application of a sufficiently strong antiseptic does, under favourable conditions as to time and the nature of the wound, materially aid in destroying the infection and preventing its spread, then it seems clear that such an application should be made in all suitable cases.

The point is, What is the best form of antiseptic to use and what is the best way of using it?

One fact which emerged from these observations is that all the antiseptics—carbolic, iodine, and mercury—when used in freshly-made aseptic wounds, seem about on a par as regards their influence on the healing of the wound.

If the conditions were the same in a wound as in a culture tube, the best form of antiseptic would have been decided in the laboratory long ago. The free use of almost any antiseptic in sufficient concentration will (apart from the question of spores) destroy or inhibit the growth of most organisms when these are present only on the surfaces, internal and external, of the wound. Hence the divergent views as to the germicidal power of different antiseptics, a divergence of opinion which indicates that in surgery as in medicine the complete control of and the curative remedy for infection in all its phases has not yet been arrived at.

We do not fully know the length of time after infection within which the application of an antiseptic to a wound holds out any prospect of doing good. Hence it is probably wise to make one efficient application of a sufficiently strong antiseptic even in doubtful cases.

If, in addition to the removal, at the proper time, of foreign bodies, bone fragments, etc., and the establishment of free drainage, one such thorough application fails to check the spread of the infection, then it is not very likely that the repeated use of weaker solutions will have a better result. Experience shows that this is true in a general sense and under these conditions reliance must be placed on stimulating the defensive mechanism of the body by vaccines and in other ways.

It is, however, not my present object to discuss infection and different methods of wound treatment generally; I desire rather to show from direct observation that the application of even a powerful antiseptic does not prejudicially affect the healing process under certain conditions, and by showing this to remove any lingering reluctance to employ suitable reagents in the treatment of infected wounds, and in this way to promote the antiseptic as opposed to the aseptic method in wounds received in war.

Hitherto I have confined my observations to wounds of the limbs and body tissues generally; I have not included wounds of the large serous cavities and their contained viscera. Although the details of application require considerable modification, I think the general principle—namely, that the efficient application on one occasion of a powerful antiseptic is better than the repeated application of weaker solutions—still holds good. One, perhaps the chief, factor influencing the result is that the destruction, by chemical or mechanical means over any considerable area, of the endothelial cells which line these serous cavities increases the risk of the transmigration of pathogenic organisms through the walls of the hollow viscera, and it also predisposes to the subsequent formation of adhesions between opposing surfaces. But bearing this fully in mind, I think that the dread of carbolic acid within the abdominal cavity under all circumstances is a somewhat unreasonable dread. From what I have seen of the application of pure carbolic acid to the stumps of amputated appendices and in some cases to adjacent areas of the caecum or small intestine, and on a still more extensive scale to the stumps of infected Fallopian tubes and abscess cavities in the female pelvis, I feel sure that the localized and careful application of even such a powerful antiseptic as pure carbolic acid at the time of operation has done good in many cases.

The governing factor is, of course, not so much the antiseptic as the mode of infection. If the infecting organisms are passing through the wall of the bowel, as in a case of general peritonitis with obstruction, then the application of any antiseptic to the peritoneal coat of the gut will only do harm. If, on the other hand, the infecting material is being introduced into the peritoneal cavity from outside, as it is in wounds of the abdomen, and as it is also in a localized perforation of a hollow viscus with escape of its contents, then after ensuring that the two urgent requirements—namely, the removal of the

extravasated material and the prevention of further leakage—are both fully carried out we must look round for further means by which to aid the organism to repel the invasion. If it is probable that in some limited area the local application of a strong antiseptic will do more good by destroying germs than it will do harm by killing a certain number of tissue cells, then it is wise to use it.

In conclusion, I hope it will not be supposed that, in recording these simple observations on the effect of antiseptics in aseptic wounds, I am advocating the routine use of these reagents in wounds made by operation under strict aseptic conditions; such a suggestion is quite foreign to my intention. What I do wish to suggest is that if it can be shown, as it certainly can be, that the proper application of strong antiseptics does not materially affect the healing of certain aseptic wounds, this fact should encourage us in the fuller use of efficient germicides in infected wounds at the earliest opportunity and under suitable conditions.

[This article was written before the publication of Sir W. Watson Cheyne's Hunterian Oration on "The Treatment of Wounds in War." We may reasonably hope that the very important researches carried out by Sir Watson Cheyne and his colleagues on the power of diffusion and bactericidal capacity of various germicides will bring the problem of the efficient disinfection of wounds received in war a step nearer solution. With increasing knowledge of the germicidal capacity of different antiseptics there still remains the need for further investigation concerning the action of these reagents on the body cells and tissues. It is this side of the problem that I have ventured to discuss in my remarks.]

Further Report

ON

THE TREATMENT OF PERNICIOUS ANAEMIA BY SALVARSAN AND NEO-SALVARSAN.

BY

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IN March, 1911, I published in this JOURNAL (p. 547) two cases of pernicious anaemia in which great improvement resulted from the intramuscular injection of salvarsan, and on June 22nd, 1912, and May 24th, 1913, I published in this JOURNAL additional papers showing the future progress of these cases and giving particulars of 10 additional cases in which the same method of treatment was employed.

