The treatment of anaemia and chlorosis by the chief iron preparations commonly in use / by Andrew Smart.

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TREATMENT OF ANÆMIA AND CHLOROSIS

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CHIEF IRON PREPARATIONS COMMONLY IN USE.

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THE

TREATMENT OF ANÆMIA AND CHLOROSIS BY IRON.[1]

PROFESSOR BUNGE, in his admirable and most suggestive lectures,[2] affirms dogmatically that no satisfactory scientific proof of the efficacy of iron as a cure for chlorosis has yet been afforded. "Chlorosis," he continues, "is well known to be a malady which disappears without medical aid. Proof that a deficiency in hæmoglobin is more rapidly cured by giving preparations of iron could only be furnished by statistics. But no reliable and satisfactory material for statistics has yet been collected; in fact, it would be a very difficult matter to do so, as the malady is seldom treated in hospital." With reference to these statements we remark that the Professor's assertion that "chlorosis is a malady which frequently disappears without medical aid" is without foundation, and opposed to all clinical experience; and, secondly, that his affirmation that chlorosis is seldom treated in hospital is also based on misconception, certainly in reference to our practice in this country at least, where chlorotic patients are numerously present in all our hospital wards; and that consequently there are abundant, accumulating, and conclusive statistics in proof that chlorosis is not only more rapidly cured, but, moreover, that as regards the restoration of the hæmoglobin, it *cannot be cured* without iron in some form being administered. As to the nature of the vital processes by which the recovery of the hæmoglobin is brought about, existing opinion is not agreed, as the point is still in doubt whether the inorganic preparations of iron are, in any degree, absorbed. It would appear, however, to matter little what iron salt is introduced into the stomach, for probably by the action of the hydrochloric acid of the gastric juice, they are all converted into chlorides, which, in contact with the carbonate of soda always present in the intestinal canal, are changed into a ferrous carbon-

[1] The substance of this communication appeared in the *Lancet* in February 1893, and my best thanks are due to the Editor for kindly permitting me to use the blocks in this place.

[2] *Text-Book of Physiological and Pathological Chemistry.* By G. Bunge, Professor of Physiological Chemistry, University, Bâle.

ate which is soluble in carbonic acid and in organic substances. Finally, by the action of the sulphur compounds and hydrogen, etc., present in the bowel, the iron compounds are converted into sulphide of iron, and eliminated with the fæces. Then the all-important question arises, if the inorganic preparations of iron are not at all absorbed, how do they promote the formation of hæmoglobin? One supposition, consistent with all the requirements of the case, is available, and Professor Bunge adopts that view, namely, that the *organic* iron contained ready made in our food is in some way preserved from being decomposed through the protecting action of the *inorganic* preparations of iron which are administered as remedies. For example, it is known that alkaline combinations of sulphur, such as are present in the intestine, if brought into contact with the *organic* iron of the food, will separate the iron from the organic compound, and, for the purposes of nutrition, destroy it. If, however, *inorganic* iron compounds are at the same time present, they will at once fix the sulphur of the alkaline sulphides before it can act upon the organic iron of the food, so that the latter is protected from decomposition, is absorbed, and goes to maintain the hæmoglobin in its normal amount and integrity. But Professor Bunge admits that, in order to render inert the decomposing activity of the alkaline sulphides upon the organic iron, it is necessary to administer large quantities of inorganic iron; whereas if iron were only given to restore deficient hæmoglobin, a very small amount would suffice. It is therefore, as will be evident, a necessary consequence of Professor Bunge's views that, in the cure of chlorosis and of other allied maladies in which there is marked deficiency in hæmoglobin, iron, in some of its inorganic forms, must be largely administered.

The patients whose cases are here reported were under treatment in my Wards during 1891-2-3.[1] The cases include those of symptomatic anæmia, chlorosis, and pernicious anæmia; and the objects chiefly aimed at by the various trials were to satisfy me as to the relative efficacy of the chief ferruginous substances employed in their treatment; as also, whether our present views in regard to them were correctly founded; and, moreover, to enable me to decide differentially as to the importance to be ascribed to the varying quantities of red corpuscles and hæmoglobin which characterize the course of these diseases. Recognising the important *rôle* which hydrochloric acid fulfils in primary gastric digestion, I was disposed to believe that, at least, one considerable group of the anæmias originated in the initial failure of the albuminoids to undergo normal transformations through deficiency or complete absence of gastric hydrochloric acid, whereby blood

[1] George Wilson, M.A., M.B., C.M., R. O. Petrie, M.A., M.B., C.M., and Hugh L. Murray, L.R.C.P.E. & G., acting in succession as my house-physicians during the periods referred to.

impoverishment resulted, not necessarily in consequence of the active destruction of corpuscles, but through defect of the gastric processes to provide sufficient and suitable material indispensable for their normal construction. To test the correctness of this supposition, I selected a case of grave chlorosis, in which there was complete absence of free hydrochloric acid in the stomach, and which I treated with hydrochloric acid for a period of forty-two days as the sole therapeutical remedy, the patient receiving 100 minims daily of the dilute acid. The results of this treatment, as shown in the progress of the case, demonstrates conclusively that while the red corpuscles slowly tended to recover their normal numbers, the hæmoglobin remained stationary until iron was given. This result is entirely opposed to the statement of Zander, as cited by Bunge, to the effect that hydrochloric acid is a more effectual remedy for chlorosis than iron.[1]

Case I.—J. I., æt. 17, a shop girl, admitted to Ward 30, May 9th, 1892, suffering from chlorosis. There was no evident decrease in the number of red corpuscles, which were about 5,000,000 per cmm. Hæmoglobin was down to 40 per cent. Blood-cells were smaller than normal, and defective in form. The corpuscles remained almost stationary, and the hæmoglobin steadily rose to 86 per cent. This deviation from the usual course is characteristic of the chlorotic type of anæmia.

Treatment:—*Sulphate of Iron, with special diet, Port Wine, and Maltine.*—The slow recovery of the hæmoglobin was peculiar to chlorosis, and treatment was prolonged to forty days.

Fig. 1.

Progress.

	R. C.	Hb.o.
May 9th, . . .	5,110,000	40 per cent.
„ 28th, . . .	6,810,000	64 „
June 7th, . . .	5,240,000	70 „
„ 13th, . . .	5,780,000	80 „
„ 22nd, . . .	5,270,000	86 „

[1] Bunge, *Text-Book of Physiological and Pathological Chemistry* (English translation), 1890.

Case II.—J. D., æt. 18, admitted to Ward 30, November 21st, 1892, suffering from **symptomatic anæmia**, complicated with intercurrent influenza. The temperature on admission was 105° F.,

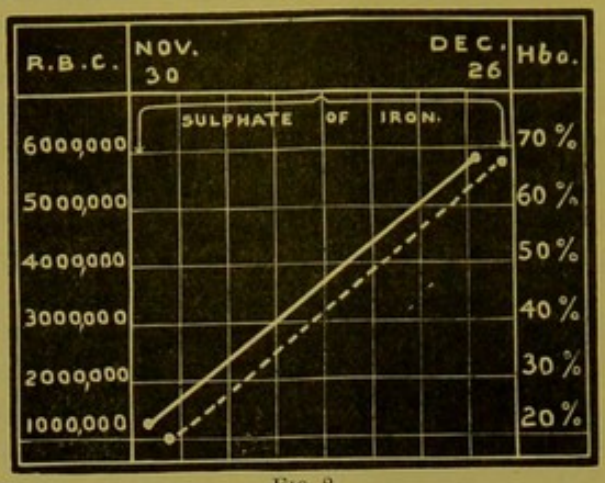

Fig. 2.

pulse 140, and respiration 48. By means of antipyrin her temperature was reduced in twenty-four hours to normal. Nine days after she was given ferri sulph. for the anæmia. The blood at the commencement of treatment was reduced to 1,150,000 red corpuscles per cmm., with 20 per cent. hæmoglobin. At the end of twenty-six days the red cells numbered 5,800,000 per cmm., and the hæmoglobin 68 per cent.

