THE EFFECT OF HORMONES ON THE BLOOD SUGAR OF THE LOWER MONKEYS

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As we showed in our previous communications [2], the state of the carbohydrate metabolism in the lower monkeys presents certain special features distinguishing it from the carbohydrate metabolism in man. The blood sugar in monkeys depends on the experimental conditions, which evoke an orienting reaction in the experimental animals. The blood sugar falls when the investigations are repeated in stereotyped conditions because of extinction of the orienting reflex to the experimental conditions.

The character of the blood sugar curves in monkeys after oral administration of sugar depends more on the experimental procedure to which the animals are subjected than on the administration of sugar itself. In control experiments in which no sugar is given the blood sugar curves are very similar to those in experiments in which sugar is given by mouth. The height to which the sugar concentration rises in these experiments when tested repeatedly in the same monkey gradually falls as a result of extinction of the orienting reaction to the experimental conditions. If the conditions favor extinction of the orienting reaction, the monkeys display a high tolerance to the oral administration of sugar. Experiments in which glucose is injected intravenously have shown that the rate of utilization of glucose when injected by this route into monkeys is from $1\frac{1}{2}$ to 2 times greater than in man.

Several other facts also demonstrate the high intensity of intermediate carbohydrate metabolism in the monkey. I. S. Kanfor [3], for instance, showed that a very marked hypoglycemia develops in monkeys during the first day of fasting. According to Maddock [7], after total extirpation of the liver in monkeys hypoglycemia develops much more rapidly and intensively than in dogs and rabbits. After adrenalectomy in rabbits [6] an extremely low blood sugar was observed (30 mg %) by comparison with other animals, and the liver glycogen content was also low (0.07 mg %), whereas the initial concentration of glycogen in the liver reached 12% in some cases.

Meanwhile, as V. S. Asatiani [1] has shown, the blood adrenalin level in monkeys is almost identical with that in man. Accordingly, the low blood sugar of adrenalectomized monkeys could have been explained by the higher sensitivity of the monkey to adrenalin. The possibility that the sensitivity of monkeys and of other animals to hormones may differ has been proved in the case of the parathyroid hormone by Brand [5]. To raise the blood calcium concentration by 5 mg % 35 units of this hormone must be administered to a monkey, compared with 1300 units to a guinea pig.

In the present investigation the indices used to qualify the effects of adrenalin and insulin on the carbohydrate metabolism were the blood sugar concentration and the rate of utilization of intravenously administered glucose. Interest in the study of the effect of hormonal preparations on the velocity of utilization of intravenously injected glucose by the tissues is determined by the findings of A. L. Mikhnev [4] and certain other workers that adrenalin inhibits the utilization of glucose by muscle tissue.

EXPERIMENTAL METHOD

Experiments were conducted on sexually mature monkeys of the species Pavio hamadryas and Macacus rhesus. The monkeys took part in the experiments at 9:30 A.M. and on an empty stomach. In order to study the effect of adrenalin on the blood sugar, after the initial sample of blood has been taken from the cubital vein, adrenalin was injected subcutaneously in a dose of 0.1 ml of the 1:1000 solution per 1 kg body weight. The next blood samples were taken 5, 10, 15, 30, 90, and 120 minutes after the injection of adrenalin. The blood samples were preserved with potassium oxalate. The sugar was estimated by the Hagedorn-Jensen method.

Blood Sugar (in mg %) of Monkeys after the Subcutaneous Injection of Adrenalin (1 : 1000) in a Dose of 0.1 ml/kg Body Weight

Monkeys	Time (in minutes)							
	0	5	10	15	30	60	90	120
	Pavio hamadryas							
Zher	125	132	133	144	176	178	196	185
Lam	114	128	165	185	195	185	133	109
Azon	116	80	149	166	204	163	129	97
"	99	123	147	164	197	177	157	119
"	92	104	138	199	173	170	145	116
"	146	145	171	186	226	190	156	120
Chernogolovyi	92	118	121	136	150	138	111	105
"	94	107	103	128	188	118	102	86
"	108	114	152	181	206	161	130	112
Angar	128	137	147	151	231	212	191	169
"	105	98	115	147	123	98	121	101
"	90	95	106	110	125	140	130	112
Mean	108	116	137	155	180	161	142	122
	Macacus rhesus							
Sobol'	63	91	108	108	138	131	—	106
Dergach	67	134	—	139	126	84	—	54
King	97	91	—	119	125	119	—	112
"	74	83	—	128	153	108	89	83
"	87	82	—	164	196	142	109	85
Mean	78	96	—	132	148	117	—	88

In the experiments to study the effect of adrenalin on the rate of utilization of intravenously injected glucose, after the initial blood sample had been taken and the adrenalin injected subcutaneously, an intravenous injection of 40% glucose solution was given in a dose of 0.3 g /kg body weight, either immediately after the injection of adrenalin or after an interval of 30 minutes. Blood was taken from the vein as soon as the glucose had been injected, and after 10, 20, and 60 minutes. Similar experiments were conducted to study the effect of insulin on the rate of utilization of intravenously injected glucose. Glucose was injected one hour after the administration of insulin in a dose of 0.5 units/kg body weight.

EXPERIMENTAL RESULTS

It can be seen from the table that after the subcutaneous injection of adrenalin into Pavio hamadryas the blood sugar, starting from a higher initial level, attained higher values than in Macacus rhesus. In proportion to the initial value, however, the increase in the blood sugar in Macacus rhesus was greater than in Pavio hamadryas. The increase in the blood sugar (in mg %) in Pavio hamadryas and Macacus rhesus may be regarded as equal. Two hours after the injection of adrenalin the blood sugar almost regained its initial level.

