A.C.T.H. or a longer course would have achieved any more striking results can be determined only by further clinical trials. All that can be said at the time of writing is that the effects of A.C.T.H. in the two cases of presumed congenital haemolytic anaemia were largely negative, in contrast to its dramatic effect in one case of acquired haemolytic anaemia.

In discussing the rationale for the use of A.C.T.H. in acquired haemolytic anaemia, Dameshek (1950) expresses the opinion that the beneficial effects may be due to a depression of antibody formation by the lymphoid tissue. Thorn (1950), on the other hand, feels that antibody formation may not be affected, but the reaction of the tissues to the antigen may be significantly altered. The fact that haemolysis was rapidly controlled in the first case while abnormal antibodies were still present does not support the view that the action of the adrenocortical steroids depends on a depression of antibody formation. An alternative hypothesis is that the damaging action of some product of the union of antigen and antibody is suppressed.

Summary

The results of the administration of A.C.T.H. in three cases of haemolytic anaemia are reported.

The administration of A.C.T.H. in a dose of 100 mg. daily for 10 days rapidly controlled the haemolytic phenomena in a case of acquired haemolytic anaemia, and symptoms have not recurred since.

In two cases of congenital haemolytic anaemia there was little or no response to the administration of A.C.T.H. in similar doses.

Evidence is brought forward to suggest that the control of haemolysis by A.C.T.H. in acquired haemolytic anaemia is not due to a suppression of the production of abnormal antibodies.

The A.C.T.H. used in these cases was supplied by the Medical Research Council, to whom we are indebted. We wish to express our gratitude to Dr. R. A. Cummings, Director of the Blood Transfusion Service, South-East Region, Scotland, who was responsible for the serological investigations.

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Speaking at Cardiff on March 12, the Minister of Health said the number of notifications of tuberculosis, which had been going up and down in the past 10 years, was now definitely showing signs of falling, and the number of deaths was going down. These developments were due to the applications of medical knowledge and skill supported by our National Health Service. In the years 1916–20 the average annual number of deaths from tuberculosis in England and Wales per million of the population had been 1,440; in 1940 it had been 670; in 1949 it had fallen to 450. Since the start of the National Health Service 3,550 additional hospital beds had been made available in England and Wales for the treatment of tuberculosis. He hoped that by the end of this year at least 2,000 more would be provided. Tuberculosis had for a long time been a more deadly enemy in Wales than in England. Mr. Clement Davies had pointed out in his report that, whereas in 1916–20 the mortality from tuberculosis had been the same in Wales as in England—namely, 1,440 per million of population—by 1936 the English figure had fallen to 680 and the Welsh only to 860. In 1949 the English figure was 415 and the Welsh 608.

EFFECT OF A.C.T.H. AND SUPRARENAL EXTRACT ON THE BONE MARROW*

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A connexion between the lymphoid tissues and the suprarenal cortex has been postulated with varying degrees of emphasis ever since Addison's (1855) classical monograph first appeared. Once Addison's disease had become recognized as a clinical entity, with its usually fatal termination, pathologists began to accumulate information about the lymphoid tissue hypertrophy which came to be regarded as one of the characteristic features of the disease, and which was even described as a "status lymphaticus" (Hedinger, 1907).

With the beginning of the modern study of the suprarenal cortex it became possible to investigate the action of individual hormones; and, of the two main groups of steroid hormones which the suprarenal cortex was known to produce, it soon became generally held that it was those with an oxygen atom at C 11 which were more especially associated with the lymphoid tissue changes. This view was challenged by Selye and his co-workers (Dontigny, 1946), but the demonstration (Hechter *et al.*, 1949), by perfusion of the isolated suprarenal with deoxycortone, that this substance could thereby be converted into 11-oxy compounds seemed to provide an obvious way of reconciling these conflicting points of view.