Treatment:—*Sulphate of Iron.*—The recovery of red corpuscles and hæmoglobin was equally progressive throughout. Cure in twenty-six days.

Progress.

	R. C.	Hb.o.
Nov. 30th, . .	1,150,000	20 per cent.
Dec. 26th, . .	5,850,000	68 „

Case III.—M. D., admitted to Ward 30, October 28th, with **symptomatic anæmia**. Red corpuscles were 1,590,000 per cmm.,

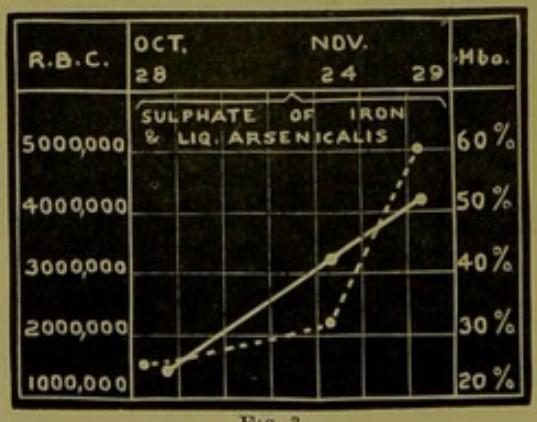

Fig. 3.

and hæmoglobin 25 per cent. Sulphate of iron and liquor arsenicalis were given. The effects were immediately apparent, and continued progressing until November 29th, when she left hospital

to resume work in a factory of her own accord. In ordinary circumstances she would not have left hospital for a couple of weeks longer, by which time the red corpuscles would have been over 5,000,000 per cmm., and hæmoglobin probably over 70 per cent. The case fairly shows the average time of recovery in symptomatic anæmia treated from the first with iron. It further shows the equal improvement in both constituents.

TREATMENT:—*Arsenic.*—Doubtful as to any specific effect on the blood corpuscles or hæmoglobin. It manifestly does not retard, and probably enhances the effects of the iron.

Sulphate of Iron.—Its twofold effect on the red corpuscles and hæmoglobin were at once apparent.

Progress.

	R. C.	Hb.o.
Oct. 28th, . .	1,590,000	25 per cent.
Nov. 24th, . .	3,240,000	31 „
„ 29th, . .	4,210,000	60 „

CASE IV.—B. R., æt. 18, admitted to Ward 30, October 24th, 1892, suffering from typical **chlorosis.** On admission she was put on ordinary ward diet, to which was afterwards added maltine and port wine, and this trial was continued for thirty-six days. During that space the red cells had increased from 1,030,000 per cmm. to 3,830,000 per cmm.; but the hæmoglobin had fallen from 38 per cent. to 32 per cent., so that as regards the hæmoglobin, the patient being on diet only, the whole of the trial had been retrograde. On December 1st perchloride of iron was given, and continued for fourteen days. At the end of that time the hæmoglobin had risen

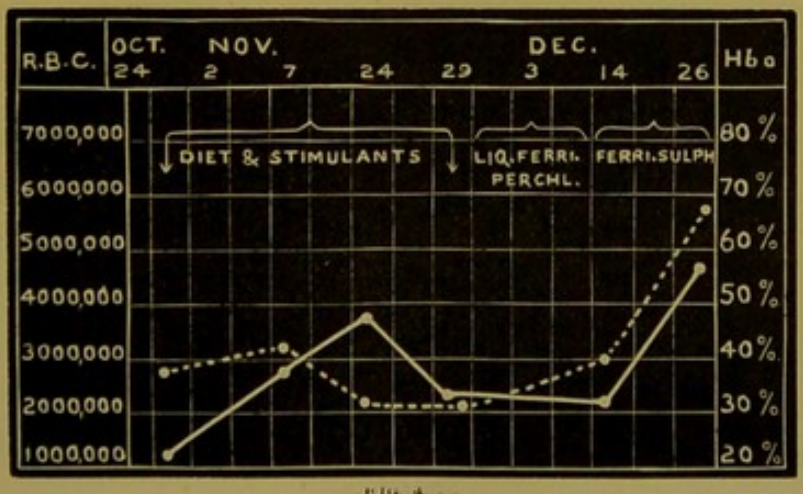

FIG. 4.

to 40 per cent., but the red cells were reduced to 2,000,000. This remedy proving unsatisfactory, the sulphate of iron was substituted for it on 14th December, and from that date there followed immediate and progressive increase in both constituents. On December 26th, when patient left hospital, the red corpuscles were 4,720,000 per cmm., and hæmoglobin 68 per cent.

Treatment:—*Diet.*—Thirty-six days. Increase of red corpuscles; diminution of hæmoglobin.

Perchloride of Iron.—Fourteen days. Increase of hæmoglobin; *reduction* of red cells.

Sulphate of Iron.—Twelve days. Progressive increase in hæmoglobin and red corpuscles.

Progress.

	R. C.	Hb.o.
Oct. 24th, . .	1,030,000	38 per cent.
Nov. 7th, . .	2,800,000	40 „
„ 14th, . .	3,800,000	32 „
„ 29th, . .	2,250,000	32 „
Dec. 14th, . .	2,100,000	40 „
„ 26th, . .	4,720,000	68 „

Case V.—K. M., æt. 21, admitted to Ward 30, June 25th, 1892, suffering from **symptomatic anæmia.** Her condition represented a severe type of the symptomatic group, with 2,600,000 red corpuscles per cmm. and 25 per cent. hæmoglobin. Both constituents remained stationary at the end of eight days on diet only. On July 3rd, 5 minims of Liquor arsenicalis were given three times daily, the dose being gradually increased to 30 minims daily. On July 10th, hæmoglobin and red corpuscles were unaltered. Sulphate of iron was substituted for the arsenic, and hæmoglobin and red corpuscles markedly increased from that date. On August 16th, when patient was discharged in perfect health, red corpuscles were 6,400,000 per cmm., and hæmoglobin 66 per cent. By comparison with chlorosis, the difference in this case of symptomatic anæmia

