

THE TREATMENT OF SPLENOMEGALY WITH  
ANÆMIA IN SYPHILITICS.

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IN a recent issue of this *Journal* I described a case of acquired hæmolytic icterus—a condition known by various names—and discussed the differential diagnosis from allied anæmias occurring in association with hepatic and splenic enlargement. It was then stated that the various members of this group were linked together by many hybrid cases. Consequently, there are occasions when the exact placing of a case requires intimate knowledge of a subject to which contemporary literature is continually adding new facts. In addition, full knowledge of all the facts of a case, derived both from bedside examination and from numerous laboratory tests, is essential if therapeutic errors of omission and commission are to be avoided. From the therapeutic point of view, a precise diagnosis is a matter of practical urgency and not merely one of academic interest. In this connection it should be remembered that responsibility rests with the physician to advise or even to urge the patient to have the spleen removed or the no less responsible duty to advise that it be retained. Fortunately, cases usually run a subacute or chronic course, and there is ample time for gathering together the information on which alone a reliable opinion can be formed.

The following record of a case that ultimately came under my charge in a General Hospital at home shows in a measure the variety of tests to which cases in this group must sometimes be submitted. Some other matters of practical interest and importance chiefly dealing with the management of such cases will be discussed in the course of a summary of the few that have already been recorded.

Private G. F., aged 44, with fifteen years' service, was admitted to a Field Ambulance in France on 6th September 1917. The diagnosis made there was severe debility and slight D. A. H., and mist. ferr. perchlor. was prescribed. Three days later he was passed on to a C. C. S., and the record made there stated that he suffered from vague abdominal pain, nausea, occasional diarrhoea, and loss of weight. There was no vomiting. He had been in the Army for twelve years, and had served in India and Aden before the present war. He had had malaria in India. Examination showed he had a large swelling in the abdomen,

presumably the liver or "at one with the liver." The surface was not nodular. The lower edge of the liver could be felt extending below the umbilicus. The spleen was also much enlarged. The urine was normal. He was emaciated. There were no physical signs of disease in the chest. The blood-count and films were practically normal on 10th September 1917. Splenic puncture on the thirteenth day of the same month gave a negative result for kala-azar. The blood films showed no abnormality morphologically and no parasites. The blood-count was as follows:—Report by Major J. W. M'Nee on 13th September 1917. Red corpuscles, 4,432,000; white corpuscles, 5500; Hb, 65 per cent. Differential.—Polymorphonuclears, 64·5 per cent.; small lymphocytes, 8·5 per cent.; large lymphocytes, 12·0 per cent.; hyalines, 2·5 per cent.; eosinophiles, 6·5 per cent.; masts, 4·5 per cent.; transitionals, 1·5 per cent.

Examination per rectum was negative. The stool was examined on 16th September, and Major M'Nee reported there were fairly numerous encysted amœbæ, but he was unable to distinguish whether they were entamœba coli or histolytica. The diagnosis made at the C. C. S. was "N. Y. D." (greatly enlarged liver and spleen).

From 10th September 1917 to 16th September 1917 the temperature varied between 97·2° F. and 99·2° F. Thereafter until his transfer to the base on 20th September 1917 it remained normal or subnormal, and also during eight days in the base hospital. There it was stated that the blood condition was of the simple anæmic type, with definite leucopenia. It was further noted that there was a chronic history dating from the first six months of 1914. The diagnosis made was "anæmia (chronic splenic) 62—Banti's disease." The following details were recorded:—He began to lose flesh early in 1914. From 1899-1904 he was in India. He had malaria, but never dysentery. He had been stationed at Armentières for one year. When there he found he was becoming gradually weaker, and before admission to the Field Ambulance he had pains in the legs for six weeks. He states he has diarrhœa occasionally, and passes slime, but no blood, in his stools. His skin is light yellow colour, sclerotics white. There is no bile in the urine. There are some crepitations over the base of the right lung. There is slight irregularity of the heart, but no murmur. The liver dulness measures vertically between the mesial and nipple line  $7\frac{1}{2}$  ins. It extends down to within  $1\frac{1}{2}$  in. of the umbilicus. The spleen extends  $3\frac{1}{2}$  ins. beyond the costal margin and 1 in. below the umbilicus and is  $2\frac{1}{2}$  ins. from the anterior superior iliac spine. The spleen moves with change of position of the body. There is no ascites. There are some varicose veins on the wall of the abdomen. Examination of the blood shows a definite leucopenia of 4375 per c.mm. and a simple anæmia. Red corpuscles, 4,650,000; Hb, 60 per cent.; colour index, 0·6. Differential leucocyte count.—Polymorphonuclears, 67 per

cent. ; small lymphocytes, 19 per cent. ; large lymphocytes, 4 per cent. ; large mononuclears, 1 per cent. ; eosinophiles, 9 per cent.