The most extensive work on the relation between the suprarenal cortex and lymphoid tissue is that of Dougherty and White (1945, 1947), who from 1943 to 1947 published a number of papers on the subject, and in 1947 summarized the results both of their own work and that of other investigators. Broadly speaking, their work followed two main lines. After the administration of adrenocorticotropic hormone and cortical hormones, they not only observed regressive changes in the lymphocytes and lymphoid tissue, but also attempted to correlate these with increased formation of gamma globulin and antibodies. The problem has been extensively reviewed elsewhere (Yoffey, 1950), and so far as antibody formation is concerned all that need be said here is that considerable doubt has been cast on either the increased production of antibodies in response to cortical hormones (Eisen *et al.*, 1947; Thatcher *et al.*, 1948) or the relationship between antibodies and lymphocytes (Fagraeus, 1948; Ehrlich *et al.*, 1949). It is doubtful, in fact, whether there is any correlation whatever between the lymphoid tissues and any of the plasma proteins (Andreasen *et al.*, 1948).

*Read by Professor Yoffey to the Section of Anatomy and Physiology at the Annual Meeting of the British Medical Association, Liverpool, 1950.

So far as the regressive changes in lymphoid tissue are concerned, four main lines of evidence have been adduced. The first line is an old observation by Downey and Weidenreich (1912), who described, in sections of lymph nodes, elongated processes of the lymphocyte cytoplasm which could then break off from the cell. This appearance we have been unable to confirm, nor, so far as we know, have other workers described it in sections, as originally noted by Downey and Weidenreich, even after the administration of A.C.T.H. and cortical hormones.

However, in smears of lymph nodes, Dougherty and White (1945) described lesser degrees of cytoplasmic budding, and they interpreted these as one way in which lymphocytes discharged gamma globulin into the blood. They also noted degenerative changes in the nuclei. One may, however, not infrequently find similarly damaged lymphocytes in "normal" lymphoid tissue, and what is therefore required is a quantitative comparison of the damaged cells in normal lymphoid tissue with those in the same tissue after the administration of A.C.T.H. or cortical extracts. Furthermore, it ought to be possible to devise a test to show increased fragility of the lymphocytes under such experimental conditions, but this we have not yet been able to do. It is pertinent to note in this connexion that A.C.T.H. and cortical hormones have no action on lymphocytes *in vitro* (Robertson, 1948; Delaunay *et al.*, 1949). Yoffey and Baxter (1946) actually observed hypertrophy of lymphoid tissue after daily injections of "eschatin" (an aqueous extract of suprarenal cortex) for one month. Their results, however, admit of several interpretations. Thus it is conceivable that the daily injections of eschatin induced a secondary atrophy of the animal's own suprarenals (cf. Ingle *et al.*, 1938), but that the eschatin was nevertheless much less potent in its action on lymphoid tissues than the secretion of the animal's suprarenals. It is not clear, also, to what extent general metabolic changes might react on lymphoid tissue.

The third line of evidence has been the observation of loss in weight of lymphoid tissue (including the thymus) after the administration of A.C.T.H., cortical extracts, or various steroid fractions. This type of change appears to be fairly well substantiated. The loss of weight might be due either to destruction of lymphocytes and inhibition of mitosis or else to their leaving the lymphoid tissues at a greater rate than usual. In the latter case they should enter the blood stream and give rise to a lymphocytosis.

This brings us to the fourth line of evidence—namely, that A.C.T.H. and cortical extracts may give rise to lymphopenia. Now lymphopenia is a phenomenon which can be observed clinically, and is therefore of immediate interest to the clinician. But, though readily observed, its significance may be very difficult to determine. Since the present work may have a direct bearing on this, a brief consideration of the factors which govern the level of the blood lymphocytes may not be out of place.

