THE INFLUENCE OF UNDER-FEEDING ON THE BLOOD.[1]

By A. E. Boycott, M.A., D.M. *Lecturer on Pathology*, and R. A. Chisolm, M.B., M.R.C.P., *Greville Research Student.*

From the Pathological Department, Guy's Hospital, London.

Apart from its theoretical interest, it is a matter of a good deal of practical importance in connection with experimental observations on the blood, to know how far small or large variations in diet are of moment. In investigations on animals suffering from acute or chronic illness, which may interfere with appetite, any changes which are found in the blood might be due to under-feeding rather than directly associated with the prevailing disease or experimental procedure. The following short series of measurements was made to examine the effect of a degree of proteid starvation which was purposely exaggerated beyond what is likely to obtain in any ordinary experiment.

Rats were used for these experiments as being convenient animals to work with, and because we had available an ample series of blood data for normal individuals.[2] The average figures for eighty-seven normal rats of between 50 and 150 grms. body weight which are required in the present connection are as follows:—

Total oxygen capacity (total hæmoglobin)	9·98 c.c. per kilo. body weight.
Blood volume	62·8 c.c. „ „
Percentage of hæmoglobin (human scale)	87·6 per cent.
Red cells	8·80 millions per c.mm.

One also wants to have some idea as to what grade of departure from the mean value is to be held to constitute an "abnormal" condition. For a series of experiments which does not comprise such a number of observations as would as a rule be inconvenient to make, and much more often for single observations, it is not easy to lay down any rule which is at once precise and convenient. With the ordinary distribution of values about the mean, all normal animals will fall between the average value plus three times the standard

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[2] Chisolm, *Quart. Journ. Exper. Phys.*, 1911, vol. iv. p. 208.

deviation (σ)[1] and the average value minus three times the standard deviation. At the same time, a number of abnormal animals will not exceed these limits, which therefore become unreasonably wide. Not many normal animals lie outside the limits defined by a departure of twice the standard deviation from the mean, and it seems convenient to use this limit in the sense that any value falling within is accepted as normal, any value varying from the average by more than twice but less than three times the standard deviation is, by itself, regarded as probably, but not certainly, abnormal; while any value varying by more than three times the standard deviation is held to be definitely abnormal. Chisolm's series of 87 "normal" rats give the following result when classified on this basis:[2]—

	Total O_2 Capacity per cent.	Blood Volume per cent.	Hæmoglobin per cent.
Deviation more than σ .	25 or 29 per cent.	30 or 34 per cent.	22 or 25 per cent.
Deviation more than 2σ	5	4	3
Deviation more than 3σ	1	0	0

We shall therefore, for purposes of discussion, regard rats as abnormal if they exceed the following values:—

	Standard Deviation.	Limits for "Normal" Animals.
Total oxygen capacity . .	0·88	8·2 – 11·7 c.c. per kilo.
Blood volume	6·7	49 – 76 ,, ,,
Percentage of hæmoglobin .	8·35	68 – 103 per cent.
Red cells per cubic millimetre .	1·00	6·8 – 10·8 millions.

In order to have a criterion of "size" which is independent of the fatness of the animal, we have also used the figures showing the relation between body weight and body length. From the body length is calculated the "normal" body weight. The relation is naturally a variable one, but the figures show that, while some were rather fat and others rather lean when the period of under-feeding commenced, most of our animals conformed pretty closely to the average standard.

The determinations were made in the usual way by taking a

[1] *I.e.* the square root of the sum of the squares of the amounts by which each observation departs from the average value divided by the number of observations.

[2] See also the distributions of rats with transplanted sarcoma: Chisolm, *Journ. Path. and Bacteriol.*, Cambridge, 1911, vol. xv. p. 360.

sample of the heart blood for the hæmoglobinometer and hæmocytometer and then washing out the vessels from the heart and titrating the solutions so obtained against standardised dilutions of blood.[1] Stained blood films were also examined. In normal rats these sometimes show a small amount of polychromasia; marked polychromasia, anisocytosis, and especially the presence of many nucleated red cells are, as in other animals, indicative of active blood formation.

