peptides in the composition of the fibrils have been shown to be associated into definite stable high-molecular-weight subunits with mol. wt. of 500,000-600,000. Disulfide bonds between the chains evidently play no part in maintenance of the quaternary structure of the amyloid fibrils.

LITERATURE CITED

1. E. M. Tareev and T. S. Korneeva, Vestn. Akad. Med. Nauk SSSR, No. 9, 3 (1970).
2. E. P. Benditt, in: Amyloidosis, London (1976), p. 323.
3. N. Eriksen, H. Ericsson, I. Pearsall, et al., Proc. Natl. Acad. Sci. USA, 73, 154 (1976).
4. G. Fairbanks, T. L. Steck, and D. F. Wallach, Biochemistry (Washington), 10, 2606 (1971).
5. G. G. Glenner and D. Page, J. Histochem. Cytochem., 19, 2606 (1971).
6. M. Harada, C. Isersky, P. Cuatrecasas, et al., J. Histochem. Cytochem., 19, 1 (1971).
7. F. Henryk et al., Pol. Arch. Med. Wewnet., 51, 375 (1974).
8. M. A. Hermodson, R. W. Kuhu, K. A. Walsh, et al., Biochemistry (Washington), 11, 2934 (1972).
9. G. Husby and J. B. Natvig, Clin. Exp. Immunol., 10, 635 (1972).
10. G. Husby, Ann. Clin. Res., 7, 154 (1975).
11. M. Levin, E. Franklin, B. Trangione, et al., J. Clin. Invest., 51, 2773 (1972).
12. A. I. Pick, R. Froelichman, and S. Schreibman, in: Amyloidosis, London (1976), p. 270.
13. M. Pras, M. Schubert, D. Zucker-Franklin, et al., J. Clin. Invest., 47, 924 (1968).
14. M. Skinner and A. S. Cohen, Biochim. Biophys. Acta, 236, 183 (1971).
15. K. Sletten and G. Husby, Eur. J. Biochem., 41, 117 (1974).

COMPENSATORY HYPERTROPHY OF THE OVARY IN ALLOXAN DIABETES AND ADRENORECEPTOR BLOCKADE

P. A. Vunder, I. I. Ivanova, V. F. Lapshina, T. G. Anishchenko, and M. D. Smetanina

UDC 616.379-008.64-092.9-07:618.11-008.66

KEY WORDS: alloxan diabetes; hypertrophy of the ovary; adrenoreceptors.

It was shown previously [3] that compensatory hypertrophy of the adrenal gland in alloxan diabetes is considerably reduced in rats and virtually absent in mice. This result indicated a disturbance of interaction between the pituitary and adrenals in diabetes. It was therefore interesting to study the course of compensatory hypertrophy of the ovary (CHO) in diabetes. Such an investigation could shed light on the state of interaction between the pituitary and gonad. Considering that adrenoreceptor blockade alleviates the course of experimental diabetes in rats [1, 2] and has a favorable effect on human diabetes [4], it was also decided to study the effect of obsidan (propranolol) and of phentolamine on CHO in rats with diabetes.

EXPERIMENTAL METHOD

Experiments were carried out on adult male albino rats initially weighing 207 g. A single subcutaneous injection of alloxan was given in a dose of 15 mg/100 g body weight. Two hours before injection of the alloxan solution, some of the animals were given an intraperitoneal injection of obsidan (3 mg/rat) or phentolamine (2 mg/100 g body weight). After the second day the adrenoblockers were injected intramuscularly: obsidan in the previous dose, phentolamine in a dose of 5 mg per rat. After the 10th day of the experiment the drugs were given on alternate days. Twelve days after injection of alloxan, the left ovary

Department of Physiology of Animals and Man, N. G. Chernyshevskii Saratov University.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, Vol. 5, pp. 548-550, May, 1980. Original article submitted October 10, 1979.

