

I. THE EFFECT OF THYROIDECTOMY ON THE BONE-MARROW
OF RABBITS. II. THE EFFECT OF THYROID FEEDING
ON THYROIDECTOMISED ANIMALS.

by

B. B. SARKAR, M.Sc.

From the Dept. of Physiology, Edinburgh University.

Thesis for the Degree of D.Sc. 1921.



The histology of the bone marrow after thyroidectomy has not been previously recorded. The effect of Thyroid feeding on the bone-marrow of normal animals was investigated by the Parhonés (1), Porrini (10) and Israelsohn (11) and by Lim and Sarkar (2). They found that there was an increase in the number of marrow cells, a marked diminution of fat and considerable congestion of blood vessels. The increase in the marrow cells after thyroid administration is specially well marked in the polymorphs. The whole appearance suggested a stimulation of the marrow by the thyroid hormone. The evidence afforded by previous observers who noted the effect of thyroidectomy on the blood picture has given no information with regard to the changes in the marrow and little to indicate the absence of a hormonal effect, which one might expect from the results of the thyroid feeding experiments.

The relation between thyroid secretion and the blood was first drawn attention to in 1885 by Horsley (3). He found after thyroidectomy in rabbits a diminution in the number of erythrocytes, with an increase in the number of white blood corpuscles in the circulating blood. Dubois (4) while investigating the/
the/

the relation between the thyroid gland, bone marrow and spleen, in Asher's Laboratory, found after the removal of the thyroid a slight decrease in the number of erythrocytes with no marked alteration in the leucocyte count; there was however a relative lymphocytosis. These observations were confirmed later by Messerli (5), who worked in the same laboratory.

It is then clear that the removal of the thyroid gland causes a diminution often not considerable, in the number of red blood corpuscles and an increase in the lymphocytes of the circulating blood. The evidence as to the change in the total number of white blood corpuscles, after thyroidectomy, is conflicting although the relative lymphocytosis is generally agreed upon. Horsley and Messerli obtained an increase in the total number of leucocytes, while Dubois found no marked change. Falta (6) states that thyroidin produces mononucleosis (Falta, Newburgh and Nobel) in normal animals; and that thyrioprivic animals show anaemia and mononucleosis which is improved by thyroid gland therapy.

A recent paper by Waser (7) on the opposite condition, that is on the effect of thyroid administration in the normal animal, described an increase in the number of red blood corpuscles, although there was no marked change in the total number of white blood corpuscles.

A relative increase in the number of polymorph leucocytes was also found.

The observations of some previous workers on the same condition, i.e. after the administration of thyroid substance to normal animals show different pictures. Blumenthal (12) obtained in dogs and rabbits after large doses of iodo-thyrin at first diminution, later increase of red blood corpuscles, with leucopaenia or at least diminution of the polymorph neutrophils. Kostling (13) found in dogs after interperitoneal injection of stroma juice first polymorph leucocytosis with relative increase of mononuclears and later lymphocytosis lasting for several days. According to Bertelli (14) under the influence of thyroid medication there is a distinct relative increase of mononuclear cells in the blood in animals as well as in man. Stachelin (15) observed in man after feeding with thyroidin tablets diminution of red blood corpuscles, distinct lymphocytosis and decrease in polymorphs; in isolated cases increase of eosinophils. The number of erythrocytes were not influenced. Mansfield (16) observed in dogs and rabbits, on administration of thyroid a decided increase of erythrocytes which continued after stopping the medication.

The evidence in connection with diseased conditions of the thyroid gland is inconclusive. Falta describes anaemia as being specially well marked in infantile myxoedema; he states that on the administration of thyroid the anaemia partially or wholly disappears. McCarrison (8) also found anaemia to be present in myxoedema and in addition a reduction in the total white blood count. The blood picture showed mononuclear and eosinophil cells predominating over the polymorphs. On the other hand, much the same changes were noted by Kocher (quoted by Falta) in the opposite condition (Graves disease). For example he found that the mononuclear percentage was higher than the polymorph; there was no marked alteration in the total blood counts. McCarrison and Jastram (9) made similar observations; Jastram found that after removal of the thyroid in hyperthyroidism, the symptoms were reduced but the blood picture was little altered.

To put the matter simply, thyroidectomy or diminished thyroid secretion results in some diminution in the number of erythrocytes and but little alteration/

alteration in the total white count, with a well marked predominance of the mononuclear cells over the polymorphs, while on the other hand the opinion as to the condition of the blood picture, after thyroid administration is not unanimous. Although the increase in the red blood corpuscles is generally agreed upon; both polymorph leucocytosis and lymphocytosis has been recorded. The blood picture, therefore, gives only a slight indication of the marked influence of the thyroid hormone on haemopoiesis.

The following paper describes the effect of thyroidectomy on the bone marrow of rabbits. The results obtained are opposite to those found after thyroid feeding, that is the marrow activity was subnormal. It was also of interest to know whether marrow activity could be raised, by feeding with thyroid substance, to normal or to a higher level. This has been found to be the case.

I GROUP. Healthy rabbits were used and were kept in a warm well ventilated room.

They were fed on cabbages and oatmeal daily. The animals were divided into three groups, which were kept separate. Each group containing animals of nearly the same age and weight.

The first group contained four animals of about ten weeks old. Of these one was kept as a control, while the others were operated upon under strictly aseptic conditions; both the thyroids were removed. In every case the animals recovered rapidly and started gaining weight in a short time.

The following table gives particulars regarding their weight and the period during which they were kept after thyroidectomy.

TABLE I.

