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A note on the desensitization of guinea-pigs.By **ALFRED H. CAULFEILD, M.B.***[From the Department of Medical Research, University of Toronto.]*

During the course of certain experiments it so happened that I desired to reinject a comparatively large number of laboratory animals with bovine protein, and because of the danger of anaphylaxis I attempted to desensitize these before giving the large amounts of protein which I subsequently wished to use. It was in fact an endeavor to safely desensitize both rabbits and guinea-pigs so that large amounts of protein could be reinjected subcutaneously, intravenously and intrapleurally. The results seemed worth recording both because of their practical bearing and because of one or two striking occurrences.

The number of animals which came into consideration were 72 guinea-pigs. On account of the character of the initial or sensitizing doses they should be divided into two groups, namely a set of 30 and a set of 42.

The former received the following initial injections:

| | | | |
|---------------|-----|----------|-----------------|
| 1915, January | 16. | 2.5 c.c. | subcutaneously. |
| " | 21. | 1.0 c.c. | " |
| " | 30. | 0.5 c.c. | " |
| February | 2. | 1.0 c.c. | " |

The set of 42 received only one initial dose of 0.5 c.c. on January 22, 1915.

The first reinjection (subcutaneous) was given on March 24, 1915, an interval of 50 days. It is perhaps advisable to explain the practical carrying out of the injections to make Chart I clear. Both sets of guinea-pigs (all of which were numerically tagged) were put in a large cage and the injections were carried out by taking the animal most convenient, without regard to its number, and transferring immediately after injection to a different cage. The dose first tried was 0.02 c.c. protein diluted to 0.5 c.c. with saline, but before the seventh animal was injected two guinea-pigs were showing toxic symptoms and died immediately. As on

account had been paid to the order in which the animals had been treated it was only possible to ascertain the numbers of the six so treated. From the time necessary, however, for the injections the animals must have died from within one to ten minutes after they had received their injection. Following this the dose was halved (*i. e.*, 0.01 c.c. diluted to 0.5 c.c.) for the remaining 66 animals without a casualty or any signs sufficiently definite that anaphylactic intoxication could with certainty be diagnosed. It so happened that the six animals receiving the higher dose of 0.02 c.c. were all from the set of 42.

The second injection (subcutaneous) was given shortly after completing the first and 0.1 c.c. protein (diluted to 0.5 c.c. with saline) was tried. As before two acute deaths occurred in the six so inoculated. Again the dose was halved, as in the preceding injections, without any fatality for the now remaining 64 animals. This time it so happened that five of the six guinea-pigs, which had received the larger dose, belonged to the set of 30, and both deaths occurred amongst the five, so that there was no evidence that the character of the initial sensitizing dose had had any bearing on the results.

In all four cases death was acute and rapid; the post mortem showed the typical emphysematous condition of the lungs.

The third (subcutaneous) desensitizing dose of 0.125 c.c. protein (diluted to 0.5 c.c. with saline) was given at 11 A.M., and the fourth (subcutaneous) of 0.5 c.c. protein at 4.30 P.M. of the following day, March 25, without any immediate ill effects. The following morning, however, one animal in the set of 42 was found dead. The post mortem showed a most marked condition of general anasarca. On cutting the skin the subcutaneous tissues were very swollen and fluid rapidly oozed from the cut surface, the serous cavities contained a very appreciable amount of free fluid, the lungs were very edematous and the tubes greatly distended with clear fluid.

Following the two injections of the 25th of March, large doses were given on subsequent days without any evidence of toxic symptoms.

Besides the two sets of guinea pigs above, there was also a small set of six which had received an initial dose of 0.5 c.c. goat

serum on January 22, 1915. Reinjection was made on March 24 of 0.01 c.c. and 0.1 c.c. (diluted to 0.5 c.c. with saline) without any ill results. Further injections of larger amounts gave negative results.

These results on guinea-pigs might be gathered together as follows:

1. While the first desensitizing dose was sufficiently strong to cause acute death in two out of the six guinea-pigs, one half the dose failed to cause any marked or certain evidences of anaphylactic poisoning in the remaining 66 animals.

2. While the strength of the second desensitizing dose was sufficiently strong to cause acute death in two out of six guinea-pigs, one half the dose again failed to cause marked or certain evidences of an anaphylactic poisoning in the remaining 64 animals.

3. Two subcutaneous desensitizing doses were given on two successive days and this proved successful in producing a fully refractive state in those that survived.

4. On the night following the fourth dose, which was 0.5 c.c. protein, one pig died and the post mortem showed a marked condition of general anasarca.

5. All injections were made subcutaneously and into approximately the same area.

6. Out of 72 guinea-pigs, previously injected with bovine protein a total of 5 died during the course of desensitization, four in acute anaphylactic shock and one later with general anasarca.

7. Six guinea-pigs showed no little evidence that they were sensitive to goat serum.

CHART I.

ILLUSTRATING FIRST AND SECOND DESENSITIZING DOSES ON GUINEA-PIGS, 50 DAYS AFTER LAST INITIAL INJECTION.

| Time and Date. | First Reinjection Subcutaneously 10:30 a. m., March 24. | Anaphylactic Death in | Second Reinjection Subcutaneously 11:45 a. m., March 24. | Anaphylactic Death in |
|-----------------------|---|--------------------------|--|--------------------------|
| Set of 30 guinea-pigs | Dose .02 c.c. for 0 | 0 | Dose 1 c.c. for 5 | 2 |
| | Dose .01 c.c. for 30 | 0 | Dose .05 c.c. for 25 | 0 |
| Set of 42 guinea-pigs | Dose .02 c.c. for 6 | 2 | Dose .1 c.c. for 1 | 0 |
| | Dose .01 c.c. for 36 | 0 | Dose .05 c.c. for 39 | 0 |