be behind the umbilicus and passing towards the pubes. These pains were almost of daily occurrence, but he had gone as long as a week without pain. For the past six weeks the pains had been more severe, and he had lost 7 lb. in weight. The pain was accompanied by flatulence and distension, and if he was able to pass flatus the pain was somewhat relieved. During his illness he had been subject to constipation. Nothing abnormal was found on opening the abdomen. He was treated with enemata and purgatives, and had no more pain. When seen about ten months after operation he continued to be free from pain.

CASE V.—*Colic resembling Intestinal Adhesions.*

Female, aged 44. Subject to marked constipation and colicky pains in upper part of abdomen for several years. For some months the pains have been more severe, more frequent, and accompanied by distension. With the pain there was a feeling as if "there was something she wanted to get rid of." Medical treatment was advised, and the pains disappeared. Three years later she was still free from attacks.

CASE VI.—*Colic resembling Cicatricial Stenosis of Intestine.*

Female, aged 44. The patient stated that she had "typhoid fever and peritonitis," during which she passed a "large quantity" of blood per anum ten years previously. Subject to marked constipation since that illness. For the past three years has been subject to abdominal pain and slight distension, and feels as if there had been a "stoppage on the left side of the bowels." Under treatment by purgatives, abdominal massage, and electricity she quickly got well, and continued so when seen four years later.

I have met with many such cases as those recorded above which sufficiently exemplify the difficulty of arriving at an exact diagnosis.

The exclusion of a malignant neoplasm is of the greatest importance. The presence of "occult blood" in the faeces may be found in cases of ulcerating growth, and the prolonged retention of a bismuth meal, as shown by the *x* rays, is of some value in suggesting a definite organic obstruction, but it is unwise to attach much importance to this symptom, and therefore it is generally desirable to keep the patient in bed under observation for a week or two. The food should be light and nutritious, the bowels should be opened regularly with purgatives and enemata if necessary, and the patient weighed at definite intervals.

If under these conditions the symptoms show no signs of improvement and there is a progressive loss of weight, an exploratory coeliotomy is desirable. Even then nothing abnormal may be found, though such cases are usually caused by some form of intestinal adhesion or new growth.

As in the acute cases, it is inevitable that exploratory operations should occasionally be necessary if we wish to safeguard the patient against the overlooking of serious organic disease, but we may justifiably delay operation where the patient shows continuous signs of improvement under the regimen referred to.

In both acute and chronic cases where coeliotomy has proved the absence of any organic lesion the patient is generally cured of his symptoms—at least, temporarily. This is, doubtless, mainly attributable to the rest in bed necessitated by the operation, accompanied by careful dieting and regular action of the bowels.

Constipation is a causative factor in so many of these cases that attention to the proper and regular evacuation of the bowels is of the highest importance if future attacks are to be avoided.

THE annual meeting and launch party of the Brussels Medical Graduates' Association will be held on Saturday, July 13th. The saloon launch *Empress of India* will start from Maidenhead at 12.30 p.m., returning about 8 o'clock. The launch is provided with a cabin and an awning, so that weather conditions are immaterial. The train leaves Paddington at 11.15 a.m. for Taplow, which is the nearest station to Maidenhead Bridge. Tickets, 12s. 6d. each, to include launch, luncheon (not including wine), and tea, may be obtained from the honorary secretary, Dr. Arthur Haydon, 23, Henrietta Street, Cavendish Square, W. At the biennial dinner of the association, which took place at the Trocadero on May 23th, the chair was taken by Dr. Arthur Haydon, owing to the absence of the president in the country. The following were elected officers for the year: President, Dr. Edward Osborne Fountain; vice-president, Dr. Robert Wilkinson; honorary treasurer, Dr. Major Greenwood; honorary secretary, Dr. Arthur Haydon; Council, Drs. Cowburn, Callender, Cullinan, Singleton, Howard Humphris, Smallwood, Fielden Briggs, Henry Dutch, and Bryce Macaulay.

C

Remarks

ON

THE SALVARSAN TREATMENT OF PERNICIOUS ANAEMIA.

BY

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IN March, 1911, I published in this JOURNAL two cases of pernicious anaemia in which great improvement resulted from the administration of salvarsan. In this paper I propose to record the future progress of these cases—they have remained well without any further treatment—and the results in five (all the) other cases treated in the same way. Since I commenced to treat cases of pernicious anaemia with arsenic in the year 1875 I have had a large experience of the disease; the impression which has been made upon my mind by the results of the salvarsan treatment in the seven cases which I am now about to record is, on the whole, very favourable. If my observations are confirmed by further experience, and by other observers, I am disposed to think that salvarsan will probably be found to be a more efficient remedy than arsenic given by the mouth, and indeed than any form of treatment which has as yet been employed in this very grave and intractable disease.

CASE I.

J. S., aged 49, married, electric hoist man, formerly a soldier, admitted to the Edinburgh Royal Infirmary on October 12th, 1910, suffering from marked pernicious anaemia.

Previous History.

