same quantity of uric acid as with a meat diet, and Douglas¹¹ found that with a diet rich in peas, beans, and lentils, the output of uric acid was 0.702 gram, as compared with 0.675 on ordinary diet. Haig¹² has recently called attention to the effect of asparagus in increasing his uric acid output. This he strangely enough ascribes to the large amount of asparagin it contains.

It will be evident from a reference to the estimations of the vegetable purins contained in Part I, and a glance at the results of the preceding experiment that certain vegetables contain considerable quantities of purin bodies, and so provide "exogenous" purin. That such an inference might be supported by experimental evidence, additional observations were made.

Dry haricot beans, after weighing, were allowed to soak in water for twelve hours, then boiled and reweighed. All three subjects of experiment ate from the same lot of beans and at the same time; otherwise, during the experiment, the food consisted solely of eggs, milk, cheese, bread, butter, sugar, and rice. Tables II, III, and IV (p. 1463) give the results obtained.

In each case there was a distinct increase in the urinary purin on the day when the beans were eaten. As Rubner and others have pointed out the small absorption of the proteids of the pulses it was in this case absolutely necessary to estimate the faecal purins. On the day in question the faeces from W. H. yielded 0.0407 N. as exogenous purin-N. Now 408 grams of haricot beans contain 0.0920 purin-N (*vide* Part I), therefore, 0.0513 purin-N. was absorbed. The increase of the urinary purin over the normal endogenous factor (0.1625 N.) was 0.0232, and thus represented 45.5 per cent. of the food purin-N. It was impossible to obtain the faeces from M and N., so that a precise calculation cannot be made. But if the absorption was at all approximate to that of W. H. there would be an absorbed amount of bean-purin 0.0162 N., an increase of 0.0090 N. above the average normal endogenous quantity of 0.1250 N., and thus an exogenous urinary purin of 56.2 per cent. With M. there was an increase of 0.0180 N. absorbed, giving an exogenous urinary purin of 55 per cent.

Thus these observations demonstrate both the presence of purin bodies in the pulses and their relation with the functional excretions. It is, therefore, apparent that in the formation of dietaries, particularly in regard to metabolic disorders, the purin contents of foodstuffs should be considered equally with their proteid percentage.

As I have elsewhere given a summary of the action of alcohol on the formation and excretion of uric acid,¹³ it is here only necessary to state that in the human body the elimination of uric acid is generally diminished after taking alcohol. Rosenfeld,¹⁴ however, had a patient whose uric acid rose considerably after a single bottle of beer, and it is common knowledge that gout is more frequent in countries where fermented drinks are taken than in those in which distilled spirits are consumed.

On a day when no laboratory work was undertaken and purin-free food was eaten I drank 1½ litre of lager beer. The urine for the following twenty-four hours amounted to 2,080 c.cm. It contained 18.2640 total N., 0.2218 total purin-N., and 0.1761 uric acid N. In the 1,700 c.cm. of beer there would be 0.090 purin-N. (*vide* Part I), and my endogenous purin quotient was 0.1625. The difference of 0.0593 might thus be attributed to substances present in the beer. The experiment, however, was not entirely free from objections. The quantity of fluid was greater than the daily average of 1,000 cc.m. of milk, and Laquer¹⁵ has shown that after 1½ to 1½ litre of water the alloxur-N. may be increased. In addition, it is contrary to my usual custom to take alcoholic beverages, and so any effects would be more pronounced; thus, although the general depression of nervous and metabolic functions might diminish the purin excretion the dilatation of the smaller arterioles might assist the removal of an abnormal amount of undecomposed tri-oxypurin. The experiment was therefore repeated in the following manner: To one litre of lager beer 1 c.cm. H₂SO₄ was added, the alcohol distilled off, the remainder evaporated to 500 c.cm., and then neutralized. The whole was drunk at 9 a.m. on the day of the experiment, and a purin-free diet observed during the several preceding and following days. An increase of 0.0175 purin-N. was obtained. As each litre of beer contains 0.05 purin-N. this quantity would represent 35 per cent. of the beer purins

appearing as urinary purins. The results of the second experiment show that the first yielded, through adverse conditions, too high an amount. The low percentage obtained in the second experiment led to an inquiry as to the form in which the purin bodies exist in beer, and further estimations were made, from which it was ascertained that each litre contained 0.0327 free purin-N.

As the addition of foods containing known quantities of purin bodies to a purin-free diet results in an increased egestion of urinary purin, varying with the nature of the food, and perhaps also with the individual, the question naturally occurs, what becomes of the balance which is not excreted as urinary purin? As the work which attempts to solve this problem is fully cited in another place,¹⁶ it may be shortly answered by the statement that the present condition of our knowledge appears to warrant the assumption that the "purin" first oxidized to tri-oxypurin is later decomposed by the liver (perhaps to a slight extent also by the general tissues) and finally excreted as urea, or the intermediate substances, allantoin and oxaluric acid.

