54. PROTEIN CATABOLISM AND PROTEIN SPARING UNDER ADRENALINE

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It has been known for many years that a subcutaneous injection of adrenaline is followed by a rise in O_2 consumption [La Franca, 1909]. Views are not unanimous regarding the nature of the foodstuffs oxidized to furnish the additional calories. To Cori [1931] it appears that under the influence of adrenaline, although the oxidation of carbohydrate is increased a relative suppression of the oxidation of carbohydrate occurs in the intact animal, even in the presence of a carbohydrate plethora, with the result that more than half of the extra calories are supplied by the oxidation of fat [Cori & Cori, 1928]. It is clear, however, from recent work on the isolated heart by Cruickshank & Startup [1934] and by Bogue *et al.* [1935] that the heart under adrenaline uses more O_2 and that the increased O_2 is used preferentially for the combustion of glucose, provided that sufficient glucose is present in the perfusing fluid. Moreover, Paton [1903] and Underhill & Closson [1906] found an increased breakdown of protein under adrenaline when the calorie value of the diet was inadequate.

The fact that adrenaline increases the blood sugar whereas insulin decreases it shows that these hormones have opposing effects as judged by the behaviour of the blood sugar, but the different behaviour of the blood sugar under adrenaline and insulin does not justify the conclusion that the metabolic actions of adrenaline and insulin are necessarily antagonistic as far as the utilization of carbohydrate is concerned.

The administration of carbohydrate lowers protein catabolism in the normal organism. This can readily be shown by giving carbohydrate to a normal fasting animal when the excretion of N promptly decreases. On the other hand, the excretion of N is not lessened by giving carbohydrate to a fasting depancreatized animal. Evidently the protein-sparing action of carbohydrate is linked in some way with the physiological role of insulin. If then adrenaline increases the breakdown of protein in the normal organism but the concomitant administration of carbohydrate prevents this, either largely or entirely, obviously adrenaline does not prevent the protein-sparing action of carbohydrate and so cannot be said to act strictly as an 'anti-insulin' hormone.

METHODS

A. *Experiments on anaesthetized cats*

Cats were fasted for 48 hr. and, after anaesthetization with chloralose, were given an intraduodenal injection of about 20 ml. warm water to maintain the flow of urine. After 2 hr. the bladder was emptied and the urine collected for an initial period of 3 hr. Then one of the following was given by slow

infusion into a vein during a period of 5-6 hr., different animals being used for each kind of infusion: (1) adrenaline; (2) glucose; (3) adrenaline + glucose; (4) adrenaline + glucose + insulin; (5) saline. Samples were taken at the beginning and at the end of the 5-6 hr. period for determinations of the blood sugar, liver glycogen, urine sugar and inorganic S. The rate of excretion of inorganic S under the above conditions was taken as indicating the rate of protein catabolism [Reid, 1936] in preference to that of the excretion of N, which is affected considerably by variations in the rate of urine flow. Observations were also made on previously depancreatized cats. The body temperature of the anaesthetized animals was kept constant by means of a rectal thermometer which acted as a thermoregulator for the animal table [Fuchs & Reid, 1937-8].

RESULTS

In intact fasting cats the excretion of inorganic S is increased by infusing adrenaline into a vein [Table 1 (1)].

The increase varies in general with the dose of adrenaline used, viz. 0.02-0.08 mg./kg. body weight/hr. [Table 1 (1)].

Table 1

Nature of infusion			Average % change in hourly rate of excretion of inorganic S during perfusion as compared with control period
Adrenaline mg./kg./hr.	Glucose g./kg./hr.	Insulin unit/kg./hr.	
(1) Intact cats: 6 experiments in each group			
Saline control	—	—	0
0.02	—	—	+22
0.05	—	—	+39
0.08	—	—	+77
0.05	0.30	—	+26
0.08	0.40	—	+32
—	0.26	—	-15
—	0.40	—	-22
0.02	0.40	0.32	-18
0.07	0.60	0.50	+8
(2) Previously depancreatized cats: 6 experiments in each group			
0.04	—	—	+53
0.04	0.40	—	+56
0.04	0.40	0.50	+2

Thus adrenaline increases the rate of protein catabolism in intact fasting cats.