The patient came under my observation as an out-patient in October, 1909, suffering from pernicious anaemia, was treated with arsenic, and rapidly recovered. He remained at work and fairly well until the beginning of October, 1910, when he got a chill and rapidly became markedly anaemic. The patient denies venereal disease. The bridge of his nose is sunken; this developed spontaneously at the age of 18, and was, perhaps, due to congenital syphilis; there are no other stigmata of that condition.

State on Admission to Hospital.

The patient presented all the typical symptoms of pernicious anaemia.

The blood count was as follows: Red corpuscles, 1,035,000; haemoglobin, 30 per cent.; colour index, 1.5; whites, 7,800. Differential count: Polymorphs, 56.6 per cent.; mononuclears, 41 per cent. (large 15 per cent., small 26 per cent.); eosinophiles, 2.3 per cent. Marked poikilocytosis, polychromasia and granular degeneration. No nucleated reds were seen.

The patient was very short of breath on exertion; his feet and ankles were oedematous; there were no retinal haemorrhages. The systolic blood pressure was 88 mm. of mercury. Blowing systolic murmurs were present in the mitral, pulmonary, and aortic areas. The tongue was clean and moist. There had been no sore spots on the tongue or mouth. The patient had had no teeth for several years; his gums were perfectly normal; the false teeth which he wears had given rise to no irritation. The urine was pale, specific gravity 1012, and contained no abnormal constituents.

Treatment and Results.

Rest in bed; milk diet; arsenic (Fowler's solution), commencing with 2 minims, three times daily. When the arsenic was increased to 4 minims three times daily, diarrhoea developed; this was, however, easily restrained (as I have found to be the case in other cases) by combining a small dose of morphine (5 minims of the liquor morphinae hydrochlor.) with each dose of the arsenic. The arsenic was gradually increased to 12 minims three times daily. The patient improved considerably under this treatment as regards his general symptoms, appearance, and the condition of the blood.

December 16th. Fowler's solution stopped. Red corpuscles, 1,830,000; haemoglobin, 52 per cent.; colour index, 1.44.

From December 16th to 21st no drugs were administered.

December 21st. Red corpuscles, 1,720,000; haemoglobin, 50 per cent.; colour index, 1.4. On this date the first dose of salvarsan (0.2 gram) was given, the remedy being injected into the left buttock. On January 5th and 19th and on February 9th the injections of salvarsan were repeated, 0.3 gram being given on each of these occasions. Each injection was followed by inflammatory hardness and pain in the buttock, but little constitutional disturbance. The first and third injections were made into the left, and the second and fourth into the right buttock. Coincidentally with this treatment very marked improvement occurred.

February 23rd, 1911. Red corpuscles, 3,580,000; haemoglobin, 78 per cent.; colour index, 1.1. The white corpuscles, which before the administration of salvarsan were 4,600, now numbered 8,000 per cubic millimetre. The systolic blood pressure had increased to 135 mm. of mercury.

Subsequent Progress of the Case.

June 23rd, 1911. The patient stated that he had been quite well since his discharge from the infirmary on February 23rd, 1911, and had had no treatment. Red corpuscles, 4,530,000; haemoglobin, 78 per cent.; colour index, 0.87.

On October 25th, 1911, the patient stated that since last seen he had continued quite well without any treatment and had been doing his full work as an electric hoist man. In July he did a march with the Territorials from Kilmarnock to Troon, a distance of twenty-five miles, without any difficulty or distress.

On March 7th, 1912, the patient stated that, owing to the coal strike, he had been unable to get a train and had had to walk ten miles to a station in order to get to the infirmary in time for the clinic. He was looking and feeling quite well, and showed no disturbance as the result of his ten mile walk. Red corpuscles, 4,680,000; haemoglobin, 94 per cent.; colour index, 1.

The condition of the blood at different dates is shown in Table I.

TABLE I.

CASE I.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
			Per Cent.	
Oct. 12, 1910 ...	Arsenic begun, 2 m., t.i.d.	1,035,000	30	1.5
Dec. 16, 1910 ...	Arsenic stopped, 12 m., t.i.d.	1,830,000	52	1.44
Dec. 21, 1910 ...	" 606," 0.2 gram	1,720,000	50	1.47
Jan. 5, 1911 ...	" 606," 0.3 gram	2,500,000	68	1.3
Jan. 19, 1911 ...	" 606," 0.3 gram	2,960,000	70	1.18
Feb. 9, 1911 ...	" 606," 0.3 gram	3,200,000	72	1.1
Feb. 20, 1911 ...	—	3,380,000	78	1.16
Feb. 23, 1911 ...	—	3,580,000	78	1.1
June 23, 1911 ...	—	4,530,000	78	0.87
March 7, 1912 ...	—	4,630,000	94	1.0

Remarks.—I have seen many cases of pernicious anaemia temporarily restored to apparent health as the result of arsenical treatment, and a few in which the patients have remained well for several years, but rarely, if ever, in the whole of my thirty-seven years' experience of the arsenical treatment, have I seen any cases in which such complete restoration to health has resulted as in this and the next case (Case II). In most cases of pernicious anaemia which apparently have recovered under ordinary arsenical treatment, and in which the normal number of red cells has been regained, the colour of the patients is not, in my experience, quite normal; there is often a yellow tinge of the skin and mucous membranes mixed with the normal red, which to the experienced eye is very suggestive that the blood is not yet quite normal, and the cure is not likely to be lasting. In this and in the next case (Case II), the colour of the patients is absolutely normal; they appear to be in robust health. The fact that this patient (Case I) could march twenty-five miles without any distress seven months after the treatment was commenced, is a striking fact. The condition of the blood (red corpuscles, 6,210,000; haemoglobin, 120 per cent.; colour index, 0.97) in the second case, fifteen months after the treatment was commenced, is remarkable. I do not remember to have seen any case of pernicious anaemia in which such a high blood count was observed as the result of treatment.