A.—In the first series fourteen rats were fed for nine or eleven days on a proteid-free diet of starch and lard;[2] on the sixth day they had a feed of corn. Four animals died on the second, fifth, seventh, and ninth days respectively. In one the experiment failed. The remaining nine gave the following results:—

TABLE I.

Number.	Sex.	Deviation of Feeding.	Initial Body Weight.	Final Body Weight.	Percentage Loss of Weight.	Body Length.	Normal Weight calculated from Length.
		Days.	Grms.	Grms.		Mm.	
1	F.	9	166	109	34	191	190
2	M.	9	106	70	34	156	96
3	F.	9	91	58	36	151	88
4	M.	9	68	47	31	140	69
5	F.	9	52	36	31	130	55
6	M.	11	97	68	30	151	88
7	M.	11	91	59	35	144	76
8	M.	11	62	42	32	135	62
9	M.	11	62	51	18	132	57

TABLE II.

Number.	Total Oxygen Capacity.			Blood Volume.			Red Cells. Millions per cub.m.	Hæmoglobin per cent. (Human Scale.)	Colour Index.[3]
	C.c.	Per Kilo. Initial Weight.	Per Kilo. Final Weight.	C.c.	Per Kilo. Initial Weight.	Per Kilo. Final Weight.			
1	1·630	9·8	14·9	7·30	44	68	10·15	121	1·2
2	1·027	9·7	14·7	4·74	45	68	11·26	117	1·1
3	0·985	10·8	17·0	4·13	45	71	12·18	129	1·1
4	0·676	9·9	14·4	3·54	52	75	10·66	103	1·0
5	0·550	10·6	15·3	2·88	55	80	10·11	103	1·0
6	0·998	10·3	14·7	5·30	56	79	10·39	100	1·0
7	1·001	11·0	17·0	4·96	55	84	10·01	109	1·1
8	0·610	9·8	14·5	4·01	65	96	8·75	82	1·0
9	0·574	9·3	11·3	3·38	54	66	8·74	92	1·1

Examination of stained films showed normal blood, except for some normoblasts and polychromasia in rat 8, and slight polychromasia (not abnormal) in rat 4.

[1] *Quart. Journ. Exper. Phys.*, 1911, vol. iv. p. 208; *Journ. Path. and Bacteriol.*, 1910, vol. xiv. p. 613.

[2] Hatai, *Am. Journ. Physiol.*, 1904, vol. xii. p. 116.

[3] On the rat scale. The average normal rat colour index is 0·5 on the human scale.

From these results it is clear that under-feeding for about ten days, to such an extent that the total body weight was reduced by about one-third, did not result in any diminution in the total amount of hæmoglobin in the circulation. Calculated on their body weights at the beginning of the experiment, all the rats had fully their normal oxygen capacity; for their weights when killed they had about 50 per cent. too much. The blood was concentrated in most of the animals, so that the volume of the blood was normal, calculated on the final body weights, in several animals; in others, however, especially in rats 7 and 8, the volume was a good deal increased, so that there was no rise in concentration (rat 8). This was perhaps a reaction against the increase in viscosity which the rise in concentration tended to produce.[1]

B.—The results of this experiment suggested that the water intake of the animals had been deficient. In the second series, therefore, twelve rats were fed for three to four weeks on mashed potatoes, sugar, lard, and filtered bovril—a diet deficient in, but not free from, proteid. One animal died on the twentieth day. The lowest weights observed were not in all cases those taken on the day of death. This and the other details are shown in Tables III. and IV.

TABLE III.

Number.	Sex.	Duration of Feeding.	Initial Body Weight.	Final Body Weight.	Percentage Loss of Weight.	Lowest Weight recorded during Feeding.	Body Length.	Normal Weight calculated from Length.
		Days.	Grms.	Grms.			Mm.	
10	F.	24	99	64	35	64*	157	98
11	M.	24	93	73	22	73	151	88
12	F.	24	75	56	25	56	139	68
13	M.	24	73	59	19	59	140	69
14	F.	24	69	57	17	56	138	66
15	F.	29	108	88	19	84	160	104
16	F.	29	98	86	12	84*	157	98
17	M.	29	92	71	23	71*	145	77
18	M.	29	90	87	3	76*	148	83
19	F.	29	81	65	20	65	148	83
20	M.	29	63	57	10	54*	137	65

* These rats between them ate their dead companion about a week before they were killed.