From the action of the body in regard to the exogenous purin it has been argued that of the purin of endogenous formation only a certain percentage is excreted as such in the urine, the remainder undergoing decomposition into urea or bodies intermediate. If from the experimental data obtained these inferences are correct, then it is obvious that the balance normally maintained between the amount of purin destroyed and the quantity excreted in an unaltered condition will depend upon the integrity of the metabolic and excretory organs. Any alteration in their functional capacity will be at once reflected in a changed purin elimination. Whether retention of purin bodies is sufficient to account for any lesions with which their non-oxidation or non-excretion may be associated is another question? When the results of similar experiments under abnormal metabolic conditions are available the relation of cause and effect may be more evident than it is at the present moment.

The precise quantities of exogenous purin taken with the food and excreted in the urine may now be somewhat easily ascertained. A knowledge of the normal and abnormal individual reactions towards purin substances permits to a certain degree the measurement of the personal metabolism of purin bodies, and thus the clinician may increase or decrease the purin-rich foods according to the activity manifested by his patient during the several stages of disease or convalescence. Another point in relation to this activity is the rate of purin elimination. Some of my experiments indicate that a fairly constant period obtains for the excretion of "free" purins, and that this is much extended before the "bound" purins appear. The subject will be more fully dealt with in a later communication.

The exogenous "purin" can thus be easily controlled, but of the endogenous purin as yet little is definitely known. That it bears a somewhat close relation to the body weight I have elsewhere shown.¹⁶ Leucocytic destruction probably only slightly affects its quantity. There is a certain amount of evidence which points to its variation with nitrogenous excretion, and it may perhaps be taken as an index of the functional activities of the body. The last word, however, has not been said upon this subject.

REFERENCES.

- ¹ Arch. f. ges. Phys., Bd. lxxx, 1900. ² *Idem*, Part I, BRITISH MEDICAL JOURNAL, D. 1461. ³ Centralbl. f. inn. Med., s. 18, 1895. ⁴ Zeit. f. klin. Med., s. 174, 1896. ⁵ Skand. Arch. f. Phys., s. 315, 1898. ⁶ Amer. Journ. Phys., p. 37, 1901. ⁷ Zeit. f. phys. Chemie., April, 1902. ⁸ Loc. cit. ⁹ Zeit. f. Biol., 1891 and 1897. ¹⁰ Verhand. f. Cong. inn. Med., s. 424, 1896. ¹¹ Edin. Med. Journal, p. 32, 1900. ¹² BRITISH MEDICAL JOURNAL, ii, 1901, p. 1078. ¹³ Walker Hall, Purin Bodies, Dissert., 1902. ¹⁴ Verhand. f. Cong. inn. Med., s. 321, 1896. ¹⁵ Verh. f. Cong. inn. Med., 1896. ¹⁶ Dissert., Purin Bodies, 1902.

REPORT LXIX.

THE OEDEMA OF ANAEMIA.

By THOMAS HOUSTON, B.A., M.D.,

Assistant to the Pathologist of the Royal Victoria Hospital, Belfast;
Research Scholar of the British Medical Association (1901).

IN the BRITISH MEDICAL JOURNAL of June 15th, 1901, I endeavoured to show that, by taking into consideration the dilution of the blood that may occur in typhoid fever, a satis-

factory explanation of the behaviour of the different varieties of leucocytes in this disease could be given. That a hydraemic plethora occurs in certain anaemic conditions appears quite clear from the observation of Professor Lorrain Smith on chlorosis and pernicious anaemia.¹ The importance of the disturbance of balance in fluid exchange between the blood and the tissues in the various forms of anaemia suggests that some light would be thrown on the allied conditions of oedema and dropsy if the occurrence of these conditions were studied in definite relationship to the various changes in the blood. In the following paper I have endeavoured, by means of the observations to be detailed, to contrast the oedema and dropsy which occurs in Bright's disease with that which frequently accompanies various forms of anaemia, such as chlorosis, pernicious anaemia, splenic anaemia, or anaemia of haemorrhage.

The systemic study of the gain or loss in weight in such conditions has been singularly neglected by investigators who are interested in the diseases which show oedema or anaemia. It is, however, a fact of common observation that patients suffering from such anaemic conditions as chlorosis and pernicious anaemia do not appear to lose weight in proportion to the severity of the disease. The observations which follow seem to furnish an explanation of this phenomenon and show that a gain of weight in an anaemic patient is by no means necessarily an indication that the patient is improving. In fact, it will be seen that in many cases of anaemia an initial loss of weight seems an essential part of the patient's progress towards recovery.

OEDEMA OF RENAL DISEASE.

Before taking up the study of the oedema associated with anaemia or changes in the blood I wish to introduce a few cases illustrating the well established fact that the oedema of Bright's disease comes and goes without simultaneous changes in the blood of the kind noticed in cases of anaemia. These cases are merely sufficient to serve as illustrations. The changes in the blood which occur in Bright's disease and in heart disease of various forms merit separate investigation.

NOTE.—The following contractions will be used for convenience in the tables given:

R. C. = red corpuscles per cubic millimetre.

W. C. = white corpuscles per cubic millimetre.

Hb. = percentage of haemoglobin compared with average normal.

Lymph. = percentage of lymphocytes (small and large varieties) in differential count.

Pmn. = percentage of polymorpho-nuclear leucocytes in differential count.

E. L. = percentage of eosinophile leucocytes in differential count.

N. B. = normoblasts } Number found in counting 500 leucocytes.

M. B. = megaloblasts }

Wt. = Weight taken in the same clothes in the case of each patient and at the same time of day.