I now propose to record the progress of the cases previously reported and the results in 9 additional cases treated in the same way. These 21 cases include every case of pernicious anaemia I have personally treated by salvarsan or neo-salvarsan, with the exception of 3 cases which have quite recently come under observation and in which sufficient time has not yet elapsed to show the effects of treatment.

One case, which was at first diagnosed as a case of pernicious anaemia and was treated by salvarsan, but which proved to be a case of malignant disease of the stomach and spleen, and 3 cases of pernicious anaemia seen once in consultation in which salvarsan was advised, but in which I do not know if the treatment was employed or not, are not included.

Since I introduced the arsenical treatment of pernicious anaemia in 1875 I have had a large experience of the disease. I have notes, more or less complete, of 141 cases. Excluding 7 cases in which arsenic was not given, the 21 cases treated with salvarsan or neo-salvarsan recorded in this paper, and the 3 cases treated by neo-salvarsan which have quite recently come under observation, there remain 110 cases treated with arsenic by the mouth in the form of Fowler's solution. Of these 141 cases, 70 were hospital and 71 were private patients.

The impression which has been made on my mind by

the comparative results obtained in the treatment of pernicious anaemia by arsenic by the mouth, given in the form of Fowler's solution, on the one hand, and by salvarsan or neo-salvarsan, given intramuscularly, on the other, is decidedly in favour of the latter plan of treatment.

Immediate Result.

A. *Arsenic by the Mouth.*—Of the 110 cases (hospital and private) treated by arsenic given by the mouth in the form of Fowler's solution, in 36 cases (32.7 per cent.) there was no improvement; in 22 cases (20 per cent.) there was slight improvement; in 40 cases (34.5 per cent.) there was marked improvement; and in 14 cases (12.7 per cent.) there was complete (? temporary) recovery.

B. *Salvarsan and Neo-salvarsan.*—Of the 21 cases treated by salvarsan or neo-salvarsan, and recorded in this paper, in 6 (28.5 per cent.) there was no improvement; in 3 (14.2 per cent.) there was slight improvement; in 5 (23.8 per cent.) there was marked improvement; and in 7 (33.3 per cent.) there was complete (? temporary) recovery.

Ultimate Result.

A. *Arsenic by the Mouth.*—Of the 110 cases (hospital and private) treated by arsenic given by the mouth in the form of Fowler's solution, in 12 cases (10.9 per cent.) the ultimate result is not known; in 4 cases (3.6 per cent.) the patients remain fairly well; in 2 cases (1.8 per cent.) the patients remain quite well; in 92 cases (83.6 per cent.) the patients have died. Of the 92 fatal cases in this series, 35 died from pernicious anaemia and 7 from other causes (4 from pneumonia, 1 from heart disease, 1 from cerebral haemorrhage, and 1 from haemorrhage from the bowel).

B. *Salvarsan and Neo-salvarsan.*—Of the 21 cases treated by salvarsan or neo-salvarsan and recorded in this paper, in 1 case (4.7 per cent.) the patient remains fairly well; in 5 cases (23.8 per cent.) quite well; in 15 cases (71.4 per cent.) the patients have died. Of the 15 fatal cases in this series, 13 died from pernicious anaemia (in one of these death was due to bronchopneumonia, which developed ten days after the first and only injection of neo-salvarsan), and 2 from other causes (one from acute croupous pneumonia and one from tuberculous disease of the pleura, peritoneum, and intestine). In the case in which death was due to bronchopneumonia the bronchopneumonia occurred a week after the administration of the salvarsan; whether the treatment had anything to do with the production of the bronchopneumonia it is, of course, impossible to say. In Case XII the pernicious anaemia was complicated with acute combined sclerosis; in Case XXI with a very bad heart; in Case XX the uterus was removed, during the course of the treatment, for profuse recurring menorrhagia (due to a fibroid condition of the uterus).

Duration.

The average duration in months after the treatment was commenced in the two series of cases was as follows:

A. Of the 110 cases treated by arsenic given by the mouth in the form of Fowler's solution, the result is not known in 12 cases; in the remaining 98 cases (6 still alive and 92 dead) the average duration since the treatment was commenced is 14.3 months.

B. Of the 21 cases treated by salvarsan or neo-salvarsan (6 alive and 15 dead), the average duration since the treatment was commenced is 12.5 months.

The comparison between the ultimate result in the two series of cases is not a fair one, for the length of time which has elapsed since the salvarsan treatment was commenced is very much shorter than that since the arsenical treatment by the mouth was commenced in the great majority of cases. Some, perhaps all, of the cases which are still living, and which have been treated by salvarsan and neo-salvarsan, will probably relapse and die. The percentage mortality in the two series of cases is therefore, in the meantime, unreliable.

The same statement applies to the average duration in months after the commencement of the treatment in the two series of cases. In 5 of the cases treated by arsenic by the mouth the duration was 165 months, 110 months, 90 months, 72 months, and 63 months respectively. The long duration in these cases materially affects the general average. Until the cases which still survive (6 cases in the series treated by arsenic in the form of Fowler's solu-

tion given by the mouth, and 6 cases in the series treated by salvarsan or neo-salvarsan given intramuscularly) die, it is impossible to give an accurate comparison of the total duration after treatment in the two series of cases.