Level of the Blood Lymphocytes

Though we are still ignorant of the part played by the lymphocyte, its association with the lymphatic vessels provides an opportunity of forming some idea of the body's lymphocyte production. Lymphocytes are formed in lymphoid tissue, and then may enter the blood directly, as in the case of the spleen, or indirectly, by first obtaining access to the lymphatics, as in the case of the lymph nodes. Even in the lymph nodes, however, it is possible that a considerable number of lymphocytes enter the blood directly, by traversing the endothelium of the blood capillaries.

So far as direct entry of lymphocytes into the blood capillaries is concerned, we are no better off than with the other blood cells from the point of view of quantitative estimation. But in the case of the lymph-borne lymphocytes nature has provided a convenient bottleneck in the thoracic and right lymph ducts, where all the lymph of the body can be collected just as it is about to enter the blood stream, and its contained lymphocytes counted. This gives a *minimal* figure for the total lymphocyte output of the body. The figure is minimal not only because of the lymphocytes which are entering the blood directly, without the intermediation of the lymph stream, but also because of the possible existence of other lymphatico-venous communications.

Once the lymphocytes have entered the blood stream they do not remain there for very long. There is no satisfactory evidence of extensive destruction of lymphocytes in the blood, and, as large numbers of newly formed lymphocytes are continually entering the blood stream, one must assume that an equal number of these cells is steadily leaving, for otherwise the level of the blood lymphocytes would not remain constant. By comparing the figures for lymphocyte output with the number of lymphocytes normally present in the circulation, it is possible to draw up a rough balance sheet and estimate the turnover of the blood lymphocytes. Thus it has been calculated that in the dog the blood lymphocytes are replaced about twice daily (Yoffey, 1936), and in the cat and rabbit four or five times daily (Sanders *et al.*, 1940). It must be re-emphasized that this is a minimal replacement figure, for in all the quantitative studies only thoracic duct lymphocytes have been counted, and the right lymph duct ignored. Furthermore, there is no way of measuring the lymphocytes which directly enter the blood. If, as some workers have concluded—for example, Sanders *et al.* (1940)—the number of these latter lymphocytes is at all considerable, and if it equals in magnitude the lymph-borne lymphocytes, then in the case of the dog the lymphocytes would stay in the blood for something like six hours, and in the cat and rabbit for two and a half to three hours.

As to the destination of the many lymphocytes leaving the blood, three regions seem to merit the most serious consideration—namely, the lumen of the intestine, the connective tissues of the body, and the bone marrow. At one time excretion into the lumen of the alimentary canal (Bunting and Huston, 1921) was considered the most likely fate of the blood lymphocytes; but this view, though it still has its supporters, has on the whole fallen into disfavour. As to the bone marrow, while it has an astonishingly high lymphocyte content (see below), the presence of these cells has become involved in one of the most long-standing haematological controversies concerning the origin of the formed elements of the blood, and has tended to be more or less ignored.

Whatever the fate of the blood lymphocytes, it is clear that the number present in the blood is the result of a balance between those entering and those leaving it. With the notation of Drinker and Yoffey (1941), if x = the number of lymphocytes entering the blood over a given period and y = the number leaving it in that time, then normally $\frac{x}{y}=1$, and the level of the blood lymphocytes remains constant. If $x>y$ over a period,

then lymphocytosis will develop. This result will be obtained equally whether x be raised above or y depressed below the normal level. In other words, lymphocytosis may be of three types—namely, $\frac{x+}{y-}$, $\frac{x}{y-}$ or $\frac{x+}{y}$. Similarly there may be three varieties of lymphopenia—namely, $\frac{x-}{y}$, $\frac{x}{y+}$, or $\frac{x-}{y+}$. To which of these three types any lymphopenia belongs it is quite impossible to decide solely on the basis of blood counts. In the case of the lymphopenia produced by A.C.T.H. or cortical extract, the work of Dougherty and White (1947) would make one incline to the view that it was $\frac{x-}{y}$ in type—a diminished entry of lymphocytes into the blood stream. Direct measurement of thoracic duct lymphocytes has in fact appeared to confirm this interpretation (Reinhardt and Li, 1945; Yoffey, Reiss, and Baxter, 1946), but the experiments were not conclusive (see also Valentine *et al.*, 1948), for they were concerned only with thoracic duct lymphocyte output, and did not pay attention to the right lymph duct. Furthermore, they could not throw light on the numbers of lymphocytes directly entering the blood stream.