Rabbit		Weight before Operat ⁿ .	Weight after the 1st week.	Weight at the time of Killing
A	Control Animal	1330 gms.	1530 gms.	1940 gms.
C	Killed on the 7th day after thyroidectomy	1270 "	1200 "	1200 "
B	Killed on the 31st day after thyroidectomy	1430 "	1570 "	1800 "
E	Killed on the 66th day after thyroidectomy	1690 "	1720 "	1920 "

None of the animals showed any marked change after the operation. They were killed by a blow on the medulla and the marrow obtained by fracturing the femur. It was not found necessary to take the marrow of other bones as they were all similarly affected. In case of the operated animals the neck was carefully searched for accessory thyroids but none were found.

The marrow was fixed in 15% Formal and sections were cut by the paraffin method. Tissues from the different animals were treated in exactly the same way and the sections were mounted and stained on the same slide. The following stains were employed:-
(1) Alcoholic Eosin and Methylene blue (2) Alcoholic Eosin and Meyer's Hematoxylin (3) Heidenhein's Hematoxylin and (4) Giemsa. The sections were stained in Giemsa from half an hour to one hour and differentiated in distilled water (15 mts. or more). This method is exceedingly good for marrow preparations.

The percentage count of the different varieties of marrow cells was determined in the sections by counting every cell in a definite area. The marrow cells were divided into the following clearly distinguishable classes.

(1)/

- (1) Large mononucleated (nucleus round, ovoid or kidney shaped) non-granular cells. (Premycocyte).
- (2) Large mononucleated (nucleus round, ovoid or kidney shaped) granular cells (Mylocytes).
The granules are oxyphil and the nucleus is large. These cells are of the same size as the large mononucleated non-granular cells.
- (3) Finely granular cells (oxyphils) containing lobed or polymorphic nuclei. These cells vary in size and the smaller of them look like the polymorph leucocytes of the circulating blood.
(Polymorphs)
- (4) Small mononucleated cells with little or no protoplasm round the nucleus. The nuclei does not stain so deeply as the nucleus of red blood corpuscles and nucleoli are present. (Lymphocytes)
- (5) Nucleated red blood corpuscles. (Erythroblasts)
- (6) Giant cells.

TABLE II.

TABLE II.

	Rabbit A.	Rabbit B.	Rabbit C.	Rabbit E.
Large mononucleated non-granular cells	6.6%	4%	4%	8%
Large mononucleated granular cells	14.9%	19%	20%	12.6%
Polymorphonucleated granular cells	35.5%	29%	34%	21.8%
Small mono- nucleated cells	30.0%	33%	31%	43.6%
Nucleated red blood corpuscles	13.0%	15%	7%	13.8%

Rabbit A. The bone marrow of this control animal on microscopical examination showed the usual aspect of normal marrow. The second column of Table II gives the percentage count of the marrow cells of this animal.

Rabbit B. This animal was killed on the 31st day after thyroidectomy. The naked eye appearance of the marrow was very pale and on microscopical examination the cellular elements were found to be almost completely replaced by fat, so that the tissue is composed almost entirely of fat cells and the few marrow cells present are scattered in/

in between the fat spaces in little groups. The proportions of the large mononucleated non-granular and the polymorph granular cells are reduced but there is a slight increase in the proportion of the small mononuclear cells. The proportion of large mononucleid granular cells is also increased.

The number of nucleated red blood corpuscles is large, although the absolute number is diminished. No mitoses are present and giant cells are almost absent. An idea of the percentages of the different cells can be obtained from Table II.

Rabbit C. The animal was killed on the 11th day after thyroidectomy. The marrow did not show any marked change in the total number of marrow cells or in the quantity of fat present. The percentages of the large mononuclear non-granular and the polymorph granular cells are slightly reduced, while the large mononuclear granular cells are slightly increased in proportion. The number of giant cells is almost normal and there is no evident mitosis.

Rabbit E. This rabbit was killed on the 66th day after thyroidectomy. The marrow is seen to have become diminished in cellular content/

content, although the diminution is not so extensive as in Rabbit B, and the quantity of fat is greater than normal. The proportion of polymorph granular to the large non-granular cells is reduced. The number of giant cells is less than in normal and there are no mitoses. The differential count of the marrow cells is given in Table II.

II GROUP. This group was composed of four somewhat younger animals (about eight weeks old).

Three of the rabbits were operated upon under strictly aseptic precautions and both the thyroids were removed. The wound healed very rapidly in every case. No marked changes were observed after the operation.

One of the operated animals was killed on the 33rd day after thyroidectomy, while the two others were fed on 1 gram of dried Thyroid gland (B.P. preparation) daily from the 33rd day after operation (i.e. the same day on which the former animal was killed). The powder was administered to the animals by mixing with oatmeal and water.

TABLE III./

TABLE III.

		Weight before Operat ⁿ .	Weight at commencement of feeding.	Weight at the time of Killing.
Rabbit K	Normal Animal	1170 gms.	1400 gms.	1370 gms.
"	L. Killed on the 33rd day after operation.	1350 "	1580 "	1580 "
"	M. Killed after 4 days of thyroid feeding	1320 "	1470 "	1100 "
"	N. Killed after 2 days of thyroid feeding	1210 "	1170 "	1100 "

The above table gives the weight and other particulars of the rabbits of this group. The two thyroid fed animals lost weight on feeding.

In this batch blood count was taken using a Thoma-Hawksley Haemocytometer and blood films were made for differential count. In each case the normal count for about a fortnight was determined before the thyroid glands were removed. Blood was obtained by pricking a small ear vein. The blood was drawn every morning before the animal was fed, so as to get as constant a count as possible. Blood films were stained in Leishman and the differential count was made under an oil emersion. An average of 300 to 400 corpuscles was taken.

The/

The animals were killed by a blow on the medulla and the bone marrow obtained and treated as stated under the first group.

