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Influence of Traumatic Shock on Blood Sugar of Adrenalectomized Rats Treated with Adrenal Cortical Extract.*

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In a previous communication,[1] we called attention to the fact that local trauma exerts a pronounced influence on the sugar metabolism of tissues. We found that the venous blood coming from a damaged area is always much poorer in glucose than is the venous blood of a non-traumatized area in the same animal. This appeared all the more surprising since the systemic blood sugar is usually very high in traumatic shock. Further experiments showed that in adrenalectomized animals, whose resistance is low, traumatic shock is not accompanied by a rise in the systemic blood sugar, and indeed often causes hypoglycemia. These observations led us to conclude that disturbances in carbohydrate metabolism play a more important rôle in the pathogenesis of shock than is generally believed. It became evident, furthermore, that the adrenal cortical hormones exert a pronounced influence on sugar metabolism during the shock syndrome.

It is well known that adrenal extracts with corticoid hormonal activity† do not significantly influence the blood sugar of normal animals, although they are highly active in restoring to the normal level both the hypoglycemia of partially hepatectomized or insulin-treated and the hyperglycemia of adrenalin-treated animals.[2,3] In these cases, as well as in the hypoglycemia caused by adrenal insufficiency, the corticoid hormones appear to be stabilizers of the blood sugar, merely maintaining the glucose concentration at the normal level.

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1 Selye, Hans, and Dosne, Christiane, PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 143.

† The term "corticoid activity" instead of adrenal cortical hormone-like activity is used here in agreement with the recently introduced terminology of the steroid hormone actions.[4]

2 Selye, Hans, and Dosne, Christiane, PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 580.

3 Selye, Hans, and Dosne, Christiane, *Am. J. Physiol.*, 1940, **128**, 729.

4 Selye, Hans, *Nature*, 1941, **148**, 84.

It appeared of interest, therefore, to determine the possible rôle played by the adrenal cortex in the production of the characteristic shock hyperglycemia.

The following experiment appears to throw some light on this problem. Eighteen adult male albino rats weighing 138 g on the average, were adrenalectomized. During the 3 days following the operation, they were given "Purina" *ad lib.* and 0.9% NaCl solution instead of drinking water. On the third day, the saline solution was replaced by tap water and the animals were fasted for 16 hours. At the end of this period, the blood sugar of these animals as well as that of 6 intact but similarly fasted controls was determined (tail blood, Somogyi-Hartman-Schaffer method). After this the rats were subdivided into 4 groups of 6, 3 of these groups consisted of adrenalectomized and one of intact animals. In 2 groups of adrenalectomized animals, surgical shock was produced by crushing the abdominal muscles, the stomach and the cecum with a hemostat. Care was taken to produce the same degree of trauma in each case. One of these 2 groups, as well as the intact and adrenalectomized but not traumatized animals, were treated with 3 ml of an adrenal-cortical extract containing 1 Selye-Schenker[5] unit in 0.01 ml. This amount was administered subcutaneously in three 1 ml doses, the first injection being made 30 minutes before crushing the tissues in order to ascertain that a sufficient amount of corticoid hormone would be present in the circulation at the time of trauma. All animals were killed 3½ hours after the first injection and the blood was collected from the transcised jugular vein and carotid artery. Table I summarizes the results of the blood sugar and hemoglobin determina-

TABLE I.

Effect of Corticoid Extract on Traumatic Shock in Adrenalectomized Rats.

Treatment	Adrenalectomized and corticoid-treated	Adrenalectomized and traumatized	Adrenalectomized, traumatized and corticoid-treated	Corticoid-treated intact
Body weight	138 (128-151)	139 (125-152)	138 (124-153)	138 (128-148)
Hemoglobin	11.6 (11.0-12.5)	17.5 (16.6-18.4)	14.6 (14.0-15.2)	8.6 (8.1-9.2)
Blood sugar (before)	63 (54-71)	64 (58-71)	63 (54-71)	77 (67-92)
Blood sugar (after)	80 (75-83)	59 (50-67)	108 (83-124)	76 (67-83)

[5] Selye, Hans, and Schenker, Victor, PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 518.

tions, the former in mg, the latter in g/100 ml of whole blood.