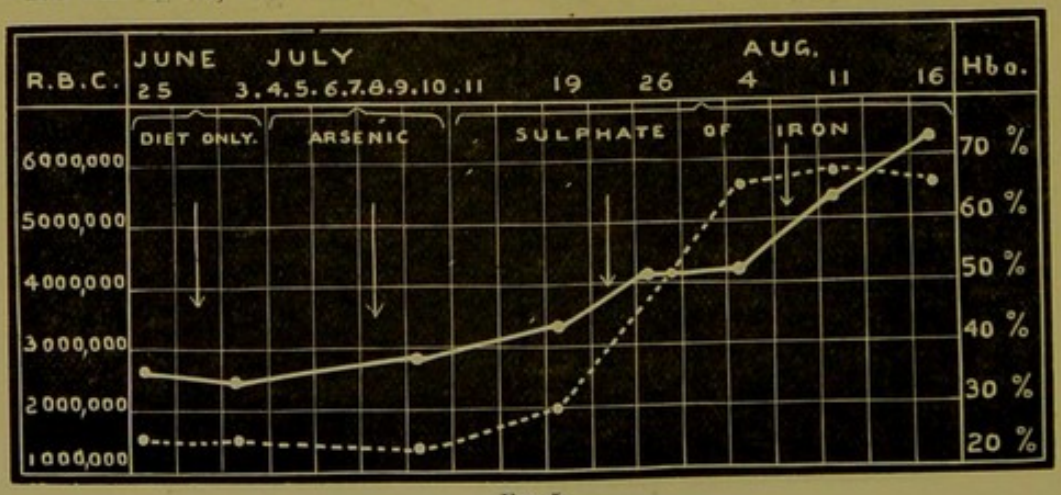

Fig. 5.

is strikingly brought out in the much more rapid and concurrent progress in both hæmoglobin and red corpuscles.

Treatment:—*Diet.*—No improvement.

Arsenic.—Improvement doubtful.

Sulphate of Iron.—Immediate and continued improvement in red corpuscles and hæmoglobin.

Progress.

	R. C.	Hb.o.
June 25th, . .	2,600,000	25 per cent.
July 3rd, . .	2,500,000	25 „
„ 10th, . .	2,900,000	25 „
„ 19th, . .	3,300,000	30 „
„ 26th, . .	4,200,000	52 „
Aug. 4th, . .	5,200,000	66 „
„ 11th, . .	5,400,000	65 „
„ 16th, . .	6,400,000	66 „

CASE VI.—M.C., æt. 20, a waitress, admitted to Ward 30, July 19th, 1892. She was suffering from advanced **chlorosis.** Red corpuscles were 1,900,000 per cmm., and hæmoglobin 40 per cent. During the first ten days, on diet alone, the corpuscles fell to 1,500,000, and hæmoglobin to 30 per cent. On July 27th she was given 15 grs. peroxide of iron thrice daily. On August 4th red corpuscles were 3,800,000 per cmm., and hæmoglobin 46 per cent. Steady progress was made, and on August 24th red corpuscles were 6,000,000 per cmm., and hæmoglobin 70 per cent. She was twenty-six days on peroxide of iron.

TREATMENT:—*Diet Alone.*—Reduction in red corpuscles and in hæmoglobin.

Peroxide of Iron.—Marked immediate increase of both constituents, with complete recovery in twenty-six days.

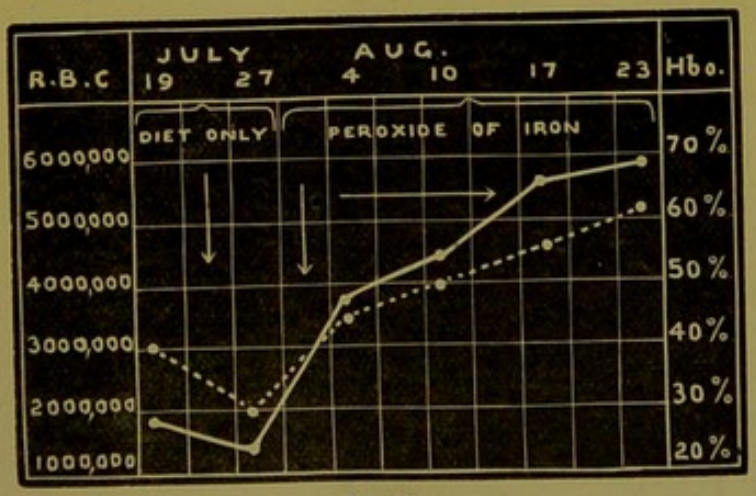

FIG. 6.

Progress.

	R. C.	Hb.o.
July 7th, . .	1,900,000	40 per cent.
„ 27th, . .	1,500,000	30 „
Aug. 4th, . .	3,800,000	46 „
„ 10th, . .	4,600,000	50 „
„ 17th, . .	5,600,000	56 „
„ 23rd, .	5,800,000	62 „

Case VII.—I. S., æt. 24, admitted to Ward 30, May 14, 1892, with marked **chlorosis**,—3,600,000 red corpuscles per cmm., and 28 per cent. hæmoglobin. At first she was put on diet with port wine and maltine, and continued for twelve days, at end of which corpuscles were 5,900,000, and hæmoglobin only 38 per cent. Notwithstanding the relatively large increase in the corpuscles, the patient did not show evidence of being in a really improved state. At this stage sulphate of iron, 7 grs. thrice daily, was begun, and there was an immediate increase in both hæmoglobin and red corpuscles; and on July 26th, when she left the Infirmary in perfect health, she had hæmoglobin 80 per cent. and 6,500,000 red corpuscles per cmm. The point of chief clinical interest to be noticed in this typical case of chlorosis is the comparatively slow rate of increase in the hæmoglobin and the rapid and excessive restoration of red blood-cells. I have found this feature characteristic of the whole group of chlorotic cases, marking a difference whereby chlorosis may generally be distinguished from symptomatic anæmia. As indicating that chlorosis is a graver type of anæmia than that of the symptomatic form, it may be added that not only does the hæmoglobin recover slowly, but that the corpuscles remain for a longer period defective in size and shape. The patient was fifty-nine days on iron treatment.

Treatment :—*Diet, with Port Wine and Maltine.*—Rapid relative increase of red blood-cells ; slight relative increase in hæmoglobin ; no change in size and shape of corpuscles.

Sulphate of Iron.—Progressive increase in hæmoglobin and red cells, and the latter recover their normal shape.

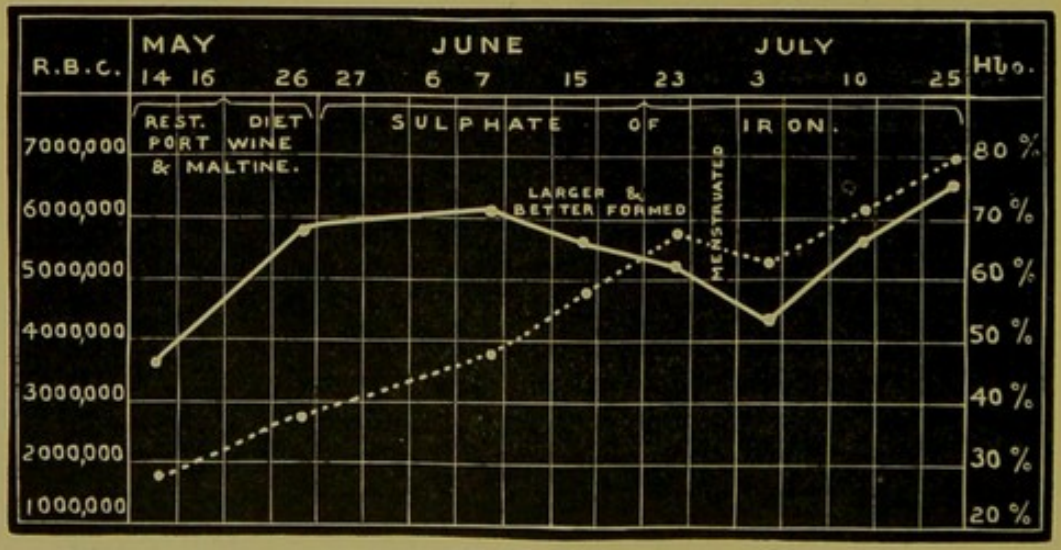

Fig. 7.

