SERUM SENSITIZATION AS RELATED TO DOSAGE OF ANTITOXIN IN MAN AND ANIMALS.*

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The results of a series of tests carried out by Lewis[1] showed that 2 units of antitoxin contained in 0.05 c.c. of horse serum given one hour previously protected rabbits which received about 10 fatal doses of diphtheria toxin. Both injections were given intravenously. When rabbits were sensitized by a previous injection of either normal or antitoxic horse serum, several times as much antitoxin was required. The amounts were not graded sufficiently to state the results more accurately.

Lewis recognizes that the experiments are limited in number and suggests that the curve of absorption of antitoxin in man as developed by J. Henderson Smith[2] be elaborated to cover the case of human beings who have received previous injections of normal or antitoxic horse serum. During the course of our studies upon the influence of protein concentration upon the absorption of antitoxin (see p. 338) we had an opportunity to make observations upon men which have a direct bearing upon this question. Also, further tests of like nature were carried out on goats. The results obtained from our tests have been plotted on charts for ease of comparison.

EXPERIMENTS WITH MEN.

The data pertaining to the men are briefly submitted, as follows: S. received on February 11, 1913, an initial injection subcutaneously of 10,000 units diphtheria antitoxin in 4.5 c.c. volume of a preparation containing 17.2 per cent of pseudoglobulin. Two months later he received a second injection of a preparation containing the same number of antitoxic units and amount of pseudoglobulin but diluted to 9 c.c. volume. This was followed by a moderate local reaction. F. received subcutaneously on February 6,

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[1] *Jour. Exper. Med.*, 1912, 16, p. 216.

[2] *Jour. Hyg.*, 1907, 7, p. 205.

1913, an initial injection of 10,000 units of diphtheria antitoxin in 9 c.c. volume of a preparation containing 8.6 per cent of pseudoglobulin. His second injection was given 2 months later. It contained the same number of units of antitoxin and the same amount of pseudoglobulin, but in a volume of only 4.5 c.c. The local reaction was moderate in amount.

The above details are given for purposes of accuracy. The protein concentration and the volume of fluid are believed by us to have practically no appreciable effect. The results of these tests are represented graphically in Chart 1 upon a 100 lb. basis.

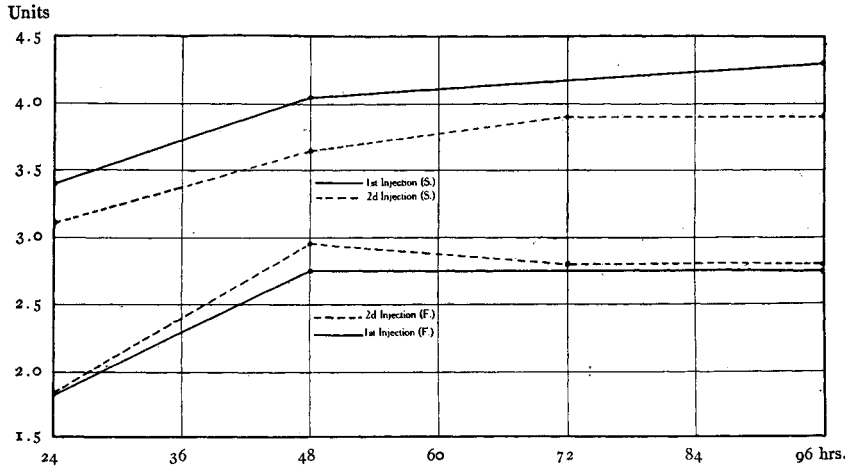

CHART 1.—Comparative tests in man.

EXPERIMENTS WITH GOATS.

Goat 5 received the first injection subcutaneously on October 17, 1912, consisting of 10,000 units of diphtheria antitoxin in a volume of 10 c.c. fluid containing 29.2 per cent of pseudoglobulin. Its weight was 47.5 lbs. Slightly over 7 months later, the same animal received an injection of an antitoxic preparation corresponding in every particular with the first injection. At this time its weight had increased to 57 lbs. Chart 2 shows the results of both tests in curves with unit value per cubic centimeter of serum (goat) based upon 50 lbs. weight.

