

PRESSURE ON SPACE.

Notice to Correspondents and Authors of Communications.

IN view of the great and constantly-increasing pressure on our space, we would urgently request correspondents and authors of communications to assist us in endeavouring to place their views before our readers by condensing their communications to the utmost extent.

THE TREATMENT OF CHLOROSIS BY IRON AND SOME OTHER DRUGS.

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MANGANESE IN CHLOROSIS.

THIS metal has a certain reputation as a hæmatinic. In this country it is never given alone for such purposes, but very frequently as compound syrups of the phosphates and hypophosphites, in which manganese is always present as an adjuvant to the iron. In France and Germany it is used to some extent. Most of the standard textbooks either deny its efficacy or speak very doubtfully regarding it, although Binz states that many experienced clinicians believe it to be a valuable aid to iron in the treatment of anæmia, and that for this reason the sulphate of manganese is included in the German *Pharmacopœia*. Bartholow also says: "There is no doubt its combination with iron much increases the efficacy of the latter." A glance at its history will show us on what foundation rests such reputation as it may have.

The black oxide (MnO₂) was first used by Bréra in Italy (1822) in atonic diarrhoea, and as an emmenagogue and antichlorotic. Kügler⁵⁹ (1838) recommends it as useful in scrofulosis. The former seems to have used it quite empirically—the latter from an idea that workers in manganese were exempt from scrofula. Various chemists have found traces of it in the bones, gall stones, liver, gastric juice, blood (Wurzer, 1830), and other tissues of man. Both in man and animals its presence seems to be purely accidental, that is to say, it is not an essential component of any tissue or organ, but is derived from vegetable food, which in turn gets it from the soil. Marchessaux (1844), Millon,⁶⁰ and Riche⁶¹ have confirmed its presence in human blood.

Renewed interest in the matter arose from the researches of Hannon,⁶² Pétrequin,⁶³ and Burin du Buisson,⁶⁴ who claimed that manganese is an essential and constant constituent of the blood of man, that it is present in the corpuscles only, and that its administration is essential for the complete recovery of many cases of anæmia. Hannon, indeed, describes three varieties of anæmia: (1) where iron is deficient; (2) where manganese is deficient; (3) where both are deficient. The results of Pétrequin, of Burin du Buisson, and of several others are completely vitiated by the fact that they always gave iron along with the manganese, and often in four times larger quantity. Hannon, however, gave manganese alone with asserted good results. On the other hand, Glénard,⁶⁵ examining the blood of forty persons in good health who were bled "in the ordinary course," found in one only a trace of manganese, and as he found none in the blood of a manganese miner, he argues that it cannot be absorbed by any channel. Kobert and Cahn have proved that manganese salts given by the mouth are not absorbed. The traces found in the tissues and urine sometimes must be due to its presence in our food. Dr. Broadbent⁶⁶ treated seven cases of anæmia with it, and believes that it has a certain value. Three of these were anæmic children suffering from ascariæ, porrigo, vaginitis, and other complications. Their recovery may be fairly ascribed to treatment directed to cure the complications, rather than to any action of manganese on the blood.

⁵⁹ Oesterr. med. Jahrb., xvi, 1838.

⁶⁰ Comptes Rendus, xxvi, 41.

⁶¹ Bull. de l'Acad. de Méd., 1877, 1, 240, Sur la Détermination du Manganèse dans le Sang.

⁶² Etudes sur le Manganèse, Brussels, 1849.

⁶³ Gaz. Méd. de Paris, 1849, 738. Bull. gén. de Thérap., 42, 193, 1852.

⁶⁴ Mémoire sur l'Existence du Manganèse dans le Sang humain, Paris, 1852.

⁶⁵ Journal de Pharmacie, xxvi, 184, 1854.

⁶⁶ Clin. Soc. Trans. II, 122, 1869, Manganese, Nickel, and Zinc in Anæmia, Chlorosis, and Allied Disorders.