TABLE IV.

	Rabbit L.	Rabbit N.	Rabbit M.	Rabbit K.
Large mononucleated non-granular cells	5.4%	18%	9.6%	9%
Large mononucleated granular cells	25.6%	14.1%	13.8%	17.8%
Polymorpho granular cells	24.6%	19.3%	34.9%	39.2%
Small mononuclear cells	31.2%	41.1%	31.6%	26.2%
Nucleated Red blood corpuscles	13.2%	7.5%	10.1%	7.8%

The above table gives the percentage count of the different cells in the marrows of the animals of the second group.

Rabbit K. The bone marrow of this control animal (Fig.1) showed the usual picture of normal marrow.

The percentage count of the different marrow cells will be found in Table IV.

The following table gives the blood count and the differential count of the control animal.

TABLE V.

TABLE V.

BLOOD COUNT OF RABBIT K.

Date.	Erythrocytes.	Leucocytes.	Polymorph Leucocyte	Lymphocyte	Macrocyte	Basophile	Eosinophile.
Oct. 7th	6,720,000	12,200	33.5	60.0	7.5	2.5	0.5
" 13th	6,320,000	12,800	28.6	62.3	3.7	3.4	2
" 14th	6,560,000	11,600	27.5	62.2	3.0	5.2	2.0
" 18th	6,720,000	10,900	28	62.8	3.2	3.5	2.5
" 20th	6,620,000	10,600	26.9	66.2	2.5	3.7	1.2
Nov. 1st	6,520,000	13,300	30	60.6	3.6	3	2
" 9th	6,670,000	12,800	31.6	60.6	3.6	3	1
" 19th	6,580,000	12,500	32.5	62.2	2.3	4	1
" 26th	6,570,000	12,200	28	65	4	2	1

Rabbit L. The bone marrow of this animal, which was killed on the 33rd day after thyroidectomy, was found to consist almost entirely of fat with very few marrow cells. (Fig. 2)

The marrow looks almost like the marrow of Rabbit B. The proportions of large mononuclear non-granular and the polymorph granular cells are reduced, while that of the large mononucleated granular and small mononuclear cells are increased. There are very few giant cells and no mitotic figures. Many of the nuclei of red blood corpuscles are distorted.

Differential count of marrow cells are given in Table IV.

In the circulating blood there was a reduction in the number of erythrocytes after the operation. The number of leucocytes show no marked change and if anything shows a reduction in the fourth week after thyroidectomy. (Table VI). The removal of thyroid was followed by lymphocytosis.

TABLE VI./

TABLE VI - RABBIT L.

Date.	Erythrocytes	Leucocytes	Polymorph. Leucocyte	Lymphocyte.	Macrocyte	Basophile	Eosinophile.
Oct. 7th	5,960,000	15,900	34.5	56.5	4.5	3.5	1
" 12th	6,760,000		34	57	4	3	2
" 14th	7,200,000	14,700	34	59	3	3	1
" 18th	6,800,000	15,000	36	59.2	3.2	2	.6
" 20th	6,920,000	14,800	34	54	2.5	9.5	1
Thyroid glands removed on the 20th.							
" 26th	6,880,000	14,700	28.5	58.5	2.5	11.5	.5
Nov. 1st	6,320,000	14,700	28	65	2	4	1
" 5th	5,920,000	15,600	25	70	2	2	1
" 9th	6,060,000						
" 10th	5,570,000	12,700	27	67	2.5	2.5	1

Rabbit N. This rabbit was fed on thyroid from the 33rd day after thyroidectomy and was killed after two days of feeding. The bone marrow on examination was found to be different from normal as well as from the marrow of thyroidectomised animals. The total number of marrow cells are less than in normal, although more than found in the bone marrow of thyroidectomised animals. (Fig. 3) The amount of fat is reduced to nearly the quantity which is present in normal marrow. Of the marrow elements the large non granular cells are present in large numbers as also the small mononuclear variety. The proportion of large mononucleated granular cells is less than normal, although the total number is increased as compared with the marrow of thyroidectomised animals. Further, these cells contain much fewer granules and some of these cells, containing just a few granules look almost like the large mononucleated non-granular cells. (Fig. 6) The polymorph percentage is less than normal. The number of giant cells, many of which are small, is increased. The total number of all the different varieties of cells is increased, the increase being most/

most marked among the large non-granular cells and the small mononuclear cells.

The reduction after thyroidectomy in the number of red blood corpuscles was considerable, as may be seen in Table VII, but there was slight increase even after two days of feeding. The number of leucocytes which showed no marked change till the end of the fourth week, fell slightly and the condition remained the same during the two days of thyroid feeding. The differential count shows marked lymphocytosis, after the removal of the thyroid. On the administration of thyroid this disappeared almost immediately after feeding.

TABLE VII./

TABLE VII - BLOOD COUNT OF RABBIT N.

Date.	Erythro- cytes.	Leuco- cytes.	Polymorph Leucocyte.	Lymphocyte	Macrocyte	Basophile	Eosinophile.	
Oct. 9th	6,800,000	13,400						
" 12th	6,800,000	14,200	39	53.2	3.9	2.3	1.5	
" 14th	7,000,000	13,125	33	62	2	2	1	
			Operated on the 20th October.					
Nov. 5th	6,300,000	14,000						
" 13th	6,190,000	13,200	19.5	73.5	3.6	2.4	1.0	
" 19th	5,280,000	11,800	25.1	68.3	2.5	1	1	
" 22nd	5,000,000	9,500	24	71	2	2	1	
		Fed on 1 gm. Thyroid daily from the 22nd November.						
" 23rd	4,930,000	8,700	37.0	55.6	4.5	6.2	.5	
" 24th	5,330,000	8,400	42.5	49.3	4.6	2.5	1	

Rabbit M. The quantity of fat and the total number of marrow cells in the marrow of this animal, which was fed for four days on thyroid, is near normal. (Fig. 4) As compared with Rabbit N the proportion of large non-granular cells is reduced, while the polymorph granular cells are increased in proportion. The granular cells contain more oxyphil granules than those of Rabbit N, and the amount is about the same as in normal. (Fig. 8) Giant cells are numerous and there are several dividing cells.

