complained of a sudden attack of confusion of vision in consequence of which he could not read figures and had to discontinue his work. Six months previously he had had a similar attack which required a week's rest. No disorder or abnormality of the eye could be detected. The patient was, however, in a poor state of health, being anæmic with a feeble circulation; the pulse was of high tension and the second heart sound extraordinarily accentuated. Everything pointed to a vaso motor disturbance in the eye. The purin nitrogen was 0.34 gramme. As he was only 21 years of age there seemed to be no objection to a drastic change of diet; accordingly all tea, coffee, and soup were excluded and also meat and fish except at one meal. This with small doses of potassium iodide produced a notable effect. Ten days later, after the medicine was discontinued but the diet maintained, the purin nitrogen was 0.19 gramme. He has since continued the diet with marked benefit.

CASE 7.—The patient was a young man who suffered from indigestion and colic and had been treated by a modified diet for six months with considerable benefit. He wished to know, as he was not perfectly well, whether anything more could be done. The purin nitrogen was 0.28 gramme. A more rigid dietary was therefore instituted, with the result that the figure was reduced to 0.17; on the stricter system all his troubles quickly disappeared.

To show the discriminating capacities of this instrument I may refer to the case of a woman recovering from influenza. Convalescence was prolonged for weeks and it looked as if she could not pick up. The amount of purin nitrogen in the urine was found to be 0.31 gramme one day and 0.51 on the following day, and gave the clue to the delay. When questioned as to the change in diet there must have been on the two days under review she at once said that there was a great difference, as on the second day, in addition to her ordinary food, she had taken two large cups of strong beef-tea, while on the first day at corresponding times she had had milk. A complete change in diet was made and rapid improvement followed.

One great advantage of the purinometer is that it enables us to check the results of treatment and so not impose more restrictions than are really necessary, and also to refrain when little benefit is likely to follow. For instance, a boy suffering from severe arthritic trouble following diphtheria, who had been treated for over 12 months without improvement, was put on this diet; previous examination had shown the purin nitrogen to be 0.12 gramme one day and 0.15 on the following day. After four weeks' treatment the figures were 0.14 gramme on each of two consecutive days. Clearly, therefore, the diet as taken was of no use. Probably the boy was bolting his food and so vitiating the good effect, for he had a dirty tongue and the teeth looked as if they were not properly used. The parents thought that eating slowly was a fad and would not insist on it; they were therefore advised that there was no difference on the new system and that no advantage could be expected from it on the present lines.

An interesting case was furnished by a woman whose husband sent me a specimen of her urine and wrote to inquire whether my treatment was likely to be of any benefit to her for recurrent headaches and general debility. The figure obtained was 0.22 gramme and as I am never satisfied till the reading is under 0.20 I replied that there were indications for treatment but that no marked result should be expected. Further inquiry elicited that the patient's diet consisted almost entirely of purin-containing substances and especially of a large amount of tea, yet the purin nitrogen was only 0.22 gramme. How was this to be explained? On examining the specific gravity of the urine—an important check—it was found to be low—1012. An obvious conclusion, as the diet was distinctly a liberal one, was that the greater part of the food passed through the bowel without being absorbed. The patient's emaciated condition justified this view, which was further confirmed by the fact that there was usually diarrhoea and the motions were always large. After six weeks' treatment, during which time tea was cut off and the amount of meat diminished, the purin nitrogen was 0.16 gramme and the general condition greatly improved. As might have been expected from the withdrawal of much irritating material, constipation was a little troublesome at first. This is often noticed early in treatment, but is not persistent, for this diet has not the constipating action of meat and tea. Really diet is the most natural and also the most successful way of treating constipation. It is also of special value in cases of recurrent appendicitis and I have now treated many in this way with the

result that once treatment was seriously commenced no further attacks occurred. When the attacks are obviously of a simple nature, without the least suspicion of pus formation, this diet ought to be tried in the first instance rather than operation.

In conclusion, I may say that, although this method of treatment is simple in the extreme, yet it requires care and discrimination in its application, and at first, at any rate, the patient must be kept under constant observation. However careful the explanation there is often some misunderstanding; and minor troubles, such as constipation and difficulty of digesting certain foods, frequently develop in the early days of treatment. To insure success thorough mastication must be insisted on. The change of food must be made gradually, not more than one meal being altered at a time in the manner suggested by Haig. At the same time careful records should be kept of the weight and other clinical tests instituted so as to measure the progress. If care is taken in such matters this method of treatment will be found of real value and deserving more general application than it has yet received.

