CONSTITUTIONAL PREDISPOSITION TO GLAUCOMA

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The onset and development of glaucoma include quite a number of facts which have not yet been convincingly explained by existing theoretical concepts. We know that individual sensitivity to glaucoma exists, and on that account an increase of intraocular pressure (IOP) in some individuals leads to glaucoma, whereas in others it does not.

In the course of the study of experimental glaucoma by reproducing it as in [5] we were quite unable to reproduce those results. When analyzing the reasons for our failure, we quite accidentally discovered differences in our technique. We found that some workers [3-5] work only on rabbits of the White Giant breed, whereas in our experiments, we used intestinal rabbits (gray and black hair color). When attempting to explain the differences in the results, we inevitably came to the conclusion that the results can be explained only from the standpoint of constitutional immunity, and its intraspecific polymorphism. However, we found such evidence in the accessible literature, although in recent years many facts indicating a role of heredity not only in the etiology, but also in the pathogenesis of this disease have been collected [9-12]. It is generally familiar that if an inherited predisposition exists in some individuals, that means that there will be an inherited insusceptibility, or resistance and, consequently, constitutional immunity also in others [7, 8].

The aim of this investigation was to study intraspecific polymorphism in rabbits of different breeds to the onset of ocular hypertension and glaucoma under the influence of catecholamines and, consequently, a link between this phenomenon and constitutional immunity. An attempt also was made to obtain a model of glaucoma in Chinchilla rabbits by means of an original method [5].

EXPERIMENTAL METHOD

An intravenus injection of 0.1 ml of a 0.1% solution of adrenalin hydrochloride was given into the auricular vein of a Chinchilla rabbit, with gray and black hair color, on alternate days for 5-18 months continuously (10 rabbits, 20 eyes). Tonometry of the eye, using a Maklakov tonometer, with a weight of 10 g, was carried out in the course of 3 weeks beforehand, and the IOP also was measured twice a week subsequently.

EXPERIMENTAL RESULTS

Typical examples of the curve reflecting fluctuations of IOP during the experimental period are given in Fig. 1. They show that IOP in both eyes did not exceed the normal level (20 mm Hg). The same result also was obtained with all other 18 eyes. Histological study of 10 experimental eyes revealed absence of pathological changes in the eye characteristic of glaucoma. In some experiments absolute glaucoma was obtained with marked excavation of the optic disc. In this case, in our opinion, we evidently were confronted by intraspecific polymorphism in the susceptibility of rabbits of different populations to an excess of catecholamines. This points to the role of constitutional immunity in the onset of raised intraoscular pressure and glaucoma.

An excess of catecholamines causes an increase in lipid peroxidation (LPO), and albino and Chinchilla rabbits, moreover, differ in their content of melanin, which influences LPO [1, 6]. These results help to explain the nature of the results we obtained, namely the absence of experimental glaucoma in Chinchilla rabbits (gray and black hair color) in the

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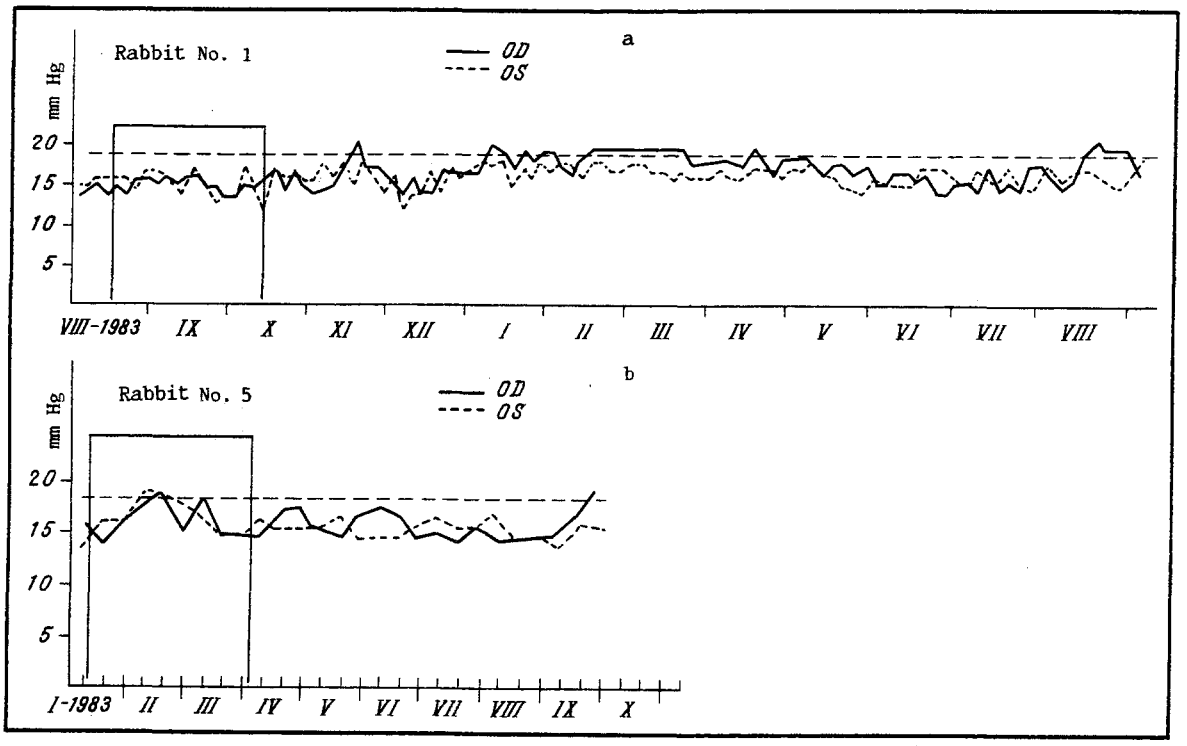

