CASE VII.—*Hydatid of Lung: Symptoms of Phthisis.*

A man, aged 34, was operated on for hydatid of the lung with haemoptysis in 1910. He joined the army in the war and went on active service. In 1916 he suffered from haemoptysis, and was invalided, under suspicion of tuberculosis. He suffers from recurrent bronchitis, and is frequently an in-patient of Dunedin Hospital, but tubercle bacilli have never been found in his sputum. He gives an intense Casoni reaction.

A case clinically resembling phthisis, but hydatid had been previously demonstrated, and the skin test was positive.

CASE VIII.—*Tuberculosis of Lung.*

A man, aged 32, was sent into Dunedin Hospital with haemoptysis and the provisional diagnosis of phthisis. Some consolidation was found at the base of the left lung, and the skiagram showed a "rounded shadow suggesting hydatid cyst." Dr. Hercus had then just completed his technique for the hydatid complement fixation test, which was negative in this case; there was no eosinophilia, and he insisted that no hydatid was present; the chest was explored and only thickened pleura and scar tissue were found, but negative results to the laboratory tests do not now carry as much conviction.

The converse of Case v; the x-ray suggestion was incorrect, the laboratory findings gave accurate information. It is thus seen that the diagnosis between hydatid of the lung and pulmonary tuberculosis may be a matter of difficulty; both are among the causes of haemoptysis. Also, hydatid of the peritoneum may be confused with tuberculous peritonitis. Barnett's colossal hydatid was diagnosed as the latter, and a child of 10 in the hospital with the diagnosis of tuberculous peritonitis was found to have an eosinophilia of 38 per cent., and proved to be suffering from hydatid disease.

I am not aware of any recorded association between hydatid disease and haemorrhage, except from the lung, but I have had experience as follows: Case ii died of haemorrhage after operation; it is true that he was deeply jaundiced, and that such cases are notoriously grave operative risks on account of bleeding; Case i, a case of hydatid of the liver, jaundiced after operation, showed no special inclination to bleed; the case may, however, be grouped with the following.

Three cases have been recently admitted to the women's medical ward with severe gastric haemorrhage; all had previously been operated on for hydatid disease. Dr. Radcliffe has informed me of a case of metrorrhagia in a young woman who was found to be suffering from hydatid of the liver; after its removal the uterine haemorrhage ceased. Certainly all cases of hydatid disease do not bleed severely, but several cases are quoted which have been found to do so; such bleeding may, possibly, be a manifestation of anaphylaxis. The fact is merely noted in this place.

Briefly to analyse these seven cases of hydatid disease. None of them had symptoms or physical signs which in themselves pointed at all strongly towards this disorder; it is extremely improbable that the diagnosis would have been even suspected except in a pastoral country. In two (Nos. i and vii) the patients' history gave the clue, hydatid material having been previously demonstrated; in one (No. iv) the family history was suggestive. These three admitted of diagnosis on ordinary clinical grounds, and in one of them this was supported by the complement fixation test and clinched by demonstrating hydatid material, and in another the Casoni test was positive. In two (Nos. ii and vi) the diagnosis was made on the operating table; in one of these the laboratory was misleading, and in the other (treated fifteen years ago) there is no record of investigation. In two (Nos. iii and v) the skiagrams gave correct information, though in No. v the complement fixation and skin tests were misleading and hydatid material had to be withdrawn to clinch the diagnosis. Excluding Case vi, which occurred before the era of specific tests, five of these cases were diagnosed before any major operation was undertaken; only one in five operations was actually discovered on the table. This is an approach to modern claims in accuracy of diagnosis.

It is evident that the diagnosis of a very serious disease, to which the inhabitants of a sheep-raising country are peculiarly liable, may present great difficulties, but that if the risk is constantly kept in mind, a study of family

and personal history, physical examination, skiagraphy, blood and skin reactions, and pathological investigations will generally discover the presence of hydatid, though any single investigation may be misleading. The treatment is evidently surgical, and it is important that cysts, if present, should be removed.