I.—J. R. Acute Bright's Disease: Anasarca well marked.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
November 27 ...	4,440,000	8,200	80	44.8	52.4	st. lb. 12 11
December 4 ...	4,100,000	9,100	79	46.4	46.4	12 8
December 20 ...	4,600,000	12,000	82	43.2	54.4	9 5

Here, although the patient has lost 3 st. 6 lb., there is hardly any effect produced on the blood. The haemoglobin seems at first to fall a little and afterwards rise a little, while the patient was losing weight or getting rid of his anasarca.

II.—J. McC. Kidney Disease with Dropsy.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
November 8, 1901	3,900,000	13,000	74	45.3	53.3	st. lb. 10 10½
November 14, 1901	3,820,000	8,500	74	25.6	70.8	10 5
November 22, 1901	3,400,000	8,500	69	41.6	56.8	10 0
November 29, 1901	3,850,000	8,100	67	38.6	60.4	10 6½

From November 8th, 1901, to November 22nd, 1901, the patient lost 10½ lb., while his haemoglobin fell from 74 to 69 per cent. He then had a slight relapse, becoming

more oedematous and putting on 6½ lb. in weight; his haemoglobin was then found to be 67 per cent. This case would seem to show that the anaemia may bear a relation to the duration of the disease but not to the oedema formation.

III.—G. L. Second Attack of Chronic Bright's Disease, Oedema, and Psoriasis.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	E. L.	Wt.
March 15, 1902	4,320,000	7,300	87.2	39.6	60	0.4	st. lb. 10 2
March 20, 1902	4,200,000	10,100	86.9	47.6	46.4	6.0	10 10
March 26, 1902	4,550,000	12,100	87.2	43.4	51.6	4.8	10 9½
April 6, 1902	4,540,000	9,100	87.2	36.8	56.8	6.4	10 10

This patient did not improve while in hospital, and left more oedematous than he was on admission. While in hospital he developed an attack of psoriasis, and it is interesting to note that during this period his blood showed an increase of eosinophile leucocytes. His haemoglobin was practically constant during his stay in hospital, although on one occasion he gained 8 lb. in five days.

IV.—W. McF., aged 39. Bright's Disease with Mitral Systolic Murmur; considerable Oedema.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
February 22, 1902	4,790,000	8,500	98.75	35.2	64.8	st. lb. 10 12
February 27, 1902	4,980,000	8,700	98.75	53.2	46.4	10 2½

In this case the patient lost 9½ lb. in five days yet no alteration could be detected in his haemoglobin.

The only deduction that can be drawn from these figures is that the condition of the blood as far as its haemoglobin percentage is concerned bears little or no direct relation to the extent of the oedema. There must be no doubt changes in the blood during oedema formation, but these changes are of such a transient nature owing to the blood's remarkable power of correcting any tendency to dilution, that they are hard to detect by the methods at our disposal.

During the time I have been making observations on this subject, I have not yet had the opportunity of observing in this manner any cases of Bright's disease with profound anaemia. The usual hospital case of chronic parenchymatous nephritis has, as a rule, little anaemia. Some cases of nephritis are profoundly anaemic, but this may not be due merely to kidney inadequacy, but possibly the result of the action of some blood poison of which the anaemia and nephritis are the symptoms, for example, lead poisoning.

CHLOROSIS.

I.—McR. Chlorosis complicated with Gastritis.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
September 10, 1900	4,375,000	5,500	56	39.4	56.4	st. lb. 7 0
September 29, 1900	4,340,000	14,000	52	30.4	66.0	7 4

This patient had a troublesome gastritis—notice the leucocytosis in the second observation—and did not improve during the period of observation. The point to be noted about this case is that, without any clinical improvement or improvement in the condition of the blood, she gained 4 lb.

II.—D. Severe Chlorosis. This Patient was kept without Iron during the Period of Observation.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
September 25, 1900	2,080,000	5,600	15	43	53	st. lb. 8 8½
October 10, 1900	1,750,000	3,700	—15	52	46	9 4

This patient made no improvement while kept without iron, as the above figures show: (1) the red corpuscles are lower; (2) the percentage of lymphocytes is higher; (3) the haemoglobin is marked under 15 per cent., but with such low percentages of haemoglobin it is difficult to be accurate; (4) her clinical condition was worse. In spite of all these points, showing that her condition was not improved, she had gained $9\frac{1}{2}$ lb. in weight.

III.—*McD. Also kept without Iron during the Period of Observation.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
September 25, 1900	3,980,000	4,000	64	42.6	54.2	7 11 $\frac{1}{2}$
October 12, 1900	3,075,000	5,000	56	44.0	54.0	8 1 $\frac{1}{2}$

This case did not improve while iron was withheld, but still her weight rose $3\frac{1}{2}$ lb.

IV.—*R. Severe Chlorosis: Oedema of Feet and Ankles.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
February 24, 1901	1,800,000	6,400	16.4	—	—	7 10
March 12, 1901	2,320,000	4,000	24.0	27	73	7 5 $\frac{1}{2}$

This patient rapidly improved under iron and rest, and although her haemoglobin rises from 16 to 24 per cent., she loses $4\frac{1}{2}$ lb. in weight.

V.—This loss of weight that appears usually to occur in chlorosis when the case is improving, does not, however, continue throughout the cure of the case.

