The certain degree of limitation of the blood supply to the heart in diabetes is probably partially compensated by increased extraction of oxygen by the myocardium. Limitation of the utilization of metabolic glucose can be explained by an increase in the contribution of NEFA and ketone bodies to myocardial energy metabolism.

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DEVELOPMENT OF DIABETES MELLITUS IN THE OFFSPRING OF FEMALE RATS WITH ALLOXAN DIABETES IN SIX GENERATIONS

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UDC 616.379-008.64-055.5/.7-092.9-07

KEY WORDS: alloxan diabetes; glucose tolerance test; latent and manifest diabetes; hypoglycemia.

Some of the first-generation offspring of female Wistar rats with alloxan diabetes, mated with healthy males, developed latent or manifest diabetes mellitus, which was either transient or permanent [1]. Meanwhile in the presence of frank alloxan diabetes in males and in the absence of diabetes in females, none of the first generation offspring developed diabetes mellitus [2]. Delay of the utilization of parenterally administered glucose, increasing in each successive generation, is observed in the offspring of three generations of rats with subclinical alloxan diabetes, associated with normoglycemia and aglycosuria [4]. The same investigators showed later a progressive disturbance of glucose tolerance in the 2nd-7th generations, reaching the stage of manifest diabetes mellitus in the 7th generation with a blood glucose level, after fasting for 16 h, of 1.32 ± 2.8 mg% in females and 1.38 ± 3.2 mg% in males [5].

This paper describes the study of the development of diabetes mellitus in the offspring of female Wistar rats with alloxan diabetes in six generations.

EXPERIMENTAL METHOD

Female rats (probands) were given alloxan at the age of 1 month by subcutaneous injection of a dose of 180-200 mg/kg. Six rats which developed permanent frank alloxan diabetes, with a glucose level of 12.1-21.1 mmoles/liter after fasting for 16 h, were used in the experiments. The blood sugar was determined by the method of Somogyi and Nelson. The morning blood sugar after fasting for 16 h was determined every 7-14 days. Female rats with alloxan diabetes were mated at the age of 3-4 months with healthy males which had received no alloxan. The glucose tolerance test (GTT) was studied in the offspring of six generations (346 rats) by injecting glucose into the stomach through a tube in a dose of 400 mg/kg at the end of the 1st, 2nd, 3rd, 4th, 5th, and 6th months of postnatal life. The offspring of rats with

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 1, pp. 13-15, January, 1988. Original article submitted September 22, 1986.

0007-4888/88/0001-0015$12.50

TABLE 1. Frequency of Hypoglycemia during First 3 Months of Life in Offspring of Female Rats with Alloxan Diabetes Depending on Number of Generations

Parameter	Generation					
	1st (31)	2nd (58)	3rd (49)	4th (71)	5th (72)	6th (39)
Frequency of hypoglycemia, %	29,5±8,2	33,3±6,2	20,9±5,8	9,2±5,1	1,3±1,3	27,3±5,5
p	>0,05	—	>0,05	<0,05	<0,01	>0,05

Legend. Significance of differences compared with 1st generation is shown. Number of rats given in parentheses.

TABLE 2. Discovery of Latent and Manifest Diabetes in Offspring in Generations Studied, Depending on Animals' Age

Age of offspring, months	No. of GTT performed	Order of generations	Diabetic type of glucose tolerance, %			
			latent	*p*	manifest	*p*
1—3	974	1—3	4,5±1,0+	<0,05	3,7—0,9+	<0,001
		4—6	2,0±0,6*		10,9±1,3*	0,001
4—6	347	1—3	12,5±3,0+	>0,05	2,5±1,4+	<0,001
		4—6	8,3±1,7		23,3±2,8	
p			+<0,05		+<0,01	
			*>0,05		*<0,001	

TABLE 3. Effect of Character of GTT of Mother-Offspring Belonging to 1st-5th Generation of Proband Female with Alloxan Diabetes on Character of GTT in Offspring of Next Generation

