IMMUNITY OF THE LENS TO TUMORS

É. V. Mal'tsev

UDC 617.741-006-092.9-035.2:617.741-097.3

KEY WORDS: lens; malignant change.

Tumors of the lens are not found in ophthalmologic practice [5]. Only spontaneously absorbing tumor-like formations (lentomas) have been produced experimentally [13] in the traumatized lens of only one species of frog *(Rana pipiens)*. In other experiments [15] foci of proliferation, invading fibers of the lens of the Canadian trout, were obtained when the fish were kept for 1 year on a diet containing thioacetamide. However, attempts to obtain the development of lens tumors in mice [10] did not give hopeful results. Accordingly, the concept of immunity of the lens to tumors has grown up in the literature [8]. To explain this phenomenon several hypotheses have been put forward [10, 14]; as a result of the anaerobic metabolism of the lens which is similar to that of tumors, the special properties of the capsule of the lens which is impermeable to chemical carcinogens, the genetically determined resistance of cells of the lens to tumor transformation, etc.

The object of this investigation was an experimental analysis of these views.

EXPERIMENTAL METHOD

Three series of experiments were carried out on 82 **chinchilla** rabbits weighing about 2.5 kg. In series I, total epithelial-capsular preparations of the lens from normal animals were used for cytochemical determination of the activity of enzymes of aerobic metabolism: dehydrogenases of the Krebs' cycle (succinate — SDH, malate — MDH, and isocitrate — ICDH), and also of NAD-diaphorase. The optical density of nitro-BT formazan formed in the cells was determined on the MTsFV-1 microscope-photometer at a wavelength of 570 nm. In the experiments of series II, 20-methylcholanthrene or 3,4-benzpyrene was injected subepithelially into the lens by an original method [3]. Every month for 20 months, lenses of the rabbits were then investigated with the ophthalmoscope and biomicroscope and also histologically. In the last case, total preparations of the epithelium and sections through the lens stained with hematoxylin and eosin or by Einarsson's method were studied. In the experiments of series III, the possible carcinogenic effect of ionizing radiation on the lens was investigated. Local x-ray irradiation of the eyes in a dose of 1600 R (4128×10^{-4} C·kg^{-1}) was given once with the following parameters: voltage 180 kV, current 10 mA, FSD 23 cm, field diameter 22 mm, filter 0.5 Cu + 1.0 Al. Ophthalmoscopy and biomicroscopy were carried out until 8 months after irradiation, and total preparations of the epithelium of the lenses, stained with hematoxylin and eosin or by Einarsson's method, were studied histologically 3 days and 5-6, 10-12 weeks, and 5 and 8 months after irradiation.

EXPERIMENTAL RESULTS

In the experiments of series I, high activity of ICDH, SDH, MDH, and NAD-diaphorase was found in the epithelium of the lenses of normal animals (the optical density of formazan in the cells was 0.181 ± 0.027, 0.248 ± 0.037, 0.180 ± 0.027, and 0.365 ± 0.054 units, respectively). Fine-grain formazan was usually uniformly distributed throughout the cytoplasm of the cells studied (Fig. 1), although sometimes it was found to accumulate in the perinuclear zone. The results indicate intensive oxidation of pyruvate in the Krebs' cycle followed by transfer of electrons thus set free to oxygen in the epithelium of the lens. Uptake of oxygen by its cells was discovered previously [11].

The experiments of series II showed that a mass containing carcinogens, injected into the lens, was located between its capsule and the cortical fibers, thus making direct contact with the epithelium. In spite of this, however, tumor development could not be observed either

Central Research Laboratory, Odessa Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Puchkovskaya.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 8, pp. 95-97, August, 1982. Original article submitted March 4, 1982.

