

HISTOPATHOLOGY OF THE ADENOHYPOPHYSIS IN EXPERIMENTAL FLUOROSIS

A. A. Zhavoronkov and A. I. Edemskii

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Fluorosis was induced in rabbits by daily subcutaneous injections of sodium fluoride in a dose of 12 mg/kg for 12 weeks. Stimulation of adenohipophyseal function was observed during the first days and weeks of poisoning. In chronic experiments depression of the function of the basophils and acidophils was observed. During the 8 weeks of the recovery period the adenohipophysis of the experimental rats was practically indistinguishable from that of the controls.

KEY WORDS: fluorine; fluorosis; adenohipophysis.

Previous investigations [4, 5] revealed changes produced by fluorine poisoning in the adaptive systems of the organism. An important role in adaptation to harmful factors is played by the pituitary gland. Meanwhile the morpho-functional state of the adenohipophysis in fluorosis has received very little study [2]. In the few investigations that have been made of this problem, little or contradictory information has been obtained [12, 13].

EXPERIMENTAL METHOD

Male albino rats (45) weighing initially 100 ± 20 g received daily subcutaneous injections of sodium fluoride in a dose of 12 mg/kg for 12 weeks. The 12-week recovery period was studied in 20 of the rats. The control consisted of 27 rats not receiving fluorine. Tests were carried out 2 days and 1, 2, 4, and 12 weeks after the beginning of poisoning and also after 1, 4, 8, and 12 weeks of the recovery period. The pituitary was fixed in 10% neutral formalin or in Zenker-formol and embedded in paraffin wax. Horizontal sections through the adenohipophysis, 4 μ in thickness, were stained for glycoproteins by the PAS reaction in Pearse's modification (counterstaining with orange G), with azan by Mallory's method in Haidenhain's modification, and with aldehydefuchsin by Halmi's method in Dyban's modification.

EXPERIMENTAL RESULTS

The morphology of the adenohipophysis of the control animals was first studied (Fig. 1a). After poisoning for 2 days, besides congestion, homogenization of the cytoplasm mainly of the gonadotrophs and thyrotrophs was observed in the adenohipophysis. Some of them contained large granules of glycoproteins. At the same time single basophils with degranulated and vacuolated cytoplasm, resembling follicle-stimulating gonadotrophs, were seen.

Marked homogenization of the cytoplasm of some acidophils also was found, and in the centers of the glands there were large acidophils with degranulated cytoplasm (Fig. 1b).

After 1 week of poisoning congestion of the adenohipophysis was present, with a decrease in the number of basophils, the cytoplasm of which was almost free from glycoproteins. The cells appeared "optically

Research Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow.
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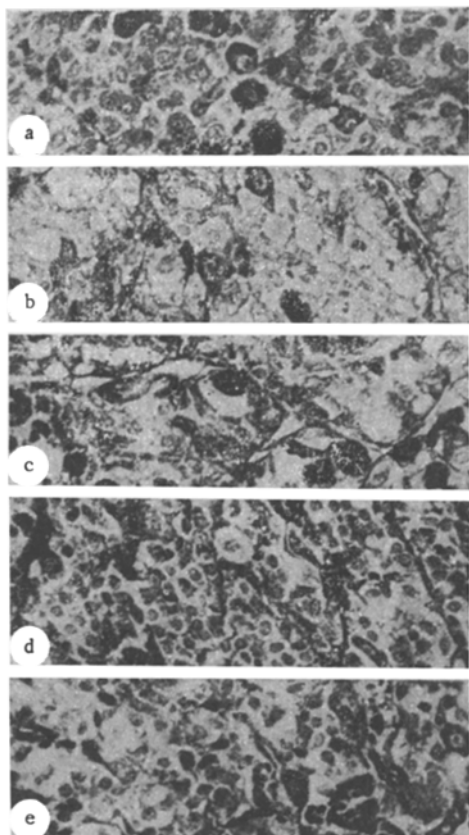


Fig. 1

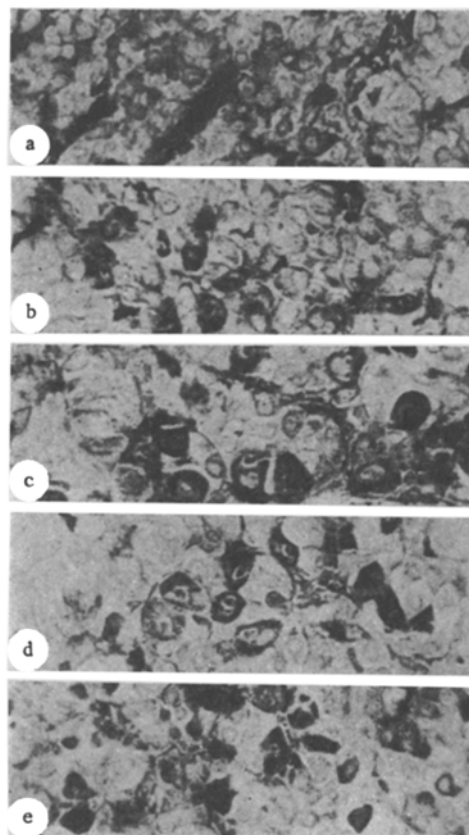


Fig. 2

Fig. 1. Histological structure of the adenohypophysis in fluorine poisoning: a) control; b) 2 days; c) 1 week; d) 2 weeks; e) 4 weeks of poisoning. PAS reaction, 500 \times .

