

# ACTION OF SOME HORMONES AND OTHER BIOLOGICALLY ACTIVE SUBSTANCES ON BLOOD BASOPHILS IN RABBITS

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Administration of hormones and other biologically active substances to rabbits, and blocking of the thyroid of these animals with methylthiouracil causes changes in the number of circulating blood basophils.

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As well as evidence of the participation of connective-tissue mast cells and basophilic granulocytes circulating in the blood stream in the genesis of allergic reactions [8, 16, 19, 21-27, 29], other results have been obtained indicating that degranulation of basophils with liberation of biologically active substances can take place not only in true allergic reactions, but also in other pathological states. In a previous investigation [1], degranulation of basophils was detected in experimental typhoid fever. It is still uncertain whether degranulation of the basophils takes place under the direct action of the toxic component of the endotoxin or under the influence of hormonal or other endogenous substances liberated during endotoxin poisoning.

According to the literature, the number of basophils in the circulating blood may change as the result of the action of hormones [4-7, 11, 13, 14] or of histamine [12] or heparin [3, 4, 17, 28]. However, these investigations are few in number and their results are contradictory.

We have investigated the effect of some hormones (ACTH, cortisone, thyroid extract), methylthiouracil, and other biologically active substances (heparin, histamine) on the blood basophils.

## EXPERIMENTAL METHOD

Blood samples were taken from the auricular veins of rabbits (weighing 2.5-3 kg) before, and 30 min, and 1, 2, 4, and 24 h after injection of the biologically active substances. Heparin was used as anticoagulant.

The leukocytes and basophils were counted by the method described previously [1]. Metachromatic granules of the basophils were stained with toluidine blue.

The effect of each preparation was investigated on 8-10 rabbits. The results were analyzed by statistical methods [2].

## EXPERIMENTAL RESULTS AND DISCUSSION

Intramuscular injection of ACTH (Exathin, Richter, Hungary) in a dose of 10-20 units was accompanied by a decrease in the total number of leukocytes. The number of basophils showed only a slight tendency to decrease, starting from 2 h after injection of the hormone. After 24 h the animals developed a mild leukocytosis and basophilia. From 2-4 h after intramuscular injection of cortisone (Cortone acetate, USA) in a dose of 10 mg/kg, the number of basophils fell by 50-70% (Fig. 1), without a change in the relative numbers of normal and degranulated forms of these cells. These results are in agreement with those obtained by other workers [5]. So far as the effect of ACTH is concerned, it may be that the doses which were used were insufficient to liberate the necessary quantity of endogenous corticosteroids. There is still no general agreement regarding the cause of the basopenia produced by corticosteroids [7, 15, 20, 24].

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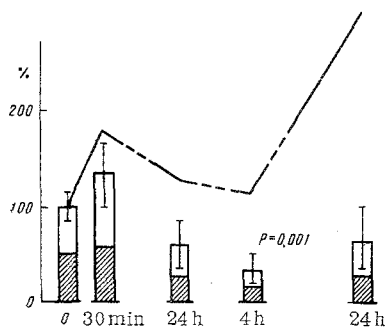


Fig. 1. Changes in basophil and leukocyte counts in rabbits' blood under the influence of cortisone. Abscissa, time of taking blood samples after injection of cortisone; ordinate, number of cells in percent of initial value. Columns indicate number of basophils; shaded part, normal basophils; unshaded part, degranulated cells. Vertical lines indicate mean error of arithmetic mean. Curve shows number of leukocytes.

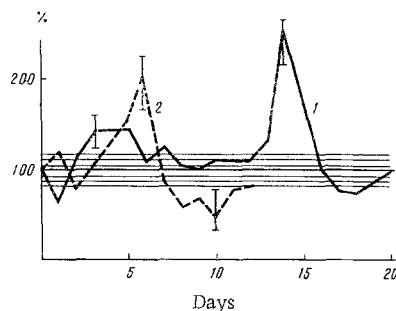


Fig. 2. Changes in basophil count in rabbits' blood under the influence of methylthiouracil (1) and thyroid extract (2). Abscissa, time (in days) after beginning of administration of substance; ordinate, basophil count as percentage of initial level. Vertical lines are confidence limits; horizontal lines are confidence limits of normal variations.

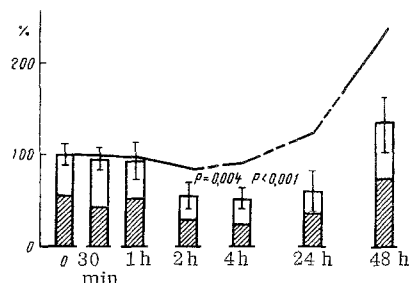


Fig. 3. Changes in blood basophil and leukocyte counts in rabbits after injection of histamine phosphate (125-150  $\mu\text{g/kg}$ ). Abscissa, time of taking samples; ordinate, number of cells in percent of initial value. Columns show basophil counts; shaded part, normal basophils; unshaded part, degranulated. Vertical lines show error of arithmetic mean. Curve denotes number of leukocytes.

Oral administration of thyroid extract (150 mg/kg for 7-10 days) was accompanied by an increase in the number of circulating basophils, reaching about 200% by the 3rd-5th day. The basophil level then began to fall. After discontinuation of thyroid administration the basophil count returned to its initial level within 3-5 days (Fig. 2). During oral administration of methylthiouracil (80 mg/kg daily for 10-14 days) the blood basophil count of the rabbits rose slightly starting on the 2nd day; the basophilia persisted for 5-6 days, and the count then returned to its initial level. After discontinuation of methylthiouracil the basophil count increased by between two and three times, and returned to its initial level after 2-3 days.

These results suggest that the basophil response to exogenous toxins is connected with the state of the thyroid function at the time of their administration. In myxedema the blood basophil count is increased [18], while in thyrotoxicosis it is reduced [9, 10, 14]. We observed that the basophil count was not increased until several days after the beginning of thyroid administration. This could be due to blocking of the liberation of thyrotropic hormone (TTH), which has a basopenic effect [13]. Basophilia after discontinuing methylthiouracil was evidently due to termination of blocking of the thyroid, the hormone of which, like exogenous thyroid extract, delays TTH liberation. As a result the basophil count rose. Prolonged administration of thyroid extract led to basopenia.

The basophil count in the rabbits' blood was reduced by about 50% 4 h after intravenous injection of histamine phosphate (125-250  $\mu\text{g/kg}$ ; Fig. 3). The relative numbers of normal and degranulated forms of basophils remained unchanged. The total leukocyte count at this time remained at its initial level.

After intravenous injection of heparin (500 units) the blood basophil count showed no significant change. According to some reports [3], heparin (5000 units) frequently causes a transient increase in the blood basophil count in man. However, in the present experiments the basophil count fell rather than rose under the influence of heparin.

These investigations suggest that the basophil count in the circulating blood is under the control of the endocrine system.

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