R. C.—*Chlorosis: Oedema of Ankles.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
August 24, 1901	4,930,000	7,400	53	56.4	43.6	9 10 $\frac{1}{2}$
August 29, 1901	Oedema of ankles disappeared.					9 6
August 30, 1901	5,380,000	7,750	59	52.4	44.8	9 7
September 1, 1901	5,000,000	6,000	64	31.6	66.4	9 7
September 6, 1901	5,280,000	5,000	70	31.6	66.4	9 10

This loss of weight here continued only for the first five days, and after this time the patient began to gain in weight. During the whole period the haemoglobin steadily increased. Since the blood in chlorosis is diluted, we may presume that in the cure of the case the loss of weight is due to the loss of fluid from the blood and tissues. The loss of fluid from the tissues is the first evident change, and therefore the oedema and puffiness first disappear. There is no doubt a continual loss of fluid during the cure, but this is masked by the fact that owing to the improved conditions of nutrition the tissues gain in weight. It thus seems evident that the gain in weight in the case of chlorosis is only an apparent one, due to the increase of fluid in the blood and tissues.

VI.—*A. M. Chlorosis.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
October 13, 1901	3,550,000	6,600	33.7	50.8	47.6	9 9 $\frac{1}{2}$
October 16, 1901			—	—	—	9 7
October 22, 1901	4,500,000	6,300	38.9	45	52	9 9 $\frac{1}{2}$
October 27, 1901	4,800,000	6,600	44.9	43.6	55.2	9 10

This is a similar case. It may be noted here that the changes occurring in the blood in chlorosis during the cure are the following: (1) A gradual rise of haemoglobin throughout the cure; (2) a more sudden rise in corpuscles (this appears to be due to the concentration of corpuscles still poor in haemoglobin by the withdrawal of the excessive fluid); (3) a decrease in the percentage of lymphocytes; (4) an increase in the percentage of polymorpho-nuclear leucocytes; (5) an initial loss of weight (no doubt due to the loss of fluid from the tissues and blood) with a subsequent gain in weight.

VII.—*M. K. Chlorosis.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
September 28, 1901	Not weighed on admission to hospital.					st. lb.
October 1, 1901	2,640,000	4,600	29.96	30	68.4	8 6
October 5, 1901	2,300,000	6,000	29.96	30	68	8 6
October 8, 1901	2,780,000	8,600	30	30	68	8 6
October 12, 1901	3,020,000	8,100	31.4	30.4	68	8 7
October 17, 1901	3,680,000	7,000	40.4	24.8	74.4	8 8

This case is noteworthy because of its slow progress at first. The weight was unfortunately not taken on admission to hospital (during this period there may have been some loss of weight). From the 1st to 9th inst. the weight remained absolutely stationary, and during this period no improvement could be detected in the blood. The patient after this began to gain in weight and rapidly improved. Here, evidently, the loss of fluid was very gradual and the tissue gain occurring as the result of rest and iron treatment prevented the gradual loss from being apparent in the weighing.

VIII.—*B. K. Chlorosis (Oedema of Ankles). Second Attack.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
November 30, 1901	2,450,000	5,500	24.6	32.4	64	7 10
December 6, 1901	Oedema of ankles disappeared.					7 6 $\frac{1}{2}$
December 14, 1901	4,100,000	8,000	69	11.6	74.8	7 4
December 21, 1901	No examination of the blood.					7 5 $\frac{1}{2}$
December 27, 1901	No examination of the blood.					7 10 $\frac{1}{2}$

This was a case of severe chlorosis with well-marked haemic murmurs and *bruit de diable*. There was oedema of the ankles. The rapid rise of haemoglobin from 24 per cent. to 60 per cent. in fourteen days is remarkable. During this period the patient lost $6\frac{1}{2}$ lb. in weight.

IX.—*N. J. Chlorosis.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
						st. lb.
January 1st, 1902	2,950,000	5,000	24.6	29.6	69.6	—
January 9th, 1902	2,440,000	5,600	29.6	27.2	72.0	8 6 $\frac{1}{2}$
January 15th, 1902	2,850,000	5,600	30.0	26.4	73.2	8 2
January 21st, 1902	3,520,000	6,000	34.5	25.9	73.6	8 8
January 28th, 1902	4,180,000	6,600	39.5	30.0	69.6	8 10

This patient was not weighed until she was nine days in hospital. She was kept fourteen days without iron. It was found by weighing the patient daily after the 9th instant that from the 9th to the 15th she lost $4\frac{1}{2}$ lb. Her weight, however, fluctuated somewhat between these dates. Her haemoglobin, it will be noted rises very slowly at first. It may be noticed in this, as in other cases, the corpuscles rise more quickly than the haemoglobin.

X.—F. O'N., age 20. Chlorosis: Cardiac Murmurs; Oedema of Ankles.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
February 15th, 1902	No examination	of blood	on this date.			st. lb. 9 3
February 18th, 1902	3,100,000	6,500	34.5	31.6	68.4	8 13½
February 22nd, 1902	3,800,000	7,000	35.5	29.6	68.0	9 0
March 1st, 1902	3,700,000	8,800	36.0	44.8	54.0	9 10½
March 15th, 1902	4,120,000	8,400	69.1	44.8	54.8	9 3½

This case also shows an initial loss of weight with a subsequent gain while the haemoglobin was steadily improving.

