1891, 473.

[3] Munch. med. Wchn., 1896, 285; Jour. Path. and Bacteriol., 1897, 4, 13; ibid., 1901, 7, 240; Brit. Med. Jour., 1898, 2, 588.

[4] Ann. de l' Inst. Pasteur, 1895, 9, 462.

[5] Semaine med., 1896, 259.

"Proc. Ind. Acad. Sci., vol. 37, 1927 (1928)."

In two previous papers presented before the Academy agglutinin production was described in which the frequency of injections was varied while the dosage and the total amount of the antigen inoculated was constant.[6] Also the converse of this experiment was discussed, namely, the frequency of injections was constant and the dosage and total amount inoculated was varied.[7]

Of the eight practical variations of these three components an experiment was undertaken in which the total amount of agglutinogen injected was varied while the dosage and frequency of the inoculations was constant.

That is, rabbits were injected at daily intervals with 1 cc. for one to ten days and consequently received from 1 to 10 cc. of a typhoid vaccine. This bacterine contained two billion typhoid bacilli per c. cm. killed by heating to 58° c. for one hour.

TABLE I. Showing Titres of Typhoid Agglutinins in Rabbits Injected* Once to Ten Times at Daily Intervals.

No. of Rabbit	No. of Injections	Total No. c.cm. Injected	Titre	Average Titre
1 2	1	1	3000 3000	3,000
3 4	2	2	1500 3000	2,250
5 6	3	3	4000 8000	6,000
7 8	4	4	3000 3000	3,000
9 10	5	5	4000 4000	4,000
11 12	6	6	5000 8000	6,500
13 14	7	7	4000 5000	4,500
15 16	8	8	8000 8000	8,000
17 18	9	9	5000 10000	7,500
19 20	10	10	16500 17000	16,750

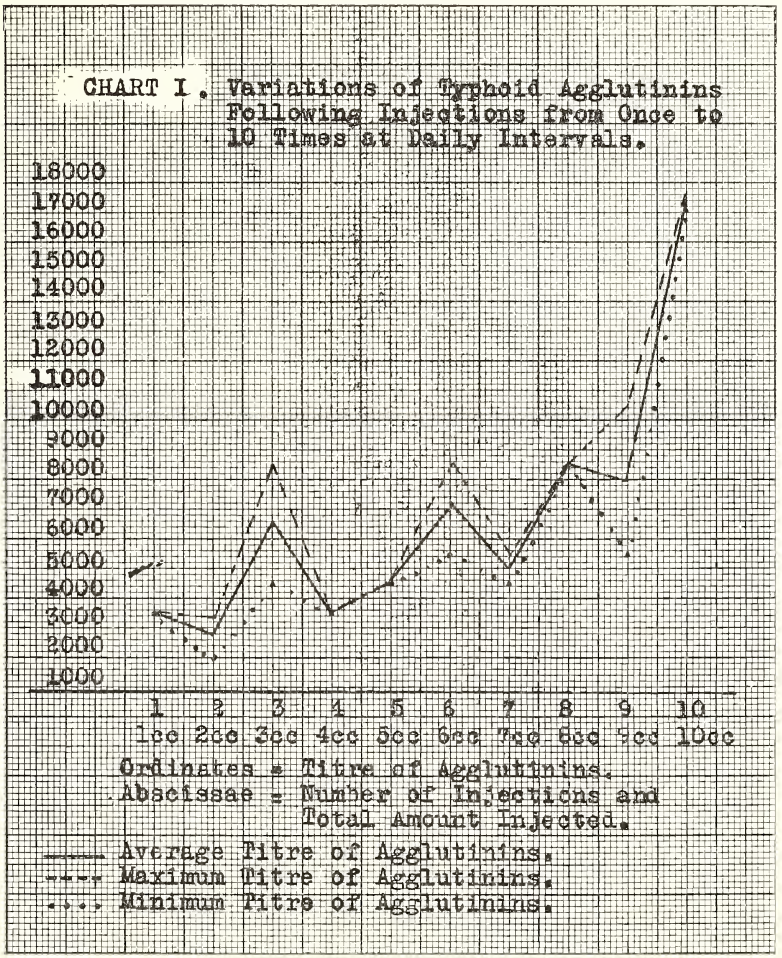
*1 cc. Intravenously.

Rabbits 1 and 2, as will be observed in Table I, received but a single injection and each developed titres of 1-3000. Rabbits 3 and 4 were inoculated once every day for two days; their agglutinin titres were 1,500 and 3,000, respectively, an average of 2,250. Rabbits 5 and 6 were similarly inoculated for three days and their titres were 4,000 and 8,000, respectively, or an average of 6,000. Likewise rabbits 7 and 8 were injected for four days and each showed titres of 3,000. Animals 9 and 10, which were inoculated daily with 1 cc. for five days and con-

[6] Proc. Ind. Acad. Sci. 1925, (1926) 34, 259.

[7] Ibid, 1926, (1927) 36, 313.

sequently received a total of 5 cc., each developed agglutinins with titres of 1-4000. Rabbits 11 and 12 were injected on six consecutive days. Their titres were 5,000 and 8,000, respectively, an average of 6,500. While rabbits 13 and 14 injected similarly for seven days had titres of 4,000 and 5,000, or an average of 4,500. Rabbits 15 and 16



injected on eight successive days developed titres of 8,000 each. Rabbits 17 and 18 inoculated for nine days showed titres of 5,000 and 10,000, respectively, an average of 7,500. While rabbits 19 and 20, which were injected consecutively at 24-hour intervals for ten days and received a total amount of 10 cc. of the vaccine, showed a marked increase of agglutinin production with titres of 16,500 and 17,000, respectively, or an average of 16,750.

The minimum, maximum, and average titres of agglutinin development in these animals is shown in Chart I.

An interpretation of these results reveals the fact that typhoid agglutinins of a high potency can be built up in rabbits by inoculating them with small amounts (1 cc.) at daily intervals for a period of days, preferably ten.

Generally speaking, there is an increase in the agglutinin development as the number of days of inoculations are prolonged.