histological findings as well as the results obtained in the author's studies on a new series of rabbits will be described in detail in another paper. In conclusion it may be stated that although thousands of doses of cobra venom have been injected by numerous physicians in different parts of the country, the authors have never received a single report describing any impairment of kidney function by this medication.

Summary. Large doses of cobra venom solution, 5 to 10 mouse units, equivalent to the ordinary and the exceptional dosage employed for adult humans, were administered to rabbits 5 or 6 days a week for periods ranging from 7 to 22 weeks. Functional tests made at the beginning and end of the investigation revealed that neither kidney nor liver function of any of the rabbits had been impaired during the whole course of experimentation.

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Relation of Suprarenal Hemorrhage to Loss of Vitamin C in Experimental Diphtherial Intoxication.

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The most characteristic lesion of acute experimental diphtherial intoxication in the guinea pig, other than the local disturbances at the site of injection, is the enlargement of the suprarenal glands with the accompanying congestion and hemorrhage, an extensive study of which was reported by Abramow.[1] Harde[2] found that the vitamin-C content of these organs was greatly diminished when death followed the injection of diphtherial toxin. Torrance[3] confirmed this finding and reported that the injection of other toxic bacterial products, such as filtrates of the meningococcus, which give rise to congestion and hemorrhage of the suprarenal glands, cause the vitamin-C concentration to fall to similar low levels.

Since the essential tissue-changes in acute scurvy are associated with alterations in the capillary walls which result in generalized hemorrhage, it seemed not unlikely that the extravasation of blood

1 Abramow, S., *Z. f. Immunitäts.*, 1912, I, **15**, 12.

2 Harde, E., *C. r. Acad. de Science*, 1934, **199**, 618.

3 Torrance, C. C., *J. Bact.*, 1937, **33**, 645.

in the suprarenal glands is a manifestation of what might be called a "localized scurvy." This hypothesis is strengthened by the experiments described.

The ascorbic-acid content of the suprarenal glands of guinea pigs was determined by a modification of the method of Bessey and King.[4] The hemoglobin-content was determined by extracting with 0.1 N hydrochloric acid the pulp obtained by grinding the tissue. Since the resultant turbid solutions of acid hematin could not be compared with the clear solutions obtained by diluting blood with the same acid, a series of standards was prepared from the suprarenal extracts themselves. Two solutions that represented the extremes of the available color range were selected and given arbitrary values of 100 units and 0. Intermediate steps in the series were attained by mixing the 2 in decimal proportions. The standards remained satisfactory for several weeks in the cold room.

Thirty-five pairs of suprarenal glands were obtained from guinea pigs that had been used for routine standardization tests of diphtherial toxin. Each gland was bisected; one half was used for the determination of the vitamin-C concentration and the other for the extraction of the hemoglobin. The correlation of the vitamin-C concentration and the hemoglobin was

$$r_{12} = -0.54 \pm 0.08.$$

This figure indicated a high degree of inverse association between the 2 substances.

Since the vitamin-C concentration of suprarenal tissue is higher than that of the blood, hemorrhage in these organs would, by dilution, reduce appreciably the concentration of ascorbic acid. The total ascorbic-acid content of the suprarenals of each of the animals was, therefore, calculated from the data available and its relation to the hemoglobin-concentration determined. The correlation-coefficient thus obtained was

$$r_{12} = -0.40 \pm .096$$

This figure, 4.2 times its probable error, is significant and indicates a degree of inverse relationship between the hemorrhage and the total vitamin C in the suprarenals at death.

Twelve guinea pigs weighing between 230 and 280 g were injected with from 0.8 to 1.2 minimal lethal doses of diphtherial toxin. Each of 10 similar animals received 100 mg of vitamin C and the same amounts of toxin. Two injected with 100 mg of vitamin C, 2 with 10 mg, and 2 uninjected guinea pigs served as controls. The animals that received toxin alone, and all but one of those given vitamin

[4] Bessey, O. A., and King, C. G., *J. Biol. Chem.*, 1933, **103**, 687.

TABLE I.
Effect of Simultaneous Injection of Vitamin C and Diphtheria Toxin on Hemorrhage in Suprarenals of Guinea Pigs.

No. of animals	Material injected	Average hemoglobin units*	Stan. dev.
10	100 mg Vit. C + 0.8 to 1.2 M.L.D. toxin	23.5	± 8.9
12	0.8 to 1.2 M.L.D. toxin	77.5	±32.5
6	Controls—no toxin	6.6	± 7.9

*Arbitrary units. 100, the greatest amount of Hb found in any suprarenal; 0, that in normal animal.

C and toxin died in less than 10 days. The 6 animals that did not receive toxin and the one that survived the toxin-vitamin injection were sacrificed. The suprarenals were removed. The right one was fixed in Zenker's fluid, the left was used for hemoglobin-determination. Since no significant differences were observed between the suprarenals of the uninjected animals and those that received vitamin C alone, the data are combined in Table I. The hemoglobin-content of the suprarenals of the guinea pigs injected with toxin alone was 2.8 times as great as that of the group that received toxin and vitamin C. These observations were confirmed by histological examination of the right suprarenals from the same animals.

Summary and Conclusions. An inverse correlation was demonstrated between the hemorrhage occurring in the suprarenals of guinea pigs injected with a fatal dose of diphtherial toxin and the total vitamin C remaining in these glands at death. When diphtherial toxin was administered simultaneously with a large dose of vitamin C, the hemorrhage of the suprarenals which customarily follows the injection of the toxin, was greatly reduced. These findings suggest that such hemorrhages follow the reduction in the vitamin-C concentration in this gland as they do elsewhere in the body, and thus result only indirectly from the action of the toxin.