0007-4888/80/8905-0595$07.50

TABLE 1. CHO in Rats Receiving Alloxan Alone or in Conjunction with Adrenoreceptor Blockers

Exptl. conditions	No. of animals	Final body weight	Blood sugar, mg %	Liver glycogen, mg/g	Weight of ovaries, mg %		CHO, %	Weight of uterus, mg %	Height of uterine epithelium, μ
					left	right			
Control	10	231,4	101,00±3,00	45,9±2,41	15,00±0,71	16,08±1,21	—	187,81±19,66	24,41±2,00
Left-sided castration	13	223,8	88,00±4,39	40,13±1,84	17,95±1,12	23,69±1,58	31,98	195,25±21,69	24,49±1,40
Alloxan, left-sided castration	12	189,9	331,00±8,62	11,06±1,52	20,07±1,5	20,71±1,85	3,19	84,27±9,73	13,55±2,33
Alloxan, obsidan, left-sided castration	8	202,8	308,00±39,25	24,94±4,42	20,36±0,89	20,16±2,86	—0,98	100,10±18,5	18,17±3,37
Alloxan, phentolamine, left-sided castration	7	181,7	305,86±28,3	13,91±1,48	22,33±1,49	19,57±3,37	—12,36	105,48±13,3	13,59±1,7

Legend. For comparison of liver glycogen content P_{1-3} and $P_{2-3} < 0.001$; CHO: P_2 (calculated relative to weight of removed left ovary in this group) < 0.001, $P_3 > 0.5$, $P_4 > 0.5$, $P_5 > 0.4$; weight of uterus: $P_{1-2} > 0.05$ $P_{1-3} < 0.001$, $P_{2-3} < 0.001$, $P_{1-4} < 0.005$, $P_{2-4} < 0.005$, $P_{3-4} > 0.4$, $P_{1-5} < 0.005$, $P_{2-5} < 0.001$, $P_{3-5} > 0.4$; height of uterine epithelium: $P_{1-2} > 0.5$, $P_{1-3} < 0.005$, $P_{2-3} < 0.001$, $P_{1-4} > 0.1$, $P_{3-4} > 0.2$, $P_{1-5} < 0.005$, $P_{3-5} > 0.5$.

TABLE 2. Pituitary Gonadotropic Activity of Intact and Diabetic Female Rats as Shown by Biological Testing on Infantile Chicks

Group of animals	Substances injected	No. of chicks	Weight of tests		Weight of comb	
			mg	mg %	mg	mg %
1	Physiological saline	6	16,83±1,76	33,77±1,88	10,83±0,95	21,73±1,47
2	Pituitary extract from control rats	10	19,10±3,99	36,66±3,39	19,00±3,84	36,47±7,30
P_{1-2}			>0,5	>0,2	≈0,05	≈0,05
3	Pituitary extracts from diabetic rats	7	23,93±1,86	47,45±3,65	24,71±3,76	49,00±6,82
P_{1-3}			<0,025	<0,01	<0,005	<0,005

was removed from some of the rats with diabetes and from intact animals. CHO was studied 21 days after unilateral castration. The degree of CHO was judged mainly from the ratio (in %) between the mean relative weight of the right and the mean relative weight of the left removed gonad. The severity of the diabetes was determined from the development of polyuria, glucosuria, and hyperglycemia and from changes in the liver glycogen content. In the course of the experiment observations were made on the vaginal sex cycle of all the animals. After decapitation of the animals their ovaries and uterus were weighed and the height of the uterine epithelium (fixed in Bouin's fluid) was measured.

EXPERIMENTAL RESULTS

On analysis of individual reactions of the ovary in the control group of rats after unilateral castration, compensatory hypertrophy of the residual ovary was found in 77% of individuals. The mean relative weight of the right ovary in the groups exceeded the mean weight of the removed left ovary by 32%. The sex cycle was preserved in all animals of this group. The mean weight of the uterus and height of the uterine epithelium were indistinguishable from normal (Table 1), evidence of complete compensation of the estrogenic function of the ovary. In rats with diabetes a marked degree of CHO was observed in only 33.3% of

