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CHANGES IN POTASSIUM ION HOMEOSTASIS IN THE LENS OF FRASER MICE WITH HEREDITARY CATARACT (LINE Cat^{Fr})

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Among human diseases that most often lead to blindness, the first place is occupied by cataract, or opacity of the lens of the eye [3]. Although there may be different causes of different types of cataract, the mechanisms of development both of the commonest type of cataract, namely senile, and the less common hereditary type of cataract, are most probably the same. We know that genetically determined cataract is characteristic not only of man, but also of other mammals: mice [12], guinea pigs [11], rats [14], and monkeys [8]. One line of mice in which opacity of the lens develops in the 2nd week after birth is the Cat^{Fr} line [12]. The morphology of the lens in these animals has been well studied [4, 7, 10], and work has recently been published on changes in crystalline structure [5, 6]. However, K^+ homeostasis in the lens of Cat^{Fr} mice has not been investigated.

The development of cataract in mice of another line (Nakano) is linked with a disturbance of K^+, Na^+-ATPase function in the epitheliocytes of the lens [12]. It has been shown [13] that that preservation of transparency of the lens in mammals is due to a high K^+ level in the cytoplasm of the fibers. The aim of the present investigation was accordingly to study the distribution of K^+ in the lens and aqueous humor of Cat^{Fr} mice.

EXPERIMENTAL METHOD

A strain of mice homozygous for the autosomally dominant Cat^{Fr} gene, generously provided by the staff of the Institute of General Genetics, Academy of Sciences of the USSR, was used. Noninbred albino mice of the same age served as the control. The animals were given a normal diet. The lenses were removed after the mice were killed by cervical dislocation.

To obtain histological specimens the lenses were fixed in 4% formalin (pH 7.4) and sections were stained with hematoxylin and eosin.

The OP-K-07118 valinomycin electrode and OP-267 ionograph (Radelkis, Hungary) were used to measure K^+ activity. An OP-0830P Ag-AgCl electrode from the same firm was used as comparison electrode. K^+ activity was estimated from the change in electrode potentials, and the steepness of the electrode function was taken into account each time. All measurements were made in a solution containing 0.15 M NaCl and 0.2 mM KCl [1].

To assess K^+ activity in the aqueous humor, it was sampled by means of a Hamilton microsyringe (USA) in a volume of 3-5 µl; the K^+ level in the lens was determined after preparation of homogenates.

EXPERIMENTAL RESULTS

A morphological manifestation of senile cataract is the appearance of so-called bullous cells, degeneration of the epithelium, and edema of the lens fibers [9]. In month-old Cat^{Fr}