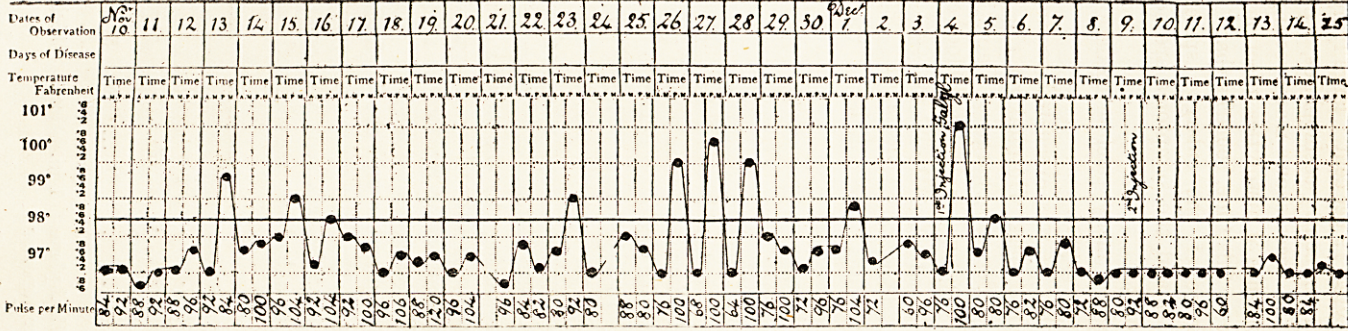
Examination of the *faeces* shows many resting *amœbæ* of the coli type. There is no evidence of *histolytica* infection. Capt. J. R. Collins, in charge of the case at this time, remarks that "the absence of fever, sweating, and presence of the enlarged spleen negatives *amœbic* abscess as a diagnosis, and the symptoms are not severe enough and too chronic for *kala-azar*."

The urine contained many calcium oxalate crystals and a few epithelial cells and leucocytes.

On 27th September he was evacuated to England, and admitted to the 2nd Scottish General Hospital on the following day. On 4th October, while under the charge of Capt. Rainy, the following observation was made on the blood:—Red blood corpuscles, 4,400,000 ; white blood corpuscles, 6400 ; Hb, 60 per cent. ; colour index, 0·8. Differential count.—Polymorphonuclears, 61·5 per cent. ; lymphocytes, 22 per cent. ; large mononuclears, 5 per cent. ; eosinophiles, 8 per cent. ; masts, 3·5 per cent.

Shortly thereafter the case came under my charge, and the following reports were obtained from Capt. J. Miller, pathologist to the hospital:—

15th November 1917.—White blood corpuscles, 5800. Differential count.—Polymorphonuclears, 63 per cent. ; lymphocytes, 18 per cent. ; large mononuclears, 6 per cent. ; eosinophiles, 9 per cent. ; masts, 4 per cent. 17th November 1917.—No *amœbæ* or cysts and no organisms of the dysentery group found in the stools. 27th November 1917.—No malarial parasites were found in the blood during pyrexia. 29th November 1917.—The Wassermann reaction of the blood was strongly positive (+ + +). The patient had previously informed me he had not had venereal disease, but now hedged when questioned further. During the first month since his admission to the 2nd Scottish General Hospital there were seven rises of temperature to 99° or 100° F. The rises recurred also throughout November. On 4th December 1917 galyl was injected at 2.45 P.M., and the temperature in the evening registered 101° F. Thereafter the temperature remained constantly normal or subnormal. He was also given pot. iodide. The general condition improved very much under this treatment. After five injections the note made on 26th December 1917 states "he has now no discomfort in the abdomen and he feels very well. The appetite is good. He is still jaundiced-looking at times after each injection, but there is no bile in the urine. On this date liq. hydrarg. perchlor. was added to his mixture. In a note made on 12th January 1918 a continuous improvement in the general condition was recorded. In all he received six galyl and three neo-kharsivan injections. The last of the latter was given on 15th February 1918. Four days later the