I have to thank both Sir Louis Barnett and my colleague Professor Hercus for kindly criticizing this paper. Several amendments and additions which it now contains were made at their suggestion. I have also to thank Dr. Roland Fulton for kindly allowing me to use his analysis of the Dunedin cases.

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THE TREATMENT OF PERNICIOUS ANAEMIA BY LIVER.*

BY

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THE liver treatment of pernicious anaemia was introduced by Minot and Murphy in America, and their first series of cases was published about three years ago. Dr. Spencer of Newcastle had some patients on this line of treatment early in 1927. One of the first, if not actually the first, in this neighbourhood was my patient W. H. P., at the beginning of July, 1927, and I had several others who started upon it about the same period. Since then I have had about forty cases under my care on this mode of treatment, and one can now draw some general conclusions as to its value, particularly its value as compared with methods of treatment previously employed.

It may be said in general that with the exception of four patients who were very ill when first seen, and who died within a few days, and the same number whom it has been impossible to trace or who failed to persevere with the treatment, all are alive and reasonably well to-day—the majority very well and following their regular work. One has died from intercurrent disease.

But at most the period of treatment has been little more than a year and a half, and a good deal less than this in many, and I find, on going through my records, almost as satisfactory results in a good many cases from our older methods of treatment. For a fair estimate of its value, therefore, it must be compared with some of the results in these older cases. Take the following cases, for example.

CASE I.

Miss G., a patient of Dr. Vipont Brown, was first seen in October, 1911; she had then been ill for about a year. Red corpuscles 2,340,000 per c.mm., haemoglobin 56 per cent., colour index 1.22. The appearance of the blood films was in every way typical. Under treatment she made a satisfactory recovery, but relapsed in the following summer, and was an in-patient under my care in the Ancoats Hospital from July, 1912, until early in 1913. In the early part of this period she proved intolerant to arsenic, but later took it well and made a good recovery. From this date she remained under the care of her own doctor. I saw her and examined her blood from time to time, but she remained free from relapse, and was able to follow her employment. About Christmas, 1925, she had an attack of influenza, and this brought on a typical relapse. She was readmitted to the Manchester Royal Infirmary early in 1926, and under treatment again made a rapid improvement. Her blood showed: on February 13th, 1926, red blood corpuscles 1,500,000 per c.mm., haemoglobin 33 per cent., colour index 1.1; on March 6th, red cells 2,100,000 per c.mm., haemoglobin 51 per cent., colour index 1.2; on March 28th, red cells 2,950,000 per c.mm., haemoglobin 62 per cent., colour index 1.05.

Unfortunately after her discharge I lost touch with her. She got into low water; she was now an elderly woman turned 60 years of age, and I learn that she died later on in that year. But she ran a course of sixteen years, during most of which time she was free from serious relapse and able to follow her employment.

* Read in opening a discussion at a meeting of the Manchester Medical Society, April 3rd, 1929.

CASE II.

A. C. was a patient in the Manchester Royal Infirmary as far back as 1899. Blood examination on June 11th, 1899, showed: red blood cells 1,210,000, haemoglobin 30 per cent., colour index 1.2; and on July 15th, 1899, red cells 3,560,000, haemoglobin 70 per cent., colour index 0.98. In all respects, both clinically and haematologically, he was a typical case. This improvement was maintained, and in November, 1901, more than two years after I had first seen him, I had him under my care at the Ancoats Hospital. A blood count in November, 1901, showed: red cells 4,180,000, haemoglobin 80 per cent.

I saw him at intervals till the summer of 1906, a period of seven years in all, or eight years from the beginning of his illness. He then had developed phthisis, and died from this without any return of his pernicious anaemia.

CASE III.

As rather a contrast to these two cases, here is the record of Miss M. She was first an in-patient at the Manchester Royal Infirmary in 1913, and had then been ill for about a year. Unlike the previous cases, she had no long period free from relapse; she had frequent relapses, and was readmitted to hospital, mostly under my care, eleven times between May, 1914, and September, 1924. On each of these occasions she made a satisfactory recovery, but only during one period—from August, 1917, to July, 1919—was she able to remain out of hospital for nearly two years. Out-patient treatment was carried out during the intervals. Finally, in 1924, associated with the relapse there were pronounced mental symptoms, which necessitated her being transferred to a Poor Law hospital, where she died.