Progress.

	R. C.	Hb.o.
May 14th, . .	3,600,000	28 per cent.
„ 27th, . .	5,900,000	38 „

	R. C.	Hb.o.
June 7th, . .	6,100,000	49 per cent.
„ 15th, . .	5,600,000	58 „
„ 23rd, . .	5,300,000	68 „
July 3rd, . .	*4,500,000	*64 „
„ 10th, . .	5,800,000	74 „
„ 25th, . .	6,500,000	80 „

* Menstruation.

Case VIII.—J. L., æt. 17, admitted to Ward 30, July 18th, with **symptomatic anæmia.** For nine days she was on diet alone, and hæmoglobin increased from 30 to 40 per cent., corpuscles remaining at 2,000,000. On July 27th phosphate of iron, 7 grs. thrice daily, was given, afterwards increased to 10 grs. The hæmoglobin and red corpuscles increased to 70 per cent. and 5,800,000 per cmm. respectively on September 9th. Patient was forty-three days on ferri phos.

Treatment:—*Diet Alone.*—Hæmoglobin moderately increased; corpuscles stationary.

Phosphate of Iron.—Hæmoglobin and corpuscles recovered but slowly.

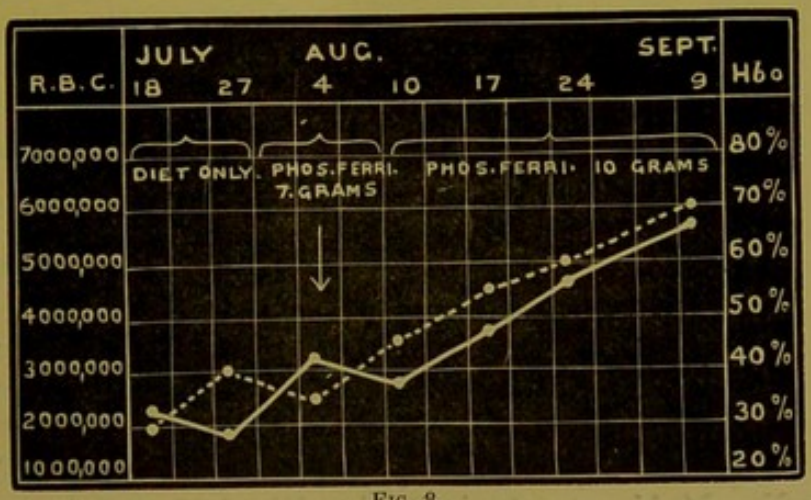

Fig. 8.

Progress.

	R. C.	Hb.o.
July 18th, . .	2,500,000	30 per cent.
„ 27th, . .	2,900,000	40 „
Aug. 4th, . .	3,400,000	35 „
„ 10th, . .	3,000,000	43 „
„ 17th, . .	3,800,000	53 „
„ 24th, . .	4,800,000	60 „
Sept. 9th, . .	5,800,000	70 „

Case IX.—M. G., æt. 19, admitted to Ward 30, November 4th, 1891, suffering from **symptomatic anæmia.** On admission red corpuscles were 1,900,000 per cmm., and hæmoglobin 10 per cent. She was put on peroxide of iron, and continued for fifteen days; the corpuscles fell to 1,640,000, but hæmoglobin increased to 26 per cent.

Six days later the red cells had increased to their original number, and hæmoglobin fallen to 20 per cent. Peroxide was now suspended,

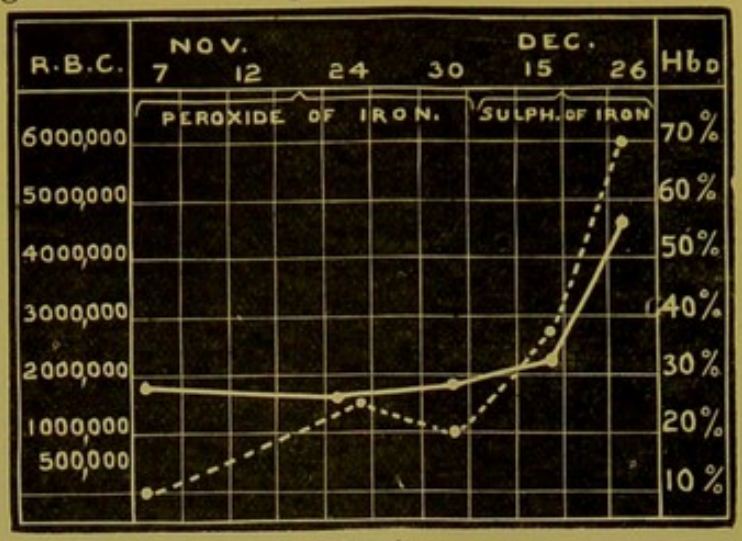

Fig. 9.

and sulphate given. After fifteen days corpuscles were 2,250,000 per cmm., and hæmoglobin 38 per cent., and seven days later cells were 4,630,000, and hæmoglobin 70 per cent. The actual time under sulphate of iron was twenty-six days. The three weeks' trial with peroxide of iron is practically out of account.

Treatment :—*Peroxide of Iron.*—Results negative.

Sulphate of Iron.—Normal restitution of corpuscles and hæmoglobin in twenty-six days.

Progress.

	R. C.	Hb.o.
Nov. 6th, . .	1,980,000	10 per cent.
„ 24th, . .	1,640,000	26 „
„ 30th, . .	1,900,000	20 „
Dec. 15th, . .	2,250,000	38 „
„ 26th, . .	4,630,000	70 „

Case X.—M. M., æt. 22, admitted to Ward 30 on July 19th, 1892,

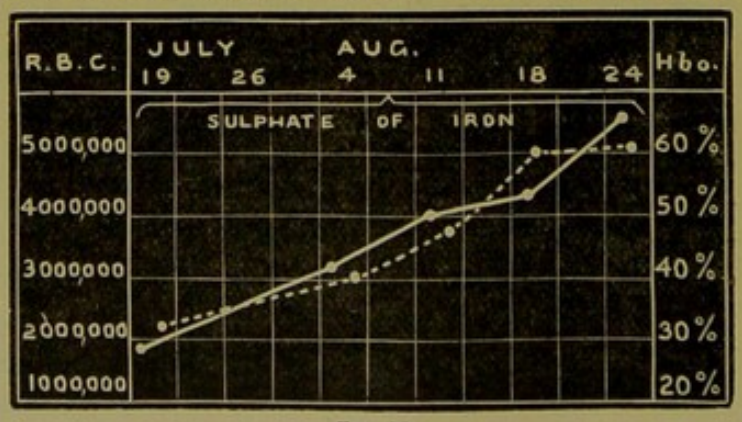

Fig. 10.

with **symptomatic anæmia,** red corpuscles being 2,000,000, and hæmoglobin 30 per cent. She was given sulphate of iron, 7 grs.

thrice daily, and in fourteen days corpuscles were 3,200,000, and hæmoglobin 40 per cent., and in thirty-five days corpuscles were 5,700,000, and hæmoglobin 62 per cent., and patient was discharged cured.