From the above 10 cases of chlorosis it will be seen that an average case will lose about 4 lb. in weight before beginning to gain after treatment has begun. Suppose, for example, we have a chlorotic of 100 lb. weight with 50 per cent. of haemoglobin. [Taking the blood in the normal person as about one-twentieth of the body weight (*Transactions of the Pathological Society of London*. Vol. li. Part iii. 1900.)]. This theoretical case may be supposed to have double the normal quantity of blood, that is about 10 lb. weight of blood, and that in improving from 50 per cent. to 100 per cent. such a patient would lose 5 lb. of fluid from the blood, or 1 lb. for every 10 per cent. of improvement in the haemoglobin. When we consider this theoretical example and the figures given above from the actual weights of chlorotic patients, it is quite clear that a good part of the fluid weight lost must be fluid in the tissues. This view is strengthened by the fact that chlorotic patients as they improve first lose any oedema that may be present about the ankles, and finally that flabby appearance so characteristic of the disease which is due to the presence of fluid in the lymph spaces of the tissues.

SPLENIC ANAEMIA.

I have made observations of other cases of anaemia with the object of determining if this initial loss of weight when the patient was improving was confined to chlorotics. The condition known as splenic anaemia may be defined as a markedly chlorotic condition of the blood with an enlarged spleen. I have made a series of observations on a case conforming to this type.

O.—*Splenic Anaemia: Profound Anaemia with History of Haematemesis, and very much Enlarged Spleen: Haemic Murmurs.*

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	Wt.
September 14, 1901	1,300,000	2,500	—16	45.0	53.6	st. lb. 7 12½
September 24, 1901	1,350,000	2,000	—16	46.6	53.3	8 0*
October 3, 1901	1,325,000	2,000	—16	46.0	54.0	7 3
October 23, 1901	1,740,000	3,000	32	38.8	60.0	7 6
November 9, 1901	4,020,000	3,000	55	30.8	68.4	7 13
November 20, 1901	3,740,000	2,400	49	37.3	61.6	8 1
November 30, 1901	4,170,000	3,000	81	26.8	71.6	8 6
December 31, 1901	4,110,000	3,200	73	32.4	66.8	9 4
February 4, 1902	5,030,000	4,000	98	34.0	62.4	9 12

* 300 oz. of urine in 48 hours.

The quantity of urine in this patient's case was carefully estimated every twenty-four hours. During the first fourteen days in hospital he passed from 40 to 50 oz. of urine in the twenty-four hours. The quantity never exceeded 50 oz. It was noted that during this period the patient was not improving; he was, indeed, supposed to be gradually dying in spite of treatment by rest and arsenic. On the 24th the patient was weighed with some difficulty on account of his great weakness, and found to have gained 1½ lb. since admission. On the 28th and 29th the patient was apparently moribund. During these two critical days he passed over 300 oz. of urine, and had some diarrhoea and melaena. From this date he began gradually to improve. The patient himself dates his improvement from the time he passed this large quantity of urine. He was weighed again on the 3rd, and found to have lost 11 lb. in weight. This loss of weight was no doubt due to the loss of fluid by the kidneys and bowel.

After this critical period of his illness during which he lost 11 lb. in weight he began steadily to increase in weight, and at the same time his haemoglobin gradually rose. It is interesting to note in this case that the haemoglobin increased inversely as the percentage of lymphocytes, and directly as the percentage of polymorphonuclear leucocytes.²

In the first three blood determinations the haemoglobin was found to be slightly under 16 per cent. No increase of haemoglobin was detected immediately after the loss of fluid. Possibly the haemoglobin was somewhat improved, but it cannot have been much. This would lead us to infer that the great loss of fluid came indirectly, at least, through the blood from the waterlogged tissues, and by its removal made it possible for the blood to concentrate, and so improve. In chlorosis, as we have seen the more gradual loss of fluid is accompanied by a gradual improvement in the blood. From this we would infer that in these cases of anaemia in which the blood is diluted the first change necessary to allow the blood to concentrate is that the tissues should get rid of their excess of fluid by the kidney or otherwise. We might also infer that the oedema and flabbiness of the tissues in such conditions is the result of the diluted condition of the blood. It seems at first difficult to understand why the draining off by the kidneys of such a large quantity of fluid should not have a very decided and immediate effect on the haemoglobin value of the blood, but we must consider that any attempt on the part of the blood to correct its dilution by getting rid of fluid by means of the kidney or otherwise may almost immediately cause an increased flow of lymph from the oedematous tissues into the blood, and thus we can explain how in this case the blood showed little immediate sign of concentration.

PERNICIOUS ANAEMIA.

Pernicious anaemia is another condition in which the blood may become diluted, and observations of the weight and haemoglobin in such cases form an interesting series.

I.—M. Pernicious Anaemia.

	Hb.	per cent.	Wt.	st. lb.
a. 21.1.00.	31	...	9	8
b. 10.2.00.	71	...	9	9
c. 28.2.00.	62	...	10	0
d. 20.4.00.	73	...	10	0½
e. 13.6.00.	57	...	9	13
f. 21.6.00.	65	...	9	7
g. 3.7.00.	59	...	9	12

In this case of pernicious anaemia the figures are taken from my notebook before this method of comparing the weight and the haemoglobin value of the blood had occurred to me.

