Between 9 and 12 months degenerative and necrobiotic changes affected all types of cells and were manifested chiefly as intensive vacuolation of the cytoplasm, amounting in some cases to baloon degeneration, karyorrhexis, and lysis followed by cytolysis. After staining by Van Gieson's method (with picrofuchsine) there was a clear tendency toward atrophy of the mucosa, evidently linked with denudation of the reticular basis of the glands as the result of death of functionally active cells.

Analysis of the results thus demonstrated the development of considerable inhibition of gastric secretory function, as shown by absence of free hydrochloric acid in the basal secretion. According to the results of maximal histamine stimulation, there was a clear decrease in excitability of the gastric glands with the development of a hyporeactive type of gastric secretion. The causes of these changes were revealed by morphological investigations. They were severe atrophy of the gastric glands, disturbances of the proportions of their cellular composition, and the appearance of functionally defective chief and accessory cells.

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EFFECT OF STREPTOZOCIN ON TEMPERATURE VARIATIONS IN RATS

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According to recent reports in the literature, the blood sugar level is not a perfect criterion for determining the state of diabetics: normoglycemia can coexist with ketonuria, debility, malaise, and worsening of retinopathy [5, 6, 10]. There is thus the need to discover new tests for the diagnosis and evaluation of the state of diabetics. At the present time, the state of these patients is determined on the basis of a whole range of parameters, both chemical and physical [1, 3, 4, 7, 8]. Physical methods of investigation are attractive because they may be noninvasive. One such method is thermometry. It reflects the state of the body's energy metabolism. In diabetes this type of metabolism can be assumed to be disturbed because 70% of it is maintained at the expense of carbohydrates [9]. This hypothesis is supported by observations showing changes in body temperature in hypo- and hyperglycemic coma [8]. It is also reasonable to expect disturbance of temperature reactions to various procedures.

The aim of this investigation was to test experimentally the effect of a disturbance of carbohydrate metabolism on the time course of the temperature reactions of the body at rest and during variations of the ambient temperatures. To do this, the difference of the core temperature of the body and the temperature of its surface layers was measured over a period of time at room temperature, and during cooling and heating of the body, under normal conditions and after administration of streptozocin.

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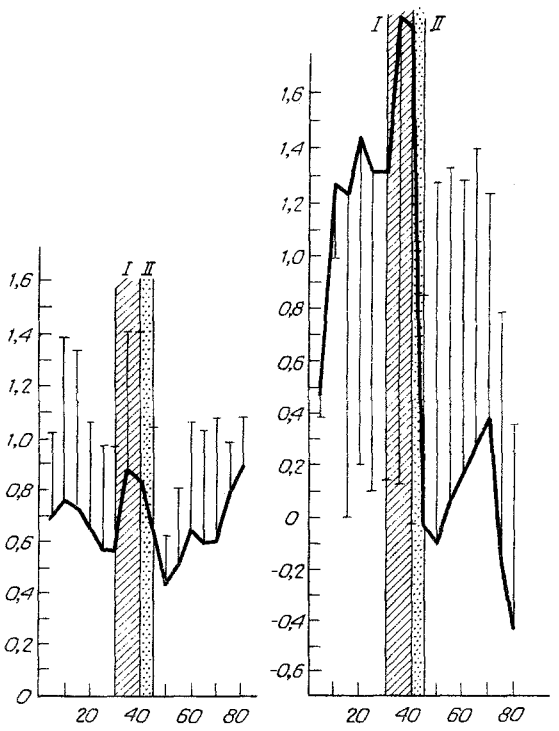

Fig. 1. Dynamics of changes in difference between core and surface body temperature (Δt) of normal rats. Here and in Fig. 2: I) Period of cooling, II) period of heating; abscissa, time (in min), ordinate, Δt, °C.

EXPERIMENTAL METHOD

Experiments were carried out on four rabbits and eighteen male laboratory albino rats weighing 200-220 g. Of this number, four rabbits and six rats were used to develop a technique of measuring temperature and establishing the values of the body temperature in the normal state and at rest. The remaining 12 rats were divided into two groups. In group 1, intact rats were studied under the following conditions: the rat was placed in special elastic restrainers, which allowed it to make limited movements (to avoid hypodynamia), the animal was observed for 30 min, then cooled for 10 min in a continuous flow of air (21°C), after which it was heated for 5 min in a flow of air at 50°C, then observed again at room temperature for 35 min (until the original parameters were restored). In group 2 the rats were tested in accordance with the same scheme before and after administration of streptozcin in a dose of 75 mg/kg body weight. The streptozocin model of diabetes is generally accepted and it reproduces sufficiently accurately type I diabetes, such as is found in man [2].

Temperature readings were taken every 5 min (449 measurements). The body temperature was measured by means of an IL 446455F catheter (to measure the rate of the blood flow by the change in body temperature), connected through a resistance bridge to a type III 43-13 digital voltmeter. The catheter was introduced into the rats' rectum so that measurements were made at a depth of 4 cm (core temperature) and 0.5 cm (surface layers). The temperature difference (Δt) was obtained from the voltmeter by means of an electronic device. The parameters were recorded in some experiments on tape by an N31 automatic writer. The animals were cooled and heated under control of a type LCK digital electronic thermometer (Hong Kong). The blood sugar was determined in the animals' venous blood by means of "Dextrostix" strips and an "Exan-1" express glucose analyzer. The numberical results were subjected to statistical and correlation analysis.

