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Observations on Hemodynamic Effect of Epinephrine in Unanesthetized Dog.

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The recent study by Luckhardt and Koppányi[1] on the hemodynamic action of subcutaneously injected epinephrine shows in a most striking way the influence of anesthetics upon the vascular response to this agent. They found that a pressor response was not readily obtained in animals under barbital after massage of the injected area, while good responses were obtained under paraldehyde. Ether was found to diminish or entirely suppress the pressor response, when administered by inhalation, and, when injected intravenously in small doses. Morphine apparently had no depressing effect. It appears, therefore, that anesthetics may have an effect upon the vascular response to epinephrine *per se*, or, by altering the acid-base balance of the blood.[2] As most of the previous work[3] in determining the minimal effective amount of epinephrine in altering the blood pressure has been done on anesthetized animals, or animals with brain and cord pithed, it seemed necessary to restudy this problem on the unanesthetized animal.

Under ether anesthesia animals were prepared by transplanting the carotid artery externally to the skin. Such animals are suitable for use within 5 or 6 hours, or can be used after several days. They were then placed on the table and a carotid cannula inserted. Some animals required small doses of morphine for the procedure, others not. Injections were made into the saphenous vein from a Woodyatt pump. Pure crystalline adrenalin was received from Parke Davis and Co., and solutions were made in slightly acidified distilled water, fresh for each experiment. We found a marked deterioration in the higher dilutions if made with Ringer's solution. Control injections of distilled water were made frequently. The injections were made as a rule for a period of 2 minutes, and not more than 5 to 8 cc. of fluid injected in this time.

In the normal, unanesthetized, undrugged dog we found pressor responses as the result of the minimal effective dose. This was also true for the normal animal, slightly narcotized with morphine, or, morphine and atropine. The latter dogs, as a rule, gave a somewhat smoother tracing on which smaller variations could be detected. We

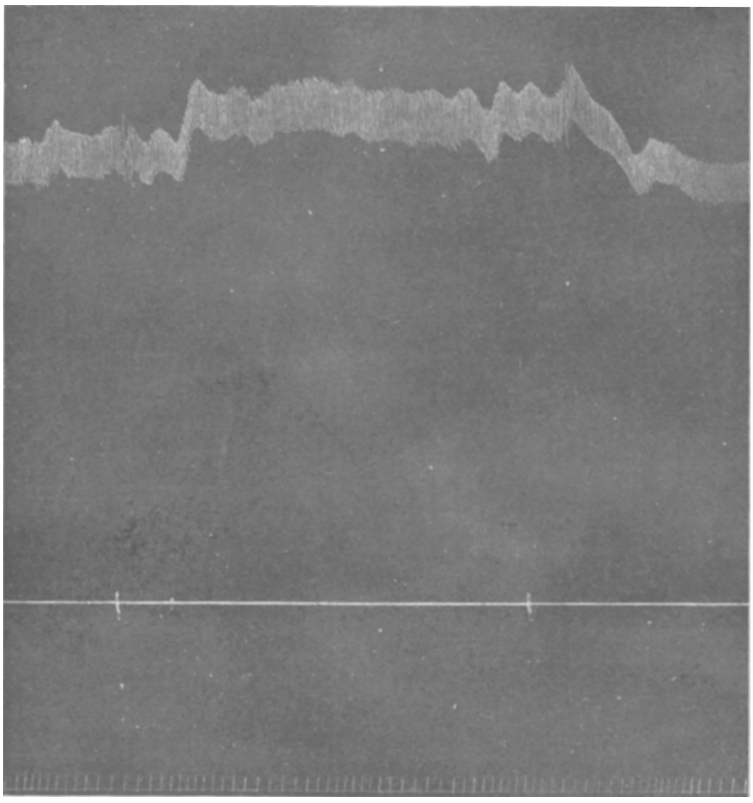

FIG. 1.

Male dog, 9 kilos, 6 hrs. after ether. Morphine Atropine narcosis. Dose: 0.18 cc. 1 to 1 million adrenalin per kilo per minute for 2 minutes.

have had pressor responses from as small amounts as 0.12 cc. of 1 to 1 million adrenalin per kilo per min. in some rather sensitive dogs, others did not give a pressor response until 0.5 cc. doses were reached. These doses are definitely under the minimal effective dose reported by Hoskins and McClure,[3] who report that the average minimal effective dose (and one which gives a depressor response) is 0.42 cc. of 1 to 1 million adrenalin per kilo per min. and that the minimal pressor amount is five times this figure. In no instance have we seen a depressor response in the unanesthetized animal. In several experiments, in which the animals were first experimented on under ether, and then allowed to recover under light morphine analgesia, we have seen depressor responses converted to pressor responses, and have then obtained pressor responses from doses which were previously ineffectual.

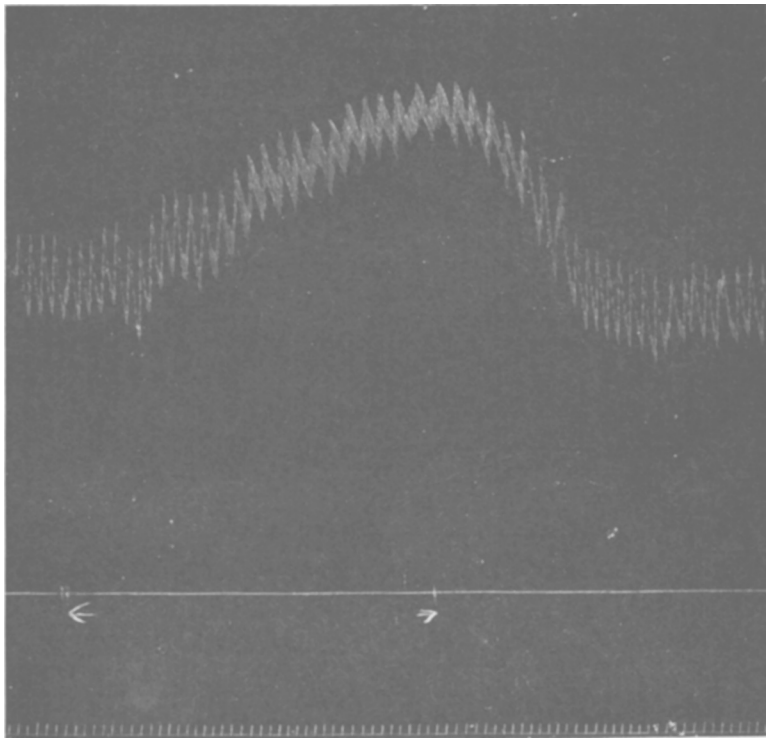

FIG. 2.

Male dog, 11 kilos. Light morphine analgesia after recovery from ether. Dose: 0.97 cc. 1 to 1 million adrenalin per kilo per minute for 2 minutes.

That these pressor responses are in reality due to epinephrine we believe to be shown by (1) the character of the response itself, (2) the absence of such responses to control injections of distilled water, and (3) a markedly augmented response seen after sensitizing the animal with cocaine.

This is a preliminary report.

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[1] Luckhardt, Arno B., and Koppányi, T., *Am. J. Physiol.*, 1927, lxxxi, 436.

[2] Burget, G. E., and Visscher, M. B., *Am. J. Physiol.*, 1927, lxxxi, 113.

[3] Hoskins, R. G., and McClure, C. W., *Arch. Int. Med.*, 1912, x, 343.