CASE II.

Mrs. E. P., aged 40, married, admitted to the Edinburgh Royal Infirmary on November 15th, 1910, suffering from marked pernicious anaemia of four months' duration. The disease commenced soon after the birth of her last child; this and her previous seven confinements were all attended with considerable haemorrhage.

Previous History.

Two years ago a tuberculous tumour was removed from the sternum, otherwise she had enjoyed good health until the present illness commenced. Some three weeks before her admission she suffered from sore spots on the mouth and tongue. For many years past her teeth have been extremely bad. There is no suspicion of syphilis, unless two miscarriages and the death of a child, aged 8 months, were due to syphilis. The patient has six children alive and well.

State on Admission to Hospital.

The patient was very pale; during the past two years she has lost more than a stone in weight. There is a curious patch of herpes on the nose.

The condition of the blood was as follows: Red corpuscles, 990,000; haemoglobin, 30 per cent.; colour index, 1.6; whites, 4,600. Differential count: Polymorphs, 74 per cent.; mononuclears, 17 per cent. (large 6 per cent., small 11 per cent.); eosinophiles, 7 per cent.; basophiles, 2 per cent. Marked poikilocytosis; some nucleated reds; no granular degeneration or polychromasia.

Blowing systolic murmurs were present in the mitral, pulmonary, and aortic areas. The pulse numbered 100. The systolic blood pressure was 108 mm. of mercury. The tongue was pale and clean; the teeth very bad. The urine was dark, specific gravity 1010, and contained no abnormal constituents. There were no haemorrhages in the retina.

Treatment and Results.

The arsenical treatment was commenced on November 15th; 2 minims of Fowler's solution three times daily. The dose of arsenic was gradually increased until December 16th, when the patient was taking 9 minims of Fowler's solution three times daily. On November 26th, 1910, a slight thrombosis developed in the lower part of the right calf, but this rapidly yielded to treatment.

December 16th. Fowler's solution stopped. Red corpuscles, 1,460,000; haemoglobin, 45 per cent.; colour index, 1.5.

From December 16th to 24th no drugs were given. December 24th: Red corpuscles, 1,760,000; haemoglobin, 52 per cent.; colour index, 1.48.

On December 24th, January 7th and 24th, and February 9th, 0.3 gram of "606" was injected into the buttocks.

Considerable swelling, hardness, and tenderness resulted from each injection, but there was little or no constitutional disturbance except after the last, which was followed for a few days by a swinging temperature.

Coincidentally with this treatment very marked improvement occurred.

February 21st. Red corpuscles, 4,020,000; haemoglobin 88 per cent.; colour index, 1.1. The white corpuscles, which before the administration of "606" were 3,000, now numbered 6,200. The systolic blood pressure remained practically unaltered during the treatment.

March 3rd. Since the last note there has been pain and pleuritic friction over the lower part of the left chest, and some painless enlargement of the glands in the neck.

March 16th. Patient discharged from the infirmary looking and feeling well.

Subsequent Progress of the Case.

October 13th. Looking and feeling well; doing all her housework. Red corpuscles, 4,800,000; haemoglobin, 96 per cent.; colour index, 1.

March 7th, 1912. Looking and feeling quite well; doing all her housework. Has had no treatment since discharged from the infirmary on March 16th, 1911. Red corpuscles, 6,210,000; haemoglobin, 120 per cent.; colour index, 0.97.

The condition of the blood at different dates is shown in Table II.

TABLE II.

CASE II.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
			Per Cent.	
Nov. 15, 1910 ...	Arsenic begun, 2 m., t.i.d.	990,000	30	1.6
Dec. 16, 1910 ...	Arsenic stopped, 9 m., t.i.d.	1,460,000	45	1.5
Dec. 24, 1910 ...	" 606," 0.3 gram	1,760,000	52	1.48
Jan. 7, 1911 ...	" 606," 0.3 gram	2,450,000	68	1.38
Jan. 24, 1911 ...	" 606," 0.3 gram	3,125,000	74	1.19
Feb. 9, 1911 ...	" 606," 0.3 gram	3,350,000	78	1.16
Feb. 18, 1911 ...	—	4,140,000	88	1.07
Feb. 21, 1911 ...	—	4,020,000	88	1.1
March 11, 1911 ...	—	4,420,000	94	1.1
June 2, 1911 ...	—	4,420,000	90	1.0
Oct. 13, 1911 ...	—	4,800,000	96	1.0
March 7, 1912 ...	—	6,210,000	120	0.97

CASE III.

