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Ineffectiveness of Adreno-Cortical Preparations in Standardized Hemorrhagic Shock.*

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In our opinion, the prophylactic or curative action of adrenocortical preparations in shock has not been tested under sufficiently controlled conditions, either experimentally or clinically. In order to do so experimentally, it is highly important to have a procedure by which irreversible shock can be produced simply and with reasonable constancy.

Standardized Hemorrhagic Shock. Having previously established that irreversible circulatory failure after extreme hemorrhage is conditioned not by the volume of blood lost, but by the degree and duration of the hypotension, Werle and Wiggers¹ recently surveyed 74 experiments and concluded that an initial period of moderate hypotension (ca. 50 mm Hg) lasting 90 min, followed by a subsequent period of drastic hypotension (ca. 30 mm) lasting 45 min, generally resulted in irreversible circulatory failure. They were not certain, however, that these represented minimal figures.

We have systematically explored this method, establishing a number of refinements in technic, and find that these represent about the minimal intervals which produces irreversible hemorrhagic shock in about 85% of dogs.

If adreno-cortical preparations are beneficial in shock, animals primed with these preparations and/or treated with them during the course of an experiment should better withstand such periods of moderate and drastic hypotension. Since reputed benefit is supposedly exerted on minute vessels, and since duodenal congestion and hemorrhage and subendocardial hemorrhages were the only observable evidences of possible capil-

lary damage, it would also be anticipated that such changes would be prevented.

Since it was questionable as to which of the substances isolated from the adrenal cortex might prove potent, it seemed desirable to limit our studies to preparations of the whole cortex. Three preparations presumably potent in maintaining adrenalectomized dogs were used: (1) Parke Davis' experimental preparation containing 40 g of fresh cortex per cc. (2) Dr. Kendall's preparation (735-736) containing 150 g of fresh cortex per cc and (3) an Upjohn Co. preparation containing 2.5 rat units per cc. Some animals were given 10 cc intramuscularly late during the day preceding an experiment, and all received 10 to 22 cc at different times during the course of the experiments.

Results. For comparison, 2 new series of animals were studied with improved technic. Of 17 untreated dogs, only 4 or 23.5% recovered on reinfusion of the withdrawn blood, and failed to show duodenal or subendocardial changes at autopsy. Of 20 animals treated with adreno-cortical preparations, 5 or 25% recovered, after the same experimental procedure. These differences are not significant in view of the facts that the course of dynamic events in dogs that died were not different from those of untreated animals, and that the congestive, edematous or hemorrhagic changes of the duodenal mucosa were often more intense than in untreated animals.

These results confirm those recently reported² in fulminant shock in a heart-lung-dog preparation. They fail to support the claims that adreno-cortical extracts exert a preventive or remedial influence in hemorrhagic shock.

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¹ Werle, J. M., and Wiggers, C. J., *Proc. Soc. Exp. Biol. and Med.*, 1942, **49**, 604.

² Wegria, R., Guevara-Rojas, A., and Wiggers, C. J., *Am. J. Physiol.*, 1943, **138**, 212.