LIPOLYTIC ACTIVITY OF THE LIVER AND LUNGS IN EXPERIMENTAL ALLOXAN DIABETES

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The results of clinical investigations[3, 4, 6, 8] have revealed an increase in the concentration of the higher free nonesterified fatty acids (NEFA) in the blood of patients with diabetes mellitus. This increase may be correlated with findings indicating increased lipolysis in adipose tissue in diabetic subjects.

Experimental investigations by N. K. Davtyan have shown that in alloxan diabetes the lipolytic activity of the adipose tissue is not increase in every case. This may be explained by the fact that, as a result of the disturbance of the conversion of carbohydrates into lipids in experimental diabetes in animals, the amount of adipose tissue is sharply reduced, and the intensity of lipolysis in the reduced adipose tissue is lowered [2]. However, the addition of glucose to adipose tissue, which in normal animals causes a considerable depression of lipolysis, hardly produces this effect. In vivo, therefore, when glucose is present in the medium bathing the adipose tissue, the lipolytic activity of the latter is higher in diabetic than in normal animals.

The object of this investigation was to determine whether the increased concentration of NEFA in the blood is also the result of changes in the lipolytic activity of the liver and lungs, organs playing an important role in the processes of lipid metabolism [1].

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing between 150 and 250 g, kept on the ordinary laboratory diet, and receiving no food for 18 h before the investigation. Altogether 58 rats with experimental alloxan diabetes and 23 control rats were used. Alloxan diabetes was induced by giving the rats 1 or 2 subcutaneous injections of a 2.5% solution of alloxan in phosphate-citrate buffer (pH 4.2) in a dose of 15 mg alloxan/100 g body weight. The rats with established alloxan diabetes were sacrificed at intervals of 9-13, 18-22, 29-33, and 72-88 days from the moment of development of diabetes, and also 3-5 days after its "spontaneous" termination and normalization of the glycemia and glycosuria.

Normal animals, and also animals not developing diabetes after receiving injections of alloxan, were used as controls.

In all the animals determinations were made of the NEFA concentration in the serum and the lipolytic activity of the liver and lungs. The serum NEFA concentration was determined by Dole's method [5] and the lipolytic activity of the liver and lungs by the intensity of hydrolysis of Twee-60 (stearic ester of polysorbitol). The extracted liver and lung tissue was dipped in ice-cold physiological saline, dried with filter paper, and minced on a glass plate. A sample of mince weighing 185-200 mg was incubated in a medium consisting of: Twee-60 2.5%, serum albumin 1% in M/15 Sorensen's phosphate buffer (pH 7.4), in the water bath of a Warburg's apparatus (37°, 120 oscillations/min) for 150 min. The lipolytic activity was expressed as the difference between the amount of NEFA contained in 1 ml of medium before and after incubation (in meq/g/liter).

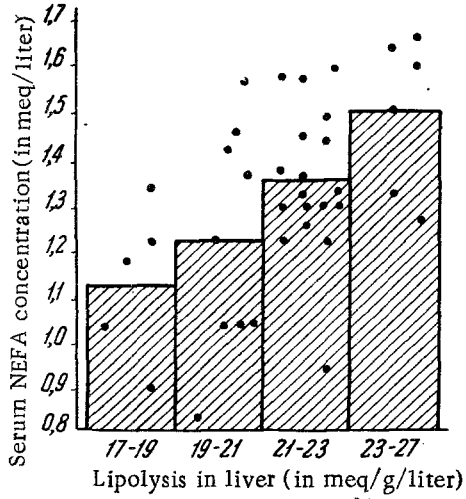
EXPERIMENTAL RESULTS

In the rats with alloxan diabetes, at all stages of the investigation the serum NEFA concentration was raised (see table). This level was maintained for 3-5 days after "spontaneous" termination of the diabetes and normalization of the blood sugar and glycosuria.

Intensity of Lipolysis in the Liver and Lungs and Serum NEFA Concentration in Rats with Experimental Alloxan Diabetes. Mean Data (M± m)

Experimental conditions	No. of animals	Blood sugar (in mg%)	Lipolysis (in meq/g/liter)		Serum NEFA (in meq/liter)
			liver	lungs	
Control (normal)	19	—	18,6±0,3	14,9±0,4	0,89±0,03
Control (after injection of alloxan but without diabetes)	4	111±17	18,0±0,9	14,5±0,9	0,87±0,02
Diabetes (9-13 days)	16	358±30	22,2 0,8 P 0,001	18,3±0,6 $P<0,001$	1,48 ± 0,05 P 0,001
(18-22 days)	6	223±24	20,6±0,6 $P=0,02$	16,9±1,1 P 0,05	1,15±0,07 $P=0,002$
(29-33 days)	11	306±23	19,5±0,7 $P>0,05$	15,8±0,6 $P>0,05$	1,38 0,06 $P<0,001$
(72-88 days)	9	308±47	20,8±0,5 $P=0,02$	16,9±1,1 $P<0,05$	1,21±0,02 $P<0,001$
After termination of diabetes*	16	105±9[1]	20,0±0,3 $P<0,001$	14,6±0,25	1,20±0,04 $P<0,001$

* On 3rd-5th day after normalization of blood sugar and glycosuria.



Serum NEFA concentration and intensity of lipolysis in the liver in rats with experimental alloxan diabetes.

The lipolytic activity of the liver was increased in the animals with diabetes lasting 9-13, 18-22, and 72-88 days, and also in the animals in which the diabetes had terminated "spontaneously," on the 3rd-5th day after disappearance of the hyperglycemia and glycosuria. In the group of animals with diabetes lasting 29-33 days, the lipolytic activity of the liver was unchanged (its increase was not statistically significant). The lipolytic activity of the lungs was increased in the animals with diabetes of short (9-13 days) and long (72-88 days) duration. The increase in the lipolytic activity of the lungs at the other periods was not statistically significant. In the animals which had recovered from diabetes the lipolytic activity of the lungs was within normal limits.

A definite relationship was noted between the degree of the increase in the serum NEFA concentration and the degree of increase of lipolysis in the liver (see figure). Hence, in certain stages of the development of alloxan diabetes, an increase in the lipolytic activity of the liver and lungs was observed. The results indicate that the increase in the serum NEFA concentration in experimental alloxan diabetes may result from release of these compounds from the liver and, to some extent, from the lungs.

SUMMARY

In experimental alloxan diabetes (lasting 9-13, 18-22, 29-33, 72-88 days) induced in rats there was an increased content of NEFA in the blood serum.

At different stages of the development of experimental diabetes there was an intensification of lipolytic activity in the liver and lungs (substrate: Tween-60) which evidently served as one cause of the increased NEFA content in the blood serum.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