Birmingham.

A CASE OF INFANTILE SPLENIC ANÆMIA.

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THE patient was a male infant, eight months old, who was admitted under the care of one of us to the Hospital for Women and Children at Leeds on March 19th, 1904, jaundiced, very anæmic, and with great enlargement of the spleen. The history was that three weeks before admission the child had been taken to the hospital for circumcision. At that time it was noticed that there was some enlargement of the spleen. After the operation there was some bleeding but otherwise all went well. There was no jaundice until some time afterwards. Careful inquiries elicited no evidence of congenital syphilis. No further history could be obtained.

On admission, when the child first came under our observation, he was obviously very anæmic and moderately jaundiced and in a very asthenic condition. There were no abnormal physical signs in the chest. The spleen extended three-quarters of the way between the umbilicus and the pubes and almost reached the middle line. The liver was slightly enlarged, its edge being about four centimetres below the costal margin in the right nipple line. No urine was obtainable for examination. An examination of the blood made the next day showed: erythrocytes, 1,831,250 per cubic millimetre; normoblasts, 7500 per cubic millimetre (approximately); megaloblasts, 400 per cubic millimetre (approximately); and leucocytes, 18,043 per cubic millimetre. A differential leucocyte count on films stained with Jenner's eosinate of methylene blue (500 cells were counted) gave the following results:—

	Percentage.	Absolute numbers.
Neutrophils	41.8	7524 per c.mm.
Neutrophil myelocytes ...	2.0	360 ..
Eosinophils	0.4	72 ..
Mast cells	2.0	360 ..
Large mononuclears ...	9.8	1764 }
Lymphocytes	42.8	7704 } 9684 per c.mm.
Large lymphocytes ...	1.2	216 }

Many of the erythrocytes and most of the erythroblasts were polychromatophilic and it was often extremely difficult to decide whether a cell was a very small lymphocyte or a normoblast nucleus with a shred of polychromatophilic cytoplasm around it. During the count of 500 leucocytes 203 normoblasts and 11 megaloblasts were seen. The original count of leucocytes in the Thoma-Zeiss chamber was 25,930 and the figure of 18,000 given above represents the corrected total after deducting erythroblasts. The absolute number of the latter was arrived at in the same way. The large mononuclears, lymphocytes, and large lymphocytes are bracketed together on account of the great difficulty in

making valid distinctions between them. The cells described as large lymphocytes are typical lymphocytes in construction and staining reactions but are extremely large. They are probably identical with Wolff's indifferent lymphoid cells and the large lymphocytes in the blood in acute lymphæmia. Death occurred at 3 A.M. on March 20th.

Necropsy.—A post-mortem examination was made nine hours after death. The body was markedly jaundiced. The thoracic viscera appeared to be normal. The thymus was large but not abnormally so and showed no gross alterations. The liver was somewhat enlarged, firm, and bile-stained. The spleen was greatly enlarged and unusually firm on section, deep red in colour, and weighed 370 grammes (13 ounces). The lymph glands all over the body were distinctly enlarged and their colour was deep red, almost as deep as that of the spleen. Peyer's patches and the solitary follicles of the intestine were also red and hypertrophied. The marrow of the femur and ribs was red. Pieces of the liver, spleen, lymph glands, bone marrow, and thymus were taken for microscopic examination. Some of the material was fixed in 75 per cent. alcohol and after going through 90 per cent. and absolute alcohol was imbedded in paraffin. Other pieces were fixed in a mixture of potassium bichromate (2.5 per cent.) and formalin (15 per cent.) for 24 hours and after remaining in 3 per cent. potassium bichromate, which was changed daily, for a week were washed out, dehydrated, and imbedded in paraffin. The alcohol material was first examined but proved unsatisfactory owing to the coarse fixation of the cytoplasm. The erythrocytes also appeared to have lost their hæmoglobin. The bichromate-formalin material, on the other hand, was very well fixed, there being an almost complete absence of shrinkage and perfect cytoplasmic, as well as good nuclear, fixation. Various staining methods were employed but the most useful was Jenner's eosinate of methylene blue in absolute methyl alcohol used as follows. Sections mounted on albuminised slides, after having the paraffin removed, are washed with absolute alcohol and put into well-corked specimen tubes of Jenner's solution for an hour to overnight. The slide is then taken out of the tube and rapidly wiped clean. A few drops of the solution are then poured over the section and an equal quantity of distilled water is added and mixed rapidly. The slide is then kept moving from side to side and the section from pale blue becomes dark blue if it has many basophil constituents, while the oxyphil elements become pink. It is found that when a scum begins to form on the surface the section is sufficiently stained. It is then washed in water and examined under the microscope (preferably with a water-immersion objective such as Zeiss D*). If there is then too much blue, either in the red cells or so as to obscure detail, it is rinsed in a weak watery solution of acetic acid, not stronger than 1 in 2000, till a little blue comes away. It is then dehydrated quickly in absolute alcohol, cleared in pure benzene (crystallisable benzene free from thiophene¹), and mounted in Grüber's pure neutral balsam dissolved in pure benzene. The method in principle is that of Leishman² for staining blood films.