TREATMENT:—*Sulphate of Iron.*—This case shows the superior efficacy of this iron salt in its comparatively quick and reliable effects on all anæmias and in chlorosis, and in the uniformity of its beneficial effects alike upon blood cells and hæmoglobin.

Progress.

	R. C.	Hb.o.
July 19th, . .	1,900,000	32 per cent.
Aug. 4th, . .	3,200,000	40 ,,
,, 11th, . .	4,000,000	48 ,,
,, 18th, . .	4,300,000	60 ,,
,, 24th, . .	5,700,000	62 ,,

CASES XI. and XIA.—J. C. and A. C., two sisters, admitted to Ward 30, one on November 11th, and other on November 28th, both suffering from **symptomatic anæmia** nearly in the same degree, except that it was somewhat more advanced in the former, and consequently somewhat longer delayed in recovery. Both were put on saccharated carbonate of iron, 20 grs. thrice daily. Between November 11th and December 13th red corpuscles increased from 3,400,000 to 6,000,000 per cmm. in J. C.'s case, and the hæmoglobin from 52 per cent. to 68 per cent., when she left the hospital cured. The red cells in A. C.'s case on admission were 3,800,000, and hæmoglobin 55 per cent., and on December 17th they were 5,500,000 and 76 per cent. respectively.

TREATMENT.—These cases of treatment by the carbonate of iron may be taken as fairly showing the effects of this preparation of iron on symptomatic anæmia and chlorosis. As a remedy it is well borne in all cases, and is rapid and curative in its effects. It is on

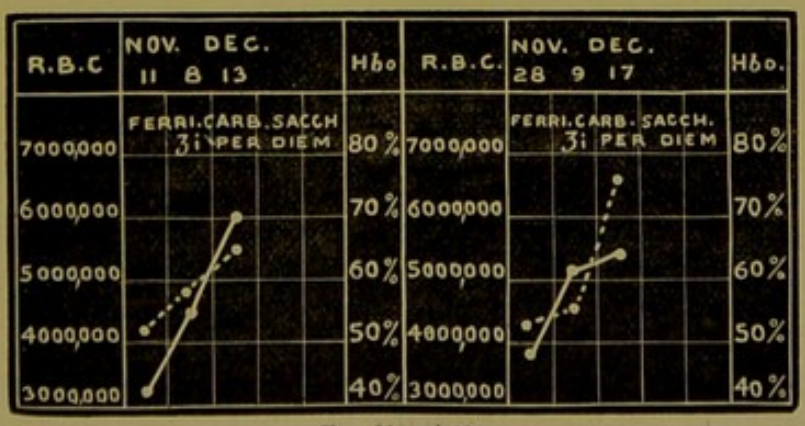

FIG. 11 and 11A.

these accounts entitled to rank as among the best of our iron remedies, and second only to the sulphate of iron, if not indeed upon a par with it.

Case XII.—J. S., æt. 20, admitted to Ward 33 on October 24th, 1892, with **symptomatic anæmia**, with progressive history of

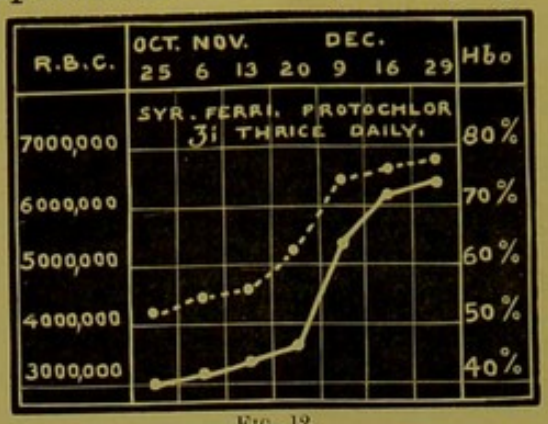

Fig. 12.

the disease. Red corpuscles were 3,400,000, and hæmoglobin 52 per cent. The diet being carefully arranged to suit her impaired digestion, she was put upon the protochloride of iron, 1 drachm thrice daily after meals.

Treatment:—*Protochloride of Iron.*—This was continued for sixty-five days, when the corpuscles were 6,500,000, and hæmoglobin 75 per cent. The drawback to the remedy was its causing sickness and vomiting, on account of which it had to be more than once suspended for a few days at a time, whereby the duration of the treatment was protracted. To avoid this, it should be given in smaller doses to begin with until toleration of the remedy is induced, increasing it from ½ to 1 drachm. Making allowance for this drawback, it is entitled to rank among the most efficient remedies.

Progress.

	R. C.	Hb.o.
Oct. 25th, . .	3,000,000	52 per cent.
Nov. 6th, . .	3,200,000	55 „
„ 13th, . .	3,500,000	56 „
„ 20th, . .	3,700,000	62 „
Dec. 9th, . .	5,500,000	76 „
„ 16th, . .	6,200,000	78 „
„ 29th, . .	6,500,000	79 „

Case XIII.[1]—M. W., æt. 18, admitted to Ward 33 on November 5th, 1892, with advanced **chlorosis.** Her condition was characterized by unusual pallor, prostration, palpitation, with loud hæmic murmurs in the neck and at base and apex of heart, amenorrhœa, and a severe type of atonic dyspepsia, the gastric contents showing absence in a marked degree of free hydrochloric acid. An examination of the blood showed 3,000,000 per cmm. of corpuscles

[1] Until after this case was published I was not aware that Dr Hale White of Guy's Hospital, London, had been making similar observations with reference to the hydrochloric acid treatment. I am pleased to find that the results obtained are in complete agreement.

and 32 per cent. hæmoglobin. The patient's condition presented a suitable opportunity of testing how far her anæmic state had been brought about in consequence of the atonic dyspepsia which had preceded and accompanied it, more especially with reference to the absence of free hydrochloric acid, so marked a feature in her dyspepsia. I accordingly decided to treat her with free HCl in the first instance. This was begun on sixth day after admission, ℥ 100 of acid hydrochlor. dil. daily being given. After seven days the red cells and hæmoglobin had remained stationary, the patient, however, taking food much better, and her dyspepsia being entirely relieved. On December 16th the corpuscles had risen to 4,000,000 per cmm., but hæmoglobin remained at 36 per cent., the latter having only increased 4 per cent. in thirty-six days. This increase was no doubt owing to the action of the phosphate of iron, which was given in 24-gr. doses during the last week of this period. At this stage of imperfect recovery the patient left the hospital to go to her home in the country much against my wish, so that we lost from that time all further account of the case. I have no doubt, however, that had she remained under the hydrochloric acid treatment the red corpuscles would have been restored to their normal number. But it is evident, from the low standard at which the hæmoglobin remained, that her condition would eventually have resulted in her disease being uncured, seeing that the defect of hæmoglobin constituted the essential feature of her anæmia, which, as I have already pointed out in previous cases, is the pathological feature which distinguishes chlorosis from symptomatic anæmia on the one hand, and from pernicious anæmia on the other. It follows from the results of this trial that, while HCl is of great value in improving the tone of the digestive functions generally, no doubt

