

DYNAMICS OF MORPHOLOGICAL CHANGES IN THE ADRENAL CORTEX AFTER WHOOPING COUGH VACCINATION

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Changes characteristic of the stress reaction were observed in the adrenal cortex of mice 3 h after immunization with whooping cough vaccine: widening of the zona fasciculata of the cortex and a decrease in the content of total lipids and birefringent lipids. Five days after vaccination (the period of maximal hypersensitivity to histamine and serotonin) morphological signs of inhibition of function of the zona fasciculata and increased function of the zona reticularis were observed in the adrenal cortex.

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Injection of whooping cough vaccine is known to produce an unusual biological effect: a marked increase of sensitivity to histamine, serotonin, cold stimulation, and so on. In particular, small doses of histamine or serotonin, hardly producing physiological changes, may cause death of 100% of mice immunized against whooping cough [2, 8, 11]. Changes in reactivity of the body after whooping cough vaccination are of great interest, because it may be connected with the high rate of reactions to whooping cough vaccine observed in immunizing practice. However, despite numerous investigations [10], the mechanism of these changes in reactivity has not yet been satisfactorily explained.

There are reports in the literature of a possible link between the stressor action of whooping cough vaccine, which has been established experimentally [1, 4, 12], and its ability to modify sensitivity of the organism to biogenic amines [5].

In the present investigation we studied morphological changes in the adrenal cortex at the height of hypersensitivity to histamine and serotonin after whooping cough vaccination.

EXPERIMENTAL METHOD

Our observations showed that the increase in sensitivity of female albino mice to serotonin reaches a maximum 5 days after intraperitoneal injection of a suspension of whooping cough microorganisms in a dose of 5 billion bacterial cells. This period after immunization, according to data in the literature, is also that of maximal sensitivity to histamine.

Changes in the effector organ of the pituitary-adrenal system (the adrenal cortex) were studied 5 days after whooping cough immunization, and also in the early period of the experiment, 3 h after intraperitoneal injection of 5 billion bacterial cells. Animals receiving 1 ml physiological saline under the same conditions and sacrificed, like the experimental mice, with ether 3 h and 5 days after vaccination, served as controls. Altogether 155 female albino mice, initially weighing about 20 g, were used in the experiments.

For histological and histochemical investigation of the adrenals the material was fixed with formalin and sections were cut on a freezing microtome. The sections were stained with a mixture of Sudan III and Sudan IV to determine total lipids, Schultz's reaction was carried out for free and bound cholesterol, and birefringent lipids were detected by examination of unstained sections of the adrenals with the polarization microscope. These investigations gave morphological evidence of the level of adrenocortical function, because we know [3, 6, 7, 9] that an increase or decrease in secretion of one or other zone of the cortex is

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accompanied by definite histological changes in the thickness of the corresponding zones, the size of the cells, and their content of total lipids, birefringent lipids, and cholesterol.

EXPERIMENTAL RESULTS

A morphological study of the adrenal cortex of mice sacrificed 3 h after vaccination revealed marked changes characteristic of the stress reaction (Fig. 1). This took the form of widening of the zona fasciculata of the cortex, congestion of the capillaries lying between the rows of cells in the zona fasciculata and of the veins in the medulla, and of a marked decrease in the content of total lipids and birefringent lipids in the epithelial cells of the zona fasciculata, especially in its inner portions.

These changes in the adrenal cortex of the vaccinated animals contrasted sharply with those in the control mice. A similar pattern was found by the use of the Schultz histochemical reaction for total cholesterol. Meanwhile, signs of increased liberation of lipids from the cells of the adrenal cortex into the blood stream could be observed, with the appearance of tiny droplets of lipids in the lumen of the capillaries lying between the radial bands of the cells in the zona fasciculata. Droplets of lipids and sudanophilic masses were also found in the dilated venous sinuses of the adrenal medulla.

The morphological picture of the adrenal cortex was completely different 5 days after vaccination, i.e., at the height of hypersensitivity of the organism to histamine and serotonin. The most marked feature of the morphological changes was considerable widening of the zona reticularis of the adrenal cortex (Fig. 2). The proliferating cells of this zone appeared to compress the zona fasciculata and to invade it in some places. Frequently cells of the zona reticularis formed bands like tentacles penetrating deep between groups of cells of the zona fasciculata. The zona fasciculata was relatively narrow and contained a moderate amount of lipids. Congestion of the capillaries of the zona fasciculata was not observed, and droplets of lipids were not present in their lumen, i.e., no signs of increased liberation of hormones from the zona fasciculata into the blood stream were observed. No difference likewise was found in the intensity of staining with the tests for lipids in the inner and outer portions of the zona fasciculata (this is always observed in the stress reaction, indicating liberation of lipids mainly from the inner portions of the zona fasciculata).

In the period of maximal increase in sensitivity of the organism to histamine and serotonin, signs of increased activity of the zona fasciculata of the adrenal cortex, characteristic of the phase of mobilization of the stress reaction, were thus observed. Conversely, however, morphological signs of inhibition of function of this zone could be also seen. At the same time, marked hyperplasia of cells of the zona reticularis of the cortex took place.