The administration of glucose along with adrenaline lessens the expected rise in the output of inorganic S [Table 1 (1)].

Glucose, therefore, can spare protein in an animal under the influence of adrenaline.

In previously depancreatized cats adrenaline increases the output of inorganic S [Table 1 (2)] and therefore the rate of protein catabolism, but protein is spared by giving glucose + insulin though not by glucose alone.

It thus seems reasonable to conclude that adrenaline is not strictly an anti-insulin hormone because it does not suppress the ability of the normal organism to use carbohydrate to spare protein. This tentative conclusion is further tested in the following experiments on non-anaesthetized dogs.

B. *Experiments on non-anaesthetized dogs*

Two bitches were subjected during 2 years to the following regime every 2 weeks with or without the administration of adrenaline:

Ordinary feeding for 10 days adjusted so as to keep their weights nearly constant throughout.

Deprivation of food, but not of water, for 2 days.

Catheterization to empty the bladder, with a further 2 days for the collection of urine during this period, and daily feeding by stomach tube with water or glucose solution.

Analysis of the 48 hr. urines for total N, inorganic S and glucose.

When adrenaline was used, it was given subcutaneously in doses of 0.25–1.0 mg. every 3 hr. Auer & Meltzer [1916] have shown that the effects of a subcutaneous dose of adrenaline last for several hours owing to slow absorption. As judged by the behaviour of the pulse rate, body temperature etc. after subcutaneous adrenaline, this certainly appears to be the case. Tissue necrosis may occur with the larger doses used unless injected at more than one site.

Table 2

Nature of experiment	Dog B (11–12 kg.)		Dog C (15–16 kg.)	
	Total N g./day	Inorganic S g./day	Total N g./day	Inorganic S g./day
Control	2.74	0.104	3.63	0.126
Adrenaline, 0.5 mg./3 hr.	3.29	0.132	4.42	0.147
Adrenaline, 0.5 mg./3 hr. + 50 g. glucose daily	2.51	0.097	3.66	0.135
Control	2.68	0.092	3.60	0.118
Glucose, 50 g. daily	2.01	0.071	3.13	0.100
Adrenaline, 0.75 mg./3 hr. + 50 g. glucose daily	2.87	0.107	3.80	0.129
Glucose, 80 g. daily	1.90	0.065	2.61	0.077
Adrenaline, 0.75 mg./3 hr.	3.40	0.121	4.08	0.123
Control	2.50	0.080	3.43	0.108

Results

Table 2 gives the data obtained from one of the 4 anoestrous periods in each bitch. Results from periods complicated by oestrus have been excluded. It is clear that, when adrenaline is given by subcutaneous injection to fasting dogs, the urinary output of total N and inorganic S rises, indicating that under these conditions protein catabolism increases. When glucose is given by stomach tube while the animals are under the influence of adrenaline, the urinary output of total N and inorganic S is significantly lessened, so that clearly protein can be spared by carbohydrate even during the acceleration of metabolic processes by adrenaline. The urine was free from sugar except on two occasions when small losses of less than 3 g. were found. The normal fasting dog likewise can use carbohydrate to spare protein (Table 2). Therefore the protein-sparing action of carbohydrate, which appears to be linked with the physiological role of insulin, is not prevented by adrenaline. The latter, accordingly, cannot be regarded strictly as an 'anti-insulin' despite the opposing effects of adrenaline and insulin on the blood sugar.

SUMMARY

Adrenaline has been shown to increase the catabolism of protein, but protein can still be spared by giving carbohydrate, even when the metabolic rate has been raised by adrenaline. The protein-sparing action of carbohydrate appears

to be linked with the physiological role of insulin, since it is not shown under ordinary conditions by the depancreatized animal without insulin. Since the protein-sparing action of carbohydrate still functions when adrenaline is given, adrenaline and insulin do not have strictly antagonistic physiological roles despite their opposing actions on the blood sugar.

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