Four were cases of chlorosis; one is stated to have improved in six weeks on 4 grains of manganese chloride three times daily, another with manganese and iron together did well, the third had quinine in addition, and the fourth only improved when iron was substituted. One case, therefore, improved on manganese alone, the others required additional treatment. Strahan⁶⁷ states that the binoxide is useful in chlorosis; Dowd⁶⁸ failed to get any result from it, while Hailes⁶⁹ also failed with 5-grain doses of the sulphate.

I have treated several cases of chlorosis with the binoxide and sulphate, and never saw the slightest improvement result. Only two of them were kept in hospital, but the failure of manganese to cure chlorosis was so marked that it seems sufficient to report one case.

CASE XV.—Girl, aged 18, ill for three years, during which time she has been treated with many kinds of iron preparations, but only improved slightly and transiently.

Date.	Medicines.	Red Corpuscles.	Hæmoglobin. Per Cent.
May 15.....	—2,425,000	26
" 16.....	Manganesii oxid purif. 10 grs. twice daily —	—
" 22.....	—2,750,000	26
" 28.....	—2,420,000	26
" 29.....	Ferri carb. sacchar. 10 grs. twice daily —	—
June 2.....	—3,020,000	30
" 8.....	—4,100,000	46
" 13.....	—3,880,000	52
" 16.....	—4,340,000	60
" 23.....	—4,580,000	72
" 29.....	—4,660,000	78

In a fortnight absolutely no improvement was made on manganese, while the substitution of iron increased the corpuscles and hæmoglobin materially in five days. I never found manganese in the urine.

HYDROCHLORIC ACID IN CHLOROSIS.

Zander,⁷⁰ arguing that the iron of the food is sufficient for the cure of anæmic conditions, and that this iron is not absorbed owing to the deficiency of the digestive juices, has used hydrochloric acid to make up this deficiency and improve digestion. He gives no exact particulars, but states that he has treated many cases of chlorosis with hydrochloric acid, sometimes with pepsin in addition, and that he has thereby obtained more satisfactory results and more lasting cures than by the iron treatment. I have been unable to confirm Zander's results. Two cases only were treated with acids, but as these made absolutely no improvement, or rather as both became worse, I thought it waste of time to pursue the matter further. Whether hydrochloric acid may not be a useful adjuvant to iron in treating the dyspepsia of chlorosis is another matter, but the attempt to determine its value exactly is met by the same difficulties as I have stated at length under arsenic. It certainly does not improve the blood condition.

CASE XVI.—Girl, aged 25, ill for two months, but has previously had several similar illnesses. In addition to the acid she had saline purgatives or an enema daily, as there was marked constipation.

Date.	Medicines.	Red Corpuscles.	Hæmoglobin. Per Cent.
Nov. 1.....	Acid. hydrochlor. dil. 10 m thrice daily in water after food3,700,000	36
" 9.....	Acid. hydrochlor. dil. 15 m thrice daily3,457,000	34
" 16.....	—3,430,000	33
" 17.....	Ferri carb. sacch. 10 gr. thrice daily —	—
" 21.....	—3,500,000	34
" 23.....	—4,457,000	40
" 28.....	—4,000,000	48
Dec. 5.....	—4,500,000	62
" 7.....	—4,700,000	76

CASE XVII.—Domestic servant, aged 18, ill for some months; appetite and digestion good.

Date.	Medicines.	Red Corpuscles.	Hæmoglobin. Per Cent.
Nov. 11.....	Acid. hydrochlor. dil. after meals2,987,000	34
" 21.....	—3,010,000	38
Dec. 6.....	—3,000,000	30

She afterwards improved on iron.

In both cases the acid agreed perfectly well, but the blood deteriorated during its administration.

Dr. Hale White⁷¹ has practically settled this question. He treated five cases with hydrochloric acid and found that the

⁶⁷ BRITISH MEDICAL JOURNAL, 1885, vol. ii, p. 473.

⁶⁸ Am. J. Med. Sci., 99, 549, 1890, The Condition of the Blood in Chlorosis.

⁶⁹ BRITISH MEDICAL JOURNAL, 1885, vol. ii, p. 629.

⁷⁰ Virchow's Archiv, 84, 177, 1881, Zur Lehre von der Aetiologie, Pathogenie, und Therapie der Chlorose.