Further, unless large numbers are compared, the comparison is apt to be fallacious, for the severity of the cases included in one series may be greater than the severity of the cases included in the other.

The comparative results in the two series of cases—110 cases treated by arsenic by the mouth, and 21 cases treated by salvarsan or neo-salvarsan (intramuscularly)—are shown in the following tables:

Immediate Result.

	No Improvement.	Slight Improvement.	Marked Improvement.	Complete (? temporary) Recovery.
A. 110 cases treated by Fowler's solution	36, or 32.7%	22, or 20%	40, or 34.5%	14, or 12.7%
B. 21 cases treated by salvarsan or neo-salvarsan	6, or 28.5%	3, or 14.2%	5, or 23.8%	7, or 33.3%

Ultimate Result up to Date.

	Not Known.	Fairly Well.	Quite Well.	Death.	
				P.A.	Other Causes.
A. 110 cases treated by Fowler's Solution	12, or 10.9%	4, or 3.6%	2, or 1.8%	85, or 77.2%	7, or 6.3%
B. 21 cases treated by salvarsan or neo-salvarsan	—	1, or 4.7%	5, or 23.8%	13, or 61.9%	2, or 9.5%

In giving salvarsan or neo-salvarsan in cases of pernicious anaemia I have always employed the intramuscular method of administration. First, because in pernicious anaemia we want, I think, a remedy which will produce a sustained and continued rather than an immediate and temporary effect. It seems probable that pernicious anaemia is due to a toxin, perhaps absorbed in repeated doses from the stomach or intestine; but, if this is so, we are quite ignorant of the nature of that toxin. Secondly, because in severe and advanced cases of pernicious anaemia (in which the patient's hold on life is often very precarious and a very little thing will turn the scale) the intramuscular has seemed, perhaps erroneously, to me to be a less hazardous procedure than the intravenous method of administration.

In my earlier cases I employed salvarsan, and in the later cases neo-salvarsan. The local effects produced by neo-salvarsan are undoubtedly much less severe—much less local pain, inflammation, hardness, and swelling—than those produced by salvarsan. The constitutional effects were slight and not more marked in the cases in which salvarsan was employed.

The injections of salvarsan and neo-salvarsan were in some cases followed by a slight rise of temperature and pulse, and in some cases by vomiting. The rise in temperature was usually from one to two degrees Fahrenheit. In the cases treated by salvarsan the rise in temperature was usually most marked on the third or fourth day after the injection, and coincided with the greatest intensity of the inflammatory hardness and swelling in the buttock. The vomiting was chiefly seen in the cases in which neo-salvarsan was given—it was, perhaps, due to the novocain, heroin, or morphine which was administered before the neo-salvarsan was injected. The local inflammation produced by salvarsan was usually relieved by an ice-bag applied locally. A dose of novocain, heroin, or morphine was usually given before each injection of neo-salvarsan, and was repeated, if necessary, two hours after the injection, and again if the pain was not relieved.

I doubt whether neo-salvarsan is so effective in the treatment of pernicious anaemia as salvarsan. The beneficial results were, on the whole, I think, more marked in the cases treated by salvarsan than in the cases treated by neo-salvarsan.

In one case (Case x) the patient refused to remain in

hospital after the first injection. I have, however, included this case in the series in order to give my complete experience of the method of treatment without in any way appearing to produce a too favourable result.

In some of the 21 cases treated by salvarsan or neo-salvarsan which died from the disease, the immediate beneficial results of the treatment were very striking (Cases IV, VIII, and XVIII). In some of the cases (notably Cases VI, XVI, and XVII), in which the improvement at first was only slight, very marked improvement ultimately occurred. I am disposed to think that in these cases the slow and gradual absorption of the remedy was probably the cause of the improvement which ultimately resulted. In all of the 21 cases treated by salvarsan or neo-salvarsan, with the exception of Cases II and X, arsenic, given by the mouth in the form of Fowler's solution, had previously been employed.

In none of the cases was there any reason to suspect previous syphilis. In those cases in which the Wassermann test was employed the result was always negative.

One advantage, and it is a great advantage, which salvarsan and neo-salvarsan possess over the long-continued administration of arsenic by the mouth, in the treatment of pernicious anaemia, is that, in my experience, salvarsan and neo-salvarsan do not produce peripheral neuritis, whereas large doses of arsenic given by the mouth in cases of pernicious anaemia often do produce, in addition to other toxic symptoms, dryness of the throat, irritation of the conjunctivae, pigmentation of the skin, keratitis, diarrhoea, vomiting, etc., and very severe and intractable peripheral neuritis.

Since I advised the administration of salvarsan in the treatment of pernicious anaemia I have received a number of communications from different physicians who have employed the remedy. In some cases striking beneficial results have been obtained, in others there has been no improvement. In some of the cases in which the remedy has been employed by other physicians and reported a failure, it was tried as a last resource after all other means had failed, some of the patients being in a moribund condition. One cannot, of course, draw true conclusions as to the value of the treatment from the results in such cases. In order to judge fairly and accurately of its value, a series of consecutive and unselected cases, slight as well as severe, in which no other treatment has been employed, should be taken, and the results compared with a series of similar cases treated by other methods. It is, however, a slow and difficult process to secure a sufficient number of "virgin" cases of pernicious anaemia for this purpose.