cases. It was completely absent in all the other animals. The mean weight of the right ovary exceeded that of the removed left ovary by only 3.19% ($P > 0.5$). The weight of the uterus and the height of the epithelium were considerably reduced, indicating a deficiency of estrogens. In the group of rats with diabetes and receiving obsidan — a β-adrenoblocker, CHO, was found in 25% of cases. For the group as a whole the mean weight of the right ovary was indistinguishable from the mean weight of the removed left ovary ($P > 0.5$). The mean weight of the uterus and the height of the uterine epithelium were below normal. It is interesting to note that the vaginal cycle was preserved in 50% of the rats with marked diabetes receiving obsidan. CHO was observed in only 14.3% of rats receiving alloxan and phentolamine (an α-adrenoblocker). For the group as a whole the mean weight of the right ovary likewise did not differ significantly from that of the removed left ovary. The uterus was atrophic. The sex cycle was disturbed in 100% of animals and in 73% was absent altogether.

The adrenoblockers thus did not restore the normal ability of the rats with diabetes to give CHO, whereas phentolamine evidently actually accelerated the disturbance of the sex cycle. At the same time it should be pointed out that the adrenoblockers reduced the mortality among animals receiving alloxan and increased the number of rats with absence of glucosuria.

The conclusion on the absence of CHO in the majority of adult rats with diabetes agrees with data on the weakening of CHO in infantile rats with diabetes [6].

What is the mechanism of this phenomenon? It might be supposed that in diabetes the gonadotrophic function of the pituitary is depressed. To test this hypothesis, in special experiments the gonadotropin concentration in the pituitary glands of intact rats and of rats with diabetes was compared in a biological test on 3-day male chicks. A saline extract of the anterior lobes of the pituitary glands in a dose equivalent to 8 mg was injected subcutaneously into the chicks for 7 days. The pituitary glands were taken on the 24th day of severe diabetes. Changes in weight of the testes and combs (Table 2) of the chicks were noted. Pituitary extract of intact rats was found to have no effect on the weight of the testes of the chicks and to increase only the weight of the combs by 68%. The same dose of pituitary extract from rats with diabetes led to an increase both in the weight of testes by 40% ($P < 0.01$) and in the weight of the combs by 125.4% ($P < 0.005$). Consequently, the content of gonadotropins in the pituitary glands of rats with diabetes was higher than in the pituitary glands of the control animals. In a special experiment on intact and diabetic (24-27th day of diabetes) adult male rats the reactivity of the ovaries to gonadotropins was investigated. Twice a day for 4 days chorionic gonadotropin (as the Soviet preparation choriogonin) was injected subcutaneously in a dose of 50 mg/100 g. The mean relative weight of the ovaries in the control rats was found to be increased by 125% and in rats with diabetes by 78%. The weight of the uterus was increased by 2 and 52.6%, respectively. However, the final weight of the ovaries in the rats of the two groups was the same: in rats with an intact pancreas 49.6 ± 4.6 mg, in rats with diabetes 50.8 ± 5.3 mg.

Despite the increased gonadotropin content in the pituitary glands and the adequate reactivity of the ovaries to gonadotropins, CHO was absent in most rats with diabetes. It can thus be concluded that in the majority of animals with diabetes the hypothalamic-hypophyseal system did not respond to removal of one ovary: Gonadotrophins evidently were not secreted to the necessary degree, and this could have led to the absence of CHO. This interpretation of the results is in agreement with the absence of ovulation in infantile rats with diabetes after injection of serum gonadotropins (pregnant mare's serum). The pituitary of such rats does not respond to estrogen secreted by ripening follicles following injection of pregnant mare's serum [5].

LITERATURE CITED

1. P. A. Vunder, I. I. Ivanova, and V. F. Lapshina, Probl. Éndokrinol., No. 4, 60 (1976).
2. P. A. Vunder, I. I. Ivanova, V. F. Lapshina, et al., Probl. Endokrinol., No. 5, 66 (1978).
3. I. I. Ivanova, Nauch. Dokl. Vyssh. Shkoly. Biol. Nauki, No. 12, 37 (1973).
4. N. A. Yukhlova, Probl. Éndokrinol., No. 5, 3 (1978).
5. H. Kirchik, P. Keyes and B. Frye, Endocrinology, 102, 1867 (1978).
6. E. Shipley and E. Danley, Am. J. Physiol., 150, 84 (1947).