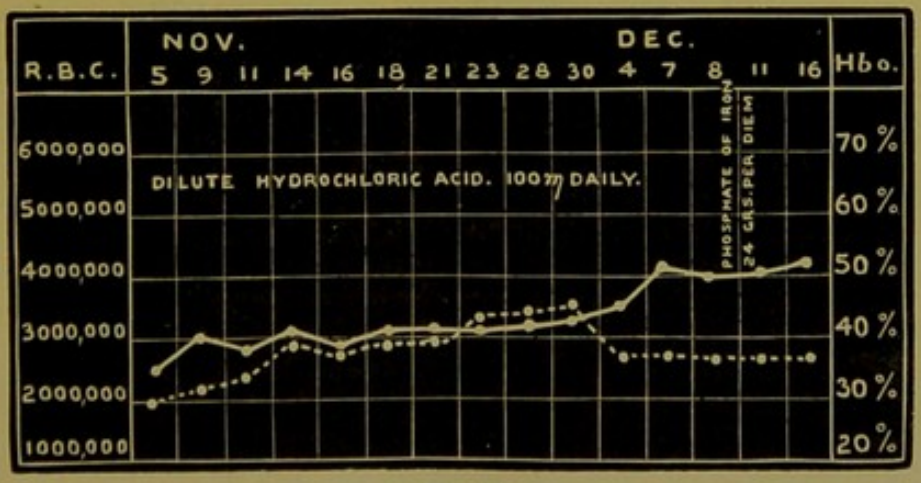

Fig. 13.

by favouring the digestion of the proteids, it nevertheless fails by itself to restore the hæmoglobin; so that in chlorosis, as in symptomatic anæmia, and even more so, it is necessary to have recourse to some form of iron in order to establish perfect recovery.

Treatment:—*Hydrochloric Acid.*

Case XIV.—A. H., æt. 26, admitted to Ward 30 on November 3rd, 1891, with **symptomatic anæmia** and secondary erythema nodo-

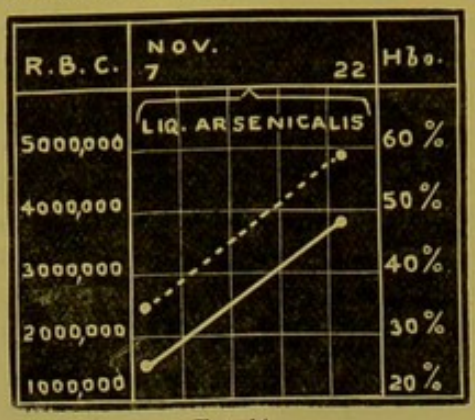

Fig. 14.

sum. Red corpuscles were 1,590,000 per cmm., and hæmoglobin 35 per cent. Fowler's solution, ℥5 thrice daily, was given, increased to ℥10. After fifteen days patient left hospital with 3,850,000 corpuscles per cmm. and 59 per cent. hæmoglobin. The arsenic in this case must be regarded as only indirectly promoting the restoration of the blood-cells and hæmoglobin by its direct and primary effect upon the constitutional condition with which the erythema was connected, the anæmia being only a secondary sequence to it. We have, however, had many proofs that arsenic when given combined with the iron, co-operates beneficially in some cases in expediting recovery from anæmia, very probably by its improving some constitutional defect upon which the anæmia may partly depend.

Treatment:—*Arsenic.*

Case XV.—Mrs A., æt. 53, came under my observation in the autumn of 1891. Her red corpuscles were 600,000 per cmm., and

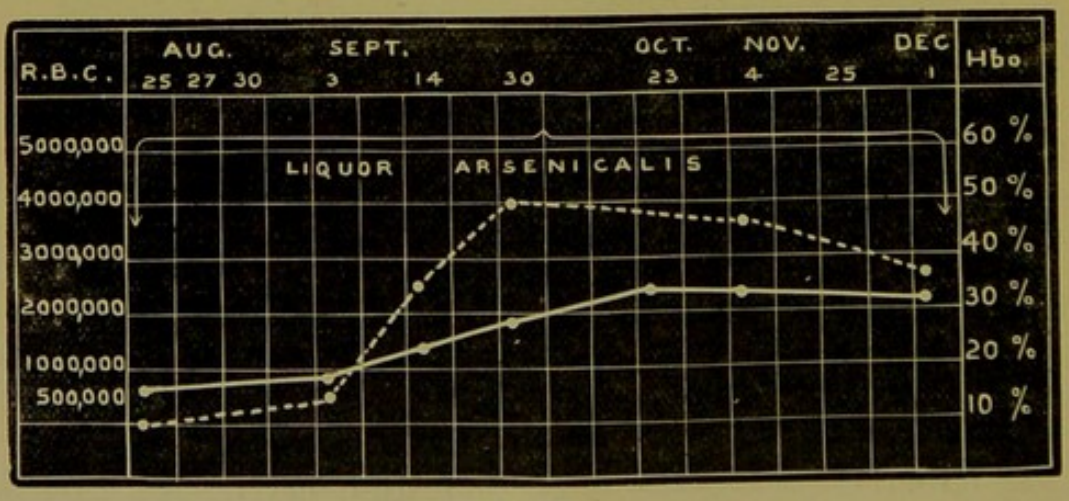

Fig. 15.

hæmoglobin 10 per cent. The irregular shapes which characterized the blood discs, the splenic enlargement, the lemon tint of the patient's complexion, and her general cachexy, left me in no

doubt that the disease was **pernicious anæmia**; and I cite her case to show by contrast that, while exhibiting iron and other tonics of the same class, there was no evident improvement in the amount of hæmoglobin or on the number and character of the red cells until arsenic was added to the treatment. Fowler's solution was given, ℥5 thrice daily, gradually increased to over double that amount. This treatment, combined with full doses of citrate of iron and quinine (10 grs. thrice daily), with a special food dietary, enhanced by the addition of port wine and maltine, after many weeks brought about an improvement in her condition, well shown by the red corpuscles having increased to 2,480,000 per cmm., and hæmoglobin to 50 per cent. At this stage in the course of her treatment, at her own request, she left the hospital for her home in the south of Scotland, where she is at present, much in the same condition of health as at the time of her discharge. It should be added that she was under arsenical treatment while in hospital for a period of three months.

Progress.

	R. C.	Hb.o.
Aug. 25th, . .	640,000	10 per cent.
Sept. 3rd, . .	910,000	15 „
„ 14th, . .	1,450,000	35 „
„ 30th, . .	1,810,000	50 „
Nov. 4th, . .	2,480,000	45 „
Dec. 1st, . .	2,160,000	35 „

Case XVI.—K. S., æt. 21, admitted to Ward 33, suffering from **chlorosis**, March 20, 1893. The blood condition was—red corpuscles 3,000,000 per cmm., and hæmoglobin 28 per cent. She was put on Liquor mangano-ferri peptonati (Hockin) in doses of a drachm thrice daily, increased subsequently to 2 drachms. It was found that the corpuscles improved considerably, but the hæmoglobin remained stationary, so that on May 1st corpuscles numbered 4,500,000, but hæmoglobin only 26 per cent. The drug was now changed, and the sulphate of iron given, with the result that the hæmoglobin at once increased, and on May 23rd it had risen to 70 per cent., the corpuscles having advanced to 5,300,000 per cmm. On admission there was considerable atonic dyspepsia, which was very much improved and relieved by hydrochloric acid before food.