blood still gave a strongly positive Wassermann reaction (+ + +). Twelve days after the last injection, *i.e.* on 27th February 1918, the examination of the blood showed:—Red blood corpuscles, 1,920,000; white blood corpuscles, 3100; Hb, 61 per cent.; colour index, 1.58. Differential count.—Polymorphonuclears, 37 per cent.; lymphocytes, 43.9 per cent.; large mononuclears, 7.9 per cent.; eosinophiles, 11.2 per cent.; masts, 0. One month later, on 26th March 1918, red blood corpuscles, 2,800,000; white blood corpuscles, 5450; Hb, 90 per cent.; colour index, 1.6. Differential count.—Polymorphonuclears, 49.6 per cent.; lymphocytes, 38 per cent.; large mononuclears, 1.7 per cent.; eosinophiles, 10.7 per cent.

On the blood, as shown by counts, the first effect was to reduce the red cells to less than one-half of their former number and to raise the colour index to 1.6. The leucopenia became more definite and the lymphocytes increased relatively at the expense of the polymorphs. There was also a considerable relative increase of eosinophiles. One month after the injections were completed the red cells showed a definite recovery of about 900,000. The colour index still remained high, *viz.* 1.6. The leucopenia was slight, and the differential count showed a definite tendency towards normal proportions.

Before passing from the consideration of the primary effect of the injections on the blood, I should record the fact that during the course of the injections, and a few days after one of these, a very remarkable differential count was made as follows:—Polymorphonuclears, 45.2 per cent.; lymphocytes, 16.3 per cent.; large mononuclears, 33.9 per cent.; eosinophiles, 3.2 per cent.; masts, 1.4 per cent. Subsequently a similar, though less marked, large mononuclear reaction was found to be constant in syphilitic patients early after injections.

From time to time during the six months of the patient's hospital treatment measurements of the enlarged organs were made. These show that no diminution of the size of the spleen or liver occurred before the antisymphilitic treatment was given. The table given below shows that between September and the beginning of December the liver did not alter and that the spleen apparently increased in size. Three months later, after the treatment was completed for the period under review, the spleen had become distinctly smaller and the liver also measured less.

	September 1917.	December.	March 1918.
Liver, vertical midway between mesial and nipple line . . .	7½ ins.	...	6½ ins.
Lower edge from umbilicus . . .	1½ in.	1½ in.	2¼ ins.
Spleen, distance horizontal from umbilicus . . . . .	...	3¾ ins.	4½ ins.
Beyond costal margin . . . . .	3½ ins.	...	2¼ ins.
Lower edge and umbilical plane	1 in. below.	1½ in. below.	1 in. above.
Distance from anterior superior iliac spine . . . . .	2½ ins.	2 ins.	4¼ ins.

The further course of the case cannot be followed, as the man was discharged from the Army medically unfit owing to splenic anæmia caused by syphilis.

The outstanding facts, so far as results of treatment are concerned, are:—(1) The general condition of the man greatly improved, and the improvement set in most decidedly soon after the antisyphilitic treatment began; the fever ceased. (2) The size of the spleen, and, to a less extent, of the liver, began to diminish only after antisyphilitic treatment was begun. (3) The action on the blood was considerable, as shown by the cellular changes, but the significance of these could not be determined at the time of the man's discharge from the Army. (4) The specific treatment had no effect on the Wassermann reaction of the blood which remained strongly positive.

While in the 2nd Scottish General Hospital he put on 12 lbs. in weight, although he again lost 4 lbs. of this at the end when he was steadily doing work in the hospital. In regard to (2) the liver and spleen became free from all tenderness, and the consistence of the liver substance gave the impression that regenerated tissue occupied the greater part of the palpable organ. A month after the cessation of the injections the blood showed a definite tendency to improve, if one excepts the colour index and the positive Wassermann reaction. Consequently, though the treatment had been beneficial, a "cure" had not been effected. I believe, also, that little prospect could be entertained that further treatment on the same lines would be more satisfactory in this particular case.