In the BRITISH MEDICAL JOURNAL of December 20th, 1913, p. 1605, the following statements with regard to the results obtained by Friedländer, Leede, and Boggs are recorded:

Comparatively few cases of pernicious anaemia in which injections of salvarsan have been tried have been reported since Dr. Byrom Bramwell communicated the results of this treatment in the BRITISH MEDICAL JOURNAL (1912, vol. i, p. 1413). Friedländer published the account of a case which, though uninfluenced by Fowler's solution, rapidly recovered after two injections of salvarsan, followed by sodium cacodylate. Leede had previously recorded 5 cases with no beneficial effect. Four of these were practically moribund before recourse was had to salvarsan. Recently Boggs (*Johns Hopkins Hospital Bulletin*, October, 1913) recounted the effect of salvarsan in 4 cases under his own care, and in 7 others treated by colleagues. Of the latter, 2 were apparently moribund, and no good effect was observed, whilst 5 showed distinct improvement after an initial drop in the blood count following injection. The interesting observation is made that previous treatment with Fowler's solution did not add to the risk of salvarsan administration. Of Boggs's own 4 cases all showed a favourable response to the drug, both in the relief of symptoms and in the regeneration of the blood. In none of the cases was there any suspicion of syphilis, and the serum and cerebro-spinal fluid were negative to the Wassermann test. Two of these cases, as the result of a single injection, became greatly improved, and the red corpuscular count increased by 2,000,000. The subsequent history is not recorded. A third case showed a very striking result. This was a patient in his fifth relapse, which remained quite refractory to Fowler's solution, and practically refractory to sodium cacodylate injections extending over four months. Salvarsan was then given intravenously in doses of 0.3 gram every four weeks, with the result that there was a steady rise in the number of red cells from an initial 500,000 to 5,000,000 at the end of sixteen weeks. The percentage of haemoglobin also rose from 23 to 90. Save for mild degenerative changes in the spinal cord the patient was quite well. During treatment he had an attack of tertian malaria, accompanied by a fall in the red cell count, but this rose again after quinine and the

next dose of salvarsan. For six months afterwards he was kept under observation whilst employed as liftman in the hospital, but was afterwards lost sight of. In the fourth case, in which nervous symptoms preceded the onset of blood changes, the red cell count rose from 1,100,000 to 3,400,000 in twenty days after the first injection, eventually attaining a level of 4,000,000 (with 85 per cent. haemoglobin), but this was not maintained. The blood regeneration failed and there was a speedy relapse, followed again by a rise to the normal after two more injections, but at no time were the qualitative changes absent from the blood picture. Relapses and recoveries went on for over a year, when the patient died of intercurrent bronchopneumonia. *Post-mortem* examination revealed the typical changes of pernicious anaemia, with funicular degeneration in the cord. In all the 11 cases it was found that the salvarsan provoked a rather sharp febrile reaction, lasting for six to twelve hours after each injection, in marked contrast to the effect produced in syphilitics. All the necessary precautions in technique for the avoidance of such reactions were taken.

In the *Albany Medical Annals*, vol. xxxv, No. 12, December, 1914, the results obtained by Barker and Thayer are noted:

The cases of Barker and Thayer were treated only in part with salvarsan. One, considered moribund on admission, received three-tenths gram and died forty-eight hours later from pre-existing myocardial degeneration, without any reaction or material change in the blood count. Another died eighteen days after admission, receiving one dose of two-tenths gram eleven days before death. There was no considerable reaction and no drop in the blood count of more than 200,000 cells. The other five cases all showed considerable improvement with initial drop in the red cell count, never more than 200,000. These cases also received sodium cacodylate or Fowler's solution, so the report is of value merely in showing that salvarsan may be given to such patients without risk.

The details of my 21 cases are given in the following notes.

CASE I.

Male (J. S.), aged 49, admitted to Edinburgh Royal Infirmary on October 12th, 1910. The red corpuscles numbered 1,035,000 per cubic millimetre, the haemoglobin was 30 per cent., and the colour index 1.5. He had four injections of salvarsan (December 21st, 0.2 gram; January 5th, 1911, 0.3 gram; January 20th, 0.3 gram; February 9th, 0.3 gram). He was discharged from the infirmary on February 22nd, 1911, looking and feeling perfectly well; the red corpuscles were then 3,580,000 per cubic millimetre, the haemoglobin equalled 78 per cent., and the colour index was 1.1.

He continued well and at work until August 31st, 1914, when he was admitted to Chalmers' Hospital with a slight relapse. The red corpuscles numbered 2,500,000 per cubic millimetre, the haemoglobin was 54 per cent., and the colour index 1.08. After 0.6 gram neo-salvarsan was injected intramuscularly on September 13th, he rapidly improved. He was discharged from hospital on September 28th. On January 2nd, 1915, the red corpuscles numbered 3,790,000 per cubic millimetre, the haemoglobin was 62 per cent., and the colour index 0.84.

Duration up to date since the salvarsan treatment was commenced, forty-eight months.