[1] *Journ. Path. and Bacteriol.*, 1910, vol. xiv. p. 303.

TABLE IV.

Number.	Total Oxygen Capacity.			Blood Volume.			Red Cells. Millions per cub. m.	Hæmoglobin per cent. (Human Scale.)	Colour Index.
	C.c.	Per Kilo. Initial Weight.	Per Kilo. Final Weight.	C.c.	Per Kilo. Initial Weight.	Per Kilo. Final Weight.			
10	0·927	9·4	14·5	4·96	50	77	10·17	101	1·0
11	0·923	9·9	12·7	6·23	67	85	7·93	80	1·0
12	0·569	7·6	10·1	5·03	67	90	6·94	61	0·9
13	0·743	10·2	12·6	4·62	63	78	9·43	87	0·9
14	0·664	9·6	11·6	4·31	63	76	7·08	83	1·2
15	0·886	8·2	10·1	5·57	52	63	9·59	86	0·9
16	0·918	9·4	10·7	6·56	67	76	7·68	76	1·0
17	0·661	7·2	9·3	5·33	58	75	7·19	67	1·0
18	0·835	9·3	9·6	6·62	74	76	5·93	68	1·2
19	0·782	9·6	12·0	6·30	78	97	7·43	67	0·9
20	0·700	11·1	12·3	4·51	72	79	8·28	84	1·0

Stained films showed normoblasts in rats 18, 19, and 20; marked polychromasia in rats 15, 16, 18, and 19; slight polychromasia, not more than normal, in rats 11, 17, and 20; the rest were normal.

None of these eleven animals show any diminution of total oxygen capacity calculated on their final weights, and only two (rats 12 and 17) are possibly abnormal in that respect with reference to their original weights. Even these, however, are within the extreme range of normal rats. The concentration of the blood (percentage of hæmoglobin) tends to be low, and the volume of the blood is increased in six of the eleven rats.

The result, therefore, of these experiments is that under-feeding of this kind leaves the blood much in its original condition, and that the blood does not waste in parallel with the other tissues.[1] The total loss of weight was such that some material wasting of important tissues may be assumed. Even if the alimentary canal were emptied (which it was not) and all the fat used up, in an average rat[2] a loss of weight of not more than about 10 per cent. would be produced. In the absence of direct evidence it would not be safe to assume that

[1] As Voit found originally in an animal starved to death, though his result has not been confirmed by other observers (*Ztschr. f. Biol.*, München, Bd. ii. S. 351, Bd. xxx. S. 510, Bd. xxxvii. S. 25, Bd. xlvi. S. 195).

[2] *Journ. Hyg.*, Cambridge, 1908, vol. viii. p. 445; *Journ. Physiol.*, 1908, vol. xxxvii. p. 25; *Quart. Journ. Exper. Phys.*, 1911, vol. iv. p. 208.

a loss of water accounted for the loss of weight beyond that referable to fat. In the first series of rats the body was pretty certainly short of water, but in the second series there was no evidence of this.

The body therefore does not feed on its red cells during proteid starvation. It is highly improbable, however, that many fresh red cells are produced under these conditions, though in a few animals there were signs of hæmopoietic activity. Hence we reach the conclusion that *the natural life of red cells in the rat is something more than three weeks.* No sound evidence on this point has ever been obtained. The data derived from the results of transfusion are of no value in this connection, since transfusion excites active destruction of the excess of red cells.[1] Since the duration of life of the individual cells of the body may be presumed to be proportional to the life of the whole organism, it follows that the duration of life of the red corpuscles in larger animals and man is probably far longer than the two or three weeks usually ascribed. How much longer it is at present quite impossible to suggest. Some further data which bear indirectly on this point are given below (p. 275).

With reference to the duration of the under-feeding in these experiments, it should be remembered that three and half weeks is about the same proportion of the life of a rat as a year in the life of a man.

SUMMARY.

1. Under-feeding with a diet deficient in proteid does not necessarily cause any wasting of the blood.

2. It is suggested that this result throws some light on the duration of life of red cells in the circulation.

[1] *Journ. Path. and Bacteriol.*, 1909, vol. xiii. p. 426 ; 1910, vol. xiv. p. 294.