It appears that the high dose of our potent adrenal cortical extract failed to alter the blood sugar level in the intact animal. In the adrenalectomized but not traumatized rat, it merely restored the low initial blood sugar to the normal level. This confirms previous observations showing that corticoid hormones are unable to raise the blood sugar above normal under these experimental conditions. It shows, furthermore, that our extracts did not contain any significant amount of adrenalin. In the traumatized adrenalectomized animals, the blood sugar did not show the usual hyperglycemia which is caused by a similar degree of trauma in the presence of the adrenals. Indeed the average blood sugar declined slightly after the intervention. On the other hand, the corticoid hormone treated adrenalectomized rats developed a distinct hyperglycemia (more than 40 mg % on the average) during the development of traumatic shock. That the trauma was sufficiently severe to cause shock was evident both from the clinical condition of the animals and from the rise in blood hemoglobin shown in our table. Judged by these two criteria, the corticoid extract-treated traumatized animals were not nearly as severely damaged as the untreated traumatized controls.

It appears from these experiments that an adrenal cortical extract capable of raising the shock resistance of the adrenalectomized rat, causes a significant elevation of the blood sugar when it is given after trauma. Since neither trauma alone, nor the extract alone, were able to raise the blood sugar after adrenalectomy, it is evident that the action of corticoid hormone on the glucose concentration of the blood is in some manner modified by tissue damage. Thus traumatic shock so modifies the action of corticoid hormones that they induce hyperglycemia. This observation is equally compatible with the toxic and with the deficiency theory of shock, since the change in responsiveness may be due either to the presence of an abnormal metabolite or to deficiency in a normal body constituent.

Summary. Experiments in the rat indicate that trauma fails to elicit the usual hyperglycemia in the absence of the adrenals. Active corticoid hormone preparations restore the low blood sugar of adrenalectomized animals to normal, but do not raise it above this level, nor do they cause hyperglycemia in intact animals. If such extracts are administered to adrenalectomized rats during traumatic shock, they cause a significant rise in the blood sugar concentration and at the same time increase shock resistance. It appears that the metabolic changes elicited by extensive tissue damage alter the action of adrenal cortical hormones on the blood sugar.

Since lactic acid production is increased in traumatic shock[6] and corticoids raise the blood sugar only in the presence of the liver,[3] it is tempting to assume that in shock, the blood sugar decreases in the absence of the adrenals because the lactic acid produced fails to be resynthesized into glucose. If, on the other hand, carbohydrate-metabolism-active corticoids are administered, the blood sugar can be raised above normal by resynthesis of the excess lactic acid. In any case, these experiments give further support to the assumption that changes in carbohydrate metabolism play an important part in the pathogenesis of the shock syndrome.

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Gas Gangrene-Toxin Production in Gelatin-Thioglycollate Medium.*

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In a recent note, Reed, Orr and Baker[1] showed that good yields of *Cl. welchii* toxin were produced in a simple gelatin-peptone medium. Since that work was done a further simplification of the medium has been found to give larger and more consistent yields of both hemotoxin and lethal toxin by the 4 principal gas gangrene species: *Cl. welchii, Cl. septicum, Cl. novyi* and *Cl. sordellii.*

1. This simplified medium was based on the observation of Koser, Chinn and Saunders[2] that certain brands of gelatin support growth of many of the more exacting aerobic species.

The growth of several species of the genus *Clostridium* was tested in a medium in which gelatin provided the only source of nitrogen. Four brands were tried. Five percent concentration of the 4 gelatins were dissolved in the following salt-sugar solution:

[6] Dosne, C., Proc. of the 7th Annual Meet., Canad. Physiol. Soc., Montebello, October, 1941.

* Part of an investigation aided financially by the Canadian National Research Council.

[1] Reed, G. B., Orr, J. H., and Baker, M. C., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 620.

[2] Koser, S. A., Chinn, B. D., and Saunders, F., *J. Bact.*, 1938, **36**, 57.