Remarks.—Notwithstanding the slight relapse in August, 1914, this has been a most successful result.

CASE II.

Female (Mrs. E. P.), aged 40, admitted to Edinburgh Royal Infirmary on November 15th, 1910. The disease was of four months' duration. The red corpuscles numbered 990,000 per cubic millimetre, the haemoglobin was 30 per cent., and the colour index 1.36. She had four injections of salvarsan (December 24th, 1910, 0.3 gram; January 7th, 1911, 0.3 gram; January 24th, 0.3 gram; February 9th, 0.3 gram). She made an uninterrupted recovery, and was discharged from hospital on March 16th, 1911, looking and feeling well; the red corpuscles then numbered 4,420,000 per cubic millimetre, the haemoglobin was 94 per cent., and the colour index 1.1.

On March 7th, 1913, the red corpuscles numbered 6,210,000 per cubic millimetre, the haemoglobin was 120 per cent., and the colour index 0.97. On December 25th, 1914, the patient was quite well.

Duration up to date since the salvarsan treatment was commenced, forty-eight months.

Remarks.—The result in this case has been very successful. It and Case XVII are remarkable, since in both of them the red blood corpuscles have gone above the normal.

CASE III.

Female (Mrs. H. P.), aged 41, admitted to Edinburgh Royal Infirmary on March 28th, 1911. Duration three months. The red corpuscles numbered 695,000 per cubic millimetre, the haemoglobin was 16 per cent., and the colour index 1.06. She had two injections of salvarsan (April 6th, 0.3 gram; April 21st, 0.3 gram). On May 5th she was obliged to go home; the red corpuscles then numbered 1,495,000 per cubic millimetre, the haemoglobin was 34 per cent., and the colour index 1.03.

Notwithstanding adverse circumstances she made a splendid recovery, apparently entirely due to the salvarsan treatment.

On December 28th, 1914, she looked and felt remarkably well.

The red corpuscles numbered 4,100,000 per cubic millimetre, the haemoglobin was 80 per cent., and the colour index 0.99.

Duration up to date since the salvarsan treatment was commenced, forty months.

Remarks.—The success of the treatment in this case was remarkable. When the patient was discharged from hospital she was very ill—profoundly anaemic, feet swollen, etc.—and she had to struggle on under great disadvantages.

CASE IV.

Female (Mrs. M. A. P.), aged 56, admitted to Edinburgh Royal Infirmary on March 30th, 1911, apparently in a dying condition. The disease was of four years' duration. The red corpuscles numbered 580,000 per cubic millimetre, the haemoglobin was 17 per cent., and the colour index 1.47. She had two injections of salvarsan (April 6th, 0.3 gram; May 4th, 0.3 gram). Remarkable improvement followed the treatment. The red corpuscles went up to 1,020,000 per cubic millimetre, the haemoglobin was 28 per cent., and the colour index 1.18. She discharged herself on July 25th, continued to improve for six weeks, then relapsed, and died on September 5th, 1911.

Duration after the salvarsan treatment was commenced, five months.

Remarks.—The improvement in this case, though merely temporary, was very remarkable. The case was a long-standing one (four years' duration); two relapses had previously occurred. When the salvarsan treatment was commenced she seemed to be in a dying condition.

CASE V.

Male (W. S.), aged 50, admitted to Edinburgh Royal Infirmary on May 12th, 1911. The disease was of seven months' duration. He died on June 24th, 1911.

Duration of the case after the salvarsan treatment was commenced, six weeks.

Remarks.—In this case the treatment produced no benefit.

CASE VI.

Male (P. S.), aged 31, admitted to Edinburgh Royal Infirmary on May 17th, 1911. The disease was of fourteen months' duration. He had three injections of salvarsan (May 29th, 0.3 gram; June 12th, 0.3 gram; July 12th, 0.3 gram). He did not improve while in hospital, and went home, apparently in a dying condition, the red corpuscles numbering 600,000 per cubic millimetre, the haemoglobin 19 per cent., and the colour index 1.6.

After going home, he remained semicomatose for ten days, then improved, and ultimately got quite well. On November 11th, 1911, he looked and felt well; the red corpuscles numbered 3,100,000 per cubic millimetre, the haemoglobin was 66 per cent., and the colour index 1.1. He had no treatment for the anaemia after leaving the hospital. He remained in good health, without any return of the anaemia, until February, 1912, when he died from acute croupous pneumonia.

Duration after the commencement of the salvarsan treatment, nine months.

CASE VII.

Male (T. S.), aged 55, admitted to Edinburgh Royal Infirmary on October 24th, 1911. The disease was of fifteen months' duration. He had one injection of salvarsan (October 27th, 0.3 gram); rapid improvement followed; he then developed bronchopneumonia, and died on November 6th, 1911.

Duration after the salvarsan treatment was commenced, two weeks.

CASE VIII.

Male (J. C.), aged 72, admitted to Chalmers' Hospital on August 29th, 1912. The disease was of eight months' duration. The red corpuscles numbered 1,055,000 per cubic millimetre, the haemoglobin was 26 per cent., and the colour index 1.3. He had three injections of salvarsan (August 31st, 0.3 gram; September 14th, 0.3 gram; September 28th, 0.6 gram). He improved to a remarkable degree, and was discharged on November 27th, 1912. The red corpuscles then numbered 3,450,000 per cubic millimetre, the haemoglobin was 75 per cent., and the colour index 1.