Mrs. P., aged 54, admitted to the Edinburgh Royal Infirmary on September 1st, 1908, suffering from profound pernicious anaemia.

Previous History.

The patient was a strong, healthy woman until three years previously; then had an attack of "jaundice" which lasted for seven weeks; has had two other attacks of the same sort since, the last about a year ago. For thirteen years has been troubled with bleeding piles, worse for the past few months. No evidence or suspicion of syphilis.

State on Admission to Hospital.

Profoundly anaemic; blowing murmur in all the cardiac areas; liver enlarged; feet swollen; no retinal haemorrhages. Red corpuscles, 545,000; haemoglobin, 15 per cent.; colour index, 1.2; white corpuscles, 3,800. Differential count: Polymorphs, 73 per cent.; mononuclears, 26 per cent. (small 19, large 7 per cent.); eosinophiles, 1 per cent. Marked poikilocytosis; no normoblasts or megaloblasts seen. Appetite poor; thirsty; bowels constipated. Patient stated that for three years she had had no teeth, and that for a long time previously she only had one or two teeth; she had not suffered from dental caries or from a sore mouth; her teeth simply dropped out, and did not decay. The urine contained a trace of albumen, but no casts or other abnormal constituents.

Treatment.

Gradually increasing doses of arsenic, commencing with 2 minims of Fowler's solution three times daily, increased every fourth day by one drop. The maximum dose which the patient was able to take was 10 drops three times daily.

Progress of the Case.

Under this treatment great improvement rapidly took place. On October 1st the patient was looking and feeling very much better: red blood corpuscles, 1,800,000; haemoglobin, 50 per cent.; colour index, 1.2. From October 1st to November 10th, although the general condition improved, there was no alteration in the state of the blood. On November 11th, Robertson's Bland's pill capsules—one No. 3 capsule (equal to three Bland's pills) three times daily—were prescribed. Under this treatment striking improvement in the condition of the blood immediately took place. November 20th. Red corpuscles, 3,100,000; haemoglobin, 60 per cent.; colour index, 0.9.

On November 21st the patient was discharged from hospital, and advised to continue the iron.

Subsequent Progress of the Case.

On January 13th, 1909, the patient stated she was perfectly well. She looked very well—many years younger than on her admission to hospital. Red corpuscles, 4,100,000; haemoglobin, 65 per cent.; colour index, 0.7.

September 15th, 1909. The patient stated that she had been well since last seen. Red corpuscles, 2,800,000; haemoglobin, 60 per cent.; colour index, 1.

Readmitted to Edinburgh Royal Infirmary on March 30th, 1911.

After her discharge from the infirmary she remained well for a year; then suffered from severe pain in the abdomen, due to gall stones; was operated upon by Mr. Miles on December 25th, 1909, fifteen gall stones being removed. Made an uninterrupted recovery, leaving the hospital at the end of January, 1910.

Readmitted eight weeks later, when a second operation was performed; an abscess of the gall bladder was opened and drained. Left the hospital three weeks later. Gradually improved and remained very well until January, 1911; then became very weak and anaemic, and has been in bed since.

State on Readmission to Hospital.

Profoundly anaemic and very weak; markedly short of breath on exertion; feet swollen; loud systolic murmurs in the mitral and pulmonary areas; spitting up a good deal of white frothy mucus; vomiting frequently; abnormally sleepy. Red corpuscles, 680,000; haemoglobin, 18 per cent.; colour index, 1.3; white corpuscles, 5,200. Differential count: Polymorphs, 52 per cent.; mononuclears, 44 per cent. (large 6, small 38 per cent.); eosinophiles, 3; basophiles, 1. Many normoblasts and megaloblasts. Coagulation time very much increased; marked poikilocytosis; granular degeneration and polychromatophilia. No retinal haemorrhages. Urine dark coloured, specific gravity 1008, containing a trace of albumen. For some months past had been taking arsenic by the mouth, but not regularly.

Treatment.

Arsenic (2 minims three times a day), digitalis, etc., prescribed.

April 5th. Patient seemed to be in a dying condition. Red corpuscles, 580,000; haemoglobin, 17 per cent.; colour index, 1.47; white corpuscles, 3,600. Arsenic by the mouth stopped.

April 6th, 0.3 gram salvarsan injected into buttock. This was followed by a slight rise in temperature and pulse, but very little local pain.

April 13th. Red blood corpuscles, 972,000; haemoglobin, 22 per cent.; colour index, 1.16; white corpuscles, 3,400.

April 15th. Hypostatic pneumonia of right base. Temperature, 101°. Strychnine, brandy, digitalis prescribed.

April 19th. Red corpuscles, 1,085,000; haemoglobin, 24 per cent.; colour index, 1.15; white corpuscles, 5,100.

April 22nd. Has gradually improved during the past few days; lung is clearing up; pulse better.

April 24th to 28th inclusive. Vomited frequently.

April 29th. All medicine and food by the mouth stopped; nutrient and medicinal enemata.