Character of GTT in mother-offspring	No. of mothers	No. of offspring	Distribution of offspring by type of GTT in first 4 months		
			consistently normal	borderline	diabetic
Consistently normal	6	36	42,1±8,0	34,2±7,7	23,7±70
Disturbance of GTT of diabetic type in at least one determination	20	118	33,0±4,5	24,0±3,9	42,4±45
p			>0,05	>0,05	<0,001

alloxan diabetes received no alloxan. Females of the five generations were all mated with intact males. Tests in which the blood sugar level after fasting for 16 h was 5.5 mmoles/liter or below, and 1 and 2 h after administration of glucose it was below 9.4 and 7.2 mmoles/liter respectively, were classed as the normal type of GTT; values of 5.5 mmoles/liter or below, 9.4-9.8 mmoles/liter and above, and 7.2 mmoles/liter and above respectively were classed as a latent form of diabetes, and values of 6.5 mmoles/liter and above, 9.9 mmoles/liter and above, and 7.2 mmoles/liter and above respectively as manifest diabetes. Tests in which the blood sugar level was below 2.8 mmoles/liter were classed as hypoglycemia. The offspring of six generations (152 rats) of two intact females, mated with healthy males, constituted the control group. The numerical results were subjected to statistical analysis by Student's and the chi-square tests.

EXPERIMENTAL RESULTS

During the first 3 months of postnatal life the frequency of hypoglycemia was studied in the offspring of six generations both in the morning after fasting for 16 h and after glucose loading (Table 1).

The presence of frequent hypoglycemias during the first 3 months of postnatal life was noted in the offspring of six generations of female rats with alloxan diabetes both after starvation for 16 h and during the GTT, with a considerable decrease in the frequency of hypoglycemia in the 4th and 5th generations, followed by a fresh increase in the 6th generation. The increase in the frequency of hypoglycemia in the offspring of the 6th generation may perhaps be explained by an increase up to 60% in the frequency of the diabetic type of GTT in the offspring of the previous generation. In the control group of 152 animals, hypoglycemia at the end of the 1st month of postnatal life was determined in only one of the offspring in the 1st generation.

It will be clear from Table 2 that in rats of the 4th to 6th generations there was a significant increase with age in the frequency of development of manifest and latent diabetes. During a study of dependence of the frequency of development of diabetes mellitus (both latent and manifest together) in the offspring of the rats with alloxan diabetes on the presence or absence of hypoglycemia in them at the age of 1-3 months showed that in a group of 100 rats of the 1st to the 3rd generations which had hypoglycemia at the age of 1-3 months, the frequency of development of latent and manifest diabetes mellitus at the age of 4-6 months was 26.0 ± 4.4%, whereas in the group of 124 animals which did not have hypoglycemia it was 8.8 ± 2.6% ($p < 0.001$). In a group of 47 rats of the 4th-6th generation which had hypoglycemia at the age of 1-3 months, the frequency of development of diabetes was 59.5 ± 7.1%, whereas in a group of 77 rats which did not have hypoglycemia it was 18.2 ± 4.4% ($p < 0.001$). The type of GTT of the mother rat of the previous generation had a significant influence on the frequency of disturbance of tolerance of the diabetic type in the offspring (Table 3).

Thus an increase in the frequency of development of diabetes was found in consecutively later generations of rats which were offspring of female probands with alloxan diabetes, and this increase was particularly marked in the presence of disturbances of GTT of the diabetic type in the mother and the presence of hypoglycemia in the offspring at the age of 1-3 months. The results of investigations which showed that removal of 95% of the pancreas from female probands and from the offspring of six successive generations causes the development of diabetic GTT in the 7th generation of offspring [3] are evidence of the role of metabolic disturbances in the development of diabetes mellitus in the offspring. However, this does not rule out the possibility that alloxan may injure the genetic apparatus.

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IMMUNOENZYME DETECTION OF BRAIN NS-2 ANTIGEN AS THE CRITERION OF ALTERED PERMEABILITY OF THE BLOOD-BRAIN BARRIER AFTER γ-IRRADIATION IN MICE

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UDC 612.824.1:613.383].014.4.82.4.08

KEY WORDS: blood-brain barrier; brain NS-2 antigen; γ-irradiation of mice.

A leading place in the mechanism of radiation damage to the living organism is occupied by disturbance of the functions of the blood-brain barrier (BBB) [1, 5, 11, 13]. The function of this anatomo-physiological system is nowadays estimated by studying changes in its permeability for low-molecular-weight substances of varied origin [3, 7, 14]. As a rule these substances are foreign for the animal and may have an independent action on the BBB, which modifies its permeability and sharply reduces the possibility of using these substances as markers of the functional state of the BBB. Meanwhile the question of the use of specific brain substances to assess the functional state of the BBB has been inadequately studied [2, 9].

The aim of this investigation was to conduct an immunoenzyme study of changes in permeability of BBB for species-specific mouse brain protein NS-2 in the early stages after acute γ-irradiation.

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 1, pp. 15-17, January, 1988. Original article submitted March 20, 1987.