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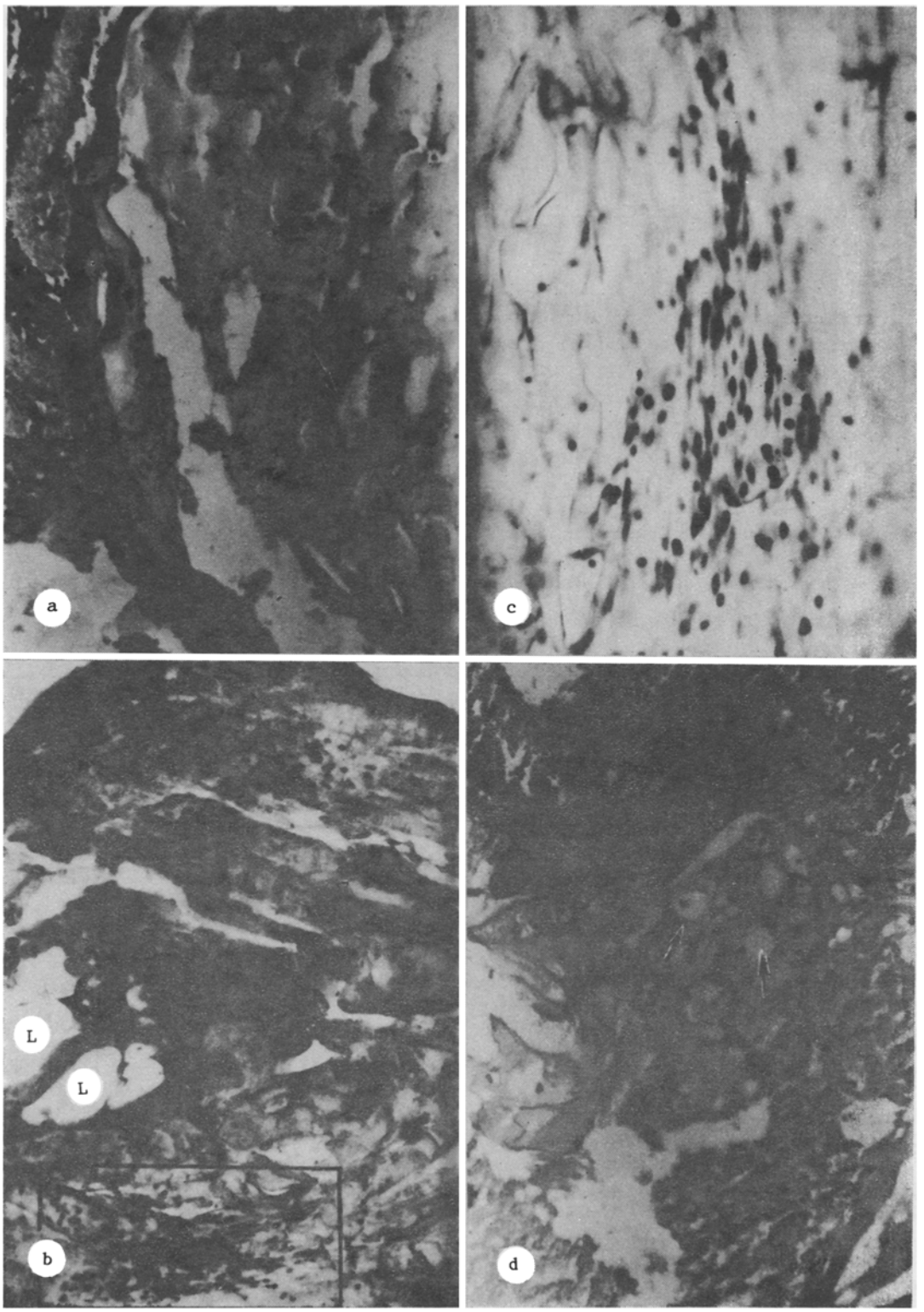

Fig. 1. Morphology of lens of Cat^{Fr} mice. Arrows indicate bullous cells; L) lacunae or vacuoles; region containing fusiform cells is outlined and shown under higher power in Fig. 1c. Stained with formalin, hexatoxylin, and eosin. Magnification: a, b, d) 9 × 12.5, c) 10 × 10. Age of animal: A, B, and C) 1 month, D) 4 months.

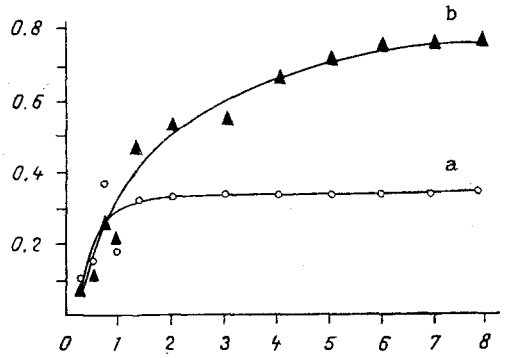

Fig. 2

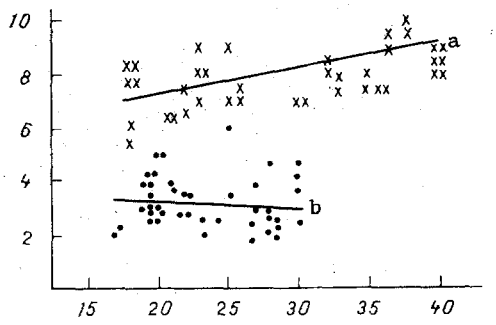

Fig. 3

Fig. 2. Outflow of K^+ into incubation medium from lens of a noninbred albino mouse (a) and a Cat^{Fr} mouse (b). Here and in Fig. 3: abscissa, incubation time (in h); ordinate, K^+ activity (in meq/liter). Incubation at 20-22°C. Incubation medium: 0.15 M NaCl, 0.2 mM KCl.