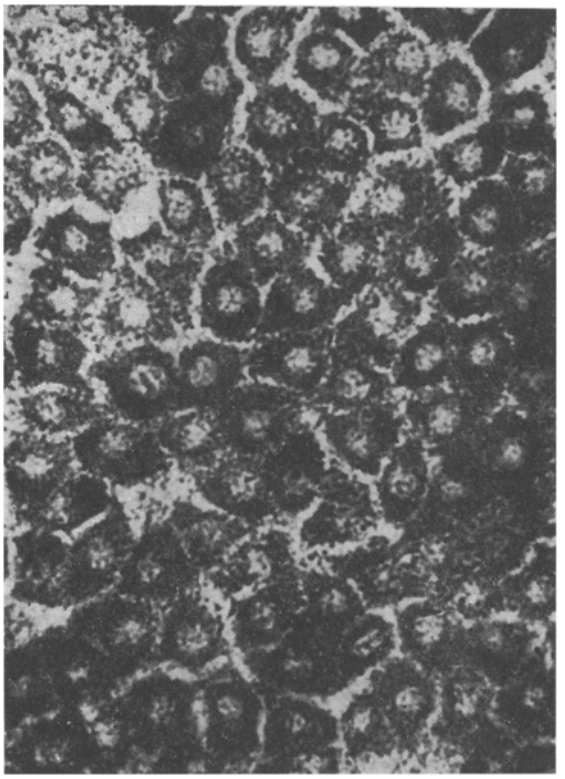

Fig. 1. Reaction for ICDH in epithelium of normal lens. Hess—Scarpelli—Pearse method. 240 ×.

macro- or microscopically in experiments lasting up to 20 months. Yet the epithelium in contact with the injected mass was thinner, some of its cells were pycnotic and others had undergone lysis, and granular debris occupied the place of necrotic cells (Fig. 2). Migration of atypical cells from the posterior capsule of the lens was observed. The number of cells undergoing degenerative and necrotic changes increased as the experiment progressed, but the epithelium at a distance from the injected mass was indistinguishable from normal. The pathological changes in the epithelium of the lens described above, it must be emphasized, did not go beyond the usual structural disturbances of an epithelial monolayer such as are characteristic, for example, of various forms of cataract.

In the experiments of series III, x-ray irradiation of the eye gradually led to complete opacity of the lens, and the appearance and progressive development of such a cataract was closely connected with radiation injury to the epithelium. However, no malignant transformation of the lens tissue could be observed, although changes in its epithelial cells were distinct. Disturbances of mitotic activity, the appearance of pathological mitoses and of atypical cells — giant, multinuclear, vacuolated, and irregularly shaped cells (Fig. 3), the development of a pseudoepithelium and, finally, the almost complete death of the epithelium were observed.

On the basis of these experimental results, the possible causes and character of the immunity of the lens to tumors can be discussed. First, there seems to be no doubt that it is not the result of impermeability of the capsule of the lens for carcinogens of chemical nature (the experiments of series II). It likewise cannot be based on an anaerobic type of metabolism common to tumors and the lens. In fact, most energy in tumors is produced by glycolysis [6], and this metabolic pathway is a feature of the lens as a whole [9]. However, the epithelium of the lens, i.e., that part of its structure which, unlike the fibers, possesses proliferative activity and could undergo malignant change, very actively utilizes the aerobic pathway of glucose metabolism (experiments of series I).

The immunity of the lens to tumors is evidently not absolute, as is sometimes considered [12], but it rather is relative in character, and it is possible in principle for tumors of the lens to arise. This view is supported by the report of a case [8] of metastasis of a melanosarcoma of the ciliary body in the lens, as well as the results of investigations by Courtois