As in the other thyroidectomised animals, the number of erythrocytes fell, after the operation, but recovered to a certain extent on feeding with thyroid. The leucocyte count did not show any steady change either after the operation or on feeding on thyroid. There was an increase in the number of lymphocytes with a corresponding decrease in the number of polymorphs after thyroidectomy. On the administration of thyroid the proportion came back to the pre-operation level and even went beyond it. (Table VIII)

TABLE VIII - BLOOD COUNT OF RABBIT M.

Date.	Erythro- cytes.	Lympho- cytes.	Polymorph	Lymphocyte	Macrocyte	Basophile	Eosinophile.
Oct. 7th	6,880,000	11,600					
" 9th	6,920,000	14,600	34	61.8	1.8	1.4	1
" 12th	7,040,000	15,000	34.5	60	3	1.5	1
" 14th	6,840,000	13,200	33.8	59.4	3	3	1
" 18th	7,120,000	14,400	33	60	4	2.5	.5
" 20th	7,200,000	15,600	32	62	2.5	2.5	1
Operated on the 20th and both the thyroids removed.							
" 26th	6,660,000	15,900	32.0	60.3	3.3	3.3	.5
Nov. 1st	6,600,000	16,500					
" 9th	6,390,000	14,100	22.4	70.6	4	2.5	.5
" 13th	6,390,000	19,000	16	80	1.5	1	1
" 18th	5,770,000	19,000	20	72.5	5	2	.5
" 22nd	5,770,000	14,100	29	65.5	3.5	1	1
Fed on 1 gm. Thyroid from the 22nd Nov.							
" 23rd	5,640,000	14,000	42.5	62	3.5	1.5	.5
" 24th	5,800,000	13,200	60	34	4	1	1
" 25th	5,880,000	12,200	49	45	4	2	1
" 26th	5,930,000	13,500	50	43	4	2	1

III GROUP. Of the five adult rabbits of this group, one was kept as control, while the other four were operated upon under strictly aseptic precautions and both the thyroids were removed. They recovered rapidly but showed no change after the operation. One of the animals was killed on the 34th day after thyroidectomy and two others were fed on 1 gram. of dried thyroid gland powder daily from the 34th day after operation for different periods. The fourth thyroidectomised rabbit was fed on .5 gram. of dried thyroid gland from the 66th day after thyroidectomy for seven days, after which it was discontinued for a period of twenty-two days. Thyroid was administered to it again for three consecutive days and was killed seven days after stopping the thyroid feeding. The following table gives particulars of these animals.

TABLE IX.

TABLE IX.

Rabbit.		Weight before operation.	Weight before Thyroid feeding.	Weight at time of killing.
H	Fed on Thyroid for 7 days - discontinued feeding for 22 days - fed again on thyroid for 3 days - discontinued for 7 days and killed.	2090	2250	1700
P.	Fed on thyroid for 7 days - from 34th day after thyroidectomy.	1800	2000	1600
Q.	Fed on thyroid for 3 days from the 34th day after operation and discontinued feeding for 12 days when killed	1700	2150	1960
R.	Killed on the 34th day after operation	2510		2440
S	Control animal	1860		1800

The rabbits were killed by a blow on the medulla and the bone marrow was obtained and was treated as stated under Group I.

The following table gives the percentage count of the different bone marrow elements in the marrow of the animals of this group.

TABLE X.

	Rabbit H.	Rabbit R.	Rabbit P.	Rabbit Q.	Rabbit S.
Large mononucleated non-granular cells	7.1	6.5%	8.2	6.5%	6
Large mononucleated granular cells	19.5	19%	10.2	40.5%	18
Polymorphonucleated granular cells	43.8	20%	37	26%	43.7
Small mononucleated cells	19.2	40%	36.4	21%	24.5
Nucleated Red blood corpuscles	10.4	14.5	8.2	6%	7.8

Rabbit S. The bone marrow of this control animal showed the usual picture of normal marrow. The blood count (Table XI) of the control animal did not show any change during the whole period of the experiment.

TABLE XI.

TABLE XI - RABBIT S.

Date.	Erythro- cytes.	Leuco- cytes.	Polymorph Leucocyte	Lymphocyte	Macrocyte	Basophile	Eosinophile.
Oct. 13th	6,860,000						
" 15th	7,100,000	11,400	35	58.5	5	2	1.5
" 21st	7,040,000	13,100					
" 23rd	7,200,000	15,000	33.5	60.5	3	1.5	1.5
Nov. 8th	7,280,000	12,500	34.5	60.9	1.8	1.9	1.4
20th	6,920,000	13,200					
Dec. 16th	7,160,000	12,800	34	58.5	4	1.5	2

Rabbit R. The bone marrow of this animal, which was killed on the 34th day after thyroidectomy, shows some reduction in the number of marrow cells and an increase in the quantity of fat. But these changes are not so extensive as that found in the marrow of Rabbits L and B. There is a reduction in the number of polymorph granular cells with a proportionate increase in the large granular cells and in the small mononuclear hyaline cells. The proportion of large non-granular cells is about normal. The number of giant cells is reduced.

