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Effect of Slowly Absorbed Epinephrine in Experimental Shock.*

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The impression is prevalent that administration of adrenalin is harmful in clinical shock.[1] Furthermore, various investigators including Freeman[2, 3] have reported that a condition which they claim is analogous to shock can be produced in experimental animals by continuous injection of large doses of adrenalin. However, other workers have been unable to produce shock by prolonged administration of this drug.[4, 5] In a recent study of traumatic shock,[6] physiologic doses of adrenalin were shown to have a more pronounced pressor action in the course of shock than before trauma.

In view of the controversy concerning the rôle of epinephrine in shock, the effect of administration of slowly absorbed epinephrine in experimental shock was investigated. Shock was produced in anesthetized cats by exposure and manipulation of the small intestine for 30 minutes. The manipulation consisted of stripping the gut forcefully throughout its length. In the control experiments this procedure produced a marked momentary spasm of the segment of gut stripped. There was considerable oozing of sanguinous fluid and the bowel became purple in color. The visible fluid loss at the time of manipulation never exceeded 5 cc. In the animals receiving adrenalin, the identical procedure resulted in less spasm, no visible fluid loss, and less discoloration of the gut.

In 14 cats, anesthetized with chloralose, 80 mg/kilo, the bowel was manipulated without aseptic precautions, using bare hands, and blood pressure was recorded with a mercury manometer from a cannula in the carotid artery. In 6 control experiments, a fall in

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1 Moon, V. H., *Shock and Related Capillary Phenomena*, Oxford University Press, 1938, p. 391.

2 Freeman, N. E., *Am. J. Physiol.*, 1933, **103**, 185.

3 Freeman, N. E., Freedman, H., and Miller, C. C., *Am. J. Physiol.*, **1941**, **131**, 545.

4 Hamlin, E., and Gregerson, M. I., *Am. J. Physiol.*, 1939, **125**, 713.

5 Van Prohaska, J., Harms, H. P., and Dragstedt, L. R., *Ann. Surg.*, 1937, **106**, 857.

6 Freedman, A. M., and Kabat, H., *Am. J. Physiol.*, 1940, **130**, 620.

blood pressure to shock level (60 mm Hg) was produced in an average of one hour and 33 minutes after beginning intestinal trauma, with a range from 35 to 195 minutes. These animals survived an average of 3 hours with a range from 47 minutes to 4 hours and 23 minutes.

Eight experiments similar to the above were performed using slowly absorbed epinephrine. The preparations used were adrenalin in peanut oil and suprarenalin-gelatin for which we are indebted to Parke, Davis & Co. and Armour and Co., respectively. The drug was administered intramuscularly in doses of 2 mg per kilo 2-3 hours preceding manipulation. Following intestinal trauma, 2 mg of epinephrine was injected every 2-3 hours until the original dose had been repeated (6-10 hours). The blood pressure at the time manipulation was begun averaged 154 mm Hg, with a range from 126-167 mm Hg. Thus "slow" adrenalin caused only a slight rise in blood pressure which was well maintained. In 6 of the 8 experiments, blood pressure was maintained at a normal level during and following manipulation of the bowel for many hours. In these experiments blood pressure fell to shock level in an average time of 8 hours and 7 minutes, with a range from 6 hours and 10 minutes to 10 hours. In 2 unsuccessful experiments with "slow" adrenalin, shock supervened in 1½ hours.

In another series of 36 experiments, intestinal manipulation was carried out aseptically, the operator wearing rubber gloves. Blood pressure was not recorded. These cats were anesthetized with nembutal, the usual dose being 25 mg/kilo intravenously. In 14 controls the average survival was 12.9 hours and the median survival was 9 hours. Except for one instance in which the cat survived for 65 hours, the survival ranged from 1 hour and 17 minutes to 17 hours and 24 minutes. At autopsy, no gross pathology was found except in the manipulated gut.

In 22 cats to which "slow" epinephrine was administered as described previously, aseptic manipulation was carried out with gloved hands. The average survival in these animals was 42.7 hours and the median survival was 27 hours. The range of survival was from 16 hours and 30 minutes to 192 hours (8 days). The longest survivals were for 8 days, 6 days, 4 days, and 2½ days. All of the "slow" epinephrine series survived longer than the average or the median of the controls. Postmortem examination revealed the cause of death in 7 animals was pneumonia, in 2 peritonitis, and in the remaining 13 cats the pathology was confined to the manipulated gut.

These experiments indicate, therefore, that "slow" epinephrine will maintain the blood pressure during and following intestinal manipulation and will increase survival 300%. This confirms the encouraging clinical results reported in shock using vasoconstrictor drugs such as adrenalin,[7] ephedrine,[8] and neosynephrine.[9] Recent experiments of Best and Solandt[10] indicate that adrenalin and other vasoconstrictor drugs may be a valuable adjunct in the therapy of some forms of shock.

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Mechanism of Intestinal Absorption of Thiamin.

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We have reported[1] that the intestinal absorption of substances whose absorption is accelerated by phosphorylation is specifically stimulated by thyroxin. Banga Ochoa and Peters[2] have demonstrated that the phosphorylated form of thiamin, cocarboxylase, is active in pyruvic acid oxidation. Therefore it seemed of interest to ascertain whether thyroxin would accelerate the absorption of thiamin from the digestive tract.

Apparently a close relation exists between thyroxin and vitamin B because the requirement for vitamin B increases when metabolism is augmented. Cowgill[3] and his coworkers have shown that the need for the vitamin B complex is greatly increased when metabolism is accelerated experimentally by the administration of thyroxin. Drill[4] has demonstrated that thiamin injections offset the loss of weight in rats caused by feeding of thyroid substance. Furthermore, Peters and Rossiter[5] have found that hyperthyroidism causes a fall in tissue

7 Mummery, J. P. Lockhart, *Lancet*, 1905, **1**, 846.

8 Johnson, C. A., *J. A. M. A.*, 1930, **94**, 1388.

9 Johnson, C. A., *Surg. Gyn. and Obst.*, 1937, **65**, 458.

10 Best, C. H., and Solandt, D. Y., *Brit. Med. J.*, 1940, **1**, 799.

1 Althausen, T. L., and Stockholm, M., *Am. J. Physiol.*, 1938, **123**, 577.

2 Banga, I., Ochoa, S., and Peters, R. A., *Biochem. J.*, 1939, **33**, 1109.

3 Himwich, H. E., Goldfarb, W., and Cowgill, G. R., *Am. J. Physiol.*, 1932, **99**, 689.

4 Drill, V. A., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 313.

5 Peters, R. A., and Rossiter, R. J., *Biochem. J.*, 1939, **33**, 1140.