

SOME ASPECTS OF ANAPHYLAXIS IN GUINEA-PIGS

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(Received on July 16, 1959)

While working on the protective action of various drugs in experimental anaphylaxis, it was observed that the survival time of guinea-pigs of heavier weight was more than that of lighter guinea-pigs, when the same amount of antigen was being used as the shocking dose. A search of the available literature did not reveal any relationship between the shocking dose and anaphylactic reaction. Coulson *et al.*, (1949) were of opinion that in anaphylactic shock it appears unlikely that LD 50 is correlated to body-weight. The results of Hoene *et al.*, (1952) indicated that there is some relationship between the dose of reinjected antigen and the percentage of fatal shock in sensitised guinea-pigs. In order to find out whether there is any relationship between the shocking dose and the percentage of mortality, the following work was undertaken.

METHOD AND MATERIALS

In this series of experiments, because of the very specific and sharp reaction, guinea-pigs were selected. The animals weighing between 250-400 gms. were selected. The diet mainly consisted of gram, bran and green vegetables. Egg albumin was taken as the antigen and a 10% solution was prepared afresh before each experiment. Active sensitisation to egg albumin was obtained by injecting intraperitoneally 0.1 ml. of the antigen (diluted 1:10) on two consecutive days. The shocking dose—a 5% solution of egg albumin—was administered intravenously on the 15th to 17th day of administration of the sensitising dose.

RESULTS

The results of these experiments are summarised in Table I below.

TABLE I

Response to various amounts of shocking dose in sensitized guinea-pigs.

Sl. No.	No. of animals	Average weight in gms.	Shocking dose of egg albumin (5% solution).		No. of animals dead	Percent mortality.
			Amount in ml.	ml. / Kg. body-wt.		
1.	20	310	0.2	0.64	17	85
2.	20	290	0.1	0.34	12	60
3.	20	315	0.04	0.12	5	25
4.	20	295	0.02	0.06	4	20

On analysis of the results of Table I it will be seen that with the increase of the shocking dose percentage mortality increased. This indicates that the antigen-antibody reaction is perhaps a quantitative response. These results were further subjected to analysis and a dose - response curve was plotted. Figure I shows that there is distinct relationship between the percentage mortality of guinea-pigs and the dose of antigen used as shocking dose.

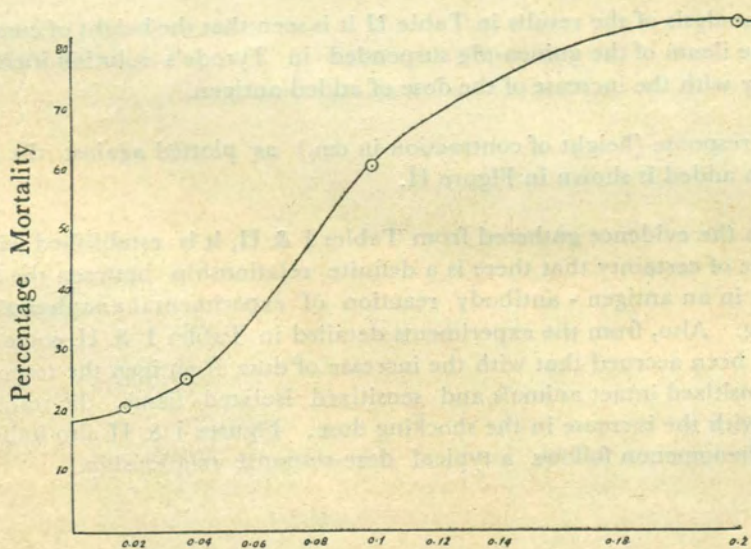


Fig. 1.

Dose of Egg Albumin in ml. (5 Percent equivalent)

Having established that in the intact animals there is a definite relationship between the shocking dose and the response, experiments were undertaken to find out if similar relationship exists between the dose of antigen and the effect in isolated strips of intestine obtained from sensitized guinea-pigs. Various doses of the antigen were added to the bath (capacity 10 ml.) containing Tyrode's solution in which the strip of intestine from sensitized guinea-pig was suspended. The results are shown in Table II,

TABLE II

Response of isolated sensitized strip of intestine to various doses of antigen.