Fig. 3. Dependence of weight of lens on body weight of mice. Abscissa, weight of mouse (in g); ordinate, weight of lens (in mg). Regression lines ($y = a + bx$): for noninbred albino mice: $a = 5.76$, $b = 0.072$; for Cat^{Fr} mice: $a = 3.59$, $b = -0.016$.

mice the lens was found to be packed with bullous cells, but to show no evidence of visible degeneration of epitheliocytes; after 3 months lacunae filled with fluid were formed, and in addition, the number of bullous cells in the lens increased (Fig. 1).

The cytoplasm of the bullous cells in an older mouse is paler, possibly indicating a lower concentration of crystallins in them (Fig. 1). Degeneration of fibers in the center of the lens also was observed. Moreover, in some preparations, elongated nucleated fusiform cells not characteristic of this part of the normal lens were identified in the central layers. They may have appeared as a result of disturbance of normal fiber maturation.

Reduction in the size of the cell nuclei, their pycnosis, swelling and vacuolation of the fibers, and the formation of amorphous eosinophilic masses, going on to total liquefaction of the lens in Cat^{Fr} mice have been observed previously by other workers also [4, 7]. The appearance of bullous cells which, in our view, are one of the earliest morphological features of developing cataract, in young mice has not previously been noted.

The study of homogenates of 34 lenses from mice with hereditary cataract revealed an increase in the K^+ concentration, calculated per total weight of the lens: 142.16 ± 6.01 and 87.54 ± 2.74 meq/liter for the pathological and normal state respectively ($p<0.001$, 38 lenses in the control). K^+ activity in the aqueous humor of these same groups of animals showed no difference: 5.92 ± 0.36 and 7.01 ± 0.58 meq/liter for the cataract and normal lens.

After removal of the lens from the mammalian eye and its transfer into incubation medium containing 30-35 times less K^+ than the aqueous humor, a rapid outflow of K^+ from the lens took place. Only epitheliocytes are characterized by tissue respiration and the transparent fiber cells do not possess mitochondria [9]. Systems of active K^+ transport in the lens are also typical of epitheliocytes only. It can be tentatively suggested that the outflow of K^+ which we observed in the incubation medium from the removed lens will depend on the functional state of the epitheliocytes.

Data indicating a difference in the outflow of K^+ from the normal and opaque lenses are given in Fig. 2. The more prolonged loss of K^+ by the lens affected with cataract compared with the normal lens may be due to several causes: first, the different concentrations of this ion which we found in transparent and opaque lenses; second, the more intensive working of the "potassium" pumps of the epitheliocytes; third, differences in the distribution of the ion in the lens tissues.

It is not yet known where the main reserves of K^+ in opaque lenses are located — in the lacunae, the bullous cells, or the unchanged fibers.

The present writers have shown [2] that K^+ flows out of the lenses of animals with a galactose cataract in vitro at the same rate as from transparent lenses. We also observed bullous cells in these animals, but there were no lacunae.

Differences in the level and velocity of outflow of K^+ in Cat^{Fr} mice may perhaps be due to morphological differences: preservation of the layer of epitheliocytes not only in the surface layers of the lens, but also in its thickness, and the formation of lacunae.

The development of senile cataract in man [13] and of hereditary cataract in mice of the Nakano strain [12] is known to be accompanied by a disturbance of the distribution of K^+ and Na^+ ions. In particular, human lenses, as they become opaque, lose K^+ and Na^+ is drawn inside. As a result, a relative increase in the content of water, transported passively with Na^+, is observed [13]. Previously the writers reported [2] an increase in the weight of the lens in mammals with diabetic cataract, and during the development of an opacity of the lens in vitro. The development of cataract in Cat^{Fr} mice probably proceeds along a totally different path. As the results in Fig. 3 show, with age or (which amounts to one and the same thing) with an increase in weight of animals the weight of the lens is reduced, and this may reflect an increase in the K^+ concentration or a decrease in synthesis of crystallins.

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ROLE OF MONOAMINE OXIDASE IN THE INTENSIFICATION OF MITOCHONDRIAL LIPID PEROXIDATION IN EXPERIMENTAL MYOCARDIAL NECROSIS

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In recent years the participation of lipid peroxidation (LPO) reactions in the pathogenetic mechanism of ischemic and anoxic heart damage has been demonstrated [6]. Analysis of the results of experimental studies of myocardial damage has shown that an excess of catecholamines and of their incomplete oxidation products during stress is one way whereby LPO is intensified [5, 7].

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