The bone marrow.—(After fixation in formalin and bichromate this was decalcified by Ziegler's sulphurous-acid method before imbedding.) Blood-cell formation is going on actively and mitoses are frequent. Megaloblasts are present. The appearances agree completely with the view originally, we believe, enunciated by Saxer and since upheld by Wolff, Pappenheim, and others. The cell from which all the others can be traced is a cell whose construction and staining reactions are those of a lymphocyte which only differs from the ordinary lymphocyte of the blood and tissues in its greater size and the fainter staining of its nucleus. This is the indifferent lymphoid cell of Wolff and the basophil myelocyte of Dominici.

From this develop the neutrophil and eosinophil myelocytes. The mechanism of their development is as follows. In the cytoplasm, generally in one spot near the nucleus, the specific granulations appear. At the same time, in this spot the cytoplasm begins to lose its basophily and the granules lie in an unstained space. More granules appear until eventually the cell body is full of granules and the cytoplasm has completely lost its basophily. Simultaneously with this granule formation the nucleus becomes smaller and more deeply staining. The myelocytes thus formed develop into the adult polymorphonuclear cell. Mast cells were almost absent in this marrow.

Between the indifferent lymphoid cells and cells like ordinary small lymphocytes there is every transition and we find it quite impossible to say where this small lymphocytic cell ends and the polychromatophilic normoblast begins. As mentioned above, there was the same difficulty of distinguishing in the blood films between the two latter classes of cells. The megaloblasts appear to originate from a cell of lymphocytic type while still large, intermediate between the indifferent lymphoid cell and the ordinary lymphocyte. The nucleus becomes deep-staining before the cytoplasm begins to alter. This transition one of us has observed recently in a case of lymphæmia.

The spleen.—There is no fibrosis or any degenerative change to be seen. The organ is densely packed with erythrocytes and various kinds of leucocytes. The Malpighian bodies appear to be normal at their centre, but at their periphery indifferent lymphoid cells, neutrophil and, in greater abundance, eosinophil myelocytes are seen. The presence of these cells and transitions from the former to the two latter is most noticeable at the edge of the Malpighian bodies and along the finest trabeculæ leading from them. They are present, however, throughout the organ, but are scarcer in the other parts, or else their presence is masked by the vast numbers of red cells and normoblasts which form the most striking feature of the section. The endothelial elements of the spleen pulp are not prominent nor have we found evidence of blood-cell destruction.

The lymph glands.—These bear no resemblance to normal lymph glands but have undergone complete transformation into red bone marrow, so much so that all stages of blood-cell formation can be seen here as well as in that tissue. Giant cells, with large, convoluted and deep-staining nucleus and homogeneous cytoplasm with little affinity for dyes, corresponding to the megakaryocytes of Dominici³ are frequent. They appear to be phagocytic, for occasional leucocytes and red cells can be seen englobed by them. There is also phagocytosis of red cells by the endothelium of the sinuses. Throughout the glands are masses of amorphous brown pigment, suggestive of broken-down hæmoglobin. These latter also contain many myelocytes and adult leucocytes and normoblasts.

The thymus.—This organ does not show the myeloid transformation seen in the spleen and lymph glands but occasional myelocytes can be seen, most of which are eosinophil. The most frequent situation is in the connective tissue between the alveoli of lymphadenoid tissue. Eosinophil cells, however, seem frequently to be found in the thymus. Normoblasts are seen occasionally in the vessels but that is of little importance since the blood contained about 7500 of them to the cubic millimetre.