May 4th. Extremely weak. Respirations 36; heart very feeble; some oedema of feet and hands. Red corpuscles, 490,000; haemoglobin, 18 per cent.; colour index, 1.8; white corpuscles, 6,100. 0.3 gram salvarsan injected into buttock.

May 6th. Somewhat brighter and feeling a little better.

May 8th. Much brighter to-day, but very restless; constantly wanting to be turned from one side to the other.

May 10th. Much better; can lie on her back, which she has not been able to do for a fortnight.

May 16th.—The buttock at the site of the last injection is red and tender. Is talking rather incoherently.

June 1st. Very bright and cheerful; much better in every respect; appetite improving. Red corpuscles, 870,000; haemoglobin, 31 per cent.; colour index, 1.8; white corpuscles, 4,200.

June 9th. General condition very much improved; enjoyed being at an open window and seeing the trees and flowers. Red corpuscles, 970,000; haemoglobin, 32 per cent.; colour index, 1.6; white corpuscles, 6,100.

June 18th. Bland's pill (one, three times daily) prescribed; increased on July 18th to two capsules.

June 23rd. Vomiting and diarrhoea due to eating strawberries and sweet cakes surreptitiously given her during Coronation festivities.

July 11th. Diarrhoea still troublesome, notwithstanding the administration of tincture of opium. Red corpuscles, 1,020,000; haemoglobin, 28 per cent.; colour index, 1.4; white corpuscles, 4,800.

July 25th. Removed home by her friends, still in a very unsatisfactory condition.

On September 5th, 1911, died. (The patient was not seen after her discharge from the infirmary.)

The condition of the blood at different dates is shown in Table III.

TABLE III.

CASE III.—*Pernicious Anaemia. Showing the Results of Treatment.*

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
			Per Cent.	
Sept. 3, 1908 ...	Arsenic, 5 m., t.i.d.	545,000	15	1.2
Nov. 3, 1908 ...	Arsenic, 10 m., t.i.d.	1,600,000	45	1.2
Nov. 8, 1908 ...	Iron begun.	1,800,000	50	1.2
Nov. 20, 1908 ...	1 Bland's pill, t.i.d.	3,100,000	60	0.9
Dec. 2, 1908 ...	Iron, 2 Bland's pills, t.i.d.	2,900,000	55	0.8
Jan. 13, 1909 ...	—	4,100,000	65	0.7
Sept. 15, 1909 ...	—	2,800,000	60	1.0
March 30, 1911 ...	Arsenic, 2 m., t.i.d.; digitalis, etc.	680,000	18	1.3
April 5, 1911 ...	Arsenic stopped	580,000	17	1.47
April 6, 1911 ...	"606," 0.3 gram	—	—	—
April 13, 1911 ...	—	972,000	22	1.16
April 19, 1911 ...	—	1,085,000	24	1.15
May 4, 1911 ...	"606," 0.3 gram	490,000	18	1.8
June 1, 1911 ...	—	870,000	31	1.8
June 18, 1911 ...	Iron begun (Bland's pill)	—	—	—
July 11, 1911 ...	Iron (2 Bland's pills)	1,020,000	28	1.4

Remarks.—This was a very severe case of pernicious anaemia. During the patient's first stay in hospital a splendid recovery resulted from arsenic by the mouth and iron (Bland's pill capsules); it is one of the few cases of pernicious anaemia in which I have seen striking benefit, with a fall of the colour index, from the administration of iron; in the great majority of the cases of pernicious anaemia in which I have given iron, I have seen either no benefit or distinct deterioration result.

When the patient was readmitted to the infirmary on March 30th, 1911, she appeared to be in a dying condition. Salvarsan was given as a last resource, but none of us who saw her expected that she would even temporarily recover. The results on paper do not perhaps look very striking, but the way in which she temporarily rallied was very remarkable; all of us who watched the case attributed the temporary change for the better to the salvarsan. I have, of course, seen many remarkable temporary rallies and recoveries in cases of pernicious anaemia, but I have seen very few cases, in which the patients were in such a grave condition as this patient was, improve and temporarily recover in the way this patient (and Case vi) did.

CASE IV.

Mrs. H. P., aged 41, admitted to the Edinburgh Royal Infirmary on March 28th, 1911, suffering from profound pernicious anaemia.

Previous History.

Since childhood has suffered off and on from diarrhoea. In March, 1905, had the appendix removed; before this the bowels used frequently to move as many as twelve times a day; after the operation the diarrhoea ceased for twelve months; then had three or four motions a day. No suspicion of syphilis.

In October, 1910, began to suffer from abdominal pains; was

at that time six months pregnant. The child was born on December 30th, 1910; the labour was normal, and there was no excessive loss of blood; she did not nurse the child. After the confinement the diarrhoea became worse—nine motions per day; at the same time she began to have a swinging temperature (between 100° and 102°) and persistent vomiting. She got paler and thinner. Her doctor prescribed arsenic, which she took for about ten days with some slight improvement; she has not, however, taken the medicine regularly.

State on Admission to Hospital.