On March 3rd, 1913, he was readmitted to Chalmers' Hospital suffering from a severe relapse. The red corpuscles numbered 1,010,000 per cubic millimetre, the haemoglobin was 36 per cent., and the colour index 1.7. As the result of one injection of neo-salvarsan (March 10th, 0.6 gram) he again improved rapidly. On May 17th, 1913, the red corpuscles numbered 2,680,000 per cubic millimetre, the haemoglobin was 55 per cent., and the colour index 1.03. He was discharged on May 22nd, remained well till the beginning of October, 1913, then suddenly relapsed and died on October 14th, 1913.

Duration after the salvarsan treatment was commenced, thirteen months.

Remarks.—The improvement in this case was very striking.

CASE IX.

Male (T. B.), aged 25, admitted to Chalmers' Hospital on October 3rd, 1912. The disease was of five years' duration. He had two injections of salvarsan (October 6th, 0.3 gram; October 13th, 0.3 gram). There was no improvement. He died on October 14th, 1912.

Duration after the salvarsan treatment was commenced, one week.

Remarks.—In this case the treatment produced no benefit. It was a very severe case. It is interesting because of the early age at which the disease commenced—20 years. The diagnosis was verified by *post-mortem* examination.

CASE X.

Male (A. D.), aged 61, admitted to Chalmers' Hospital on November 2nd, 1912. The disease was of two months' duration. He had one injection of salvarsan (November 4th, 0.3 gram); refused to stay in hospital, discharged himself, and died on April 17th, 1913.

Duration after the salvarsan treatment was commenced, five and a half months.

CASE XI.

Male (J. T.), aged 50, admitted to Chalmers' Hospital on December 9th, 1912. The disease was of eight months' duration. The red corpuscles numbered 1,045,000 per cubic millimetre, the haemoglobin was 24 per cent., and the colour index 1.14. He had two injections (December 13th, 0.3 gram salvarsan; January 9th, 1913, 0.5 gram neo-salvarsan). He rapidly improved and was discharged on February 22nd, 1913.

On April 8th, 1913, he looked and felt quite well; the red corpuscles numbered 3,850,000 per cubic millimetre, the haemoglobin was 78 per cent., and the colour index 1.01. He continued well until September, 1913, when he had two attacks of diarrhoea. On January 25th, 1914, the red corpuscles numbered 3,360,000 per cubic millimetre, the haemoglobin was 60 per cent., and the colour index 0.89.

On May 15th, 1914, he was readmitted to Chalmers' Hospital, suffering from acute pleurisy with effusion. He died on June 29th, 1914.

Post-mortem examination showed tubercle of the pleura, peritoneum, and intestine. The liver showed slight Prussian-blue reaction; the bone marrow of the femur and ribs was soft and of a deep red colour.

Duration after the salvarsan treatment was commenced, eighteen and a half months.

Remarks.—This was one of the most successful cases I have had. The anaemic symptoms seemed to have entirely disappeared as the result of the salvarsan treatment. Death was due to tubercle of the pleura, peritoneum, and intestine, and not to pernicious anaemia.

CASE XII.

Male (W. H. L. H.), aged 42, married, admitted to Chalmers' Hospital on December 16th, 1912, suffering from subacute combined paralysis and pernicious anaemia. The disease was of three and a half years' duration. He had two injections of neo-salvarsan (December 23rd, 1912, 0.4 gram; January 24th, 1913, 0.6 gram). There was a slight improvement in the condition of the blood, but no improvement in the nervous symptoms. He died on March 22nd.

Post-mortem examination showed all the typical appearances of pernicious anaemia and subacute combined degeneration of the spinal cord.

Duration after the salvarsan treatment was commenced, three months.

CASE XIII.

Male (J. R.), aged 58, admitted to Chalmers' Hospital on January 11th, 1913. The disease was of one year's duration. The red corpuscles numbered 1,690,000 per cubic millimetre, the haemoglobin was 48 per cent., and the colour index 1.4. He had three injections of neo-salvarsan (January 14th, 0.6 gram; February 14th, 0.6 gram; March 14th, 0.6 gram). He was discharged from hospital on March 28th, feeling well; his colour was better, he had gained 1½ lb. in weight; the red corpuscles numbered 2,560,000 per cubic millimetre, the haemoglobin was 56 per cent., and the colour index 1.1.

At the beginning of June, 1913, he got a chill, developed congestion of the lungs, and died on June 17th.

Duration after the salvarsan treatment was commenced, five months.

Remarks.—The improvement in this case was only slight.

CASE XIV.

Male (A. G.), aged 41, admitted to Chalmers' Hospital on March 23th, 1913. The disease was of two years' duration. On March 30th, 0.6 gram of neo-salvarsan was given intramuscularly. There was no improvement. He died suddenly on April 16th, 1913.

Duration after the salvarsan treatment was commenced, two weeks.

Remarks.—In this case there was no improvement.

CASE XV.