The blood count of this animal did not show any change after the operation, as can be seen from the following table. The differential count showed the usual picture found after thyroidectomy, that is, an increase of lymphocytes with a diminution of polymorphs.

TABLE XII.

TABLE XII - BLOOD COUNT OF RABBIT R.

Date.	Erythro- cytes.	Leuco- cytes.	Polymorph	Lymphocytes	Macrocytes	Basophile	Eosinophile.
" 15th	6,600,000	15,600					
" 21st	7,240,000	14,500	31.3	64	1.3	2.2	1.2
" 23rd	6,640,000	12,200	32	60	3	4	1
" 25th	7,240,000	14,600	32.5	62	3	2	.5
Operated on the 25th Oct.							
" 30th	7,200,000	14,100	32	63	2.5	2	.5
Nov. 8th	6,820,000	15,000	28	62.5	5.5	2	1
" 12th	6,880,000	14,200	26	69	2	3	1
" 20th	7,220,000						
" 27th	7,340,000	13,700	23	70.5	2.5	3	1

Rabbit P. This animal was fed on thyroid from the 34th day after thyroidectomy and was killed on the 7th day after feeding.

The bone marrow of this animal contained more cells than normal and very little fat was present. The percentages of the different varieties of cells were near normal, although the total number of cells was increased. The number of giant cells was slightly above normal.

The red blood count fell after the operation, though there was a slight improvement on the fourth week. The blood count came back to normal on feeding. The white blood count did not show any constant change. In the differential count an increase in the number of lymphocytes and a diminution in the number of polymorphs were obtained after the operation, while on feeding on thyroid (7 days) the number of polymorphs increased to a higher level than normal with a corresponding diminution in lymphocytes.

Rabbit Q. The rabbit was fed on thyroid for three days commencing from the 34th day after thyroidectomy, after which it was kept for twelve days, when it was killed. The marrow on examination was found to be very rich in cellular elements, and the amount of fat present was near normal. The proportion of large granular cells is very high and a large number of large non-granular cells are present. In fact there is a larger number of granular cells in this marrow than was found in the marrow of the other animals and the whole tissue is packed with these cells. The proportion of polymorph granular cells is less than in the marrows of Rabbits P and S, although more than found in the marrow of Rabbit R. The number of small mononuclear cells is diminished as compared with Rabbits P and S. The number of giant cells present is less than that in Rabbits P and S. (Fig. 5)

Table XIV shows the blood count of this animal. The erythrocyte count which fell after the operation recovered slightly on the fourth week. On feeding on thyroid the red blood count came back near normal and when the administration was withheld fell slightly again/

again. The white blood count showed no constant change. The lymphocytosis which developed after thyroidectomy disappeared on the administration of thyroid and the polymorph count rose above normal. The polymorph percentage fell again after thyroid administration has been withheld for twelve days. (i.e. at the time of killing).

TABLE XIV./

TABLE XIV - RABBIT Q.

Date.	Erythro- cytes.	Leuco- cyte.	Polymorph	Lymphocyte	Macrocyte	Basophile	Eosinophile.
Oct. 15th	6,920,000	12,900	33.4	58.8	2.8	3.8	1.2
" 19th	7,160,000	12,800					
" 23rd	7,040,000	15,700	37	58	2	2.5	.5
" 25th	7,280,000	14,100	31.5	63.2	2.3	2	1
Operated on the 25th and both the thyroids removed.							
" 30th	6,770,000	15,600	33.1	60.9	2.1	2.5	1.4
Nov. 12th	5,400,000	13,700	24	71.5	2.5	1	1
" 20th	5,930,000	12,800	21.3	73.2	2	3	.5
" 29th	6,390,000	14,000	18.6	77.9	1.5	1.5	.5
" 30th	6,640,000	13,400	21	72	2	3	2
Fed on thyroid from the 30th Nov.							
Dec. 1st	7,040,000		30	62.5	3	3	1.5
" 2nd	6,810,000	15,600	41.4	53.6	2.1	2.4	.5
Stopped feeding from the 2nd Dec.							
" 3rd	6,970,000	14,000	42	50	4.5	3	.5
" 7th	6,540,000		41.8	49	3.5	3.0	.8
" 14th	6,480,000						
" 15th	6,640,000		32	61	3	3	1

Rabbit H. This rabbit was fed faily on .5 gms. thyroid for seven days from the 66th day after thyroidectomy, after which the feeding was stopped for twenty-two days. The feeding was commenced again (on 1 gm. thyroid) for three days and was again stopped for seven days when it was killed. The bone marrow looked like normal, except that it contained a large percentage of polymorphonuclear granular cells with a diminution of small mononuclear cells than normal.

In the blood a diminution in erythrocyte count was obtained after thyroidectomy. During the administration of thyroid (.5 grm. daily for 7 days) no marked increase occurred and the erythrocyte count did not become normal till about 10 days after the feeding was commenced. The number of red blood corpuscles fell slightly again as thyroid was withheld but rose on feeding on thyroid (1 gm. daily for 3 days). The white blood corpuscles showed no marked change as regards their total number, but the lymphocytosis which appeared after the operation, disappeared on the administration of thyroid (.5 grm. daily) and the polymorph count rose higher than normal. On discontinuing the feeding the lymphocytes increased slightly again, at the expense of the polymorphs. Table XV shows the blood count of this animal.

TABLE XV - BLOOD COUNT OF RABBIT H.