She was discharged cured on May 27th. The sudden rise of hæmoglobin on changing the drug was very marked.

Treatment:—(1) *Peptonate of Iron and Manganese;* (2) *Sulphate of Iron.*

Progress.

	R. C.	Hb.o.
March 20th, . .	3,000,000	28 per cent.
May 1st, . .	4,500,000	26 „
„ 23rd, . .	5,300,000	70 „

Case XVII.—J. C., æt. 28, admitted to Ward 33 on April 8th, 1893, suffering from **symptomatic anæmia**. Her red corpuscles were 2,800,000 per cmm., and hæmoglobin 34 per cent. She was put on bipalatinoids (ferri sulph. exsic., gr. j., and sodii sulph. exsic., gr. $\frac{5}{8}$), three being given thrice daily. This was increased to first six and afterwards nine thrice daily. On April 20th there was but slight improvement, red corpuscles being 3,500,000 per cmm., and hæmoglobin 33 per cent.

The ferri sulph. was given now alone, with the result that there at once was a marked rise in hæmoglobin, so that on May 3rd corpuscles numbered 4,300,000, and hæmoglobin 60 per cent.

Progress.

	R. C.	Hb.o.
April 8th, . .	2,800,000	34 per cent.
„ 20th, . .	3,500,000	33 „
May 3rd, . .	4,300,000	60 „

Case XVIII.—M. F., æt. 18, admitted to Ward 33 on April 1st, suffering from symptomatic anæmia. The red corpuscles were 2,300,000 per cmm., and hæmoglobin 22 per cent. She was given the bipalatinoids, three thrice daily, and in ten days corpuscles were 2,800,000, and hæmoglobin 25 per cent., there being but slight improvement in the latter. The drug was now changed to the sulphate of iron, 8 grs. thrice daily, with the result that the hæmoglobin increased markedly, being on April 26th 52 per cent., with corpuscles at 5,800,000 per cmm.

Treatment:—(1) *Bipalatinoids;* (2) *Sulphate of Iron alone.*

Progress.

	R. C.	Hb.o.
April 1st, . .	2,300,000	22 per cent.
„ 11th, . .	2,800,000	25 „
„ 26th, . .	5,800,000	52 „

Case XIX.—Mrs G., æt. 33, was admitted to Ward 33 on May 30th, 1893, suffering from **chlorosis**. The red corpuscles were 3,300,000 per cmm., with the hæmoglobin at 36 per cent. She was given ferri sulph. from the date of admission, and on June 30th the red corpuscles were 5,800,000 per cmm., with the hæmoglobin at 60 per cent.; and on August 1st, when she was discharged, red corpuscles were 6,500,000, with hæmoglobin at 72 per cent.

Treatment:—*Sulphate of Iron.*

Progress.

	R. C.	Hb.o.
May 30th, . .	3,300,000	36 per cent.
June 30th, . .	5,800,000	60 „
Aug. 1st, .	6,500,000	72 „

Case XX.—L. I., æt. 19, admitted to Ward 33 on April 4th, suffering from **chlorosis**. Her corpuscles were 2,200,000 per cmm., and hæmoglobin 28 per cent. The sulphate of iron was again given,—at first in 4-grain doses thrice daily, afterwards increased to 8 grs.; and on May 15th, forty days after admission, her corpuscles numbered 5,600,000, with hæmoglobin at 78 per cent.

Treatment:—*Sulphate of Iron.*

Progress.

	R. C.	Hb.o.
April 4th, . .	2,200,000	28 per cent.
May 15th, . .	5,600,000	78 „

General Conclusions.

1. *Sulphate of Iron.*—Of the varieties of iron used in the trials here recorded, the best results have been obtained from the sulphate. This accords with my previous experience of all the trials made. It is the preparation which undoubtedly possesses the greatest therapeutical activity, and the one which, in the different varieties of the disease and constitutional differences of the anæmic patients, may most uniformly be depended upon for satisfactory results. In anæmic patients who suffer markedly, as many of them do, from atonic dyspepsia, and in whom consequently the hydrochloric acid is either greatly deficient or absent, it is of great advantage to their recovery to prescribe 15 to 25 minims of dilute hydrochloric acid shortly before meals, the iron salt being taken shortly after meals. But, on the contrary, to those patients whose stomach complaints are of an opposite nature, being due to excess of acid (pyrosis), acid in any form cannot be given; the substitution in these cases of 10 grains each of bicarbonate of soda and carbonate of potash before meals will be of material assistance to the stomach by inducing tolerance of the iron, and thereby expediting recovery. In assigning the first place to the iron sulphate as a remedy, I am guided by the whole of the circumstances connected with each case in which trial was made. As a remedy it is exceptionally active in restoring the deficient corpuscles alike in their number and character, and also is notably active in restoring hæmoglobin in chlorosis.

2. *Saccharated Carbonate of Iron.*—Numerous trials with this preparation, only two results of which are shown on the Charts (Fig. 11 and 11A), were uniformly of a favourable character in the different types and stages of the disease in which it was given. It is invariably well tolerated, whatever be the nature of the dyspepsia from which the patient suffers. It is given in doses varying from 20 to 30 grains thrice daily, with, or immediately after, meals. On these grounds I consider it entitled to rank as second best therapeutic iron.

3. *Protochloride of Iron.*—This preparation was given, in the form of the syrup, in 1 drachm doses thrice daily after meals. Each drachm of the syrup contained 7 grains of the protochloride. As during its administration it repeatedly brought on nausea, and had consequently to be suspended for a time, it would be better to avoid this drawback by giving it at the commencement in smaller doses, and increasing it gradually to the 1 drachm dose as mentioned above. Making allowance for the delay caused in this way by the suspension of the remedy, and its liability to induce intolerance, it is entitled to hold at least a third place in the grade of efficacy of these remedies. Recovery under its administration is otherwise in every respect satisfactory and complete.

4. *Phosphate of Iron* yielded excellent results only in some of the patients treated by it; but in others it apparently failed, its effects being only appreciable after considerably protracted treatment. The beneficial character was apparent in those types of the disease in which there existed constitutional conditions allied to neuroses.

5. *Peroxide of Iron.*—This iron in some cases yielded only negative results, but in other cases its effects were satisfactory. This difference may depend upon individual peculiarities of constitution. It cannot, therefore, as a remedy be relied upon in all cases.

6. *Perchloride of Iron.*—The same may be said of this iron as of the preceding, but less satisfactorily. The results of trials with it were in most cases negative.

7. *Peptonate of Iron and Manganese.*—This makes rather a pleasant mixture, and is not accompanied by any disagreeable stomach troubles if given in small doses to start with. I gave a drachm, and gradually increased the dose to two. The results as regards the corpuscles were good; but it was not until adding the sulphate that the hæmoglobin advanced to a proportionate extent. Consequently, by itself it is not equal in value to several of the other salts of iron mentioned above.