Profoundly pale and anaemic. Red corpuscles, 695,000; haemoglobin, 16 per cent.; colour index, 1.15; white corpuscles, 3,200. Marked poikilocytosis; many megaloblasts and normoblasts; coagulation time increased. Very short of breath on exertion; palpitation and dizziness on assuming the upright position. Systolic murmurs in all the cardiac areas. Numerous small retinal haemorrhages. Tongue large, flabby, and pale, but clean. Teeth all false; has had no teeth for four years; before the teeth were removed the gums used to be sore, but there has been no trouble about the mouth since she was fitted with false teeth. Urine amber colour, specific gravity 1010; no abnormal constituents.

Subsequent Progress of the Case.

April 6th, 0.3 gram of salvarsan was injected into the right buttock. This was followed by considerable swelling, pain, and tenderness; $\frac{1}{4}$ grain of morphine was administered on the evening of the injection.

April 12th. The patient looked and felt decidedly better. Red corpuscles, 1,260,090; haemoglobin, 31 per cent.; colour index, 1.24; white corpuscles, 3,400.

April 21st. Second injection of "606" (0.3 gram); this was followed by very little pain or discomfort.

May 2nd. Looking and feeling very much better. Red corpuscles, 1,495,000; haemoglobin, 34 per cent.; colour index, 1.2; white corpuscles, 2,200.

May 6th. Insisted upon going home in order to nurse her young baby and look after her husband and family. Was warned as to the serious nature of her condition.

April 17th, 1912. Nothing more was heard of this patient until she called to see me by request. Though still somewhat pale, she was looking wonderfully well. She stated that since her discharge from the infirmary she had had no treatment of any kind. For the first three weeks after her discharge, her feet remained swollen and she was very pale and weak. Since then, she had slowly and gradually improved. Since her discharge she had done all her housework, washing, etc., herself; she has four children, aged respectively 15, 12, 9 years, and 15 months. Her husband only earns a small wage, and she had not been able to procure proper or sufficient nourishment. She spontaneously stated: "My case has been a marvellous case, and the talk of a great many people." She stated that for the past week she had had a cold and had not been so well; the cold produced herpes oris and diarrhoea. The condition of the blood was: Red corpuscles, 3,880,000; haemoglobin, 54 per cent.; colour index, 0.7; white corpuscles, 7,800. Considerable poikilocytosis, some myelocytes and nucleated reds. Differential count: Polymorphs, 39 per cent.; mononuclears, 52.5 per cent. (small 29, large 23.5 per cent.); neutrophils, 4 per cent.; basophiles, 2 per cent.; myelocytes, 2 per cent.; nucleated red, 0.5.

The condition of the blood at different dates is shown in Table IV.

TABLE IV.

CASE IV.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
March, 28, 1911...	—	695,000	Per Cent. 16	1.15
April 6, 1911 ...	"606," 0.3 gram	820,000	24	1.49
April 12, 1911 ...	—	1,260,000	31	1.24
April 21, 1911 ...	"606," 0.3 gram	1,230,000	34	1.4
April 28, 1911 ...	—	1,260,000	34	1.3
May 2, 1911 ...	—	1,495,000	34	1.2
April 17, 1912 ...	—	3,880,000	54	0.7

Remarks.—This also was a very severe case of pernicious anaemia. The improvement which has resulted—and it was apparently altogether due to the two injections of salvarsan—is very striking, for since her discharge from hospital this patient has been heavily handicapped by her circumstances and surroundings. The condition of the blood shows that she is still suffering from the disease, but her general appearance and condition are remarkably improved.

CASE V.

W. S., aged 50, married, mason, admitted to Edinburgh Royal Infirmary on May 12th, 1911, suffering from profound pernicious anaemia.

Previous History.

For the past five years has occasionally, for a day or two at a time, suffered from diarrhoea, but in other respects was a strong, healthy man until six months ago.

In October, 1910, began to feel his hands numb and sleepy, and gradually lost strength and colour. Eight weeks ago became short of breath on exertion. A week ago had a sore tongue; had never suffered from sore tongue before. Had lost 2 st. in weight during the past six months. Denies syphilis; no appearances suggestive of that disease.

State on Admission to Hospital.

Very pale and anaemic. Red corpuscles, 970,000; haemoglobin, 28 per cent.; colour index, 1.4; white corpuscles, 5,400. Marked poikilocytosis and polychromatophilia. Differential count: Polymorphs, 76 per cent.; mononuclears, 23 per cent. (small 17, large 6 per cent.); eosinophiles, 1 per cent. Systolic murmurs in all the cardiac areas. Some retinal haemorrhages. Urine amber coloured, specific gravity 1009; no abnormal constituents.

May 15th, 0.3 gram of "606" injected into the left buttock; this was followed by a rise of temperature to 100° F., and a good deal of pain, with subsequent hardness and tenderness.

May 21st. Temperature continues to rise at night to about 100° F.; buttock pain and tenderness still marked. Blood somewhat improved (see Table V).

June 9th. The local pain and tenderness have almost disappeared, but the temperature still continues swinging. The patient looks much worse. Blood worse (see Table V).