CASE IV.

J. B., a patient of Dr. Bisset of Heywood. There was some suspicion when I first saw him that this patient had carcinoma of the stomach, but the examination of a blood film, on October 31st, 1917, was diagnostic of pernicious anaemia. He improved under treatment, but was a very difficult patient, and when he felt better he ceased attendance on his doctor. Consequently after his initial improvement he relapsed and in April, 1918, a blood count showed 2,220,000 red cells per c.mm. With the resumption of active treatment he made a rapid improvement, and by July, 1918, his red cells had risen to 4,600,000 per c.mm. Once more he neglected treatment, and by November, 1918, the red blood cells had again fallen to 1,970,000. From this date his response to treatment was less satisfactory; he made a partial recovery, which was followed by a speedy relapse, and in May, 1919, he dragged himself with difficulty to my consulting rooms and I concluded that that was the last time I should see him. His red blood cells were then down to 1,570,000 per c.mm. However, this was by no means the end. He took things to heart and stuck close to his treatment, and in October, 1919, when I fully expected to hear that he was dead, he appeared in bounding health with red cells 4,050,000 per c.mm. From this date he never looked back; he presented himself for examination in July, 1920, and his corpuscles were then up to 4,820,000. He had no further relapse; he remained perfectly well, although following out little if any treatment, and died from pneumonia in 1925, eight years after the disease first manifested itself.

It must be confessed, of course, that not all the cases under my care in these earlier days made such satisfactory recoveries or ran this long course. The reason in many cases, however, is not far to seek. Treatment on these older lines, which included full doses of arsenic, a variety of intestinal antiseptics, intramuscular salvarsan, and vaccine, requires great care. The dosage must be carefully adapted to the patient's condition. The dose of arsenic which is required during the active stages of the disease closely approximates to the toxic dose. During stages of recovery active treatment must be judiciously diminished or intermitted; the patient must be under constant supervision and, if practicable, periodic blood examination should be made in readiness to return to more active treatment on the first sign of relapse.

As a result inquiries have shown that cases that have been under careful medical treatment in hospital with surprisingly complete temporary recovery may, on leaving hospital, very commonly relapse, and may speedily die unless readmitted promptly, because it was impossible to get this careful and difficult treatment continued satisfactorily after leaving hospital; and the same must be said of only too many cases seen in private on single occasions, when an initial recovery has been only too liable to be followed by relapse and a fatal ending. But fortunately I can recall many exceptions where I have found practitioners who have collaborated enthusiastically, or where I have had the opportunity of seeing the patient from time to time and giving continued advice as to treatment. All the following cases are of interest from this point of view, and more especially so that they all show the transition from "pre-liver" to "post-liver" period of treatment.

CASE V.

Mrs. C. (the late Dr. Derham Reid of Bolton and his successor, Dr. Brown). Blood examination showed:

	Red Cells per c.mm.	Haemoglobin per cent.
June 18, 1925	735,000	22
" 27, "	915,000	—
July 4, "	1,275,000	38
" 12, "	1,905,000	48
Aug. 17, "	3,142,000	72
Oct. 20, "	3,740,000	92
Dec. 1, "	3,740,000	86
Jan. 19, 1926	3,610,000	90
Mar. 2, "	3,880,000	100
Apr. 30, "	4,210,000	94
July 6, "	3,620,000	86
Nov. 18, "	3,680,000	87
Mar. 31, 1927	2,990,000	75
Aug. 2, "	3,390,000	80
Liver added.		
Feb. 12, 1928	4,290,000	95
Feb. 7, 1929	4,600,000	93

The patient had been ill for over a year before coming under treatment in a rather desperate state, with red corpuscles down to 735,000 per c.mm. She continued under treatment without relapse, though with a slight setback in March, 1927. She is perfectly well now and shows no signs of the disease.

The diagram below shows more graphically the progress of this case over nearly four years. The broken lines represent the course after start of the liver treatment.

CASE VI.