Sl. No.	Doses of Antigen 1% solution in ml.	Average height of contraction in cm.
1.	0.1	0.64
2.	0.2	1.30
3.	0.3	2.60
4.	0.4	3.23
5.	0.5	4.74
6.	0.6	5.45

On analysis of the results in Table II it is seen that the height of contraction of the ileum of the guinea-pig suspended in Tyrode's solution increases effectually with the increase of the dose of added antigen.

The response (height of contraction in cm.) as plotted against the dose of antigen added is shown in Figure II.

From the evidence gathered from Tables I & II, it is established with a fair degree of certainty that there is a definite relationship between the dose and effect in an antigen - antibody reaction of experimental anaphylaxis in guinea-pig. Also, from the experiments detailed in Tables I & II, some evidence has been accrued that with the increase of dose of antigen the response, both in sensitized intact animals and sensitized isolated tissue, the response increases with the increase in the shocking dose. Figures I & II also indicate that the phenomenon follows a typical dose-response relationship.

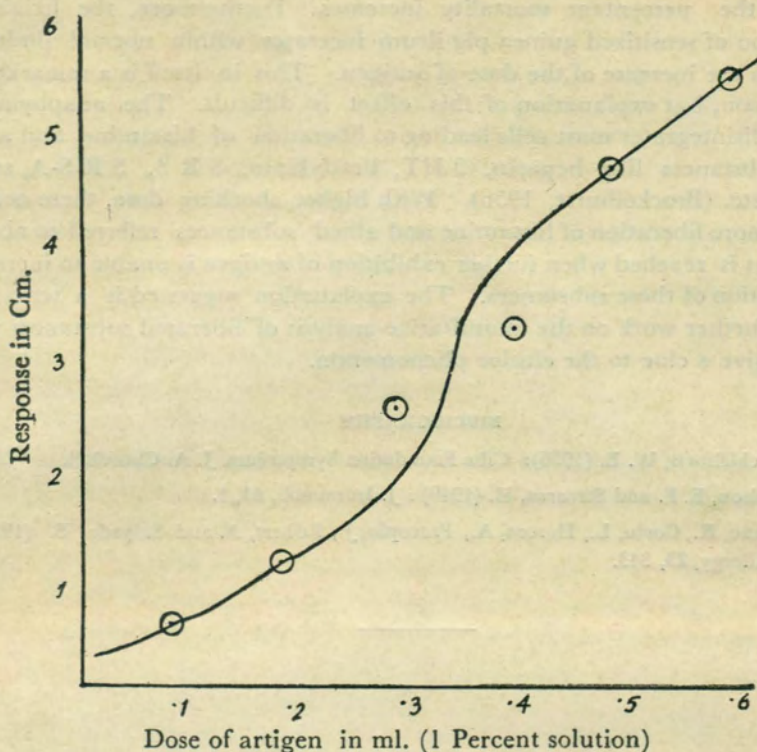


Fig. 2.

DISCUSSION

The available literature indicates that antigen-antibody reaction is a quantal phenomenon. The reaction is determined by the species of animals employed and not by the individual character of the antigen. Of all the animals, guinea-pigs are perhaps the best type of animals for this type of reaction as the end point is sharp, characterised by profound bronchial spasms and asphyxia. This in itself led us to use guinea-pigs in these experiments.

The antigen-antibody reaction occurs in the cells to which the antibody is fixed, leading to cell injury. This in its wake disintegrates most cells leading to liberation of histamine which creates a diffusion gradient. Histamine, however, does not explain the whole issue. The reaction leads to liberation, by some unknown mechanism, of a large number of substances like histamine, heparin, bradykinin, 5-hydroxytryptamine, choline, substance P, SRS, and SRS-A.

The experiments carried out in this series go to show that the reaction in the intact animals (guinea-pigs) shows that with the increase in dose of the

antigen, the percentage mortality increases. Furthermore, the height of contraction of sensitized guinea-pig ileum increases within normal limits of error with the increase of the dose of antigen. This in itself is a remarkable phenomenon, but explanation of this effect is difficult. The anaphylactic reaction disintegrates mast cells leading to liberation of histamine and associated substances like heparin, 5 HT, bradykinin, S R S, S R S-A, substance P. etc. (Brockelhurst, 1956). With higher shocking dose, there occurs perhaps more liberation of histamine and allied substances referred to above till a point is reached when further exhibition of antigen is unable to increase the liberation of these substances. The explanation suggested is a tentative one and further work on the quantitative analysis of liberated substances will perhaps give a clue to the elusive phenomenon.

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