Fig. 1. Experiment with adrenalin. Rectangle indicates period of injections. Horizontal broken line shows upper limit of fluctuations of IOP before beginning of experiment; a) rabbit No. 1, b) rabbit No. 5.

presence of a raised body level of catecholamines, and the onset of glaucoma of primary type in White Giant rabbits [2-5].

Thus the result we obtained revealed intraspecific polymorphism in rabbits, depending on the constitutional features of their melanogenesis in different populations of animals. From this standpoint it becomes clear why in absolutely every study conducted by V. N. Filatov's school a model of glaucoma was obtained in the presence of an excess of adrenalin only in White Giant rabbits, i.e., in albinos, although there is no mention in any of their publications on the reason why these workers were so attached to albino rabbits.

From the standpoint of the theory of constitutional immunity in glaucoma, there is good reason to examine the previously clinically unknown facts of congenital tolerance and intolerance to particlar biochemical ingredients, coupled with predisposition to glaucoma.

It can be considered that hereditary tolerance to a pathogenic biochemical factor (an excess of catecholamines) and to a physical factor (raised introocular pressure) exists in albino rabbits. This may be called intraspecific (population) polymorphism of constitutional immunity to glaucoma in the rabbit. Population polymorphism, incidentally, is manifested in the fact that glaucoma develops in experiments on rabbits of some populations (in albinos) with a raised adrenalin level, whereas in others (gray and black) it does not develop. This is to some extent reminiscent of the known fact relating to specific inheritance, which first and foremost must be studied by methods appropriate for constitutional immunity, i.e., methods of determination of genetic markers must be used, and it is also possible that it is advantageous to use the method of cell and tissue culture in order to study the concrete mechanisms of this immunity in the case of glaucoma.

On the basis of the theory of constitutional immunity, inherited antihyperbaric intraocular immunity can be defined as a state of specific resistance to the pathogenic action of a raised intraocular pressure, caused by molecular features of the constitution of the individual, as a result of which the structures of the eye do not obey the action of a mechanical and chemical influence arising on account of the increased IOP. From the practical point of view, however, the discovery of correlations between glaucoma and genetic markers in each individual region with its ecologic features may help to improve work in the field of prevention of the disease, with the identification of a group of persons or, more correctly populations with increased risk of developing the disease with respect to different tissue systems, to the development of retention, hypertension, and glaucoma. It can be tentatively

suggested that this will lead to improvements in the outpatient supervision and treatment of glaucoma patients.

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CHANGES IN THE LIVER OF RATS EXPOSED IN UTERO TO CHRONIC HYPOXIA

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Disturbance of cell division and an increase in the level of pathological mitoses (PM) may be the structural trace of disadaptation. Disturbance of cell division and elevation of the PM level in the corneal epithelium are observed under the influence of various experimental conditions: hypoxia, hypothermia, hyperthermia [3, 6-8]. The corneal epithelium is not actively involved in the process of adaptation. To evaluate the role of a raised PM level in the formation of the structural trace and morphological changes, it was decided to analyze disturbances of cell division in fetal and neonatal rat hepatocytes and also in month-old rats exposed to hypoxia during intrauterine development.

EXPERIMENTAL METHOD

On the 5th or 6th days of pregnancy famale mice were placed in an SKB-48 pressure chamber and raised to an altitude of 9000 m, corresponding to a pressure of 224 mm Hg. Every day the animals were exposed for 4 h from 9 a.m. to 1 p.m. for 7 days as described in [3]. Control animals were simply placed in the pressure chamber. The offspring of rats exposed during pregnancy to hypoxia and the control animals were divided into three groups. Group 1 comprised 104 fetuses at 16-17 days of intrauterine development (the 4th day after final exposure to hypoxial), Group 2 comprised 166 newborn rats, 2 days after birth (10th day after the final session of hypoxial), and Group 3 comprised 76 rats aged 80 days (40 days after the final session of hypoxia). The total body weight of the fetuses and newborn rats was determined, and after the animals had been humanely killed, the liver was removed and weighed. Pieces of tissue were fixed in Carnoy's fluid and histological sections were cut from them and subjected to systemic morphometric analysis [1]. The state of DNA synthesis was judged by autoradiography with ^{3}H-thymidine. For this purpose, pieces of liver measuring 0.2 mm^3 were incubated, immediately after sacrifice of the animals, in 5 ml of medium 199 for 60 min at 37°C with ^{3}H-thymidine (5 μCi in 1 ml, specific radioactivity 70 Ci/mmole). Autoradiographs were prepared by the method in [5]. The index of labeled nuclei of the hepatocytes (ILN) was determined after examination of at least 3000 nuclei. The labeling intensity (LI) was

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