

Effect of Adrenalectomy upon Survival Time of the Eviscerated Rat.

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This is one of a series of studies of endocrine deficiency and excess in the eviscerated rat. It was shown that removal of the adrenal glands shortens the survival of the eviscerated rat under several experimental conditions.

Methods. Male rats of the Sprague-Dawley strain were fed Purina Dog Chow. At a weight of 185 to 205 g. the inferior vena cava was ligated between the liver and kidneys to cause the development of a collateral circulation. Asepsis was preserved. When the animals reached 250 ± 2 g they were anesthetized (intraperitoneal injection of 18 mg of cyclopentenyl-allyl-barbituric acid sodium) and eviscerated.¹ The vascular supply of the adrenals and the kidneys was ligated and these organs removed at the time of evisceration.

The temperature of the room was 75° to 78°F and the humidity 30 to 35% of saturation. Crystalline zinc insulin (Lilly) was given to some of the animals (Exp. 3 and 4). It was injected into the saphenous vein of the right hind leg with an initial dose of 4 units and a subsequent steady rate of 40 units per 24 hours by means of a continuous injection apparatus. Injections were started within 2 minutes following removal of the liver. Cessation of heart beat was the criterion used to judge the time of death.

Experiments and Results. Ten adrenalectomized and 10 nonadrenalectomized rats were studied in each experiment. Comparisons of adrenalectomized and nonadrenalectomized animals were always made simultaneously on pairs.

In Exp. 1 (kidneys intact, no insulin) the nonadrenalectomized animals survived an average of 870 minutes with a range of 535

to 1467, and the adrenalectomized an average of 361 minutes with a range of 125 to 724 minutes.

In Exp. 2 (nephrectomized, no insulin) the nonadrenalectomized animals survived an average of 183 minutes with a range of 152 to 222, and the adrenalectomized an average of 139 minutes with a range of 67 to 175.

In Exp. 3 (kidneys intact, insulin) the nonadrenalectomized rats survived an average of 86 minutes with a range of 65 to 123, and the adrenalectomized an average of 72 minutes with a range of 57 to 99.

In Exp. 4 (nephrectomized, insulin) the nonadrenalectomized rats had an average survival of 76 minutes with a range of 64 to 85, and the adrenalectomized an average of 61 minutes with a range of 43 to 70 minutes.

In 39 of the 40 pairs of rats studied in these experiments the adrenalectomized animal survived a shorter period than its nonadrenalectomized control.

Discussion. The study of the effect of hormone deficiency and excess upon short survival times may, as in the present experiment, provide one index of the time required for hormonal effect.

It was previously known that either nephrectomy² or the administration of insulin³ hastens the onset of hypoglycemia and death of the eviscerated rat. In these experiments it was found that the survival time of the eviscerated-nephrectomized rat is decreased still further by the injection of insulin. All of the animals dying under these conditions show marked hypoglycemia, and die with convulsions and respiratory failure. In each case the symptoms can be prevented and survival greatly prolonged by the administration of glucose.

¹ Ingle, D. J., and Griffith, J. Q., Chapter 16. *The Rat in Laboratory Investigation*, J. B. Lippincott Co., Philadelphia, 1942.

² Reinecke, R. M., *Am. J. Physiol.*, 1942, **136**, 167.

³ Ingle, D. J., and Sheppard, R., *Endocrinology*, 1945, **37**, 377.

The presence or absence of the adrenal glands modifies the survival of the eviscerated and the eviscerated-nephrectomized rat either with or without insulin. This effect of adrenalectomy can be observed within 2 hours following operation. The data do not permit a differentiation between the relative importance of the adrenal medulla and the adrenal cortex in effecting the survival of the

eviscerated rat.

Summary. The survival of the eviscerated rat is shortened by either nephrectomy or insulin. Insulin shortens the survival of the eviscerated-nephrectomized rat. Adrenalectomy at the time of evisceration shortens the survival of the eviscerated and eviscerated-nephrectomized rat either with or without insulin.

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Enhancement and Depression of Neuromuscular Transmission by Intra-arterial Injection of Potassium Chloride in the Dog.

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Rosenblueth and Cannon¹ observed that intra-arterial injection of KCl, during indirect stimulation of muscle in the cat at a high frequency, produced marked depression of muscle tension. More recent studies^{2,3} have shown that intraperitoneal injection of KCl improved neuromuscular transmission in the rat and that intra-arterial injection of KCl in the nerve-muscle preparation from the frog first augmented and then depressed neuromuscular transmission. The present paper is concerned with the effect of varied rates of intra-arterial injection of KCl on the development and maintenance of muscle tension during stimulation of the nerve at a high frequency. Nine dogs anesthetized with sodium barbital were used in the experiments. Both *Triceps surae* were prepared as previously described for the rat.² Spring levels were used for the recording of muscle tension. The muscles of each leg were stimulated simultaneously through the cut sciatic nerves with electrodes connected in parallel and led from a Thyatron stimulator. The stimulus strength was about 6 times threshold

and the frequency of stimulation was 275 to 300 shocks per second. The duration of stimulation was usually 5 or 10 seconds with an equal interval of rest between periods of stimulation. In some experiments stimulation was continuous during the period of injection. In a few experiments the muscles were stimulated with single shocks during the period of injection. Injections were made into the femoral artery. Two rates of injection were employed: slow, 2 to 3 mg of KCl (1.12% solution) per second; fast, 15 mg of KCl (4.2% solution) per second.

Results. During indirect stimulation at 300 shocks per second the peak of tetanic tension was followed immediately by a rapid decline of tension to a much lower level which was either maintained or slightly increased during continued stimulation (Fig. 1, 1A). Slow injection of KCl gradually reduced the rate and the extent of decline of tension in the perfused muscles during successive periods of stimulation. The maximal enhancement of tetanic tension was attained approximately one minute after the beginning of injection (Fig. 1, 1B). In the contralateral muscles, not subjected to KCl perfusion, little change in the tension curve occurred during the same interval (cf. 2A and 2B of Fig. 1). By the end of 2 minutes of slow injection

¹ Rosenblueth, A., and Cannon, W. B., *Am. J. Physiol.*, 1940, **130**, 205.

² Walker, S. M., *Am. J. Physiol.*, 1947, **149**, 7.

³ Walker, S. M., and Laporte, Y., *J. Neurophysiol.*, 1947, **10**, 79.