fected extrinsically by various factors. The two most important are (1) the affinity of fibrin for the walls of the container and (2) the cell volume. Thus, normal blood will show clot retraction in a glass test tube, but not in a collodion-coated tube (6). Presumably, fibrin becomes more firmly attached to a collodion than to a glass surface. Since the erythrocytes and leucocytes are noncompressible, it follows that the greater the cell volume, the less will be the clot retraction. Retraction is generally marked in anemic blood and almost absent in polycythemic blood. The clinical significance of these observations has been discussed elsewhere (7).

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The Adrenal Gland and Hemopoiesis[1]

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Accumulating evidence indicates convincingly that the endocrine gland system exerts a regulatory influence on certain phases of blood formation and destruction in the vertebrate organism (1, 2). The glands that appear to be implicated in these processes include the pituitary, thyroid, gonads, and adrenal. More recently, considerable attention has been focused on the effects produced by adrenal cortical factors upon the white blood cell elements (3, 4, 5). A decrease in the circulating lymphocytic and eosinophilic levels has now become recognized as a sensitive indicator of the presence of extra quantities of adrenal cortical or adrenocorticotropic factors in the blood stream (3, 6, 7). Although some data have appeared on the manner whereby the cortical hormones influence lymphocytic numbers in the peripheral blood (8, 9), only fragmentary information is available concerning the mechanism by which they affect the granulocytic and erythrocytic levels and, more particularly, concerning their effects on the site of blood formation, the bone marrow. The need for such information and, in addition, the current application of the adrenal cortical factors in the treatment of myelogenous leukemia (10) make important an experimental investigation of the effects of chronic adrenal insufficiency and replacement therapy on the hemopoietic processes. This report describes some preliminary results obtained in one phase of this research.

TABLE 1

EFFECTS OF ADRENALECTOMY AND REPLACEMENT THERAPY UPON BONE MARROW CELLULAR PERCENTAGES (MEAN ± STANDARD ERROR)

Elements*	Controls (14)†	Adrenalec- tomized (8)	Adrenalec- tomized + Com- pound E, 0.5 mg (4)	Adrenalec- tomized + Com- pound E, 1.0 mg (4)
Blasts	1.6 ± 0.1	3.2 ± 0.5	0.8 ± 0.2	0.8 ± 0.1
Neutrophiles Promyelo- cytes and myelocytes	10.9 ± 0.6	17.1 ± 1.1	6.6 ± 1.0	6.3 ± 1.3
Metamyelocytes and seg- menters	21.1 ± 1.4	24.6 ± 0.7	36.1 ± 1.8	39.4 ± 4.5
Eosinophiles (all forms)	9.1 ± 0.8	14.2 ± 0.8	9.0 ± 1.8	8.2 ± 2.5
Total granulocytes	41.6 ± 2.4	55.9 ± 1.8	51.6 ± 4.3	53.7 ± 6.7
Nucleated erythrocytes	56.5 ± 2.1	40.5 ± 2.2	47.5 ± 4.2	43.7 ± 4.9
Erythrocytes/ myelocytes	1.46 ± 0.1	0.73 ± 0.1	0.96 ± 0.2	0.85 ± 0.2

* Lymphoid cell elements, which are not included in the myelograms, were not affected by the experimental treatments and did not exceed 2% of the total population in the control or adrenalectomized animals of the particular strain of rats employed.

† Numbers of animals employed are given in parentheses. All adrenalectomized animals were observed and treated for a 2-week period beginning with the first day of operation.

Groups of young adult female rats of a hardy, closely inbred strain, weighing 140–170 g, were adrenalectomized and maintained on 1% sodium chloride given as drinking water. Eight of the 14 controls were sham-operated and injected with 1–2 ml of 1% saline daily.

The peripheral blood of the adrenalectomized rat is characterized by the development of an anemia that attains its maximum (20–25% below normal) 2–3 weeks after the operation. The red cell counts and hemoglobin tend to rise following this time, but normal values are not reached up to 8 weeks subsequent to the operation. These results are in agreement with the data reported by Crafts (11). Associated with the anemia is an increased resistance of the red cells toward hypotonic saline. Their decreased fragility attains its maximum at about the time the anemia has reached its peak. No significant alterations in the peripheral total white cell and differential counts were observed during the experimental period.