⁷¹ Guy's Hosp. Rep., 48, 1891.

increase of corpuscles and hæmoglobin was trifling, no more in his opinion than complete rest and full diet might account for.

PURGATIVES: DIETETIC TREATMENT: REST IN BED.

Sir Andrew Clark⁷² is of opinion that constipation with consequent absorption of ptomaines is the primary cause of chlorosis, and that purgation with salines is the best method of treatment. His purgative saline mixtures, however, contain ferrous sulphate, of which the patient gets no less than 8 grains daily. This is far more than sufficient iron to effect a cure, and hence the exact value of the purgative remains undetermined. Hamilton⁷³ had previously treated anæmia by purgation, along with tonics, diet, and fresh air, but his results are not striking. Dowd⁷⁴ in one case gave laxatives for ten days with very slight improvement, but improvement began at once when iron was substituted. Cosgrove⁷⁵ finds that iron cures without purgation, and further that many cases of chlorosis do not suffer unduly from constipation.

I have treated five cases in hospital on Sir Andrew Clark's plan, omitting the iron. In the first case, after eleven days' treatment there was 2 per cent. diminution in the hæmoglobin; in other two cases, after eleven and twenty-one days, 1 per cent. diminution; in another, after fourteen days there was a loss of 4 per cent; and in the fifth, after fourteen days a gain of 4 per cent hæmoglobin. The addition of iron caused rapid improvement in them all. I have besides observed several cases outside the hospital, and never found that improvement took place until iron was given in addition to, or in place of, the purgatives.

The same is true of purely dietetic treatment, either alone or combined with outdoor exercise or rest in bed. Hollis⁷⁶ found that a week's rest in bed only caused an average increase of 1 per cent. hæmoglobin; Graeber⁷⁷ that improvement ceased whenever he stopped iron, and then began again when iron was resumed. This accords entirely with my own results in several carefully observed cases. To regulate the bowels and to use a nutritious and digestible dietary are general rules of living both in health and sickness; they contribute greatly to bodily comfort and well-being, but they cannot be regarded as specific for the cure of anæmia, or more valuable in it than in many other morbid conditions.

Many cases do not begin to improve on iron until they have rest in bed. This is matter of common experience, and I have frequently found it occur. It is impossible to discuss the reason in this paper, as it would carry us far beyond its assigned scope.

FORM IN WHICH INORGANIC IRON IS ABSORBED.

It is usually assumed by those who believe in its absorption that iron is absorbed from the alimentary canal as chloride or albuminate, but the results of some uncompleted experiments have convinced me that iron may be absorbed in other forms also. In fact, it seems probable that any combination may be absorbed. We have, however, no exact knowledge on this point. Bubnow⁷⁸ has shown that if ferric salts be given by the mouth they gradually become reduced to ferrous during their passage along the intestinal canal, until in the fæces he found mere traces of the persalts; a large portion is converted into ferrous sulphide. Glaevecke, after subcutaneous injection of ferric salts, found only ferrous salts in the urine, but ferric in the blood and peritoneal fluid. What further happens is unknown. When iron is given intravenously or subcutaneously, it is caught and stored up chiefly by the liver, where it is converted into an organic combination, which gradually supplies the iron for the red blood corpuscles. Zaleski⁷⁹ has demonstrated the presence of several such combinations in the liver, but at the present time our exact knowledge on these matters consists chiefly of gaps. It has never been traced from the intestinal canal to the liver. If the liver catch it as it leaves the

bowel, we can understand why it does not circulate in the blood, and is not excreted in the urine. The quantity absorbed is also unknown, but is almost certainly small.

BEST FORM OF ADMINISTRATION AND DOSE OF IRON.

At present this is largely a matter of opinion; different practitioners use different preparations, apparently with equally satisfactory results. Formerly the astringent preparations were most in fashion, now it is the milder preparations and proto-salts. No proof has yet been given that any one preparation of iron cures chlorosis more quickly than another, and we shall probably make little progress in this direction until we know more about the form and conditions of absorption. Hayem holds the oxalate to be most satisfactory, while others think they get the best results from the protochloride, carbonate, perchloride, double salts, etc. Meanwhile it seems most rational to use those preparations which disturb digestion least. Latterly I have employed chiefly reduced iron and freshly prepared carbonate. Frequently, if there be gastric dyspepsia, 1 grain of reduced iron along with bismuth subnitrate agrees perfectly well if given before food.