June 16th. Temperature has been better lately. The patient says he feels better, but there is no improvement in the condition of the blood.

June 19th, 0.3 gram "606" injected into the right buttock. Very little pain or tenderness resulted.

June 22nd. Looks very ill; diarrhoea. Red corpuscles, 810,000; haemoglobin, 24 per cent.; colour index, 1.5; white corpuscles, 5,400.

June 23rd. Diarrhoea worse; patient collapsed; temperature, 96.2° F.; pulse very feeble, only just perceptible. Transfused with 1 litre of normal saline solution.

June 24th. Temperature fell to 96° F. Vomiting. Died at 5.30 p.m.

Post-mortem examination showed all the typical appearances of pernicious anaemia.

In the left buttock a deep incision showed an extensive necrosis of the muscle substance surrounded by a zone of well-formed fibrous tissue infiltrated with inflammatory cells. In the right buttock deep incision showed a more recent but extensive necrosis of the muscles with marked polymorph infiltration at its margins, but no fibrous tissue formation.

In the midst of each of the necrotic areas there was a large mass of unabsorbed salvarsan.

The condition of the blood at different dates is shown in Table V.

TABLE V.

CASE V.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
May 12, 1911 ...	—	970,000	Per Cent. 28	1.4
May 15, 1911 ...	"606," 0.3 gram	1,030,000	30	1.4
May 21, 1911 ...	—	1,440,000	36	1.25
June 3, 1911 ...	—	1,120,000	28	1.3
June 9, 1911 ...	—	750,000	22	1.45
June 16, 1911 ...	—	825,000	26	1.5
June 19, 1911 ...	"606," 0.3 gram	860,000	26	1.5
June 22, 1911 ...	—	810,000	24	1.5

Remarks.—In this case a slight temporary improvement in the condition of the blood followed the injection of salvarsan, but there was no real improvement; the treatment was entirely unsuccessful.

Post-mortem examination, six weeks after the first injection, showed that a large mass of the salvarsan emulsion was encapsuled in the depth of the gluteal muscles. This is, I think, suggestive and instructive. When I commenced the salvarsan treatment of pernicious anaemia I selected the intramuscular method of administration for two reasons. First, it seemed to me that in pernicious anaemia it would be best to give the remedy in a way which would tend to its gradual absorption and prolonged action. We are yet ignorant as to the exact cause of pernicious anaemia. In syphilis the object is to give it in such a way as to kill outright the spirochaete. In pernicious anaemia no definite micro-organism has as yet been demonstrated. If the disease is due to a micro-organism, that organism is possibly ultra-microscopic.

Secondly, I was afraid that the intravenous injection of salvarsan in severe cases of pernicious anaemia, in which the blood is so profoundly affected, might be attended with dangerous results. Perhaps I am wrong in reasoning in this way; perhaps it would be better to administer the remedy intravenously. My friend, Dr. John Love, who did me the honour of frequently coming through from Glasgow to attend my Wednesday clinic, and who saw some of the cases which I am now recording, tells me that he has treated several cases of pernicious anaemia by the intravenous method with good results.

CASE VI.

P. S., aged 31, married, farm griever, admitted to the Edinburgh Royal Infirmary on May 17th, 1911, suffering from profound pernicious anaemia.

Previous History.

The patient was quite well till a year ago. In March, 1910, he was confined to bed for ten days with an attack of influenza, and was unfit for work until the middle of May. He was at work from May till September; then the weakness increased, he became anaemic and short of breath, his feet swelled, etc. He was treated with arsenic, which caused diarrhoea and had to be discontinued. A few days before his admission to hospital he had a severe epistaxis. Denies syphilis; no appearance suggestive of that disease.

State on Admission to Hospital.

Profoundly anaemic. Red corpuscles, 955,000; haemoglobin, 26 per cent.; colour index, 1.4; whites, 3,900; marked poikilocytosis and polychromatophilia. Differential count: Polymorphs, 44 per cent.; mononuclears, 56 per cent. (small 44.5, large 11.5 per cent.). Considerable number of nucleated reds present. Systolic murmurs in all the cardiac areas; no retinal haemorrhages. Has never had a sore mouth or tongue. Several of the molars are carious. Tongue pale, clean, and moist.

May 22nd. Complained of pain in the left ear, followed by a purulent discharge and rise in temperature.

May 29th. 0.3 gram salvarsan injected into buttock. Still complaining of pain in the ear; temperature still continues to rise at night; pulse quick.

June 5th. 3 grains of quinine sulphate, three times daily, prescribed.

June 12th. Ear discharge slightly less; 0.3 gram salvarsan injected into the buttock, followed by a good deal of local pain and tenderness; relieved by morphine hypodermically and an ice-bag.

June 16th. Much *in statu quo*. Red corpuscles, 920,000; haemoglobin, 28 per cent.; colour index, 1.55; white corpuscles, 5,300.

July 3rd. Has been in much the same condition till last night, when his temperature went up to 102° and pulse to 120; he complained of some pain and tenderness behind the ear in the region of the mastoid. Red corpuscles, 620,000; haemoglobin, 23 per cent.; colour index, 1.5; white corpuscles, 4,200.