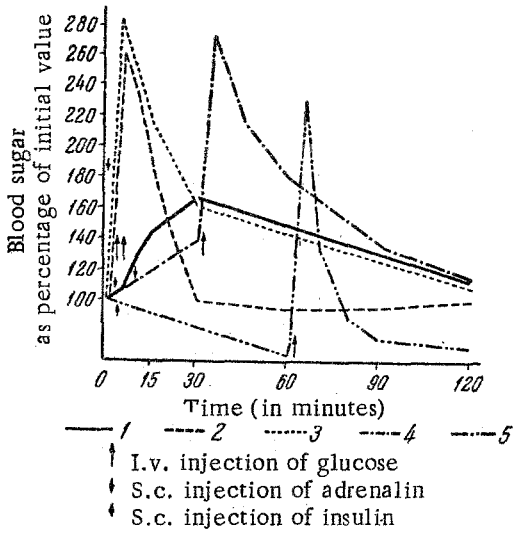

Fig. 1. Blood sugar curves in Pavio hamadryas. 1) After subcutaneous injection of adrenalin; after intravenous injection of glucose; 3) following preliminary administration of glucose, 2 minutes after subcutaneous injection of adrenalin; 4) following preliminary administration of glucose intravenously, 30 minutes after subcutaneous injection of adrenalin; 5) following preliminary administration intravenously, 60 minutes after subcutaneous injection of insulin.

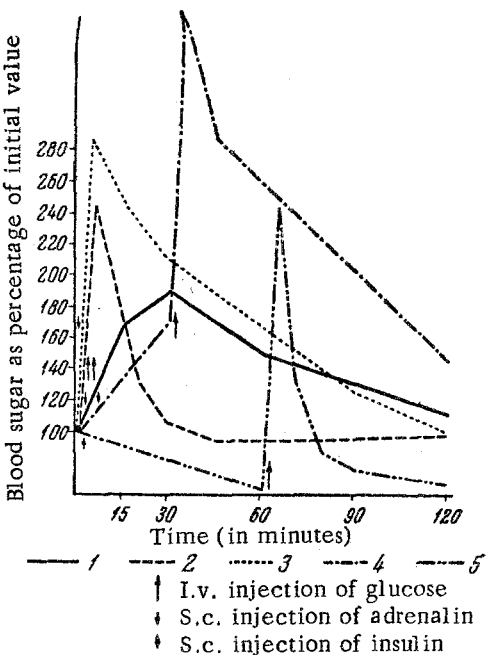

Fig. 2. Blood sugar curves in Macacus rhesus. Legend as in Fig. 1.

Attention is drawn to a slight difference between the character of the blood sugar curves in the various experiments In 8 of the 12 experiments on Pavio hamadryas the blood sugar reached its maximum after 30 minutes, in one after 60 minutes, in one after 90 minutes, and in 2 experiments 15 minutes after the injection of adrenalin. The time of onset of the maximal blood sugar varied in different experiments on the same animal. This suggests that the intensity of the reaction of the monkey to adrenalin is possibly determined by a difference in the initial functional state, the conditions and character of which were not revealed by our experiments. A different degree of hyperglycemia was observed in different monkeys and in different experiments on the same monkey.

As the experiments in which glucose was injected after the preliminary injection of adrenalin showed (Fig. 1, 2), the rate of utilization of intravenously injected glucose by the tissues brought about a return to the initial blood sugar level 1-$1^1/_2$ hours after the injection of glucose equally in Pavio hamadryas and Macacus rhesus. The injection of glucose without a preliminary injection of adrenalin was followed by a return to the initial blood sugar level

after, as a rule, 30 minutes. This fact confirms the conclusions of several writers [4] that adrenalin diminishes the glucose utilization by the body tissues. These conclusions were based on organ perfusion experiments and on the fact that an arteriovenous difference in the blood sugar is present in association with the action of adrenalin. Consequently, the hyperglycemia developing under the influence of adrenalin is due, not only to the mobilization of the liver glycogen, but also to a decrease in the rate of transfer of glucose from the blood into other tissues.

If a preliminary injection of insulin was given, the velocity of utilization of intravenously injected glucose restored the normal blood sugar level 20 minutes after the injection of glucose. The fall in the blood sugar one hour after injection of insulin was the same in Pavio hamadryas and Macacus rhesus.

According to A. L. Mikhnev [4], the hyperglycemia in man after subcutaneous injection of adrenalin reached its maximum in most cases after 60 minutes, and after 2½ hours the blood sugar level almost regained its initial value. In our experiments on monkeys, the subcutaneous injection of adrenalin caused a more rapid rise in the blood sugar and a more rapid return to the initial values.

The rapid increase in the hyperglycemia in monkeys may evidently be interpreted as the result of an increased sensitivity of the carbohydrate metabolism of the monkey to adrenalin. The earlier fall in the blood sugar level in the monkey than in man to its initial level is possibly the result of the more rapid inactivation of the injected hormone. The inhibition of the utilization of the intravenously injected glucose at the height of the adrenalin hyperglycemia is evidence of the continuing action of adrenalin 30 minutes after its administration. The inhibition of the utilization of intravenously injected glucose suggests a possible role of adrenalin as an inhibitor of the hexokinase reaction.

We consider that the method of intravenous glucose loading may be used as a test of the sensitivity of the carbohydrate metabolism of the monkey to hormones.

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