In view of all these facts, it was thought worth while to investigate the lymphocyte content of bone marrow after the administration of A.C.T.H. and cortical extracts. Attention was further attracted to the marrow because these substances produced changes in several other blood cells, giving rise to neutrophilia, eosinopenia, and perhaps even some degree of erythraemia (cf. also the occasional erythraemia of Cushing's syndrome). It seemed a not unreasonable working hypothesis that an effect on several different types of blood cells might be due to action on a single tissue—the bone marrow. Apart from these considerations, however, another reason for directing attention to the bone marrow was the fact that a technique had already been employed (Yoffey and Parnell, 1944) for making absolute counts of the nucleated cells of bone marrow. In view of the finding of Dougherty and White (1945), that after the administration of A.C.T.H. and cortical extracts there was destruction of marrow lymphocytes, it was thought that such a technique of quantitative analysis would demonstrate the change most convincingly

Material and Technique

The technique employed in the examination of the bone marrow is designed to give absolute counts of nucleated cells per unit of marrow volume. The principle of the method is to mix together known weights of bone marrow and oxalated plasma, and then shake up the marrow to obtain an even suspension of cells, which can be counted and from which smears can be prepared and stained in the usual way. The technique described previously (Yoffey and Parnell, 1944) has been improved upon by determining the specific gravity of both bone marrow and plasma, instead of assuming them both to be 1. Further, after many trials the marrow of the guinea-pig humerus was found to be the most suitable. It is far superior to the costal marrow of the rabbit, on which the previous counts were made, for it contains very little fibrous or fatty tissue and yields an admirable cell suspension

The marrow is obtained after the anaesthetized animal has been killed by bleeding in order to drain away from the marrow any excess blood. It is the admixture of marrow tissue with varying and unknown amounts of blood which renders the ordinary marrow biopsy so unsuitable for quantitative work. No doubt even with the present technique some blood was still retained in the marrow, the red cells in which ranged from 574,000 to 2,080,000 per c.mm., while those in the blood ranged from 4,330,000 to 7,000,000 per c.mm. Thus the method is still not perfect, and, depending upon the proportion of red cells which are mature marrow cells about to enter the blood to those which are blood cells contained in the vessels of the marrow, the counts obtainable will be somewhat below the true absolute count. In other words, the absolute figures for marrow lymphocytes are minimal.

From the cell suspension, counts were made with the haemocytometer in the usual way, and smears, with or without preliminary fixation in pure methyl alcohol, were stained with Wright's stain; the diluting fluid was at *p*H 6. For absolute counts it is of course necessary to include all cells, even those which are damaged. This was in any case no disadvantage, for special interest attached to changes in the number of damaged cells, which were fully expected to be increased. It will be seen from Table I that the number of these damaged cells is quite appreciable. It is to be noted, however, that both in the counting chamber and in wet preparations examined by phase contrast there was remarkably little evidence of cell damage in either the normal or the treated animals, and it was only in the dry smears that appreciable cell damage was observed. The tendency to cell damage, a recognized drawback of the dry-smear technique to be offset against its well-known merits, was regarded as a positive advantage in the present experiments, as it would presumably accentuate any trend towards increased fragility of the cells. It is worthy of note that, despite the cell trauma associated with the dry-smear technique, the figures obtained for mean lymphocyte percentage in normal marrow were of the same order as those found in guinea-pig marrow by Epstein and Tompkins (1943), both by supravital staining (11.3%) and in sections (10.2%).