From a to b we notice that although the patient rises from 31 per cent. to 71 per cent. of haemoglobin, he only gains 1 lb. in weight. This would probably have been explained had more observations been made between January 21st and February 10th been made, as it is more than likely that the patient would first have been found to lose weight and then to gain a little. From b to c the patient gains 3 lb. in weight, but loses 9 per cent. of haemoglobin. From c to f he loses weight, but gains in haemoglobin; and from f to g he gains in weight but loses in haemoglobin. Such results can only be explained on the supposition that there is also in this disease a tendency to dilution of the blood and exudation of plasma into the tissues. No doubt if the disease is progressing there is also a progressive real loss of weight in this as in other fatal diseases, but this real loss of weight may often become masked by the dilution of the blood and accumulation of fluid in the tissues. Some other examples will make this more clear.

II.—S. M., age 52. Pernicious Anaemia.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	N. B.	M. B.	Wt.
Jan. 11, 1902	1,080,000	4,500	29.6	49.2	50.8	—	2	st. lb. 7 9½
Jan. 18, 1902								7 9½
Jan. 25, 1902	890,000	4,100	22.7	49.6	48.3	12	24	7 11½
Jan. 27, 1902	Oedema	increasing				in counting 500 leucocytes.		7 12½

This patient lost ground from admission till her death.

During this time she continued to gain in weight. During the last fourteen days of her life she was not weighed owing to her great weakness, but as she became markedly more oedematous there can be no doubt that her weight still increased. The necropsy showed the pathological condition of liver, bone marrow, and heart usually found in pernicious anaemia.

III.—M. S. Pernicious Anaemia.

Date.	R.C.	W.C.	Hb.	Lymph	Pmn.	N.B.	M.B.	Wt.
								st. lb.
Dec. 5, 1901	1,020,000	2,400	26.0	75.0	34.4	2	10	8 11½
Dec. 14, 1901	840,000	2,300	25.0	66.5	32.5	4	18	8 11
Dec. 20, 1901	1,140,000	2,250	25.6	62.5	37.0	6	14	8 11
Dec. 31, 1901	910,000	2,500	25.0	65.6	34.0	4	12	8 11
Jan. 21, 1902	794,000	2,300	23.7	67.5	32.5	2	12	8 9½
Jan. 25, 1902	720,000	2,900	22.2	82.8	17.5	0	14	8 9½
Jan. 28, 1902	720,000	4,000	19.75	65.2	34.4	2	8	8 9½
Feb. 4, 1902	630,000	4,250	15.8	64.4	35.2	14	10	8 13½
Feb. 18, 1902	590,000	3,500	15.0	66.0	34.0	54	12	9 11
Feb. 27, 1902	925,000	3,200	25.6	31.0	68.0	4	6	9 9½
March 14, 1902	1,105,000	3,800	20.0	64.0	34.0	—	8	8 7½
March 22, 1902	1,110,000	2,300	28.0	46.0	51.2	2	14	8 7
April 16, 1902	1,230,000	3,700	39.5	52.4	43.6	2	2	9 3

This was a case of pernicious anaemia which for the first two months in hospital responded to no treatment. She was treated for the first month on injections of cacodylate of sodium, and for the second on antistreptococcus serum. Neither treatment seemed to improve her condition. During the first month she very gradually lost in haemoglobin, falling from 26 per cent. to 22 per cent. during this period; she lost only 2 lb. in weight. During the second month she got more quickly worse, her haemoglobin falling from 22 per cent. to 15 per cent. from January 15th to February 18th. During this period it will be noticed that her weight rose from 8 st. 9½ lb. to 9 st. 11 lb.; in other words, while she lost 7.2 per cent. of haemoglobin, she gained 15½ lb. in weight during this time. She became markedly oedematous, and was so weak that it was thought advisable not to give her the usual injection of antistreptococcus serum. In the above table it will be noticed that at this critical period in her illness, when her haemoglobin was lowest and her weight was greatest, a very large number of nucleated blood corpuscles were found on examining her blood films; 66 were found in counting 500 leucocytes. This number, it will be noticed, is very greatly in excess of the nucleated corpuscles found in any of the other examinations. This makes it probable that at the stage when her oedema was greatest and her haemoglobin lowest, there was a "blood crisis" present. After this critical period it will be seen from the table that she rapidly lost weight and gained in haemoglobin. From February 18th to March 14th she lost 15½ lb. in weight and gained 14 per cent. of haemoglobin. From this period on until she left hospital she gained both in weight and in haemoglobin. We may therefore divide the progress of this case into the following stages:

First stage: Gradual gain of weight, with oedema increasing and haemoglobin falling.

Second stage: More rapid loss of weight, with oedema decreasing and haemoglobin rising.

Third stage: Gradual gain in weight, with haemoglobin also improving.