Fig. 2. Histological structure of adenohypophysis during fluorine poisoning and in the recovery period: a) 12 weeks of poisoning; b) 1 week, c) 4 weeks, and d) 8 weeks of the recovery period; e) control. PAS reaction, 500 \times .

empty," and their nucleus was large and pale. Vacuolation of the cytoplasm was well marked in the follicle-stimulating and luteinizing gonadotrophs. Homogenization of the cytoplasm and pycnosis of the nuclei of the thyrotrophs and acidophils were seen (Fig. 1c). The content of colloid in the pars intermedia was reduced, as it also was after poisoning for 2 days.

After poisoning for 2 weeks the congestion of the adenohypophysis remained; an increase in the intensity of the PAS-positive staining of the blood vessel walls and a decrease in number of basophils and the content of colloid also were observed. Bright crimson granules of glycoproteins appeared in the cytoplasm of the gonadotrophs. Few degranulated basophils and cells with homogenized cytoplasm and a pycnotic nucleus were present (Fig. 1d). The number of acidophils with homogenized cytoplasm and a small pycnotic nucleus was increased.

Four weeks after the beginning of poisoning the number of basophils remained low. The follicle-stimulating gonadotrophs and thyrotrophs had degranulated cytoplasm (Fig. 1e). At the same time thyrotrophs with homogenized cytoplasm could be seen. The content of glycoproteins in the cytoplasm of the luteinizing gonadotrophs was increased. The number of acidophils was low, and at the periphery of the gland there were many cells with a dark, pycnotic nucleus and with homogenized cytoplasm. Conversely, in the central zones of the adenohypophysis there were very large acidophils with a pale nucleus.

After poisoning for 12 weeks the number of basophils was reduced and the content of glycoproteins in their cytoplasm was low (Fig. 2a). In individual basophils the granules of glycoproteins were present only in the peripheral zones of the cytoplasm. The number of acidophils was low, and acidophils with degranulated and with homogenized cytoplasm were found equally often. Colloid was absent.

One week after the last injection of sodium fluoride into the rats (the recovery period) there was some increase in the number of basophils (Fig. 2b) and also, to a lesser degree, of acidophils and colloid had accumulated. The 4th week of the recovery period was characterized by hyperplasia and marked hypertrophy of the basophilic cells with the accumulation of glycoproteins in their cytoplasm (Fig. 2c). The luteinizing gonadotrophs were the first to recover functionally and morphologically, followed by the thyrotrophs and the follicle-stimulating gonadotrophs. The number of acidophils, as well as the colloid content, increased. After 8 weeks of the recovery period the adenohypophysis of the experimental rats (Fig. 2d) no longer differed significantly from that of the control animals (Fig. 2e). After 12 weeks of the recovery period the histological picture of the adenohypophysis of the experimental rats was indistinguishable from the control.

The morphological and histochemical changes observed in the rat adenohypophysis during fluorine poisoning reflect morphological and functional changes both in its cells responsible for the production of the various hormones, and in the colloid. The colloid appeared and accumulated in the adenohypophysis in definite phases. Monastyrskaya [8] regards the "colloid edema" of the anterior lobe of the pituitary as a product of an after-response following alarm. "Colloid edema" of the adenohypophysis was observed by Akmaev under experimental conditions [1]. The present writers consider that the state of the colloid in the adenohypophysis, as well as in its cells, may be reflected in the morphological and functional state of the gland.

The beginning of poisoning was accompanied by activation of the functions of all the basophils. The accumulation of large granules of glycoproteins in the cytoplasm of some basophils and the presence of degranulated basophils are evidence of their increased function [7, 9].

Further poisoning led to a gradual but progressive decrease in function of the basophils and acidophils. Consequently, experimental fluorosis was accompanied by inhibition of both gonadotropic and thyrotrophic functions. If it is remembered that the function of ACTH production is connected with the basophils located in a zone bordering on the pars intermedia [10], changes in these cells must indicate inhibition of ACTH production. This is also shown by clinical investigation revealing marked hypocorticism [3].

The inhibition of function of the acidophils in the adenohypophysis, cells responsible for producing growth hormone and lactogenic hormone, is reflected in the slower gain in weight of experimental animals [13] and disturbance of lactation in female workers exposed to chronic fluorine poisoning [6]. The author cited also confirmed this observation in experiments on rats in which not only was lactation severely disturbed, but the weight of the mammary glands also decreased in fluorine poisoning.

The earlier study of the morphological and functional state of the hypothalamic-hypophyseal neuro-secretory system of rats with experimental fluorosis showed increased activity of that system during the first days of poisoning, followed by inhibition of its function [5]. Comparison of these findings with the changes observed in the adenohypophysis revealed the close connection between them in experimental fluorosis. Reliable correlation is also found with the changes in the adrenal cortex of these rats [4].

Experimental fluorosis in rats is thus accompanied by interconnected and interdependent changes in various endocrine glands and, in particular, in the hypothalamic-pituitary-adrenocortical system responsible for adaptation of the organism to extremal factors, exemplified in this investigation by administration of toxic doses of sodium fluoride.

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