Mrs. R., a patient of Dr. Church Mann of Radcliffe. She was seen first on March 6th, 1926, but she had been ill then, with several ups and downs, for about two years. Her course under treatment is shown by the following figures:

	Red Cells per c.mm.	Haemoglobin per cent.
Mar. 6, 1926	1,530,000	35
Apr. 19, "	3,000,000	82
June 25, "	3,740,000	94
Oct. 12, "	3,760,000	88
Jan. 6, 1927	3,650,000	90
Apr. 27, "	3,580,000	90
Sept. 28, "	3,430,000	90
Liver treatment commenced.		
Apr. 1, 1928	4,320,000	95

and she is still, up to date, keeping quite well.

CASE VII.

Mrs. M. (a patient of Dr. Berry of Pendlebury). She was first seen on September 2nd, 1926, as an out-patient at the Manchester Royal Infirmary, and was an in-patient from September 7th to November 6th of that year. Following is a record of her blood:

	Red Cells per c.mm.	Haemoglobin per cent.
Sept. 13, 1926	650,000	14
Oct. 7, "	2,340,000	45
Oct. 20, "	2,800,000	63

She improved very rapidly under treatment, from an extremely low figure, but after leaving hospital she gradually went back.

Dec. 27, 1926	3,900,000	75
Apr. 1, 1927	2,960,000	70
July 22, "	2,160,000	52

Active treatment was then resumed with the addition of liver, and she was again an in-patient from August 16th to September 17th, 1927.

Aug. 17, 1927	2,250,000	56
Sept. 17, "	3,530,000	76
Nov. 25, "	4,488,000	91

But now, with the addition of the liver, she did not relapse on leaving hospital. On July 13th, 1928, the red cells numbered 4,576,000 per c.mm., and the haemoglobin was 90 per cent. She continued well until a few weeks ago, when she was taken ill

with some subacute abdominal trouble—probably tuberculous peritonitis—and died, without, however, any sign of a return of her anaemic condition.

It is of interest to note that the improvement after the addition of liver was little, if any, more rapid than on her previous admission without it, but that the red corpuscles rose to a higher figure, and that no tendency to relapse remained so long as she continued the treatment.

CASE VIII.

Mr. W. H. P. (a patient of Dr. Sidley of Eccles). I saw him first in August, 1926, but he had been recognized as suffering from pernicious anaemia since early in 1924, and had been ill for some little time before that date. The record of his blood shows:

	Red Cells per c.mm.	Haemoglobin per cent.	Colour Index.
Aug. 29, 1926	1,200,000	—	—
Sept. 20, "	948,000	20	1.05
Oct. 15, "	850,000	25	1.47
Nov. 25, "	1,090,000	32	1.6
Dec. 18, "	1,190,000	30	1.3
Jan. 17, 1927	1,440,000	35	1.3

It is noticeable how slow and imperfect was the response to treatment in this case, so that when he left hospital after four months' treatment, although he was a good deal better, the red corpuscles had not reached one and a half million per c.mm. As an out-patient on February 21st, 1927, the red blood cells numbered 1,624,000 per c.mm., haemoglobin 36 per cent.; on July 7th the red cells numbered 1,160,000. In the course of these months there had been a gradual falling back in spite of careful treatment. So he was readmitted and was restarted on active treatment, including now minced liver.

	Red Cells per c.mm.	Haemoglobin per cent.
Aug. 24, 1927	3,340,000	—
Oct. 10, "	4,264,000	—
Jan. 9, 1928	3,544,000	—
Jan. 9, 1929	1,640,000	20
Feb. 1, "	1,510,000	34
" 16, "	2,730,000	58
Mar. 15, "	3,064,000	70

Here it is of interest to note that, in contrast to the slow improvement in 1926, the addition of the liver to his other lines of treatment brought about a much more rapid and complete amendment, and this was equally evident early this year when in consequence of some neglect of treatment he had a serious relapse at the end of 1928. This is all the more distinctly brought out by the following graph.

Here, then, we have this patient after some six years back at work and feeling quite well.

I will briefly refer to two other cases that have responded satisfactorily to treatment, part of the time without the addition of liver, part with.

CASE IX.