The proof of failure is not complete, although the prospect that the Wassermann test will yet become negative is remote. Is it probable the prospects would be brighter in cases in which the history of syphilis is recent? Even in the present case the result to date is that the activity of the process has been, for the present, arrested, and the treatment has not been wholly in vain. The literature dealing with this matter has so far, and for obvious reasons, been meagre. It was in 1914 that Osler first drew attention to cases of syphilis of the liver with the picture of Banti's disease, and the period begun then has furnished few and not sufficiently explicit records on the antisyphilitic treatment of this condition. Giffen has found that in a series of three cases this form of treatment was of little use. He, unfortunately, does not furnish the details necessary for others to judge of the adequacy of the treatment given to his patients. Thus, in his first case, he

merely states that antisyphilitic treatment proved unsatisfactory. In his second case the patient "remained under observation for one month, during which time she received three injections of neosalvarsan, and mercurial inunctions and potassium iodide. She gained somewhat in strength and 7 lbs. in weight. The hæmoglobin, however, remained low (58 per cent.)—a gain of 8 per cent.—and the size of the spleen was not reduced, although the liver seemed to be smaller. Splenectomy was decided upon." But, as this patient was first examined on 6th March and the operation occurred on 1st April, the period of treatment was much less than a month, and the result of the treatment, incomplete though it was, was not awaited. In his third case the information is still less satisfactory. The physician who referred the patient stated "that while the Wassermann reaction had become negative and he had improved to a considerable extent under salvarsan and mercury, on the other hand improvement reached only a certain point, and then his recovery seemed to be at a standstill." I have found reference to only two other cases in which the point being discussed is mentioned. Hartwell's patient denied the possibility of syphilitic infection, but a Wassermann reaction was positive. Neosalvarsan, mercuric salicylate, potassium iodide, iron, and arsenic had been administered while the patient's condition became less satisfactory. French and Turner's case was that of a boy aged five years, in whom there was a blood-count suggestive of the splenic anæmia of infancy. A Wassermann test had been positive several times, and the patient had received antisyphilitic treatment without benefit.

The seven cases, including my own, therefore give the following results. Reported by Box:—A child given mercurial inunction which "brought about marvellous improvement with great alteration in the blood-count; the spleen had also diminished in size." Reported by Giffen:—(1) A case in which antisyphilitic treatment for six months gave unsatisfactory results. The details of treatment are not given. (2) This patient gained strength and weight. The spleen was not affected in size by the treatment, but the liver was possibly smaller. The hæmoglobin remained low, but improved. The treatment was inadequately given—three injections of neosalvarsan, mercurial inunctions, and potassium iodide for, it seems, a period of three weeks. (3) In this case the Wassermann test became negative. Improvement occurred to a certain extent, then stopped. Salvarsan and

mercury. Reported by Hartwell:—Under treatment the condition became less satisfactory; given neosalvarsan, mercuric salicylate, potassium iodide, iron, and arsenic. Reported by French and Turner:—No benefit from antisyphilitic treatment (salvarsan, mercury, potassium iodide) nor from iron and arsenic, X-rays over spleen. Case of v. Jaksch type; Wassermann test positive; not stated whether rendered negative by treatment. Case now recorded; Wassermann test positive before and after treatment; general condition materially improved, spleen definitely lessened in size and fever abolished; six injections of galyl, three of neo-kharsivan, mercuric chloride, potassium iodide for three months.

In only one of these seven cases is it known that the Wassermann test became negative. In one case the condition became less satisfactory; in two no benefit was derived; in three some improvement occurred.

In the period preceding the publication of Osler's paper it is probable that some cases of this syphilitic type were treated by splenectomy as cases of the orthodox Banti type. Subsequently, in the period of three years the operative treatment has not had adequate trial, the number of recognised cases being too small and the post-operative periods too short. It appears, however, that uniform post-operative improvement was an early result in the few cases reported up to the present time. The following are the results of splenectomy in syphilitic splenomegaly with anæmia. In Hartwell's case very prompt improvement occurred. After two weeks the hæmoglobin had risen from 25 per cent. to 80 per cent. In Giffen's case (1), one year after operation, the patient's physician stated that she had gained much strength, had put on 15 lbs. in weight, and was feeling well. Her blood-count was as follows:—Red blood corpuscles, 3,552,000; hæmoglobin, 80 per cent.; white blood corpuscles, 11,000. The differential count was not abnormal. In case (2), eight months after operation, the patient had improved markedly in weight and strength and the anæmia had disappeared. In case (3) the patient was in excellent condition three months after operation with hæmoglobin at 99 per cent. In French and Turner's case the patient was apparently well in two months. In few of these cases do the records show whether antisyphilitic treatment was given subsequent to operation. As regards the duration of the improvement following upon splenectomy there is little that can yet be learned. One case, however, may be cited relevantly to show that this may be