Goat 25, weight 47.5 lbs., was given subcutaneously a sensitizing dose of 10 c.c. normal horse serum on March 19, 1913. On

May 21, 1913, the animal was given a second injection subcutaneously of a diphtheria antitoxin preparation containing 10,000 units in 2.7 c.c. volume with 29.2 per cent of pseudoglobulin. Two animals weighing 54 lbs. and 46.5 lbs., respectively, which

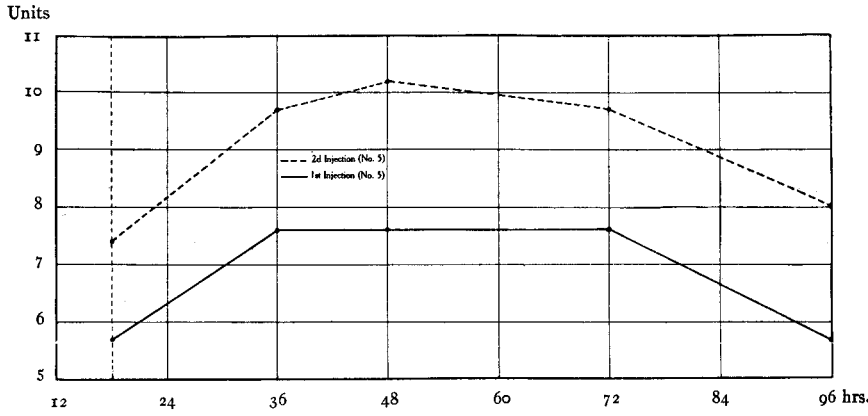

CHART 2.—Absorption curves of first and second injections of antitoxin in Goat 5.

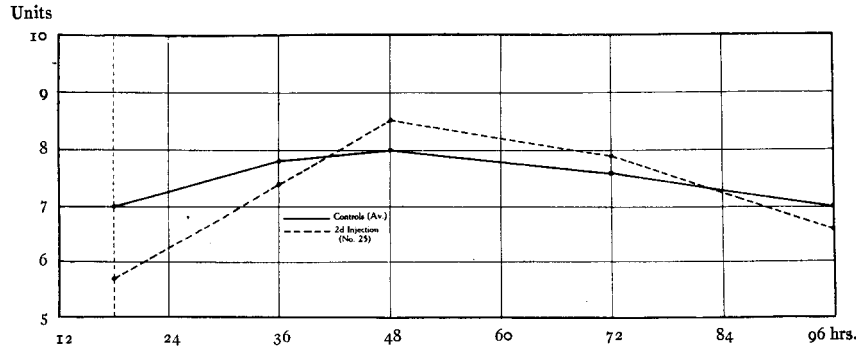

CHART 3.—Average antitoxin content in 2 goats receiving first injections, and of Goat 25 receiving a second injection.

had received primary injections of an antitoxic preparation corresponding in unit strength, volume, and protein concentration with that given to Goat 25, were used as controls. The unit values of the serum samples from each animal were brought to the 50 lb. basis, and in case of the 2 controls the average taken, and then comparative curves were plotted as shown in Chart 3.

SUMMARY AND CONCLUSIONS.

The results obtained in 2 men and in 2 goats showed no appreciable difference in the absorption curves of antitoxin before and after sensitization. The variations that occurred in the cases appeared to be due to the inherent individual characteristics of the persons and animals injected and not to the sensitization.

We conclude that the large amounts of antitoxin injected in the treatment of diphtheria are neither bound nor destroyed appreciably by any globulin antibodies present in the blood of those previously injected. The same quantity of antitoxin is therefore indicated in the treatment of diphtheria whether the case has or has not received a previous injection of horse serum or globulins.