8. *Bipalatinoids.*—A combination of iron sulphate and exsiccated sulphate of soda. This combination was tried in several cases with more or less success. At first three bipalatinoids were given thrice daily, but the results were very slight. The dose was increased, and six and afterwards nine were given thrice daily. It is an undoubtedly elegant preparation, and patients take them without difficulty; but beneficial results are too long delayed to be satisfactory and to render the treatment by them generally useful.

9. *Arsenic.*—This remedy when combined with iron is evidently useful as an alterative; but, as the results of the trials made with it as the sole remedy showed, it did not appear to exert any direct or appreciable effect on the renewal of the red blood-corpuscles and hæmoglobin in the cases of symptomatic anæmia and chlorosis in which it was tried. When, however, combined with an iron salt, especially the sulphate, I could not avoid being convinced that the efficacy of the iron was enhanced by the combination.

10. In pernicious anæmia, however, as is well seen in Case 15, arsenic exerts a distinctly noticeable effect in promoting recovery, alike of red blood-corpuscles and hæmoglobin. Although iron was long and freely exhibited in Mrs A.'s case, no evident effects of a constructive kind were produced upon the corpuscles and hæmoglobin until arsenic was added to the treatment; and not even then until full doses (20 to 30 minims of Fowler's solution daily) had been continued for some time. It is, however, rare, and indeed exceptional, in pernicious anæmia, to be able to administer arsenic in almost any dose except the smallest,—that is, only a few minims daily,—on account of the extreme intolerance of it, so that in the majority of cases it is practically out of account as a remedy.

11. It will doubtless have been observed that in several of the cases referred to the red corpuscles numerically exceeded, in some instances by 2,000,000 per cmm., the usual standard number of 5,000,000 per cmm. This excess having been found repeatedly, I am led to believe that, by the treatment being continued, a similar result would have been obtained in most, if not all, the cases. It would appear from this discrepancy that an estimation of red corpuscles at 5,000,000 per cmm. is too low a standard.

12. On the other hand, speaking with reference to the hæmoglobin, I must observe that I have never yet succeeded in raising the hæmoglobin to a standard of 100 per cent. The highest obtained has never exceeded 90 per cent., and that amount only in instances of exceptionally robust health. My experience, therefore, leads me to believe that 80 per cent. is a good health standard, and that 70 per cent., or even under, may be taken as a fair average estimate at which patients may be discharged from hospital treatment, provided that the red cells are over 4,000,000 per cmm. It would appear from these results that our views in regard to the relative estimation of the red corpuscles and hæmoglobin require to be modified in accordance with these trials.

13. I have repeatedly had occasion to notice certain differences between symptomatic anæmia and chlorosis which I have not before seen referred to, but which are of importance as diagnostic signs. In the latter the red cells and hæmoglobin do not bear the same definite relation to one another in their decrease and increase which may be observed in symptomatic anæmia. I have several times recorded cases of advanced chlorosis in which there was present a high numerical standard of red corpuscles (over 5,000,000 per cmm.), while at the same time the hæmoglobin did not exceed 25 per cent. Such cases might not improperly be designated hæmoglobin anæmia in the same sense as we speak of a pernicious anæmia as corpuscular. The low standard of hæmoglobin in chlorosis represents the chief pathological feature in that disease, as do the reduced numbers and defective morphological characters of the red globules in pernicious anæmia. In consequence of the comparatively slow recuperation of the hæmoglobin in chlorosis,

the recovery of these cases is longer delayed than in those of symptomatic anæmia, and besides this there is observed in the red globules a decided proclivity to undergo morphological degeneration. These special differences lead us to regard chlorosis pathologically as a graver type of anæmia than symptomatic anæmia, although at the same time it specifically differs from the pernicious type.

14. I would here again revert to the very severe type of anæmia referred to at the outset as being put under treatment by hydrochloric acid as the sole therapeutic remedy. I am not aware of this treatment having previously been tried.[1] Many anæmias doubtless originate in defects of the primary gastric digestion caused by either deficiency or complete absence of free hydrochloric acid in the stomach, the consequence of which is that the proteids, not undergoing normal metamorphosis, are largely thrown out of the system as waste, and lost. This method of treatment by hydrochloric acid can only be of use in cases in which there is present that condition of atonic dyspepsia in which the hydrochloric acid is, as I have said, markedly deficient or entirely absent. This type of dyspepsia, however, is characteristic of a large number of anæmias at the commencement of as well as throughout their entire course. The result of the trial by hydrochloric acid will be seen by referring to Case 13. During the forty-two days the patient was under this treatment the red corpuscles increased from 2,500,000 to 4,200,000 per cmm., and during that long period the hæmoglobin only rose from 30 to 36 per cent. The patient at this stage of incomplete treatment left the hospital of her own accord. It was evident, however, that whilst longer continued treatment would have raised the corpuscles to 5,000,000 per cmm., it would not have materially increased the hæmoglobin from the low standard at which it had apparently become stationary. The result of this clinical experiment, as that of every other, proves that iron in some form is absolutely indispensable in the treatment of chlorosis as well as of symptomatic anæmia to effect complete recovery.

15. In each of the anæmias here reported there co-existed chronic constipation, and the urine in each case yielded the roseate colour with nitric acid, referred to by M'Munn in his *Chemistry of the Urine*, as an indication of the destruction of red blood-corpuscles. To what extent, if at all, this colour reaction indicates blood destruction through the agency of reabsorbed toxic materials from the *prima via*, as Sir Andrew Clark suggested, remains to be determined by further investigation.

The following anatomical and pathological distinctions have been suggested in the course of these trials as marking off diagnostic differences between the three grades of anæmia :—(1.) In symptomatic anæmia there exists a constant proportionate relation

[1] See footnote, page 14.

between the number of red corpuscles and the amount of hæmoglobin. They diminish relatively during the course of the disease, and increase relatively during recovery, the iron being deficient as to the whole blood and each cell relatively. (2.) In chlorosis the relation between the number of red corpuscles and the hæmoglobin is entirely broken. The hæmoglobin is markedly deficient relatively to each cell and to the whole blood. The low relative amount of hæmoglobin is the chief pathological determining feature in chlorosis, and points to the low amount of iron, which in this type of the disease is, *par excellence*, to be regarded as the specific remedy in its treatment. (3.) In pernicious anæmia the normal relation between the red cells and the hæmoglobin is also disturbed. The iron is in excess in each cell, and also in proportion to the whole blood. The great diminution in the number of red cells, and the relative excess of the hæmoglobin in relation to them and to the whole blood, are the distinguishing features in this anæmia, so that as chlorosis may be regarded as a hæmoglobin anæmia, pernicious anæmia may be viewed as a red corpuscular anæmia, that being the chief point of difference between them. The excess of iron present in the blood of pernicious anæmia plainly contra-indicates its employment in the treatment of that disease, except, in small quantities as an alterative. Arsenic (Fowler's solution), when tolerated and continued by a patient suffering under pernicious anæmia, is a preferable remedy. It is, however, only borne in certain cases, and in every case the tolerance of it is to be acquired by giving it in small doses at the beginning and gradually increasing it. Quinine is markedly useful in that group of pernicious anæmias in which there is splenic enlargement, and its beneficial effects are enhanced when combined with moderate doses of iron. The best drug in such a case is the citrate of iron and quinine given in full doses. My recent experiences in connexion with the treatment of pernicious anæmia by the transfusion of healthy blood is leading me to attach much importance to that mode of treatment.

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