Male (W. A.), aged 49, admitted to Chalmers' Hospital on May 21st, 1913. The disease was of three years' duration; had improved and relapsed twice; previously treated by arsenic and iron for two and a half months. On May 22nd the red corpuscles numbered 3,030,000 per cubic millimetre, the haemoglobin was 60 per cent., and the colour index 1. He had one injection of neo-salvarsan (June 13th, 0.6 gram). He was discharged on July 1st, 1913, considerably improved; the red corpuscles numbered 4,380,000 per cubic millimetre, the haemoglobin was 75 per cent., and the colour index 0.8.

He continued much *in statu quo* for some time after his discharge, then relapsed, and died on December 6th, 1913.

Duration after the salvarsan treatment was commenced, five and three-quarter months.

Remarks.—The improvement produced by the treatment in this case was only slight; he only had one injection of salvarsan.

CASE XVI.

Male (E. D.), aged 55, admitted to Chalmers' Hospital on June 12th, 1913. The disease was of a year and a half's duration; previous treatment arsenic by the mouth. On admission,

the red corpuscles numbered 2,070,000 per cubic millimetre, the haemoglobin was 45 per cent., and the colour index 1.1. He had four injections of neo-salvarsan (June 14th, 0.4 gram; July 2nd, 0.6 gram; July 16th, 0.6 gram; August 1st, 0.6 gram). Marked improvement in the general condition resulted, but the blood showed little change. On August 4th, 1913, the red corpuscles numbered 2,300,000 per cubic millimetre, the haemoglobin was 40 per cent., and the colour index 0.9. On August 12th, 1913, he was discharged from hospital feeling greatly improved.

After getting home he continued to improve. On February 19th, 1914, his wife wrote me: "The change for the better in my husband is most remarkable; he has been back to business since Christmas, and in his spare time plays golf. All my friends say he looks better than he has done for years." On December 30th, 1914, he was well.

Duration up to date since the salvarsan treatment was commenced, nineteen months.

Remarks.—The improvement, which at first was very slow, has been very striking.

CASE XVII.

Male (T. H.), aged 39, admitted to Chalmers' Hospital on July 27th, 1913. The disease was of one year's duration; previous treatment, arsenic by the mouth. Colour very yellow; feet and legs oedematous. On the day after admission the temperature rose to 102.6°; pulse 103. He vomited several times, was delirious, and apparently in a dying condition; the red corpuscles numbered 1,380,000 per cubic millimetre, the haemoglobin was 30 per cent., and the colour index 1.1. He had four injections of neo-salvarsan (August 7th, 0.4 gram; August 15th, 0.6 gram; August 25th, 0.6 gram; September 23rd, 0.6 gram). He slowly but steadily improved. He was discharged from hospital feeling very well on November 7th, 1913; the red corpuscles numbered 2,015,000 per cubic millimetre; the haemoglobin was 40 per cent., and the colour index 1.

On March 20th, 1914, the patient wrote me: "I now write to tell you of my wonderful improvement. I have got much stouter. I am enjoying very good health; I can walk three or four miles at a time. I am doing a lot of domestic work. Everybody about here is surprised at my improvement."

When seen at Chalmers' Hospital on April 11th, 1914, his weight was 12 st. ½ lb. (he had gained 3 st. since his discharge from hospital); the red corpuscles numbered 5,480,000 per cubic millimetre, the haemoglobin was 80 per cent., and the colour index 0.7. On December 27th, 1914, he was quite well.

Duration up to date since the salvarsan treatment was commenced, fifteen months.

Remarks.—This was one of the most successful cases which I have had. For several days after the patient's admission to hospital he seemed to be in a dying condition. On October 5th, 1913, 10 grains of boric acid, three times a day, were prescribed, with 4 minims of Fowler's solution. He continued to take this medicine for some time after his discharge from hospital.

CASE XVIII.

Female (Mrs. A.), aged 34, admitted to Chalmers' Hospital on October 15th, 1913. The disease was of eighteen months' duration; previous treatment, arsenic by the mouth. The red corpuscles numbered 1,270,000 per cubic millimetre, the haemoglobin was 40 per cent., and the colour index 1.4. She had two injections of neo-salvarsan (October 16th, 0.4 gram; November 4th, 0.6 gram). Great improvement resulted. She was discharged on December 20th, 1913; the red blood corpuscles numbered 3,360,000 per cubic millimetre, the haemoglobin was 65 per cent., and the colour index 0.87.

On March 15th, 1914, her doctor wrote me that she was not so well; after this, she rapidly relapsed, and died at the beginning of April, 1914.

Duration after the salvarsan treatment was commenced, five months.

Remarks.—In this case the immediate result of the treatment was great improvement, but a relapse and death speedily followed.

CASE XIX.

Male (A. C.), aged 44, admitted to Chalmers' Hospital on October 17th, 1913. The disease was of eleven months' duration, previously treated with arsenic by the mouth.

In November, 1912, he complained of stomach symptoms, for which the abdomen was opened on November 15th by Mr. Stiles; the appendix was found to contain two or three concretions, and was removed. The patient rapidly became weaker and more anaemic after the operation, though there was no loss of blood. On November 23rd I diagnosed pernicious anaemia; the red corpuscles numbered 1,450,000 per cubic millimetre, the haemoglobin was 55 per cent., and the colour index 1.8. He was treated with arsenic by the mouth. On January 3rd, 1913, when he was discharged, the red corpuscles numbered 3,390,000 per cubic millimetre, the haemoglobin was 80 per cent., and the colour index 1.1.