July 10th. Looks very ill; blood condition not improved.

July 12th. 0.3 gram salvarsan injected into buttock; this caused considerable local reaction.

July 28th. No improvement; temperature still swinging; pulse 92 to 124; respirations slow, 12 to 20; passing large quantities of pale urine (to-day 112 oz.). Red corpuscles, 585,000; haemoglobin, 17 per cent.; colour index, 1.45; white corpuscles, 4,500.

August 7th. Removed by his wife to Kinross; not expected to survive the journey.

Subsequent Progress of the Case.

I heard nothing more of this patient until the middle of October, when his doctor told me that he was quite well. For ten days after leaving the infirmary he continued in a semi-

TABLE VI.

CASE VI.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
May 17, 1911	—	955,000	Per Cent. 26	1.4
May 21, 1911	—	1,180,000	32	1.4
May 29, 1911	"606," 0.3 gram	—	—	—
May 30, 1911	—	1,300,000	34	1.3
June 12, 1911	"606," 0.3 gram	810,000	23	1.45
June 16, 1911	—	920,000	28	1.55
July 3, 1911	—	620,000	23	1.5
July 12, 1911	"606," 0.3 gram	730,000	22	1.55
July 28, 1911	—	585,000	17	1.45
Aug. 5, 1911	—	600,000	19	1.6
Nov. 11, 1911	—	3,100,000	66	1.1

comatose condition, then began to improve slowly, and in the course of a short time improved more rapidly.

November 11th. The patient saw me by request at the infirmary. He said he felt quite well and was able to walk considerable distances. He looked somewhat pale. Red corpuscles, 3,100,000; haemoglobin, 66 per cent.; colour index, 1.1.

He continued in good health and without any return of the anaemia until February, 1912, when he took an attack of acute croupous pneumonia and died.

The condition of the blood at different dates is shown in Table VI.

Remarks.—This was a very severe case of pernicious anaemia, complicated with otitis media. During the patient's stay in hospital the salvarsan treatment seemed to produce no benefit; when he left the hospital he was apparently in a dying condition; no one who saw him expected him to rally even temporarily; and yet, after getting home and being in a semi-conscious condition for ten days, he made a splendid recovery. Now, seeing that one knows that the salvarsan remains for many weeks encapsulated in the gluteal tissues and in a position to be absorbed into the system, I am strongly tempted to attribute the recovery to the salvarsan. The way in which Case iv has gradually improved during the past year, without any other treatment, lends, I think, some support to this view. I am, of course, aware that remarkable temporary rallies and apparent recoveries sometimes occur, apparently spontaneously, in cases of pernicious anaemia. I do not wish to attribute too much importance to the result in this case; all I say is that it is, I think, suggestive that it was perhaps due to the salvarsan.

CASE VII.

T. S., aged 55, married, foreman warehouseman, admitted to the Edinburgh Royal Infirmary on October 24th, 1911, suffering from profound pernicious anaemia.

Previous History.

Was well until July, 1910; then became weak, had occasional diarrhoea, and was confined to bed for two months; was treated with arsenic, recovered, and was able to work for eight or nine months. In May, 1911, had an attack of sciatica; has gradually got paler and weaker since, notwithstanding arsenical treatment. Denies venereal disease; no appearances suggestive of that disease.

State on Admission to Hospital.

The patient is feeble and old-looking, profoundly anaemic, very short of breath, feet swollen. Red corpuscles, 790,000; haemoglobin, 27 per cent.; colour index, 1.7; white corpuscles, 9,600; marked poikilocytosis, many megaloblasts, some normoblasts. No retinal haemorrhages.

October 27th. 0.3 gram "606," given subcutaneously produced very little pain and local reaction. Red corpuscles, 1,030,000; haemoglobin, 26 per cent.; colour index, 1.3.

November 4th. The patient has improved considerably. Red corpuscles, 1,460,000; haemoglobin, 25 per cent.; colour index, 0.8; white corpuscles, 5,600.

On the evening of this day he had a rigor, followed by a rise of temperature and the development of acute bronchopneumonia; he died on November 6th.

Post-mortem examination showed acute bronchopneumonia, with all the characteristic appearances of pernicious anaemia in the different organs and tissues.

The condition of the blood at different dates is shown in Table VII.

TABLE VII.

CASE VII.—Pernicious Anaemia. Showing the Results of Treatment.

Date.	Treatment.	Red Corpuscles.	Haemoglobin.	Colour Index.
Oct. 24, 1911	—	790,000	Per Cent. 27	1.7
Oct. 27, 1911	"606," 0.3 gram	1,030,000	26	1.3
Nov. 4, 1911	—	1,460,000	25	0.8

Remarks.—In this case bronchopneumonia occurred, and caused death a week after the administration of salvarsan. Whether the treatment had anything to do with the production of the bronchopneumonia it is, of course, impossible to say. During the week which supervened between the administration of the remedy and the occurrence of the bronchopneumonia, the general condition of the patient and the condition of the blood showed a distinct improvement.