Date.	Erythro- cyte.	Leuco- cyte.	Polymorphs	Lymphocyte	Macrocyte	Basophile	Eosinophile.
1st Oct.	6,080,000		34.5	59.5	3.0	2.0	1.0
4th "	6,720,000	11,400	32.0	63.0	2.0	2.0	1.0
6th "	6,800,000	11,400	31.0	62.5	3.5	2.0	1.0
8th "	6,500,000	13,900	32.0	62.0	3.0	2.5	.5
Both the thyroid glands removed on the 18th Oct.							
22nd "	5,860,000	15,300	27.0	66.0	3.0	3.0	1.0
10th Nov.	5,520,000	12,500	24.0	70.5	3.0	1.0	1.5
11th "	5,800,000	13,400	23.0	72.0	2.5	1.5	1.0
13th "	5,900,000	12,200	24.0	70.0	3.0	2.0	1.0
Fed on .5 gm. Thyroid daily from the 13th Nov.							
16th "	5,660,000	12,800	34.0	59.5	4.0	2.0	.5
17th "	5,920,000	13,700	35.5	57.5	4.0	2.0	1.0
18th "	6,250,000	15,300	49.0	41.0	6.5	3.0	.5
19th "	6,400,000	15,000	53.0	41.0	4.0	1.0	1.0
20th "	5,730,000	15,600	50.0	42.5	4.5	2.0	1.0
21st. /							

Date.	Erythro- cyte.	Leuco- cyte.	Polymorphs	Lymphocyte	Macrocyte	Basophile	Eosinophile.
21st Nov.	5,440,000	14,100	45.0	49.5	5.0	1.0	.5
23rd "	5,720,000	13,800	41.2	49.7	6.0	2.0	1.0
24th "	5,420,000	14,600	38.5	53.5	5.0	2.0	1.0
26th "	6,400,000	13,200	35.5	59.5	5.0	.5	.5
27th "	6,800,000	13,600	32.0	64.0	2.5	1.0	.5
30th "	6,790,000	12,800	31.5	57.5	6.5	3.5	1.0
6th Dec.	6,400,000	12,600	32.5	58.5	4.0	3.0	2.0
15th "	6,510,000	12,800	32.0	62.5	2.5	2.0	1.0
16th "	6,600,000	13,800	32	61.0	3.0	2.5	1.5
19th "	6,700,000	13,400	43.0	49.0	4.0	2.5	1.5
23rd "	7,360,000		60.5	34.0	2.5	2.0	1.0
24th "	7,360,000	14,200	58.5	37.5	2.5	1.5	1.0

Fed on 1 gm. Thyroid daily from the 15th Dec.

Stopped feeding on Thyroid from the 18th Dec.

DISCUSSION. No marked effect was found in the bone marrow eleven days after thyroidectomy except a slight increase in the quantity of fat in the marrow. But the effect of thyroidectomy on bone marrow is very pronounced after four weeks. There is an absolute reduction in the total number of every class of marrow cells with a preponderance of fat. The reduction affecting specially the polymorph and the large non-granular cells. Consequently the proportions of large mononucleated granular and small mononucleated cells is higher. The almost total disappearance of giant cells is also very striking. There are quite a large number of nucleated red blood corpuscles; specially in one of the rabbits (Rabbit B) the percentage is high. This evidence of the subnormal activity of the bone marrow is very distinct in the Rabbits B and L, which were young animals; but the changes are not so strikingly pronounced in Rabbit R, which was an adult animal. It is of interest to note here that the changes in the blood and especially in the bone marrow is more pronounced in the Groups I and II than in the Group III. The two former groups consisted of young animals, while the animals in the latter group were adults./

adults. Thus the absence of thyroid affected the blood and bone marrow of young animals more than the adults. The same thing has been noticed by Falta, who found more pronounced changes in the blood of young than old patients suffering from myxoedema.

The bone marrow of an animal (Rabbit E) killed two months after thyroidectomy shows evidences of the same kind of subnormal activity as has been noticed in the marrows of Rabbits B and L, killed one month after thyroidectomy, although there are more cellular elements in the former animal than in the latter two.

The effect of thyroid feeding on the bone marrow of thyroidectomised rabbits is very rapid, the marrow being thrown into activity almost immediately. The bone marrow after two days of feeding showed an enormous increase in the number of cellular elements as compared with the marrow of a thyroidectomised animal. The greatest increase is found at this stage in the number of the large non-granular and the small mononucleated cells, and the percentage of these cells are higher than in normal. Although large mononucleated granular and the polymorph granular cells are increased, yet the percentages of these cells are below the normal level. Most of the granular cells/

cells contain fewer granules than found in normal marrow, and some of these which contain just a few granules look almost like the large non-granular cells. The normoblasts and megaloblasts shared in the general increase. The total number of giant cells is increased and some of them are unusually small.

The stage which was obtained after four days of feeding showed still further changes, and the marrow approached a more normal aspect. There was further increase in the total number of cells in the marrow with a diminution in fat. The best marked change is in the polymorph granular cells, the proportion of which is increased. There is also an increase in the number of the large mononucleated granular cells. The giant cells are still further increased in number at this stage.

The bone marrow of the rabbit fed on thyroid for seven days after thyroidectomy has a normal appearance, but the total number of cells, including the giant cells, is higher than normal.

From these observations it is evident that the activity of the bone marrow is diminished by thyroidectomy; the inactivity affecting all the different varieties of marrow cells and specially the production and maturation of polymorph leucocytes (the fine oxyphile/

oxyphil leucocytes in Rabbits). The almost total disappearance of the giant cells after thyroidectomy is very striking. The first effect of the administration of thyroid to these animals was the rapid multiplication of the marrow cells, specially the small mono-nuclear and the large non-granular cells; although no mitosis was found. The giant cells increased rapidly. The large mono-nucleated granular cells followed rapidly and many of them seem to be formed from the large non-granular cells by developing granules in them. The next step (after 4 days of feeding) was the rapid production of polymorphs (amphophil cells in Rabbits). Nucleated red blood corpuscles shared in the general increase. The marrow assumed almost normal condition in a short time (feeding for 4 days on 1 gr. thyroid daily).