He continued fairly well until September, 1913, when the symptoms of pernicious anaemia returned. On October 17th, 1913, the red corpuscles numbered 1,600,000 per cubic millimetre, the haemoglobin was 50 per cent., and the colour index 1.5. He had three injections of neo-salvarsan (October 20th, 0.4 gram; November 1st, 0.6 gram; December 7th, 0.6 gram). He was discharged from hospital on December 17th, 1913, feeling very well. On February 23rd, 1914, he looked and felt extremely well; the red corpuscles numbered 4,600,000 per cubic millimetre, the haemoglobin was 90 per cent., and the colour index 0.97.

On January 9th, 1915, the red corpuscles numbered 4,320,000

per cubic millimetre, the haemoglobin was 85 per cent., and the colour index 0.99.

Duration up to date since the salvarsan treatment was commenced, fourteen months.

Remarks.—In this case great improvement resulted.

CASE XX.

Female (Mrs. W.), aged 43, treated in a nursing home. First seen May 17th, 1913. The disease was of two years' duration, but had been worse for three and a half months; previous treatment, arsenic by the mouth. On April 29th, 1913, the red corpuscles numbered 1,575,000 per cubic millimetre, the haemoglobin was 44 per cent., and the colour index 1.3. She had had arsenic continuously for a few weeks before coming under my observation. On May 22nd, 1913, the red corpuscles numbered 1,970,000 per cubic millimetre, the haemoglobin was 40 per cent., and the colour index 0.93. She suffered from very profuse menorrhagia. From May 28th to June 2nd and from June 25th to July 5th two "periods" occurred; both were very severe, particularly the latter. On July 14th the red corpuscles numbered 1,370,000 per cubic millimetre, the haemoglobin was 36 per cent., and the colour index 1.3.

Hysterectomy.—After anxious consultation with two leading gynaecologists and Dr. Lovell Gulland (who agreed with me that the case was a typical case of pernicious anaemia complicated with menorrhagia), it was decided to remove the uterus at the commencement of the next "period." The operation was most successfully performed on July 29th; the uterus was enlarged and fibroid; there was no loss of blood. For forty-eight hours after the operation the patient was extremely ill; she then recovered slowly.

She had four injections of neo-salvarsan (June 7th, 0.4 gram; July 8th, 0.6 gram; August 13th, 0.6 gram; September 1st, 0.6 gram). Remarkable improvement occurred as the result of the first three injections; no improvement followed the fourth injection. On August 29th the red corpuscles numbered 2,020,000 per cubic millimetre, the haemoglobin was 45 per cent., and the colour index 1.0. On October 12th, 1913, the red corpuscles numbered 1,620,000 per cubic millimetre, the haemoglobin was 43 per cent., and the colour index 1.3. The patient went home on October 13th.

After returning home she suffered severely from inflamed piles, relapsed, and died on November 30th, 1913.

Duration after the salvarsan treatment was commenced, five and three-quarters months.

Remarks.—In this case striking improvement resulted from the first three injections of salvarsan; the fourth injection seemed to do harm rather than good.

CASE XXI.

Male (W. R.), aged 62, admitted to a nursing home on December 25th, 1913, suffering from well marked pernicious anaemia and degeneration of the cardiac muscle. The anaemia was of one year's duration, during which time he had lost 3 st. in weight. The red corpuscles numbered 2,180,000 per cubic millimetre, the haemoglobin was 45 per cent., and the colour index 1.04. The heart was in a very unsatisfactory condition—very quick and irregular action with triple rhythm. He had one injection of neo-salvarsan (0.4 gram). He remained in the home for three weeks and did not improve. The condition of the heart was so unsatisfactory that it was decided not to repeat the injection. Mental symptoms developed. He returned home on January 17th, 1914. His mental condition gradually became worse and his heart more and more unsatisfactory; he died on January 26th.

Duration after the salvarsan treatment was commenced, one month.

Remarks.—In this case no improvement resulted from the treatment.

N.B.—Cases I, II, III, IV, V, VI, VII, VIII, IX, XI, XII, and XIII were more fully reported in the *BRITISH MEDICAL JOURNAL*, May 24th, 1913, p. 1093.

BENZOL THERAPY IN LEUKAEMIA AND LYMPHO-SARCOMA.*

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DURING the last year I have had an opportunity of testing the reputed action of benzol as a useful therapeutic agent in leukaemia. I have now treated altogether four cases with this drug—one of myelogenous leukaemia, one of lymphatic leukaemia, one of lympho-sarcoma, and one of what was regarded as osteo-sarcoma.

The introduction of the drug and its mode of action have been very fully discussed in recent papers, many of which contain a full bibliography up to the date of publication. In consequence, I only propose to refer to those facts which it is essential to bear in mind in order that the reasons for employing the drug at all may be understood, and I will omit practically all reference to the literature of the subject.

In 1910 Selling reported in the *Johns Hopkins*

* A paper read before the Royal Academy of Medicine in Ireland.