The experiments fall into four groups. In the first group 25 normal marrows were counted. In Group II (nine experiments) marrow counts were made six hours after the intraperitoneal injection of 0.1 ml. of eschatin per 100 g. body weight, while in Group III marrow counts were made six hours after the injection of 1 mg. of pituitary A.C.T.H. (in 2 ml. of saline) per 100 g. of body weight. In Group IV 10 guinea-pigs were given intraperitoneal injections of saline (2 ml.) as controls; in five of these we used saline which had been in stock for some time, while in the other five pyrogen-free saline was employed.

TABLE I.—*Absolute Counts of Nucleated Cells per c.mm. of Guinea-pig Bone Marrow*

Type of Experiment	No. of Animals	Total Nucleated Cells	Total Myeloid Cells	Total Erythroid Cells	Damaged Cells	Lymphocytes	Monocytes	Reticulum Cells
Normal	25	1,235,000	404,800	153,000	457,000	144,800	54,800	7,200
Saline controls	10	1,500,000	520,000	239,000	451,000	183,000	76,800	8,000
Eschatin	9	1,151,000	363,400	105,900	379,000	269,000	38,500	2,400
A.C.T.H.	10	1,059,000	302,900	134,800	357,600	203,400	33,830	6,400

For supplies of eschatin we are indebted to the courtesy of Dr. J. Stanley White, of Messrs. Parke, Davis & Co., while the A.C.T.H. was kindly placed at our disposal by Dr. M. Reiss (cf. Reiss and Halkerston, 1950).

Results

Table II gives the mean results of the lymphocyte counts in the four series of experiments, expressed both as percentages and in absolute figures. The percentage of lymphocytes in the 25 normal marrows was 11.3 ± 1.4, and the absolute count $142{,}100 \pm 16{,}000$ per c.mm. of marrow. This corresponds quite closely with the counts obtained by Epstein and Tompkins (1943). Earlier counts on rabbit marrow (Yoffey and Parnell, 1944) gave the lymphocytes as 12–48% of the total nucleated cells of the marrow, and the mean absolute count as 61,000 per c.mm. Apart from the possibility of species differences, the present guinea-pig counts, for the reasons already mentioned, were technically much more satisfactory.

Substance Administered:	Eschatin	A.C.T.H.	Normal	Saline Controls
Number of Experiments:	9	10	25	10
Lymphocytes per cent of total nucleated cells of bone marrow	23.1 ±1·8	19·1 ±1·4	11·3 ±1·4	12·1 ±1·6
	t 4·63, $p > 0.001$	t 3·29, $p < 0.01$		t 0·347, $p \gg 0.1$
Lymphocytes in absolute numbers per c.mm. of marrow	269,000 ±32,000	203,400 ±30,000	142,000 ±16,000	183,000 ±26,000
	t 3·55, $p < 0.01$	t 1·804, $0.05 < p < 0.1$		t 0·142, $p \gg 0.1$

TABLE II.—Lymphocyte content of bone marrow in normal and experimental animals.

In the nine eschatin experiments the mean lymphocyte count was $269{,}000 \pm 32{,}000$ per c.mm. of marrow, and the percentage was 23.1 ± 1.8, while in the ten A.C.T.H. experiments the mean lymphocyte count was $203{,}400 \pm 30{,}000$, with a percentage of 19.1 ± 1.4.

The total absolute count of nucleated cells per c.mm. of marrow was $1{,}295{,}700 \pm 55{,}000$ in the normals, $1{,}151{,}000 \pm 105{,}000$ in the eschatin series, and $1{,}059{,}000 \pm 88{,}000$ in the A.C.T.H. series. The true absolute count is almost certainly somewhat higher, as already noted. Kindred (1942), working with paraffin sections of costal marrow in the rat, found an average count of 1,960,000 nucleated cells per c.mm. of marrow. In addition to differences in technique, however, there arises here also the question of species differences.

