THE EFFECT OF REPEATED INJECTIONS OF ADRENALINE ON THE HAEMOPOIETIC TISSUES OF THE RABBIT*

BY F. N. GHADIALLY†

From the Department of Pathology, Prince of Wales Hospital, London

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SUMMARY

The effect of repeated injections of adrenaline on the blood and haemopoietic tissues of the rabbit was studied. A "panhyperplasia" of the marrow was produced. No change was detected in the lymph nodes. The peripheral blood showed no significant change in the total erythrocyte, total and differential leucocyte and Cook-Arneth counts.

A single injection of adrenaline can produce a well-marked lymphocytosis and granulocytosis in the peripheral blood of man. This phenomenon is probably produced by mobilization of cells from the bone marrow and lymphoid tissues [Ghadially, 1952]. Further, a salivary leucocytosis can be demonstrated concurrently with the decline of the circulatory leucocytes when the effect of the drug wears off, suggesting that this is perhaps one of the mechanisms by which the blood picture is restored to normal [Ghadially, 1952]. Therefore, it would appear that the net result of an injection of adrenaline would be a loss of leucocytes from the circulation.

The experiment described in this paper was carried out to test whether repeated injections of adrenaline would make an animal lose a sufficient number of cells, so that hyperplastic changes might become demonstrable in the haemopoietic tissues.

The rabbit is believed to be less sensitive to adrenaline than man [Cameron, 1947]. Hence a preliminary experiment was performed in which 1 ml. of a 1:1000 solution of adrenaline was given intramuscularly to a rabbit weighing 2.8 kg, and the changes in the blood picture were followed over a period of 50 min by counts done on samples of blood obtained from the ear veins. Results showed that the response in the rabbit was similar to that in man [Ghadially, 1952], except that although weight for weight the rabbit had received a considerably larger dose, quantitatively the haematological response appeared to be less pronounced.

METHODS

Eleven, approximately 1 year old Agouti rabbits, weighing between 2.6 and 2.9 kg, were divided into an experimental and a control group. All animals received a diet consisting of bran, oats, carrots and a daily supply of greens. Adrenaline hydrochloride was administered intramuscularly to the experimental group three times a day each day of the week, except Wednesday and Sunday (see Table 1).

At autopsy, carried out on all rabbits, the spleen, right and left inguinal, right and left axillary and mesenteric lymph nodes were removed and kept separately for

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† Present address: Department of Pathology, The University, Sheffield.
Table 1. **Treatment of experimental and control animals**

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<thead>
<tr>
<th>Duration of treatment (days)</th>
<th>Experimental animals</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>R1</td>
<td>R2</td>
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<td></td>
<td>12</td>
<td>34</td>
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**Results**

**Peripheral blood.** No significant quantitative variation was found in any of the cellular components of the peripheral blood.

**Lymph nodes.** There were no significant macroscopical or microscopical changes.

**Spleen.** No striking difference between the test and control groups was seen, except that the spleen of two of the test animals showed a rather large number of phagocytes laden with haemosiderin and extracellular granules of pigment.

**Bone marrow**

**Macroscopical appearance.** Marrow from the experimental animals was redder and more cellular than that obtained from the control animals (Pl. 1, fig. 1). The increased cellularity and correspondingly diminished fat content was clearly demonstrated by the fact that most of the marrow from the experimental animals sank in the fixation fluid, while that from the controls floated.

**Microscopical appearance.** A comparison of the marrow from similar sites from the various animals showed that the marrow of every test animal was decidedly more vascular and cellular than any from the control group (Pl. 1, figs. 2–5). Differential counts done on Leishman-stained marrow films showed no difference between the control and experimental groups.

later study. Smears were made from the spleen and mesenteric lymph nodes and stained with Leishman’s stain. Haematoxylin and eosin sections were prepared from all the above-mentioned tissues. The humerus, femur and tibiofibula of both sides were removed in each animal, cleaned and sawn open longitudinally with a fine fret-saw. Each pair of bones split produced four ‘halves’; these (femora, tibiae and humeri) were examined as follows. The marrow of the first portion was removed entire, fixed in formol saline, and paraffin sections, stained with haematoxylin and eosin, were prepared. The second portion was fixed in Kaisering’s solutions and kept for macroscopic comparison with similar portions from other rabbits. Smears were prepared from the third portion stained with Leishman’s stain, and differential counts were done on the three specimens from each animal, dividing the cells into four large groups; the granulocyte series, the lymphocyte and monocyte series, nucleated red cells and megakaryocytes. The fourth portion was discarded. Studies of the peripheral blood were made on all the animals at the commencement of the experiment and shortly before each animal was killed. The determinations made were: total erythrocyte, total and differential leucocyte, and Cook-Arneth counts.


EFFECT OF REPEATED INJECTIONS OF ADRENALINE 11

DISCUSSION

The results of the experiment reported show that injections of adrenaline produce a well-marked hyperplasia of the bone marrow. Although such a marked degree of change was produced, no definite increase in the percentage of any particular series of cells was observed. This suggests that the various cellular elements must have all undergone a hyperplastic change. Broadly speaking, the degree of hyperplasia appeared to be proportional to the intensity and duration of treatment. However, rabbit R6, which received 168 mg adrenaline, showed less marked hyperplastic changes than R5, which received 102 mg.

The mechanism by which this ‘panhyperplasia’ of the marrow, with an unaltered peripheral blood picture, is produced is not quite clear. The granulocytic hyperplasia seen may have been produced in response to the loss of cells that occurs after each injection of adrenaline [Ghadially, 1952]. Goldzieher [1944] states that there is an increased erythrophagocytosis by the reticuloendothelial cells as a result of repeated injection of adrenaline, and in two of the six animals reported in this paper there was a suggestion of an increased erythrophagocytosis in the spleen. It is possible, therefore, that the erythroid hyperplasia is secondary to an increased destruction of red blood cells.

The unchanged peripheral blood picture may then be explained by assuming that the hyperplastic marrow succeeds in rapidly replacing the lost leucocytes and erythrocytes; on the other hand, the ‘panhyperplasia’ seen may be due to a direct stimulant action of the drug on the bone marrow, and both the erythrophagocytosis, as well as the escape of leucocytes in the saliva might be looked upon as mechanisms by which the excess of cellular elements mobilized is disposed of.

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REFERENCES


DESCRIPTION OF PLATE

Fig. 1. Photograph showing the halves of two femora. The lower one is from a control animal (R11), while the upper one is from a test animal (R5). The rather fatty acellular appearance of the former is well contrasted with the intensely hyperplastic nature of the latter.
Fig. 2. Marrow from upper end of the femur of a control animal showing paucity of cellular elements and abundance of fat (×15).
Fig. 3. Marrow from upper end of the femur of a test animal (×15). Note increased cellularity.
Fig. 4. Same as fig. 2 (×324).
Fig. 5. Same as fig. 3 (×324). Note increased vascularity and cellularity.