

ify the resultant reaction, it seemed desirable to test the above hypothesis of the mechanism of action of Vitamin C in a histamine liberating reaction that is apparently not dependent upon an antigen-antibody reaction. Such a reaction occurs in peptone shock. We have demonstrated that peptone shock in dogs is accompanied by an explosive liberation of histamine and that the degree of shock is proportional to the amount of histamine liberated.³ We have, therefore, studied the effect of the prior administration of Vitamin C upon the severity of peptone shock in dogs.

Eleven dogs were anesthetized with ether and sodium barbital and the carotid blood pressure tracings recorded to provide an objective record of the severity of the shock reactions. Cevitamic acid* was injected intravenously in amounts varying from 25 to 100 mg per kilo and after varying intervals of from 15 to 45 minutes an injection of 2 cc per kilo of a 10% solution of a proteose peptone† was made. Definite shock reactions occurred in 10 animals, 2 being rapidly fatal, 5 quite severe, and 3 mild. The distribution of the varying grades of severity of shock was similar with that in a large number of controls.³ Blood samples were drawn approximately 5 minutes after the peptone injection and the presence of histamine demonstrated in all instances in which the reaction was severe.³

It is concluded that the prior administration of Vitamin C to dogs does not protect against peptone shock and that correspondingly it does not prevent the liberation of histamine from the fixed cells of the body into the blood.

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Vitamin C and Anaphylactic Shock in Dogs.

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Contradictory reports upon the effect of Vitamin C on the anaphylactic reaction of guinea pigs have appeared. Hochwald,¹

³ Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Ther.*, 1937, **59**, 429.

* We are indebted to Merck and Co. for the Cebione used in these experiments.

† Bacto-Protone-Difco was used in these experiments.

¹ Hochwald, A., *Z. f. d. ges. Exp. Med.*, 1935, **97**, 433.

Lemke,² and Solomonica³ have reported protective effects, while Schwartz and Cisloghi⁴ and Van Niekerk⁵ have reported negative effects. Giroud and Giroud⁶ have reported protective effects in rabbits. To our knowledge no study of the effect of administered Vitamin C on the anaphylactic reaction in the dog has been reported.

Eighteen dogs were sensitized to horse-serum. After incubationary periods of 15 to 20 days they were anesthetized and the blood-pressure reactions recorded to provide an objective record of the degree of shock produced by the intravenous injection of horse-serum. Four dogs were given 250 mg of cevitamic acid* daily by mouth throughout the incubationary period, 5 dogs were given intravenous injections of 200 mg prior to the sensitization, a daily oral dose of 500 mg during the incubationary period and a final intravenous injection of 500 mg before the provocative injection of horse-serum, and 9 dogs were given intravenous injections of 100 mg per kilo during the last 45 minutes before the provocative injection of horse-serum. Sixteen animals showed anaphylactic reactions, of which 4 were rapidly fatal and 9 were quite severe. The distribution of the various grades of severity of shock were similar with that in a large number of controls.⁷ Through the courtesy of Professor C. J. Farmer, the concentration of Vitamin C in the blood was determined in some of the animals.

We are thus enabled to say that the blood concentration was elevated from normal levels of approximately 0.20 mg % to around 0.6 mg % in the first group, that in the second group the blood concentration was moderately high at the time of sensitization (2.0 to 4.0 mg %), was maintained at fairly high levels during the incubationary period (around 1.0 mg %) and was considerably elevated (11.0 to 20.0 mg %) at the time of the provocative injection of horse-serum, and that in the third group the blood concentration was above 20 mg % at the time of the provocative injection of horse-serum. It is therefore believed that the amounts of cevitamic acid used were adequate to influence the reactions if such administration has any specific effect.

² Lemke, C. H., *Monatschr. f. Kinderh.*, 1936, **67**, 244.

³ Solomonica, B., *J. Immunol.*, 1936, **31**, 209.

⁴ Schwartz, E., and Cisloghi, F., *Minerva Medica*, 1935, **2**, 522.

⁵ Van Niekerk, J., *J. Allergy*, 1937, **8**, 446.

⁶ Giroud, P., and Giroud, A., *C. R. Soc. d. Biol.*, 1936, **121**, 1588.

* We are indebted to Merek and Company for the Cebione used in these experiments.

⁷ Dragstedt, C. A., Mills, M. A., and Mead, F. B., *J. Pharm. and Exp. Ther.*, 1937, **59**, 359.

Although the number of animals used is not large enough to detect a slight change in response it is evident that the administration of Vitamin C in the manner and amounts here employed has no marked effect either upon the phenomena of sensitization or the subsequent anaphylactic reaction in dogs.

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An Antidiuretic Substance Present in the Urine of Dehydrated Rats.

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Gilman and Goodman^{1, 2} have reported the discovery of an anti-diuretic substance, which they identify as pituitrin, in the urine of animals dehydrated for varying periods of time. These authors have suggested that the effective concentration of a hormone responsible in any part for the reabsorption of water in the renal tubules must increase as the demand for reabsorption becomes greater, as in states of dehydration. It has, further, been reported by Heller^{3, 4} that a portion of pituitrin injected into the animal body appears in the urine.

We have repeated a part of the work of Gilman and Goodman, and are able to confirm their statement that an antidiuretic substance can be recovered from the urine of dehydrated rats.

Healthy, adult male rats were deprived of water for periods of 24, 48, and 72 hours. Their urine was collected during 24-hour periods in sufficient 1% acetic acid to keep the samples weakly acid. An attempt was made to keep the samples free from contamination with fecal matter by lining the collecting funnels with glass wool. In most cases, this was successful. Urine so collected was filtered and dialyzed from 5 to 8 hours against running water, through a "viscose" membrane with a wall thickness of 0.0008 inch. It was then concentrated *in vacuo* to approximately 10 cc. When it was

¹ Gilman, A., and Goodman, L. S., *Science*, 1936, **84**, 24.

² Gilman, A., and Goodman, L. S., *J. Physiol.*, 1937, **90**, 113.

³ Heller, H., and Urban, F. F., *J. Physiol.*, 1935, **85**, 502.

⁴ Heller, H., *J. Physiol.*, 1937, **89**, 81.