Discussion

The present data (average of 142,100 lymphocytes per c.mm. marrow) confirm the earlier findings of the high absolute count of lymphocytes in normal marrow. Since the average blood lymphocyte count in the series was 9,048 per c.mm., this is clearly not explicable as due to contamination with lymphocytes from the circulating blood. So far as the percentage of lymphocytes in human marrow is concerned, most clinical haematologists give a figure of the same order. Thus according to Whitby and Britton (1946) the lymphocytes form 5–20% of all the nucleated marrow cells. Very few absolute counts are available, but those reported in man (Lossen, 1910; Isaacs, 1937; Gordon, 1939) are of the same order as the present counts in the guinea-pig, which would suggest that there is also a similar absolute lymphocyte count in man.

Roughly, then, one in every ten of the nucleated cells of the adult bone marrow is a lymphocyte. This astonishingly high proportion of lymphocytes has, however, tended to be disregarded, for current haematological theory denies any genetic relationship between the lymphocytes and the erythrocytes and granulocytes. Thus, to quote one example of many, Piney and Hamilton-Paterson (1946) state that the lymphocytes constitute 14–21% of the marrow cells—that is, about one cell out of five—but then proceed to add that nevertheless "they are not part of the myeloid tissue proper." It certainly seems a little odd that one out of every five nucleated cells found in the marrow should have no real connexion with it.

Another factor which has made it somewhat easier to ignore the high lymphocyte content of the bone marrow has been the absence of quantitative data. To think of the lymphocytes as 10% of the nucleated cells of the marrow may not convey much. But if one translates this percentage into absolute figures, and considers the bone marrow as a whole, it becomes obvious that we are dealing here with one of the largest collections of lymphocytes in the body.

The high lymphocyte content of normal bone marrow is clearly something which calls for an explanation, and no satisfactory explanation has yet been forthcoming. The chief reason perhaps why the problem has not been more clearly envisaged is because it has become entangled with the numerous conflicting theories of blood formation. In general, clinical haematologists have tended to adopt a polyphyletic approach to the problem of haemopoiesis, according to which erythrocyte, granulocyte, and monocyte each arise from a specific stem cell; and the lymphocyte does not fit into this scheme of things. In consequence, its presence in the bone marrow has come to be regarded as a somewhat awkward phenomenon which is best ignored. But, irrespective of whatever theory of blood formation one accepts, the number of lymphocytes in the bone marrow ought to be an objective fact capable of being established quite independently.

Unfortunately the identity of the small lymphocyte has been the subject of controversy on so many occasions that almost any data appertaining to it have become suspect. An excellent instance is afforded by the bone marrow of the rat, in which the lymphocyte percentage has variously been estimated as 0.5% (Stasney and Higgins, 1935), 20% (Overbeck and Querido, 1938), 2.96% (Higgins and Macella, 1939), 21.7% (Aschkenasy, 1946), and 13.3 ± 4.27% (Endicott and Ott, 1945). Apart

from the question of true variation in the number of lymphocytes, the gap between the figures of the various workers seems to be due to difficulties of cell identification as much as anything else. In the example just quoted (rat), Aschkenasy (1946) considers that the confusion is chiefly between the small lymphocyte and the early erythroblast. We have on occasion experienced this difficulty in the guinea-pig. Another source of trouble is the cell which Cunningham *et al.* (1925) termed the primitive cell, which at first they thought could be clearly differentiated from the small lymphocyte, though at a later date Sabin *et al.* (1936) seem to have come to the conclusion that this was not the case. Yet another source of confusion is with the cell which Rohr (1949) and others have termed the small reticulum cell.

While fully appreciating these difficulties in the identification of the small lymphocyte, we have endeavoured to overcome them in all cases by making in each animal suspensions of lymphocytes from a lymph gland, and examining these in stained smears before performing the differential count on the marrow. This, of course, still bases the identification of the small lymphocyte on morphological criteria alone, but, subject to that limitation, we believe that our data for marrow lymphocytes are reasonably accurate.