It is evident from the observations made in this case that the weight in a case of pernicious anaemia furnishes no indication of the progress of the case unless it be taken in conjunction with the haemoglobin value of the blood. During the period that this patient was most oedematous and at her worst she had two severe attacks of epistaxis. This was the only period during her stay in hospital that she had any haemorrhage, and it is interesting to note that it occurred during the period in which her haemoglobin was falling most rapidly and in which her oedema was increasing. The explanation of this seems to be that the volume or dilution of her blood was increasing, and that the epistaxis and oedema were merely Nature's method of getting rid of the excess of fluid in the vessels. For more reasons than one this period may be regarded as a critical period of her illness.

IV.—Mrs. H., age 50. Pernicious Anaemia. Ill since April, 1900. Epistaxis and Haemoptysis: Septic Condition of Mouth and Teeth.

Date.	R. C.	W. C.	Hb.	Lymph.	Pmn.	N. B.	M. B.	Wt.
								st. lb.
July 12, 1901	810,000	3,900	19.4	56.4	38.0	10	22	7 6½
July 22, 1901	Dropsy	and as	cites in	creasing				8 0
July 29, 1901	"	"	"	"				8 5
Aug. 10, 1901	2,260,000	4,400	46.0	55.6	42.8	—	—	7 5½
Jan. 25, 1902	2,400,000	3,000	49.5	45.6	54.4	—	—	9 4½

This case of pernicious anaemia made a wonderful recovery, and is still alive in fairly good health, that is, having about 50 per cent. of haemoglobin. She is very prone to slight relapses, and at these periods she develops some oedema. She has so far improved under treatment by arsenic. When she came into hospital she was profoundly anaemic, with 19 per cent. of haemoglobin, and up to the 29th little improvement was noted in her clinical condition. During this time it was noted that her oedema and ascites increased. From July 29th she rapidly lost weight and as rapidly improved. On August 10th her haemoglobin was 46 per cent., and her weight 7 st. 7½ lb., that is, practically a stone lighter than on the 29th.

V.—M. McK., age 46. Pernicious Anaemia: Ill for One Year: Some Oedema: Septic Mouth and Teeth.

Date.	R. C.	W. C.	Hb.	Lymph	Pmn.	N. B.	M. B.	Wt.
								st. lb.
March 31, 1901	1,000,000	2,000	25.6	32.0	67.0	16	14	7 5
April 16, 1902	963,000	7,300	23.7	18.4	81.2	4	4	7 6½

This patient a few days after admission to hospital became extremely ill, with very high temperature; she was semi-comatose, and had incontinence of urine. During this period she became markedly oedematous, but, owing to her extreme weakness, no observations were made. On the 16th, when she had considerably improved, and the oedema had almost disappeared, her blood was found to be as above. In this case, again, the patient first becomes oedematous and extremely ill, and then improved.

This case is still in hospital and under observation.

From my observations in these cases and from several other cases I have seen, I do not think that oedema is an altogether unfavourable sign. In several cases it would appear that the oedema is the first step towards an improvement of the blood condition. (The oedemas here referred to were all developed in bed.) The patient suffering from pernicious anaemia may get steadily worse for some time, then become oedematous, and then improve.

I made a few observations on another case of pernicious anaemia which present some interesting features in this connexion. This patient was not a hospital patient, and her weight was therefore not observed.

VI.—Mrs. G., aged 42. Ill since Christmas time. No Septic Condition of Mouth or Teeth. Irregular Temperature.

	R.C.	W.C.	Hb.	Lymph	Pmn.	N.B.	M.B.	Remarks.
March 6, 1902	1,130,000	4,200	30	49.2	46.6	2	10	Slight oedema.
April 3, 1902	1,500,000	5,100	33	47.5	51	300	75	Marked oedema.
April 19, 1902	1,560,000	5,000	35	63.2	36.8	16	10	Oedema disappearing.

On March 6th, 1902, I examined this patient's blood, and obtained the figure given above. The case was therefore a typical one of pernicious anaemia. At this time there was a very slight amount of oedema about the ankles. On March 4th her blood was again examined, and her haemoglobin was found very slightly higher. She was at this time very

oedematous, and the abdominal wall greatly distended with oedema, although there did not seem to be much free fluid in the peritoneal cavity. During this time she was passing an average of 40 to 50 oz. of urine in the twenty-four hours, and was very restless and sleepless. Her blood at this period, as seen in the above table, presented a very interesting feature, namely, a blood crisis—the blood films contained a great number of nucleated red corpuscles. Many of their nuclei were bilobed or trilobed as if dividing. It will be remembered that a somewhat similar condition of the blood was found in Case III where she was most oedematous. The presence of a blood crisis is said to be a favourable sign in prognosis. From this period until the present date she made a gradual improvement, and her oedema almost entirely disappeared. From April 8th to the 19th, while her oedema was passing off, she passed from 130 to 150 oz. of urine in the twenty-four hours.

HAEMORRHAGE.

VII.—The next case is one of haemorrhage that presented the clinical appearance of pernicious anaemia, he had, however, bleeding piles and made a remarkable recovery. On admission to hospital his tissues appeared very flabby, although there was but slight evident oedema. He entirely lost this flabby appearance as he improved.

R. B. Bleeding Haemorrhoids.

	R. C.	W. C.	Hb.	Lymph	Pmn.	N. B.	M. B.	Wt.
Sept. 25	1,680,000	5,000	20	23	76.5	0	0	st. lb. 11 10½
Oct. 27	3,100,000	4,100	55	40.6	58.8	0	0	11 4
Nov. 8	4,350,000	5,900	74	34.8	63.6	0	0	11 6

For the first month in hospital this patient lost steadily in weight, falling from 11 st. 10½ lb. to 11 st. 4 lb. At the same time the haemoglobin rose from 20 per cent. to 55 per cent. From the 27th he began to gain slowly in weight while his haemoglobin continued to rise.