A continuation of thyroid administration (seven days of feeding) called forth a larger increase in the number of marrow cells, without any marked changes in the proportion of the different varieties of cells.

These observations are further supported by the conditions found in the bone marrow of Rabbit Q, which was killed after discontinuing the thyroid feeding for twelve days. There are more cells in this marrow than found in normal marrow, and the increase/

increase was clearly evident, specially in the large mononucleated granular cells; the large non-granular and the small mononuclear cells are also slightly increased. The number of polymorph granular cells was reduced. Under the stimulus of thyroid hormone the marrow cells multiplied but when the stimulus was withheld (after three days of feeding) the further change towards the production of polymorph was retarded. Consequently the marrow was packed with an abnormal number of large mononucleated granular cells.

My observations on the effect of thyroidectomy and of feeding such animals on thyroid, on the circulating blood, supports the findings of others (Falta and others). The white blood count did not show any steady change in either conditions. In the case of adult animals they seem to recover slightly from the anaemia, from the 4th week. One of the adult rabbits did not show any reduction in the red blood count after thyroidectomy although the lymphocytosis which set in after the operation was well marked. The lymphocytosis, which developed after the removal of the thyroid gland, disappear rapidly on the administration of thyroid and there is even a slightly higher percentage of polymorph after about four days. No constant changes were found in the numbers of the eosinophile, the basophile and the macrocytes either after operation or after feeding.

The changes in the blood corresponds with the changes in the marrow, and with the increased percentage of polymorphs in blood, there was the indication of increased production of these cells in the marrow.

S U M M A R Y.

1. The removal of the thyroid gland is attended by a subnormal activity of the bone-marrow.
The marrow shows an extreme poverty in all the varieties of cells, with an increase in the amount of fat cells.
2. On administering thyroid substance to thyroid-ectomised animals, the marrow regains its activity in a very short time, and on continuing the feeding the number of marrow cells increases beyond normal.
3. The first effect of the administration of thyroid is the rapid production of the non-granular varieties (both large and small) of cells followed by the granular variety. From these the polymorph granular cells are produced, but on withholding the thyroid administration the further production of these cells is arrested.
4. The giant cells almost disappear from the marrow after thyroidectomy but they increase after the administration of thyroid.

5./

5. Erythroblasts diminish in number after thyroidectomy but increase after thyroid administration.
6. The anaemia and lymphocytosis which is produced after thyroidectomy disappear rapidly on administering thyroid.

The expenses of the research has been defrayed by a grant from the Earl of Moray fund.

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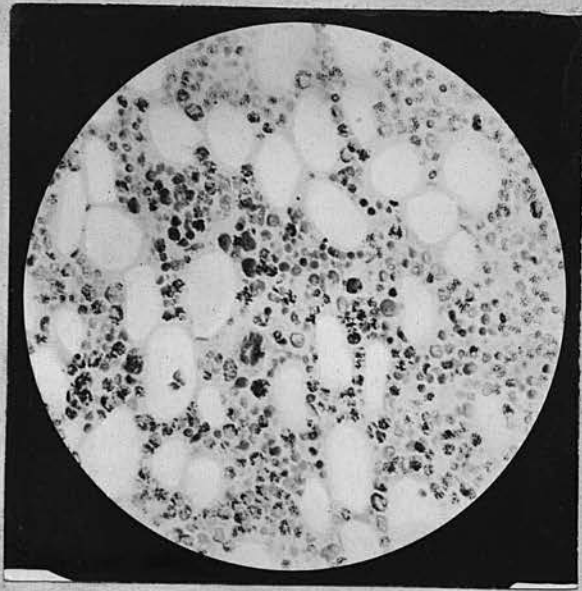


FIG. 1.

Magnified 300 diameters.

Bone-Marrow of Normal Rabbit.

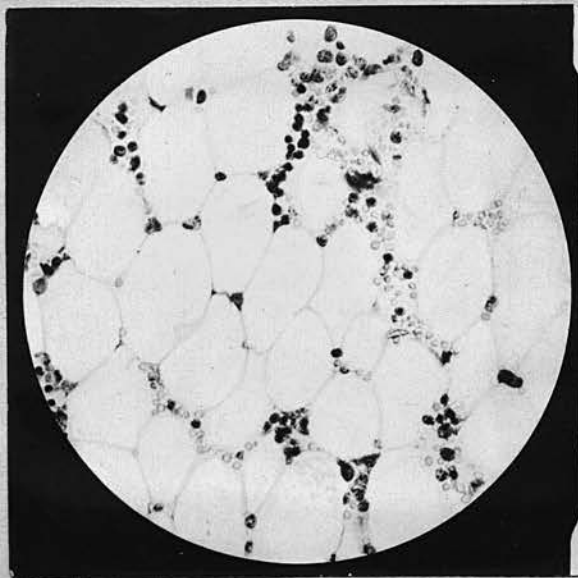


FIG. 2.

Magnified 300 diameters.

Bone-marrow of thyroidecto-
mised Rabbit. (Rabbit L)

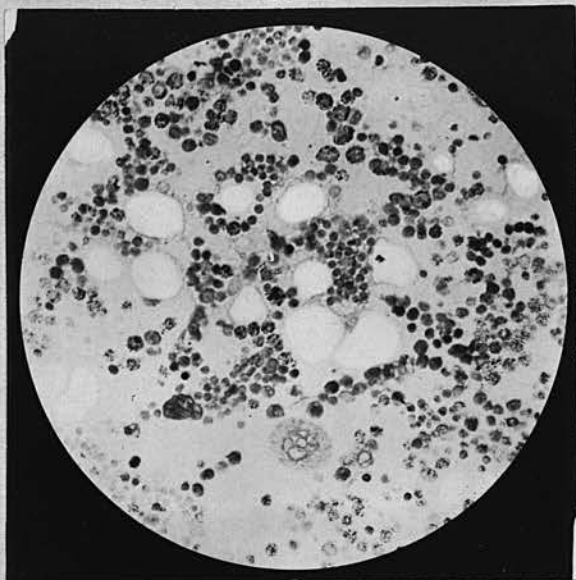


FIG. 3.