All animals were killed by exsanguination, and marrow cell counts made from combined femoral and tibial marrows suspended in homologous serum and Giemsa-stained. A total of 1,500 nucleated cells was counted for each animal by use of the method of classification suggested by Endicott and Ott (12). It will be seen from Table 1 that 2 weeks after the adrenalectomy there occurs a rise in the percentages of total granulocytes in the marrow. The increase is due to significant elevations in the percentages of all myeloid components, including blasts,

eosinophilic, and young and mature neutrophilic elements. These changes are accompanied by a significant diminution in the percentages of nucleated erythroid elements, with a consequent decrease in the values of the erythroid-myeloid cell ratios, as compared with the untreated and sham-operated controls.

Administration of whole adrenal cortical extract[3] (1–2 ml daily) to adrenalectomized rats, beginning with the first day of operation, although effective in preventing the development of the peripheral anemia and increased red cell resistance, is without significant influence upon the marrow components, except for a concomitant decrease in the percentages of blast cells. Table 1, however, indicates that Compound E (17-hydroxy-11-dehydro-corticosterone acetate[4]), in dosages of 0.5–1.0 mg daily, is partly effective in restoring the bone marrow myelograms to normal values. This substance significantly reduces the degree of myeloid immaturity, and the most significant decreases occur in the eosinophilic and young neutrophilic cell groups, with accompanying increases in the percentages of mature neutrophilic forms. Erythroid-myeloid cell ratios are increased, but completely normal values are not obtained with these dosages of hormone. Significant decreases in the eosinophilic levels of the peripheral blood are also observed when this hormone is given to the adrenalectomized animal.

It is thus apparent that the marrow of the adrenalectomized rat is characterized by increased percentages of myeloid elements, associated with elevated levels of eosinophilic and young neutrophilic forms, tending toward a leukemoid state. The decreased nucleated erythroid cell percentages could account for the peripheral anemia that develops in the salt-maintained adrenalectomized animal. Despite the changes that occur in the granulocytic percentages in the marrow, however, no consistent trends were observed in the peripheral white cell picture with chronic adrenal insufficiency. It should be borne in mind that peripheral blood cell values may be influenced by a variety of processes, of which type and rate of cell production are only two. A complete elucidation of the question as to how the adrenal cortex influences the numbers of circulating blood cells can be achieved only after the effects of adrenal insufficiency and replacement therapy are studied in connection with such additional factors as total functional marrow mass, rate of release of cells from the marrow, longevity of the cells in the circulation, and possible redistribution of the cells to other organs.

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Modified Laboratory Lyophil Apparatus

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A modification of the lyophil apparatus of Holzman (2) has been in use in this laboratory for several months and has been free from one objectionable feature of the original design. The ring seal at the top of Holzman's apparatus is a point of weakness, since any movement of the center tube will cause breakage, even though this tube is supported on glass pins.

Our apparatus replaces the sealed-in center tube with a female standard taper joint, so that the body of the apparatus consists of six 34/45 female joints arranged symmetrically and at right angles to each other (Fig. 1).
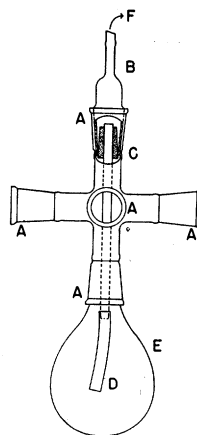

FIG. 1. Lyophil apparatus, side view: A, ports, ST 34/45 female, for flasks; B, exhaust tube, ST 34/45 male; C, cork insert in exhaust tube; D, removable glass center tube with flexible end (Tygon) extending into receiver flask; E, receiver constructed from 800-ml Kjeldahl flask; and F, connection to vacuum.

A male joint is drawn and sealed to 10-mm glass tubing, and the center tube of the same diameter is inserted through a cork in the lower end of this joint. It is not necessary to achieve a completely gas-tight seal by insertion of the cork, as there is no restriction on gas flow through the center tube, the purpose of the latter being