S. G. (Dr. Burrows Brown of Failsforth). Seen first on January 18th, 1924. A blood examination on that date showed: red blood cells 1,530,000 per c.mm., haemoglobin 38 per cent., colour index 1.24. Seen again in January, 1925; no count made, but doing well. January, 1928: Continued well, but recent partial relapse; red cells numbered 2,770,000 per c.mm.; liver added to treatment. In March, 1929, the patient was doing well; no sign whatever of anaemia; working, after a course of five to six years.

CASE X.

W. S. F. (Dr. Myers of Radcliffe). Seen first on November 26th, 1926. He had then been ill through the greater part of that year. His red corpuscles were down to 1,440,000 per c.mm. On March 30th, 1927, they numbered 4,220,000 per c.mm., haemoglobin 90 per cent.; on December 17th, 1927, 3,930,000 per c.mm., haemoglobin 86 per cent. From this date onward liver was added to the treatment, and he has continued perfectly well up to date.

It may be noted in these, as in other cases that have been published, that when under other methods of treatment the number of red corpuscles tends to stand at between 3,000,000 and 4,000,000 per c.mm., the addition of liver commonly brings the number to over 4,000,000. In some cases, however, this difference is not particularly striking; in others the rise with the addition of the liver may be still more remarkable. Thus, in one patient the red corpuscles rose from 2,770,000 to 6,000,000 between November 14th, 1927, and March 12th, 1928.

In every case I have given the liver in addition to the already described methods of treatment. This may be unscientific, but in such a grave disease I do not think we are justified in abandoning any line of treatment that has been well tried and has proved successful. When, however, recovery from the active phase of the disease has taken place it may be maintained, as a rule, with the liver alone, with little, if any, further aid from our other lines of treatment.

Summary.

From my study of these cases there are certain general conclusions at which I have arrived.

1. On our older lines of treatment, if efficiently carried out, many, if not most, cases of pernicious anaemia may be given many years of useful life; but there are practical difficulties in getting the treatment effectively applied, which consequently result in a large proportion of failures.

2. The introduction of the liver treatment has undoubtedly greatly increased our power of dealing with the disease; the improvement is more rapid and the advance in the number of red corpuscles is higher.

3. Continued treatment by liver will maintain the improvement, and it will do this more easily and with less meticulous attention to details than will our older methods alone. Consequently, though not necessarily more successful—as I have already demonstrated—it is undoubtedly more simple to carry out, and so there is much less risk of failure.

4. At the same time, whilst relieving the symptoms it does not appear to strike at the root of the disease, so as to produce a complete and lasting cure. So far as we can say at present, treatment must be continued, and, if given up, or insufficiently followed out, relapse will occur.

5. Though 6 or 8 ounces of minced liver ("potted liver") in the day is usually advocated, I have found in general that when combined with the older methods of treatment 4 ounces or even 3 ounces may be quite effective. This is of importance in the case of those who dislike the liver and take it only with reluctance.

6. When the red corpuscles have been raised to 4,000,000 or over a smaller amount of liver—3 or 4 ounces every other day, or even as little as 1/2 lb. in the week—will maintain the improvement, at any rate, if combined with some continued or occasional courses of treatment, in moderate degree, of the older methods of treatment.

7. It is important not to push the dose of liver too high or to keep on with the use of full doses too continuously. There is some reason to suppose that over-use may risk the production of gout or chronic nephritis. As in all other methods of treatment, its use must be guided by the consideration of the condition of the blood.

8. In those who have insuperable difficulty in taking the fresh liver, liver extracts, either solid or liquid, may be used. They appear to be equally effective with the fresh, but are very expensive.

9. Although it has been supposed that the liver treatment leaves the nervous symptoms untouched, I am not sure that this is the case. In three cases in which these symptoms were prominent and in which arsenic had appeared, whilst curing the anaemia, to aggravate the nervous symptoms, slow improvement has occurred with the use of liver and dilute hydrochloric acid. In many cases the slighter nervous symptoms, the numbness and tingling about the fingers and toes, have been materially improved.

10. Lastly, accurate diagnosis of the disease is of greater importance than ever it was.