STATE OF THE PANCREATIC ISLETS, FETAL WEIGHT, AND GLUCOSE TOLERANCE TEST IN OFFSPRING OF MALE RATS WITH ALLOXAN DIABETES

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The body weight and morphometric parameters of the state of the pancreatic insular apparatus (the relative percentage of islet tissue, of A- and B- cells, the number of islets) in fetuses and the adult offspring of healthy female rats and male rats with alloxan diabetes were studied. No change in these parameters was found, indicating that under these conditions the genetic systems of the males are undamaged and that these lesions are not transmitted to the progeny. On the basis of these findings and of the importance of diabetes in the female in the development of insular deficiency in the progeny demonstrated previously, the role of the environment in which the fetus develops in the formation of the diabetes is emphasized.

KEY WORDS: alloxan diabetes; heredity; pancreas.

It was shown previously that the fetal mortality is increased in female rats with alloxan prediabetes and also with latent and manifest diabetes, and the weight of the fetuses is greater than that of healthy rats [1]. Morphometric features of increased activity of the B-cells of the pancreatic insular apparatus have also been found in such fetuses [3]. In individual animals born from females with alloxan diabetes, particularly in the period of sexual maturation, the spontaneous appearance of glucose tolerance tests of the diabetic type and of latent and manifest diabetes was observed [2]. These observations suggest that stimulation of the fetal insular B-cells when diabetes is present in the mother may induce damage to these cells that may remain without clinical manifestation for a long time. Only at certain periods of life and under the influence of unfavorable external conditions do disturbances of diabetic type develop in some of the animals. These disturbances may be produced by genetic factors [5] and by factors of the environment in which the fetus develops in the sick mother.

To study this problem the state of the offspring of healthy females and males with alloxan diabetes was investigated.

EXPERIMENTAL METHOD

Sexually mature male Wistar rats received a subcutaneous injection of alloxan in a dose of 170-500 mg/kg [4]. From the time of appearance of hyperglycemia and glucosuria the fasting blood sugar level (by the Somogyi–Nelson method), the diuresis, and the excretion of sugar in the urine were determined every 5-7 days. After the period of sexual maturation the diabetic males were mated with healthy females in which vaginal smears were studied every hour. Fetuses were extracted from the uterus 522 h after the

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TABLE 1. Morphometric Parameters of State of Pancreatic Insular System in Adult Progeny of Healthy Female Rats and Males with Alloxan Diabetes

Group	No. of fetuses	Relative percentage in whole parenchyma of gland			B/A	Number of islets per 10 mm² parenchyma of gland
		insular tissue	B-cells	A-cells		
Control	56	3,32±0,04	2,69±0,03	0,40±0,01	6,72	7,1±0,15
Experimental	68	3,36±0,07	2,75±0,06	0,41±0,01	6,70	7,3±0,18

TABLE 2. Morphometric Parameters of State of Pancreatic Insular System in Adult Progeny of Healthy Female Rats and Males with Alloxan Diabetes

Group	No. of animals	Relative percentage in whole parenchyma of gland			B/A	Number of islets per 10 mm² parenchyma of gland
		insular tissue	B-cells	A-cells		
Control	28	0,83±0,04	0,59±0,02	0,11±0,002	5,27	14,2±0,8
Experimental	102	0,85±0,06	0,58±0,04	0,11±0,005	5,25	16,3±1,3

discovery of spermatozoa in the vagina; these were weighed; and the morphometric parameters of the state of the pancreatic insular system were recorded.

In special experiments on rats born from healthy females and males with alloxan diabetes the glucose tolerance test was carried out during the first 3 months of life. The blood sugar was determined in the fasting state and 1 and 2 h after oral administration of glucose (400 mg/100 g body weight). Rats born from healthy females and males served as the control. On attaining sexual maturation, experimental and control animals were transferred to a high-sugar diet. After 1.5 months the animals were killed. The pancreas was stained with hematoxylin-eosin and with Weigert's iron-hematoxylin. Differential staining of the A- and B-cells of the islets was carried out by Gomori's aldehyde-fuchsin method, by Paccini's polychrome method in Nikitin's modification, and by a method using hematoxylin phosphotungstate. The relative percentages of insular tissue and also of A- and B-cells throughout the parenchyma of the gland were determined planimetrically. The B/A ratio and the number of islets per 10 mm² of parenchyma of the gland were calculated.

EXPERIMENTAL RESULTS AND DISCUSSION

There was no difference between the body weight of the fetuses (68) removed 522 h after mating the healthy female rats with males with alloxan diabetes (5.16 ± 0.07 g) and control fetuses (56) at the same period of development (5.24 ± 0.05 g). The morphometric parameters of the state of the pancreatic insular system (Table 1) in the control and experimental fetuses also were virtually identical.

In rats born from healthy female rats and males with alloxan diabetes the glucose tolerance tests at the end of the first, second, and third months of life, and also later when maintained on a high-sugar diet, were indistinguishable from the corresponding tests on the control rats. The results of morphometric investigation of the pancreatic insular system also were identical in the control and experimental series (Table 2).

The presence of alloxan diabetes in the male parents, if the females are healthy, thus does not lead to the development of diabetic changes in the offspring (whether in the prenatal or in the postnatal period). This is evidence of the absence of genetic disturbances in alloxan diabetes. Meanwhile the appearance of changes in the pancreas and in carbohydrate metabolism in the progeny of females with alloxan diabetes [1-3] points to the role of a disturbance of metabolism in the mother in the production of hyperstimulation of B-cells in the fetal islets; these changes are probably connected with the increase in body weight of these fetuses and with the frequent subsequent development of diabetic disturbances.

Considering the data described in this paper it can be postulated that pathology in the progeny of females with alloxan diabetes is an example of acquired and not genetically determined spontaneous diabetes.

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