EXPERIMENTAL RESULTS

Preliminary experiments showed that the absolute values of the core and superficial temperature varied during the 24-hour period between limits of up to ±1°C, and their difference Δt by a rather smaller amount, up to 0.5°C. However, these fluctuations, like the original levels in different animals, are highly individual. For instance, the value of dis-

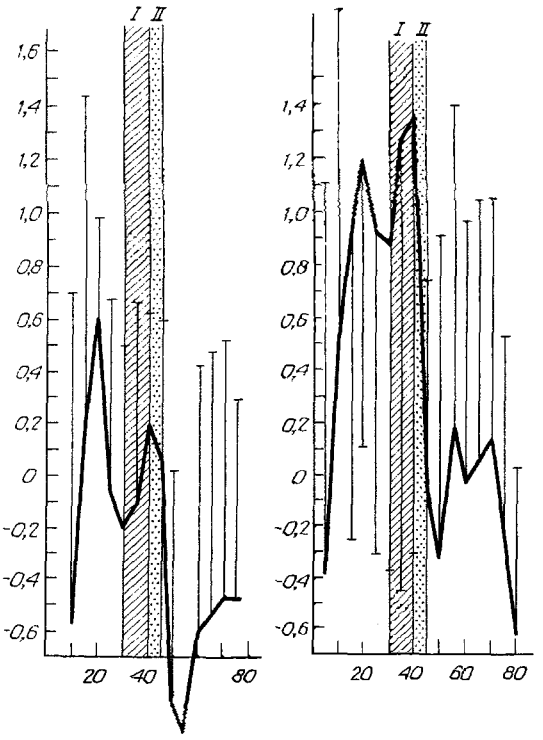

Fig. 2. Dynamics of mean changed in rats receiving streptozocin in a dose of 75 mg/kg 3 days before measurement.

persion in healthy rats tested in the same state of food satiation and at the same time of day, in the same ambient temperature (variations between limits of ±0.5°C), varied from 0.3 to 0.6°C (Fig. 1).

The response of healthy rats to cooling was on the whole consistent: there was a tendency for it to increase (Fig. 1). However, different versions were noted: an increase only, an increase followed by a fall of Δt, and fall of Δt followed by an increase, although admittedly, only amounting to 0.1-0.15°C. Subsequent heating of healthy animals led on the whole to reduction of Δt from 0.4 to 1.0°C in most cases. After heating, as a rule, Δt continued to fall for a short time, and later, it returned with fluctuations to its original level in the course of 20 min, and then to exceed it after 30-40 min, but not significantly. In this case also, the reaction of the animals was highly individual, as shown by the high values of dispersion. On average Δt remained all the time within its initial limits. On repetition of the test on individual animals no changes in the response recorded previously in them could be detected.

Considering the individual nature of the temperature curves, in the last series of experiments involving creation of an experimental model of diabetes, the rats were tested before and after receiving streptozocin. Control determination of the blood sugar in these animals enabled them to be divided at once into two groups: normoglycemic and hyperglycemic. As the results in Fig. 2a, b show, in both groups both the level and the intensity of the temperature reactions were changed compared with the normal state. Initial levels of Δt also were changed. While normoglycemia remained, the original value of Δt and its scatter were observed to increase. During cooling, Δt increased. This was followed by a sharp fall of Δt, which continued into the heating period. Later Δt remained below its initial values (Fig. 2a). In the hyperglycemic animals, the initial Δt was low and remained at that level when the ambient temperature conditions changed (Fig. 2b). On average, rats receiving streptozocin differed from the intact animals in the width of the individual variations of Δt, changes in this parameter during cooling and heating of the body, and also its decrease in the recovery period, which was proportional to the blood sugar level (Fig. 2c).

Analysis of the results indicates that in healthy animals the difference between the core and surface body temperature is a variable (oscillating) value, which evidently reflects the search for equilibrium between heat production and heat loss. During changes in ambient temperature corresponding variations of Δt are observed: an increase during cool-

ing (more heat is produced), a decrease during heating (heat production is reduced). Under all conditions, however, fluctuations of Δt and of the core temperature remain within limits not differing significantly from the original values. After injection of streptozocin the reaction of the animal was disturbed. Irrespective of the presence or absence of hyperglycemia, deviations of the temperature reactions from the normal oscillations are present. Moreover, a marked after-reaction is observed, in the form of preservation of the deviation of Δt for a long time. As a rule, under these circumstances, Δt is depressed, indicating insufficient heat production, for under those conditions, when the external temperature was restored to its initial level, Δt fell only as long as the internal temperature was falling. It can be tentatively suggested that in diabetes, in connection with the inability of the tissues to utilize glucose completely as a result of the inhibition of insulin secretion by streptozocin, the body is unable to maintain the temperature balance. As regards differences in the reactions observed under both normal and pathological conditions, they may have been caused by the fact that the state of the energy reserves and, in particular, the liver and muscle glycogen, initially may vary in different animals even if all of them are kept together.

Consequently, measurement of Δt under ordinary conditions and, in particular, during heat loading may be a valuable method of finding a disturbance of carbohydrate metabolism. This method was used in clinical practice in the investigation of 23 patients, in whom diabetes had not previously been diagnosed. In 21 of them Δt corresponded to its value in healthy individuals, i.e,. it exceeded 0.6°C, whereas in two patients Δt was below 0.6°C (0.33 and 0.49°C respectively). The fasting blood sugar of both these patients did not exceed 70 mg %. However, in a standard glucose tolerance test, a disturbance of the blood sugar curve was observed in these two patients, unlike in the others, and was expressed as an increase in the level of the maximal rise (up to 230 and 170 mg % respectively) and the duration of the hyperglycemic period (more than 2 h). In this way a latent form of diabetes was detected.

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