This case was undoubtedly one of severe secondary anaemia due to haemorrhage. It has been often contended that severe long continued haemorrhage may produce a blood picture in all respects similar to pernicious anaemia. In this case and in all the others I have examined it was quite possible from the blood to distinguish the two conditions. It is unfortunate that those authorities who make this contention give no accurate details of the blood examination of such secondary anaemias which present all the features of pernicious anaemia.

CONCLUSIONS.

In conclusion, I may sum up the points of interest suggested by these observations:

1. The absence of loss of weight in anaemic conditions, and the fact that the patient seldom seems emaciated is mainly due to the fact that there is abnormal accumulation of fluid in the blood and tissues. If this excess of fluid were deducted it would probably be found that in these, as in other chronic illnesses, there is a progressive loss of weight in proportion to the severity and duration of the disease.
2. In the cure of such anaemic conditions, especially chlorosis, the first stage seems to be the getting rid from the blood and tissues of this excess of fluid.
3. A gain of weight in a case of pernicious anaemia under treatment, and without any improvement in the haemoglobin, is to be regarded as an unfavourable sign, indicating dilution of the blood and consequent escape of serum into the tissues. It may, however, be a critical phase of the disease, and indicate the first step towards concentration of the blood. Immediately after this sudden increase in oedema there is either a marked improvement or the patient dies.
4. The oedema of anaemic conditions seems to result from a hydraemic plethora of the blood, and is somewhat different in origin and nature from the oedema usually found in Bright's disease.
5. Careful observations in the manner indicated of anaemic conditions, namely, a record of the weight and haemoglobin value of the blood may furnish very interesting results. The points to direct attention to are the occurrence of haemor-

rhages (epistaxes, etc.), oedema, diarrhoea, and profuse sweating. My observations convince me that these symptoms are often the result of dilution of the blood, and may be merely Nature's method of counteracting the excessive and abnormal volume of the blood.

REFERENCES.

- ¹ *Trans. Path. Soc. Lond.*, vol. 11, part 3, 1900. ² See former paper in *BRITISH MEDICAL JOURNAL*, June 15th, 1901.

REPORT LXX.

ABSTRACT OF A REPORT ON THE FORMATION OF LYMPH BY THE LIVER.*

By F. A. BAINBRIDGE, M.B., M.R.C.P.,

Junior Demonstrator in Pathology, St. Bartholomew's Hospital.

In 1899 Asher found that the intravenous injection of ox bile, blood serum, and other substances produced an increased flow of lymph from the thoracic duct; he considered that these substances increased the metabolism of the liver, that the lymph came from the liver, and that it was formed as a result of the increased activity of the liver cells.

In the present research pure taurocholate of soda, pure haemoglobin, and certain ammonium salts have been injected intravenously, and the effects of such injections on the lymph flow have been studied.

RESULTS.

I.—*Taurocholate of Soda.*

Slow injections of small amounts invariably lead to an increased flow of lymph. The flow is doubled or trebled, begins ten to twenty minutes after the injection is begun, reaches its maximum in twenty to thirty minutes, and lasts about two hours. The extra lymph is derived entirely from the liver, since after ligature of the portal lymphatics, injections of bile salt cause no increased flow of lymph.

The lymph contains a slightly-increased percentage of solids, and usually also a small amount of free haemoglobin.

Observations on the blood pressures show no change in the arterial or vena cava pressure; there is a slight rise of portal pressure, but it falls within the limits of a physiological rise accompanying the increased flow of bile also produced by injecting bile salt.

When the bile and lymph are collected simultaneously, the variations in the rate of flow are very similar in the two cases; the most important difference is that the increased bile flow sets in earlier than the increased flow of lymph.

II.—*Haemoglobin.*

The injection of haemoglobin in dilute solution leads to results very similar to those obtained with bile salt, except that the bile becomes more concentrated, though its amount is not as a rule increased.

III.—*Ammonium Salts.*

The salts used were the tartrate, carbonate, and chloride. Intravenous injection sometimes leads to an increased lymph flow, but more often a negative result is obtained. The experimental conditions were so unsatisfactory, and toxic symptoms so prominent in the case of ammonium salts that no conclusion could be drawn from them.

COMMENTARY.

The injection of bile salts (and haemoglobin) does not cause blood-pressure changes similar to those produced by bodies either of the peptone class or of the sugar class; in fact, bile salts differ in very many respects from peptone in their mode of action. Consequently they do not belong to either of Heidenhain's classes of lymphagogues.

On the other hand, bile salts do increase the metabolism of the liver and also the formation of lymph; this increased metabolism does not merely accompany, but is the actual cause of the increased flow of lymph. In this respect Asher's view is fully confirmed, and these bodies constitute a "third" class of lymphagogues.

It is further supposed that this suddenly-increased metabolism leads to the setting free in the liver cells of crystalloid metabolites. These enter the surrounding lymph spaces

* The full text is published in the *Journal of Physiology*.