It is evident that the signs of a stress reaction observed in the early stage (2 h) after whooping cough vaccination are a response to introduction of toxic substances contained in the vaccine into the body. On the other hand, absence of signs of a stress reaction at the height of sensitization after whooping cough vaccination showed that the sensitization produced by whooping cough vaccine is unconnected with its toxic action.

The marked hypertrophy of the zona reticularis of the adrenal cortex observed 5 days after whooping cough vaccination is evidence of increased formation of its hormones, the anabolic steroids. This is evidently associated with the increased requirement of hormones promoting protein synthesis and, in particular, synthesis of antibodies, characteristic of the body at this period of immunogenesis.

Participation of hormones in the regulation of protein synthesis and, in particular, of antibody formation has recently been conclusively proved by investigations carried out especially by P. F. Zdrovskii's school. However, among the hormones participating in antibody formation, it is our opinion that the internal secretions of the zona reticularis of the adrenal cortex which have received least study. Further investigations must be carried out to determine the role of these hormones in immunogenesis and in post-vaccinal sensitization.

The inhibition of function of the zona fasciculata which we discovered at the height of sensitization after whooping cough vaccination is of considerable interest. Hormones liberated by the zona reticularis of the adrenal cortex, which are glucocorticoids and have catabolic action, possess a powerful desensitizing effect. Possibly, therefore, a decrease in the production of these hormones on the 5th day after whooping cough vaccination may play an important role in sensitization of the recipient at this period of immunogenesis.

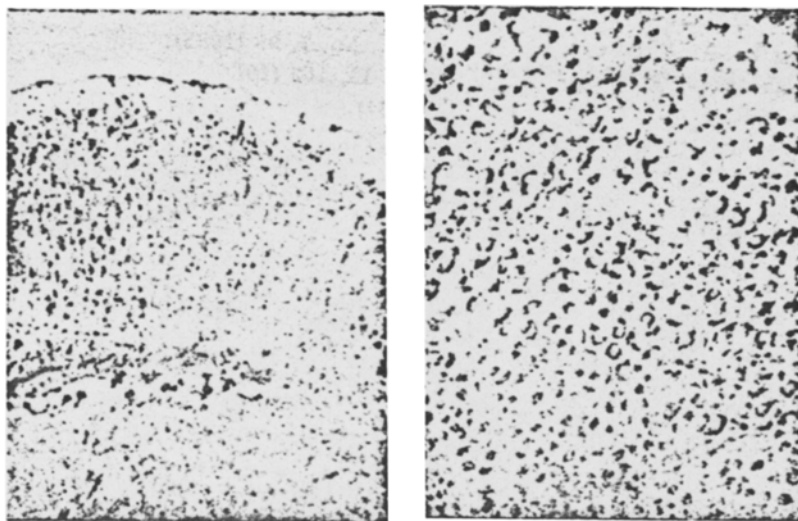


Fig. 1. Signs of the stress reaction in the adrenal cortex 3 h after whooping cough vaccination. Broadening of the zona fasciculata of the adrenal cortex, with decrease in lipid content of its inner portions. Stained with a mixture of Sudan III and Sudan IV and counterstained with hematoxylin. Magnification: 70 \times (A), 200 \times (B).

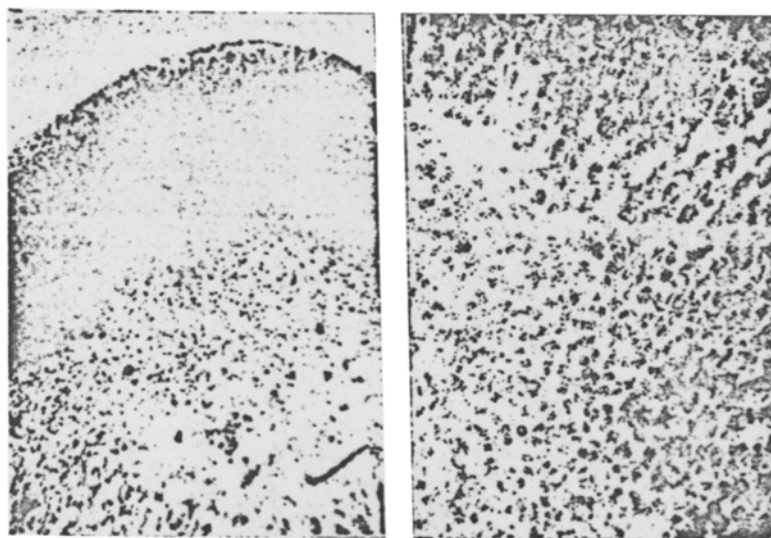


Fig. 2. Marked broadening of zona reticularis of adrenal cortex with relative narrowing of zona fasciculata 5 days after whooping cough vaccination. Staining as in Fig. 1. Magnification: 70 \times (A), 200 \times (B).

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