The liver.—The lobular arrangement is not at all clear. There does not appear to be any fibrosis or inflammatory change. The cytoplasm of the liver cells is scantier and more reticular than in the adult, somewhat resembling that of the foetal liver. Some of the cells are degenerate and have homogeneous, diffusely staining nuclei. Bile is seen frequently in the intercellular bile capillaries and occasionally in what appear to be intracellular bile canaliculi. In the connective-tissue spaces of the portal tract and the capillaries throughout the liver there can be seen indifferent lymphoid cells with erythrocytes and myelocytes, both neutrophil and eosinophil, developing from them as in the bone marrow, spleen and lymph glands. Mast cells are scanty. One megakaryocyte was seen in the examination of many sections. In short, it is a foetal—i.e., a hæmopoietic—liver, to which are superadded some parenchymatous degeneration and the injection of the bile capillaries met with in obstructive jaundice.

We have, then, in this case complete myeloid transformation of the lymph glands and spleen; in fact, the former are as myeloid as the marrow itself. The liver also participates in blood-cell formation, behaving as a foetal liver.

Dominici,⁴ working on animals in experimental infections and anæmia produced by frequent abstractions of blood, has found that in these conditions the spleen takes on the functions of red bone marrow. Hirschfeld,⁵ examining the spleen and lymph glands of the human subject post mortem, has found that in severe infections the spleen assists the bone marrow in the production of neutrophil myelocytes and polymorphonuclears and that, to a lesser extent, the

¹ Mann: Phys. Histology, Oxford, 1902, p. 378.

² Brit. Med. Jour., Sept. 21st, 1901.

³ Cornil and Ranvier, Manuel d'Histologie Pathologique, tome ii., p. 593.

⁴ Archives de Médecine Expérimentale, 1900, 1901, 1902.

⁵ Berliner Klinische Wochenschrift, 1902, No. 30.

lymph glands participate in this function. He frequently found eosinophilic myelocytes in them but very rarely normoblasts. When we turn to anæmias we find less written about the spleen and lymph glands. Wolff⁶ found in a case of anæmia due to chronic lead poisoning that the bone marrow was defective in the production of neutrophils, but that the spleen, although not enlarged, was producing them freely. Hirschfeld⁷ quotes Rindfleisch as having, in 1881, found normoblasts in the lymph glands of a child with anæmia and marked rickets. Fowler⁸ and Melland,⁹ discussing splenic anæmia of infants, have very little to say about the histology of the condition, with the exception that Fowler found eosinophilia of the spleen in two cases. R. Hutchison¹⁰ in his Goulstonian lectures for 1904 reviewed the reports of the histological findings recorded by various observers. From these reports it appears that we can as yet postulate no definite morbid anatomy and histology for the condition. He quotes, however, Luzet, Mya and Trambusti, and Hunt as having, in their cases, found the liver to be foetal as in our case. Fowler¹¹ mentions jaundice as occurring in three cases, twice transient and once associated with acute hepatitis. We can offer no satisfactory explanation of it in this case. The results of the blood examination were not abnormal for infantile splenic anæmia, and accord well with those given by Fowler, Melland, and Hutchison, except that the count of erythroblasts was very high, 7500 normoblasts and 400 megaloblasts per cubic millimetre. Melland mentions one case with 9353 erythroblasts.

As to the production of the anæmia our investigations give us no clue. The phagocytosis of erythrocytes in the lymph glands was not a very marked feature, while we have seen none of that in the spleen, as opposed to the findings of Harris and Herzog¹² in splenic anæmia of adults. If there had been no blood examination the histology of the blood-forming organs would have suggested myelæmia but the blood examination negatives that supposition. Of course, it is *a priori* possible to say that the child may have died in the pre-leukæmic stage of myelæmia, or that the blood picture of myelæmia was altered by an infection; but the former proposition is susceptible of neither proof nor disproof, while there is no evidence in favour of the latter. Also myelæmia is very rare in children. Infantile splenic anæmia is common enough clinically; many cases thus classified are really examples of anæmia due to rickets or congenital syphilis, but in this case there was no evidence of either. On the other hand, they do not frequently come to the post-mortem room, and as their pathology is obscure we have thought the case worth publishing. The chief importance of it, however, lies in the fact that it shows that under suitable stimulation the indifferent lymphoid cells of the lymph glands can evolve exactly as they do normally in the red bone marrow.

RAPID GENERAL MYASTHENIA GRAVIS.

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As so little is known of this interesting condition it is well to record the notes of every case.