Magnified 300 diameters.

Bone-marrow of thyroidecto-
mised Rabbit fed for 2 days
on thyroid. (Rabbit N)

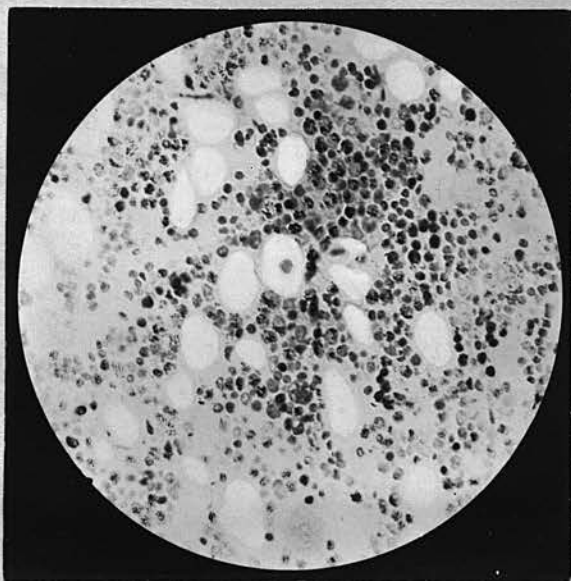


FIG. 4.

Magnified 300 diameters.

Bone-marrow of thyroidecto-
mised Rabbit fed for 4 days
on thyroid. (Rabbit M)

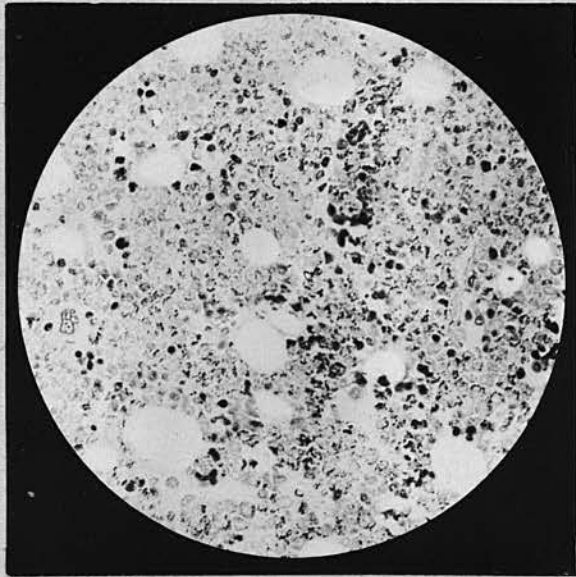


FIG. 5.

Magnified 300 diameters.

Bone-marrow of thyroidecto-
mised Rabbit fed on thyroid
for 3 days and killed 12
days later. (Rabbit Q)

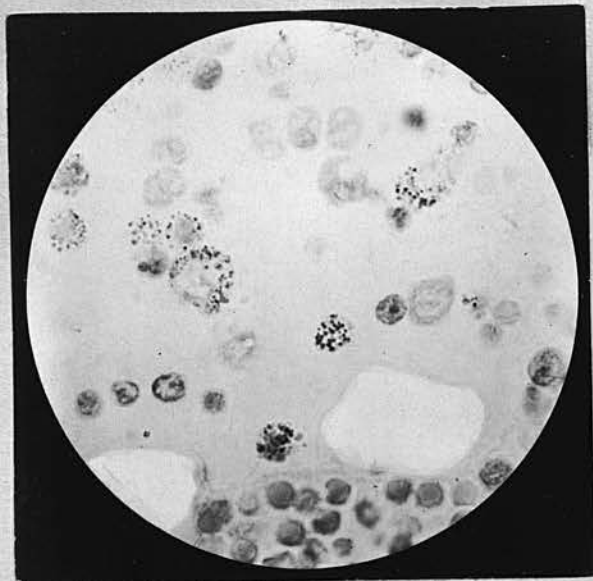


FIG. 6.

Magnified 1000 diameters.
High power view of Fig.3.

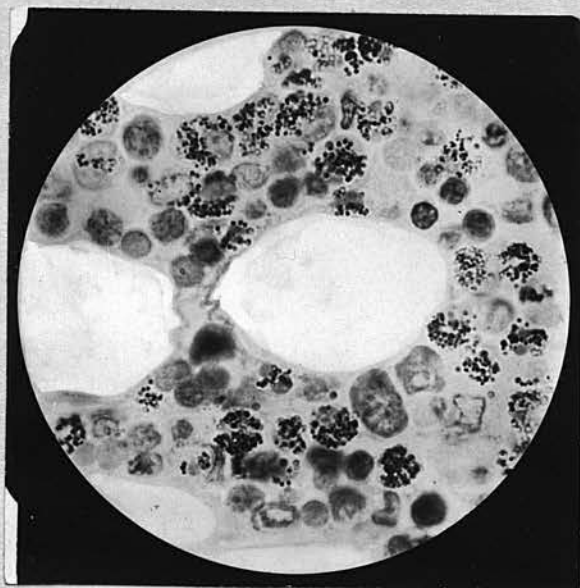


FIG. 7.

Magnified 1000 times.
High power view of Fig.4.