INFLUENCE OF CORTISONE ON THE BASOPHIL GRANULOCYTES AND THE TOTAL WHITE CELL COUNT IN RABBIT BLOOD

By

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Several investigators (Ehrich, 1953; Asboe-Hansen & Kaalund-Jørgensen, 1956; and Boseila, 1958) have suggested that the basophil leucocyte and the tissue mast cell have some functional relationship in addition to their morphological similarities.

Systemic cortisone administration results in a reduction of the number of the tissue mast cells, as well as degranulation or conglomeration of their granules (Asboe-Hansen, 1950; 1952; Videbæk et al., 1950); and oral cortisone administration induces a fall in the absolute count of circulating basophil leucocytes in man (Code et al., 1954).

Injected subcutaneously, cortisone brings about a marked decrease in the total leucocyte count in rats (Hamilton, 1957). A single injection of adrenal cortical extract, corticosterone or cortisol produced lymphopenia in rabbits within few hours (Dougherty & White, 1944). In rabbits, as in rats, the lymphocyte is the predominant circulating white cell, and hence a total leucopenia might be expected along with the lymphopenia.

The present investigation was carried out in order to elucidate the mechanism of the action of cortisone on the circulating basophils, and especially, the problem as to whether this effect is direct and/or part of a generalized leucopenic reaction.

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Sixteen white rabbits of a body weight of about 2000 gm. were used. The animals were kept in separate cages and were not used for at least one week and until they had become accustomed to handling and blood sampling.

A saline suspension of cortisone acetate\(^a\) (25 mg./ml.), was injected intramuscularly into the legs of the animals in daily doses of 20 mg. per kg. body weight every morning (9 a.m.) for a period of four successive days. Blood samples for basophil and total white blood cell counts were obtained from the ear veins, immediately before, as well as 4 hours after the injections. Morning counts were then followed up for about two weeks after cortisone withdrawal. Control counts were obtained from the same animals, injected with corresponding volumes of sterile physiological saline for 4 successive days prior to cortisone treatment. A modified Moore & James (1953) diluting fluid, was used for direct basophil counts in Fuchs-Rosenthal counting chambers. The same chambers were used for total white cell counts.

### RESULTS

To eliminate the differences in the individual counts, the mean of 4 control counts (morning as well as afternoon) for each animal was considered the 100 \(\%\), level to which the counts during and after cortisone treatment were related. Then the data obtained for all the animals were pooled and the means ± standard error calculated and used for plotting the curve of Fig. 1.

A significant total leucopenia (43 \(\%\)), and a pronounced basophil leucopenia (72 \(\%\)), was observed within 24 hours after the injection of the first dose of cortisone (Fig. 1). The decreased values were maintained during the period of cortisone treatment. The maximal fall in the number of basophil leucocytes was observed 24 hours after the last dose of cortisone, while that of the total white blood cells was reached 5 days later. During the period in which the level of the basophils was rising gradually, following cortisone withdrawal reaching its pre-cortisone level within two weeks, the total white cell count level lagged behind rising more slowly.

### DISCUSSION

The results obtained in this investigation, indicated that in the rabbit, in addition to a generalized leucopenic response to repeated cortisone injections, an even more pronounced basophil leucopenia was produced.

Mast cell granules which – like those of the basophil leucocytes – stain metachromatically, contain acid mucopolysaccharides of the hyaluronic acid and heparin type (Asboe-Hansen, 1954), as well as histamine (West, 1955). If corti-

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3. Cortisate Leo, Leo Pharmaceutical Products, Denmark.

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morning count (9 a.m.) • afternoon count (11 a.m.) • mean ± st. error

White blood cells (total)

Basophils

Fig. 1.

Effect of intramuscular injection of cortisone acetate (20 mg./kg. daily) on the counts of circulating basophils and of all white cells in rabbit blood (mean of 16 animals). The difference between control counts and the basophil and total white cell counts from the 6th day up to the 13th day is highly significant (P < 0.01); thereafter the P value is at the 1% level, except for the last basophil count which represents no difference from the control.

Cortisone has a direct degranulating action on the circulating basophils as it has on the mast cells, some of them may, according to the extent of granule release, escape detection by microscopy. The count would consequently fall. Code & Mitchell (1957) gave support to this idea of a direct action, when they suggested that cortisone apparently «unloads» the human and dog eosinophils and basophils of most of their histamine content.

The comparatively long period of two weeks after cortisone withdrawal needed for the basophil leucocytes to regain their pre-cortisone level in the circulation, indicates the probability of a depressing effect of cortisone on basophil leucocyte regeneration by the bone marrow. The findings of Resegotti (1957) on the life span of the granulocytes in rabbit blood, estimated to range between 4.4 and 13.2 days may provide further support to this assumption.

In the rabbit, tissue mast cells are comparatively few, while the number of blood basophils is relatively high. Hence, if cortisone administration leads to a condition requiring histamine and/or hyaluronic acid liberation in the tissues, and if basophil granulocytes and tissue mast cells are the only or the main
stores of these substances then the basophils of the rabbit might act as a substitute for the mast cells and migrate to the tissues.

The problem whether the behaviour of blood basophils under the influence of cortisone is induced by one or more of the above-mentioned factors, needs further investigation.

**SUMMARY**

Intramuscular injections of cortisone acetate in rabbits produce a pronounced basophil leucopenia in the blood lasting for 14 days, as well as a moderate decrease in the total white blood cell count.

The possible mechanisms of action of cortisone on the basophil leucocytes as well as the functional relationship between these cells and tissue mast cells are discussed.

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**REFERENCES**