The patient, married, aged 25 years, a copying clerk, was admitted into the Royal Free Hospital on Nov. 10th complaining of weakness. The history of the illness dated back only six weeks. Previously the patient had always been a healthy man and, in fact, was playing football two days before the "feverish attack" about to be described. About the beginning of October he had "influenza" with bad pains in his back and legs, running from his nose and eyes, and

feverishness. The attack lasted for about a week but did not stop the patient from continuing at his work. After this he felt weak and four weeks ago noticed a slight difficulty in chewing his food. His jaw muscles seemed to get tired after he had partaken of a few mouthfuls. At about the same time he noticed weakness of the right leg and a few days later difficulty in holding up his head while at work. When tired his head used to droop till his chin touched his chest. His shoulders ached constantly and he could with difficulty hold himself erect. Walking fatigued him quickly. Within the last two weeks the patient had noticed dropping of his eyelids, the left eye being affected first. Since then he had not been able to open his eyes fully, this condition progressing during the day till towards evening he could barely hold them open. As night approached he had difficulty in taking liquid food and said that it had occasionally returned through his nose. Subsequently he noticed weakness in the hands. Two days before admission he suddenly became so much weaker that he fell down once or twice and eventually had to lie down. There was no history of syphilis, alcohol, or pulmonary tuberculosis. There was nothing in the family history bearing on the case. When first seen the patient was very pale and rather thin. The face had a listless, apathetic, mask-like expression. The jaw was generally slightly dropped. There was marked and constant ptosis of the left eye and occasionally less marked ptosis of the right eye. The lower lids always showed two or three millimetres of sclerotic below the corneæ. The quality of the voice appeared to be unaltered. The lips and mucous membranes were rather pale. There were no enlarged glands and his skin was quite normal. There were no developmental defects of the hands or feet.

An examination of the various systems showed the following phenomena:—There were no deformity and no tender area in the skull. The superciliary ridges were extremely prominent. This, with a somewhat prominent lower jaw, gave the face something of an acromegalic appearance. The spinal column showed nothing abnormal. The patient could walk, performing the movements correctly but very weakly and soon got tired. When in bed he could only raise himself with difficulty to the sitting posture. If he read aloud his eyes, jaws, and hands soon became fatigued in the order mentioned, so that his eyelids drooped, he had to support his lower jaw with his hand, and finally allowed the book to fall.

There were no fibrillary tremors of the muscles. An examination of the individual muscles showed that on both sides the triceps, deltoid, and pectorals were very weak and the supinator longus and biceps fairly good; the intercostals acted well, erector spinæ, trapezius, and infraspinatus weakly, while the rhomboids were fairly strong. The grip on both sides was extremely feeble. In the legs no definite paralysis of the posterior or anterior tibial groups was noticed but both were slightly affected, so that they were not as strong as the quadriceps extensor. The adductors were weak. All the muscles reacted well to faradism but as the examination proceeded the contractions became intermittent and finally ceased. This phenomenon was best seen in the muscles markedly paretic but was present also to some extent generally. The reaction to galvanism was normal. Coördination and sensation were unaffected. On testing the reflexes the plantar response was found to be flexor in character and occasionally absent altogether. The knee-jerks were exaggerated but decreased gradually if the attempts to elicit them were persisted in. Ankle clonus was present sometimes. The supinator longus and the palate reflexes were present. Jaw clonus was marked. The lumbar centres were unaffected. There was no loss of control over the acts of defæcation and micturition.

The cranial nerves are best considered seriatim. I. Olfactory normal. II. Optic discs normal. The vision and visual fields were normal. There was no alteration of colour vision and no scotomata were to be found. III., IV., and VI. There were marked ptosis, no squint, and no nystagmus in any position of the eyes. Diplopia was occasionally complained of. The movements of the eyeballs were incomplete, the downward movement being better than that in any other direction. The pupils were about four millimetres in diameter and equal. They reacted to light, accommodation, and convergence. As convergence was imperfect the patient could read better with one eye at a time than with both. V. Sensation over his face was unaffected. The muscles of mastication acted feebly and soon became fatigued. VII. The occipito-frontalis muscle acted pretty well. The

⁶ Ibid., No. 36, and Brit. Med. Jour., Epitome, Feb. 7th, 1903.

⁷ Loc. cit.

⁸ Brit. Med. Jour., Sept. 6th, 1902.

⁹ Ibid.

¹⁰ THE LANCET, May 7th, 1904, p. 1253.

¹¹ Loc. cit.

¹² Annals of Surgery, July, 1901.