Effects of A.C.T.H. and Cortical Extract

There was no increase in the number of damaged cells after the administration of A.C.T.H. or eschatin. In fact, the percentage of damaged cells was slightly lower than the normal, though not significantly so, in both the A.C.T.H. and the eschatin series. This finding would appear to argue against changes, in either the lymphocytes or any other marrow cells, of the nature described by Dougherty and White (1945) in lymph nodes and thymus. It is no doubt conceivable that there may have been rapid and complete disintegration of the lymphocytes present in the marrow at the beginning of the experiment, and that there were no cell remnants to tell the tale. But if this were so, one would have to postulate either a rapid new formation of lymphocytes *in situ* from a non-lymphocytic precursor, or else the migration into the marrow from the blood of even greater numbers of lymphocytes than those which had been destroyed. In either case the response of the marrow lymphocytes would be radically different from that described by Dougherty and White in lymphocytes elsewhere.

In most of the experimental animals sections of cervical lymph nodes and thymus were examined, and no evidence was found of marked degenerative changes in individual cells, though in a number of instances the lymphoid masses appeared to be less densely packed than usual.

Instead, then, of the expected increase in damaged cells, the results indicate that one of the effects of A.C.T.H. or eschatin is to cause an increase in the marrow lymphocytes. This result was statistically significant in the eschatin experiments, and nearly so after A.C.T.H. Since there was nothing to indicate multiplication of the marrow lymphocytes *in situ*, the alternative explanation seems the more probable—namely, that there was an increased uptake by the marrow of lymphocytes from the blood. This might well be an important contributory, if not the main, factor in the development of lymphopenia after the administration of steroid hormones.

The increase in marrow lymphocytes just described occurred six hours after a single injection of A.C.T.H. or steroid hormones. What would be the effect of repeated injections? We have as yet no evidence to offer on this point, but it would seem reasonable to expect a steady growth in the lymphocyte population of the marrow. It is all the more interesting, therefore, to note that precisely the opposite effect may result. Thus Dameshek *et al.* (1950) obtained remissions in five cases of lymphatic leukaemia, with marked decrease in marrow lymphocytes, but "extraordinary rises in reticulocytes and platelets." They believe their findings to suggest "that a long-sought-for marrow stimulant may be at hand." It is to be noted that they concentrated their attention on the increase in the number of red cells rather than the decrease in the number of lymphocytes, presumably because they accepted the view that A.C.T.H. and steroid hormones caused lymphocyte dissolution, in which case the rapid disappearance of large numbers of lymphocytes presents no problem. But so far as bone marrow is concerned this does not appear to be the case, and it would seem that the rapid disappearance of marrow lymphocytes needs to be considered more carefully in relation to augmented erythropoiesis. In this connexion one may refer to the earlier findings of Dameshek and Valentine (1937) in pernicious anaemia, where before the beginning of liver therapy 27% of the myeloid cells were "typical lymphocytes having the characteristic size, shape, and staining reactions of the mature, or small, lymphocytes of the peripheral blood." Presumably, in the case of pernicious anaemia and liver therapy the question of lymphocyte dissolution does not arise: Dameshek and Valentine (1937) do not appear to have thought so. While there is not as yet enough evidence to warrant any definite conclusion, it seems clear that A.C.T.H. and the