brief. Coupland in 1886 reported a case of this kind operated upon by Mr. Pierce Gould. The patient died two years after splenectomy with melæna, hæmatemesis, and ascites. The liver was a typically scarred syphilitic one. On the other hand, if the procedure is based on a good *rationale*, the prognosis in favour of early cases may be regarded hopefully. The *rationale* of the treatment may well be based on the idea that the spleen acts as a cesspool and that our present methods of administering anti-syphilitic treatment do not effectively cope with spirochætes lodging there. It is maintained, further, that the Wassermann test seldom gives a negative result after a full course of anti-syphilitic treatment given while the spleen remains *in situ* in these cases. The facts have received another interpretation. Dr. Parkes Weber has said: "It was an unfortunate fact that antisyphilitic treatment did not do these cases good in every instance; hence one was driven to the conclusion that the splenic enlargement in these cases was not always itself actually syphilitic, though it arose and flourished on a syphilitic basis." Giffen has also said: "Cases undoubtedly occur, however, in which a luetic history is obtained which seems to have no etiological relationship to the splenomegaly." On the other hand, cases which have improved little on antisyphilitic treatment and which continued to give a positive Wassermann reaction, promptly improve and become negative to the Wassermann test on the resumption of antisyphilitic treatment after splenectomy. As Mayo states, spirochætal "hibernation in the spleen is not unusual." Personally, I think it is more accurate to speak of the splenic cesspool rather than of splenic hibernation, as the latter term suggests a resting phase of which there is no knowledge. Mayo goes on to say that failure to eradicate syphilitic disease by inadequate treatment may result in a syphilitic spleen, which permits not only luetic reinfection of the body, but also causes a high grade of chronic anæmia. "In four cases of this type (probably three of these were in Giffen's series) removal of the spleen promptly cured the anæmia, and the lues thereafter quickly responded to *renewed treatment*. In all of these spleens either spirochætes were found or gummata in the spleen or liver were demonstrated." It is essential, of course, that *renewed* anti-syphilitic treatment should follow operation, although published case reports do not always state that this has been done.

From this consideration of the subject I decided to inform the patient regarding the benefits and attendant risks of operation.

Before leaving France he had already been told he was being returned to England for operation, but as his general condition was now greatly improved the patient declined to have surgical treatment.

With regard to the management of such cases of syphilitic origin simulating Banti's complex, I believe that in the first instance all cases should have very thorough antisyphilitic treatment. No great harm and much improvement may result from this when carried out with care while watching the effect of each injection on the blood. If this has been done, and the Wassermann test still remains positive, operation then becomes almost as necessary as for cases of the orthodox Banti type. The need for operation would not be quite so urgent if from time to time renewed specific treatment were known to re-arrest activity. As this prospect is meantime based solely on hypothesis, the indication for operation is practically the same as in Banti's disease, if specific treatment has already failed. The results of successful operation have already been stated. The operative risk cannot be assessed on a flat mortality rate. Special operative experience is bound to reduce the risk considerably, as shown by the uniformly successful results in published cases.

*Summary.*—A case of splenic æmia is recorded in which the Wassermann test was positive and antisyphilitic treatment produced definite improvement. The Wassermann test remained positive. The results obtained from specific and surgical treatment are compared by reference to seven collected cases. The late result in one operation case is also noted. The *rationale* of the surgical treatment is briefly considered. Recommendations are made for the management of such cases of syphilitic origin simulating Banti's complex.

LITERATURE.—H. Z. Giffen, *American Journal of Medical Sciences*, July 1916, p. 5. J. A. Hartwell, *Medical Record*, 1914, lxxxv. 593. H. French and P. Turner, *Proceedings, Royal Society of Medicine*, 1913-14, vii. 77-78, Clinical Section. Parkes Weber and Box, *ibid.* Wm. Osler, *Clinical Journal*, 1914, xliii. 462. S. Coupland, *British Medical Journal*, 1886, viii. 1445.