

EFFECT OF ADRENERGIC β -RECEPTOR BLOCK ON EARLY RESPONSES OF THE HEMATOPOIETIC ORGANS TO STRESS

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Changes in the cell composition of the hematopoietic organs of rats in response to injection of adrenalin were investigated after blocking of the adrenergic β -receptors with propranolol. After the injection of adrenalin the number of lymphocytes in the spleen fell but the number in the bone marrow rose, and at the same time the number of mature neutrophils decreased. Preliminary injection of the β -adrenergic blocking agent considerably reduced migration of the lymphocytes into the bone marrow but did not affect the intensity of cellular depopulation of the spleen. It is concluded that β -adrenergic mechanisms play an important role in the early response of the bone marrow to extremal factors.

KEY WORDS: stress response; hematopoiesis; adrenergic block.

Investigations in the writers' laboratory have shown [1-5] that the most characteristic early changes arising in the hematopoietic organs in response to the action of extremal stimuli are a decrease in the number of mature granulocytes, an increase in the number of lymphocytes in the bone marrow, and a simultaneous decrease in the number of cells in the lymphoid organs (the thymus and spleen). The investigation of the mechanisms of regulation of the early response of the hematopoietic organs is very interesting. In an earlier paper [3] the writers showed that injection of adrenalin gives rise to changes in the hematopoietic organs similar to those produced by the action of extremal stimuli, whereas blocking the α -adrenergic receptors prevents cellular depopulation of the spleen without, however, affecting the degree of depopulation of the thymus or changes in the cell composition of the bone marrow.

This paper describes the results of an investigation of the changes taking place in the hematopoietic organs under the influence of adrenalin after blocking of the adrenergic β -receptors.

EXPERIMENTAL METHOD

Wistar rats of both sexes weighing 160-180 g were used. Adrenalin hydrochloride was injected subcutaneously in a dose of 1 mg/kg. The effective dose of the adrenergic α -blocking agent, dihydroergotoxin (Spofa, Prague) and the dose of the β -blocking agent propranolol (Obsidan, East Germany) were determined by the usual method [5, 6, 11]. After subcutaneous injection of dihydroergotoxin in a dose of 0.25 mg/kg, the α -adrenergic effect of subsequent injection of adrenalin was almost completely blocked for 2.5-3 h; injection of 5 mg/kg propranolol blocked the β -adrenergic depressor effect of isoproterenol for the same period [6].

The number of cells in the spleen and thymus [1] and the number of nucleated cells in the fema [9] were determined; with the aid of the myelogram calculated from squash preparations the absolute number of cells of the various generations was determined. The hematopoietic organs were investigated in the rats 3, 6, 12, and 24 h after injection of the drugs. From 10 to 15 rats were used at each period.

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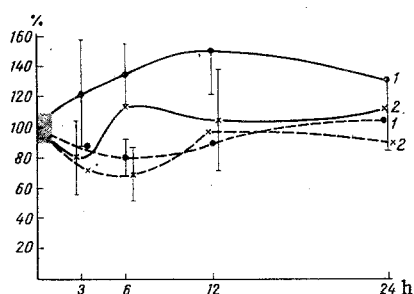


Fig. 1

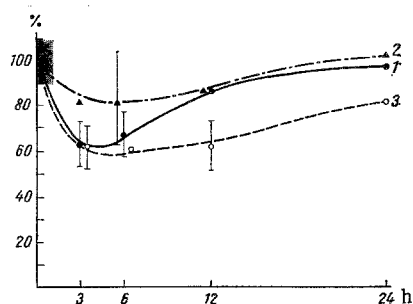


Fig. 2

Fig. 1. Change in cellular composition of bone marrow after injection of adrenalin with (1) and without previous administration of propranolol (2). Continuous lines denote lymphocytes; broken lines polymorphs. Confidence limits calculated for $P=0.05$ are shown. Abscissa, time after injection of drugs (in h); ordinate, number of cells (in % of initial level).

Fig. 2. Number of cells in spleen after injection of adrenalin (1), propranolol (2), and propranolol followed by adrenalin (3). Remainder of legend as in Fig. 1.

EXPERIMENTAL RESULTS

After injection of adrenalin the number of lymphocytes in the bone marrow increased by 50% and then fell (Fig. 1). A previous investigation [3] showed that dihydroergotoxin, a toxic α -blocking agent, produced the same increase in the number of lymphocytes as adrenalin. Injection of propranolol (a β -blocker), on the other hand, caused no increase in the number of lymphocytes. Preliminary injection of propranolol, moreover, prevented the increase in the number of lymphocytes 3 and 12 h after the injection of adrenalin. At other times the effect of the adrenergic β -receptor block on the lymphocytes was less marked. Combined preliminary injection of α - and β -blocking agents reduced the degree of increase in the number of lymphocytes in the bone marrow in response to injection of adrenalin only very slightly.

As regards the decrease in the number of mature cells in the bone marrow (following their discharge into the peripheral blood), the adrenoblocking agents had no significant effect on this response.

Unlike dihydroergotoxin, propranolol had no effect on the degree of cellular depopulation of the spleen caused by adrenalin (Fig. 2).

As regards the effect of propranolol on the changes in the cell composition of the thymus after injection of adrenalin, the results obtained were not consistent.

Lymphocytosis followed by neutrophilia has been described in healthy and splenectomized persons after injection of adrenalin [12]. On this basis it was concluded that contraction of the spleen does not play an important role in the development of the leukocytosis. No evidence of increased discharge of lymphocytes through the thoracic duct likewise has been obtained. It has also been shown that the separate administration of α - and β -adrenergic blocking agents does not change the character of the lymphocytosis induced by adrenalin and that this leukocytosis is not the result of mobilization of the intravascular leukocyte pool.

The writers have found that adrenalin, like stressors, causes changes in the cell composition of the hematopoietic organs. Whereas the α -adrenergic blocking agent prevented cellular depopulation of the spleen [3], evidently by preventing constriction of the capsule and vessels of the spleen, the β -blocking agent had no such effect. Evidence of the absence of β -receptors in the splenic capsule of rabbits and dogs has been obtained [7, 11]. The possibility that they are absent also in rats cannot be ruled out. On the other hand, the increase in the number of lymphocytes in the bone marrow under the influence of adrenalin evidently takes place with the participation of β -receptors.

The response of urgent mobilization of mature granulocytes from the bone-marrow pool, however, was not reduced by preliminary injection of α - or β -blocking agents. Consequently, this effect of adrenalin could hardly be direct. These observations on the effect of adrenalin on the number of mature granulocytes in the bone marrow agree with data in the literature [13].

The regulation of lymphopoiesis in the thymus takes place chiefly through local humoral effects of reticular and epithelial cells [10]. Lymphopoiesis in the lymph glands and spleen takes place chiefly under the influence of antigenic stimulation. So far as regulation of the cell composition of the bone-marrow lymphoid tissue is concerned, this problem remains almost completely unstudied. To judge from the present findings, this regulation may take place with the participation of adrenalin.

The increase in the number of lymphocytes in the bone marrow precedes the activation of myelopoiesis, restoration of the cellular composition of the bone marrow, and even the development of transient hyperplasia of the myeloid tissue [4]. These results are evidence of the adaptive and trophic influence of the sympathetic nervous system on hematopoiesis during exposure to stress.

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