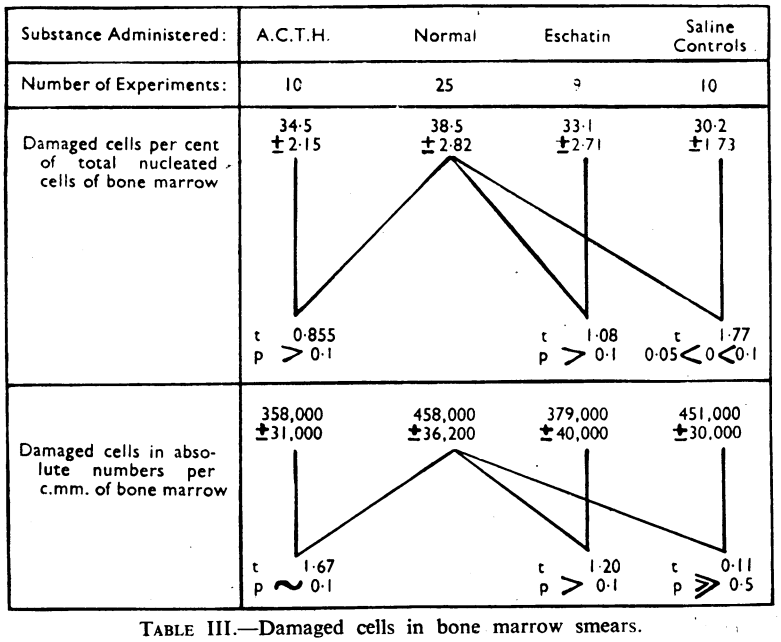

TABLE III.—Damaged cells in bone marrow smears.

steroid hormones are likely to reawaken interest in the problems of haemopoiesis and the possible part played in them by the lymphocyte.

Summary

A quantitative technique has been employed to study the nucleated cells of the bone marrow, both in normal guinea-pigs and in guinea-pigs which were killed six hours after the administration of a single dose of A.C.T.H. or of cortical extract (eschatin).

In the normal guinea-pig red marrow was found to contain on the average 1,236,000 nucleated cells per c.mm., of which 144,800 were lymphocytes. The high lymphocyte content of bone marrow is not attributable to blood contamination.

There was no demonstrable increase of damaged cells in the marrow six hours after giving either A.C.T.H. or eschatin, but there was a statistically significant increase in the lymphocyte content after eschatin and an increase almost reaching the significant level in the case of A.C.T.H.

It is possible that increased uptake by the bone marrow of lymphocytes from the blood may be a contributory factor in the lymphopenia which may follow the administration of A.C.T.H. steroid hormones.

Whatever may be the effect of steroid hormones on lymphoid tissue in other parts of the body it has not been found possible by quantitative methods to demonstrate a destructive action on the lymphocytes of the bone marrow.

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SYMPATHECTOMY FOR HYPERTENSION

BY

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This paper presents a series of cases of severe essential and malignant hypertension which have been treated by thoraco-lumbar sympathectomy at Hammersmith Hospital since 1945, and which have been followed up in detail. A study of this material has given us some useful data on the early effects of sympathectomy for hypertension.

From November, 1945, to January, 1950, 35 carefully selected patients were operated upon. They were all in the care of the surgical unit under Mr. R. H. Franklin. Most of the operations were performed by him, the remainder by his assistants.

These patients were referred to us for surgery by the Department of Medicine or sent from other hospitals, and before submitting them to operation extensive investigations were carried out to confirm their suitability for sympathectomy.

Routine for Investigation and Criteria of Operability

Apart from a thorough clinical examination, the routine investigation of all patients included electrocardiograms, *x*-ray screening of the heart and lungs, a study of the fundi, and the sodium amytal sedation test. An assessment of renal function was made by urine analysis, culture, and microscopy, specific gravity studies with concentration and dilution tests, blood-urea levels, urea-clearance tests, and intravenous pyelography.

With the aid of the information provided by the foregoing investigations, patients were selected for operation on the basis of the following criteria:

1. The patient must be under 55 and preferably under 50 years of age.

2. The diastolic blood pressure must be over 100 mm. Hg and the systolic level preferably over 200 mm. Hg.

3. There should be definite symptoms referable to hypertension, particularly severe headaches or disturbances of vision.

4. The patient must not be in cardiac failure.

5. Renal function must be adequate—that is, a blood-urea level of under 50 mg. per 100 ml. and a urea-clearance value of over 50% of normal. The intravenous pyelogram should not show any gross defect in outline or in rate of excretion.