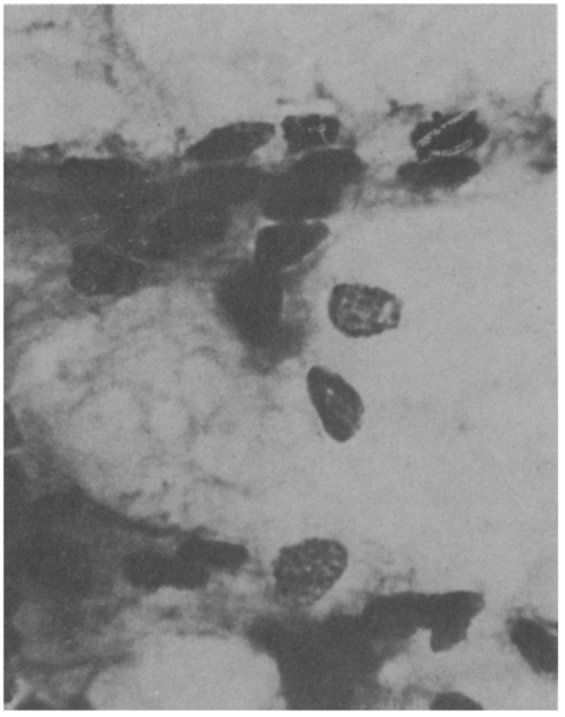

Fig. 2

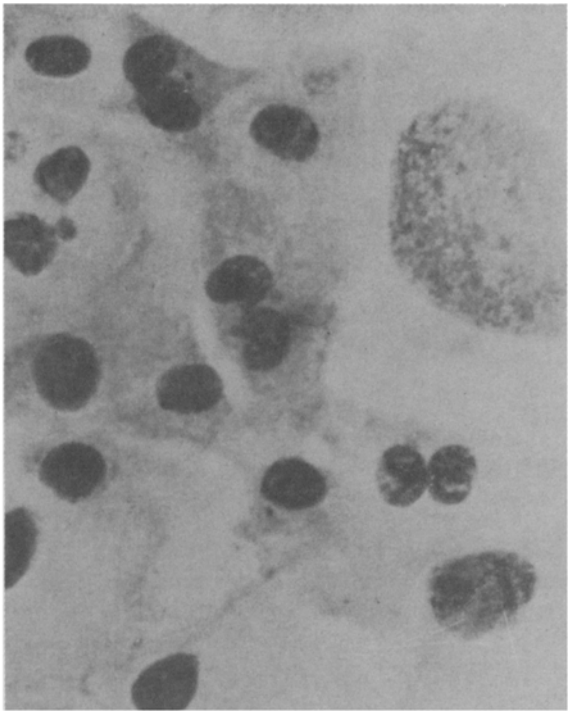

Fig. 3

Fig. 2. Epithelium of lens in contact with 20'-methylcholanthrene for 16 months. Einarsson's method, 320 ×.

Fig. 3. Atypical epithelial cells of lens 5 months after x-ray irradiation. Hematoxylin—eosin, 320 ×.

et al. [7]. They showed that subcutaneous injection of 10^6-10^7 epithelial cells from the bovine lens, transformed during prolonged (over 150 passages) culture, subcutaneously into nude mice caused the development of a tumor synthesizing the specific lens protein α-crystallin, at the site of inoculation.

Very probably the relative immunity of the lens to tumors is due to a highly active system for repairing various DNA lesions, whose role in the process of carcinogenesis is currently the subject of intensive research [2]. It may perhaps be for this same reason that malignant transformation of lens tissue has not been successfully obtained by the use of ionizing radiation [4] (the results of experiments of series III), although we know [1] that if the appropriate type of radiation, dose, and conditions of exposure are chosen, neoplasms in any situation and histogenesis can be obtained.

LITERATURE CITED

1. S. N. Aleksandrov, Vopr. Onkol., No. 7, 108 (1972).
2. G. D. Zasukhina, Arkh. Patol., No. 10, 79 (1978).
3. É. V. Mal'tsev, Oftal'mol. Zh., No. 3, 231 (1977).
4. I. A. Milovidova, Med. Radiol., No. 8, 77 (1975).
5. A. I. Paches, A. F. Brovkina, and G. G. Ziangirova, Clinical Oncology of the Organ of Vision [in Russian], Moscow (1980).
6. N. T. Raikhlin, Oxidation—Reduction Enzymes in Tumors [in Russian], Moscow (1967).
7. Y. Courtois, L. Simonnaey, J. Tassin, et al., Differentiation, 10, 23 (1978).
8. W. Hallermann and G. Meisner, Klin. Mbl. Augenheilk., 124, 159 (1954).
9. J. F. R. Kuck, in: Biochemistry of the Eye, ed. C. N. Graymore, London (1970), pp. 183-373.
10. I. Mann, J. Cancer, 1, 63 (1947).
11. U. Mayer, Albrecht von Graefes Arch. Ophthalmol., 183, 137 (1971).
12. L. Nieznanski, Klin. Oczna, 46, 559 (1976).
13. N. S. Rafferty, Anat. Rec., 153, 111 (1965).
14. E. Sachs and R. L. Larsen, Am. J. Ophthalmol., 31, 561 (1948).
15. L. von Sallmann, J. Halver, E. Collins, et al., Cancer Res., 26, 1819 (1966).