As regards dosage, there is a general idea that very large doses give the most satisfactory results, but on looking over the literature I find that large doses of iron have often been protested against on the ground that they tend to disturb digestion, and also that small doses act equally well. I am not yet able to express any decided opinion on this point, but latterly I have been using much smaller doses (1 to 2 grains of reduced iron or carbonate of iron twice or thrice daily), and find that the cases recover quite satisfactorily.

Of one thing I feel convinced—namely, that in chlorosis the ordinary inorganic preparations of iron cure much more quickly than organically-combined iron does. Patients fed on even a rich and varied diet, containing plenty of organic iron, do not, as a rule, recover until inorganic iron is administered. I have tested this frequently, and have no doubt it holds good in the great majority of cases, although some cases of chlorosis do recover spontaneously and without any treatment (that is, on the iron of the food alone). From an experiment of Subbotin's⁸⁰ it does not seem to be the case that a diet rich in organic iron causes a high percentage of hæmoglobin, although one would have expected it to be so. He fed two pigeons on yolk of egg for twenty-six and thirty days respectively, but at the end of that time their hæmoglobin was considerably less than that of two pigeons which had been fed on grain. Now yolk of egg is particularly rich in organic iron.

Blood given subcutaneously (Ziemssen,⁸¹ Silbermann⁸²) or by the stomach (Benczur⁸³) will cure anæmia, but Gherardini⁸⁴ has shown that it is extremely indigestible, that the hæmatin is very partially absorbed, and that it is a very undesirable form in which to give iron. In persons with weak digestion it does harm. Kobert⁸⁵ agrees with this, but as he is strongly of opinion that organic iron only is useful in chlorosis, he has prepared from blood two substances which he calls hæmol and hæmogallol, and which contain all the iron of the hæmoglobin in organic combination. They are insoluble brown powders, tasteless and uniritating. He finds that this iron combination is readily absorbed from the intestinal canal, and states that it is a successful method of treating chlorosis. Two cases, however, treated with these preparations did not give me very encouraging results.

CASE XVIII.—Domestic servant, aged 22, ill for about six months.

Date.	Medicines.	Red Corpuscles.	Hæmoglobin, Per Cent.
Feb. 20.....	Hæmol, 5 grs. thrice daily.....	2,700,000	34
" 29.....	"	2,720,000	35
Mar. 1.....	Hæmogallol, 10 grs. thrice daily.....	"	"
" 4.....	"	2,720,000	33
" 5.....	Ferrum redactum, 2 grs. thrice daily	"	"
" 11.....	"	3,110,000	35
" 15.....	"	3,080,000	42
" 23.....	"	4,100,000	60
" 28.....	"	3,900,000	70

⁸⁰ *Ztschr. f. Biologie*, vii, 185, 1871: Einfluss der Nahrung auf den Hæmoglobingehalt des Blutes.

⁸¹ *Deut. Archiv f. klin. Med.*, xxxvi, 269, 1885, Die Subcutane Blutinjection.

⁸² *Deut. med. Wochenschr.*, 1885, 445.

⁸³ *Deut. Archiv f. klin. Med.*, xxxvi, 365, 1885.

⁸⁴ *Revue des Sciences Méd.*, xxxix, 88, 1892.

⁸⁵ *St. Petersburg. med. Wochenschr.*, 1891, Ueber resorbirbare Eisenpräparate.

⁷² *Lancet*, 1887, ii, 1003.

⁷³ *Observations on the Utility and Administration of Purgative Medicines in Several Diseases*, Edinburgh, 1806.

⁷⁴ *Loc. cit.*

⁷⁵ *BRITISH MEDICAL JOURNAL*, 1888, i, 688.

⁷⁶ *BRITISH MEDICAL JOURNAL*, 1890, i, 1239, On Chloræmia and its Treatment.

⁷⁷ *Therapeutische Monatshefte*, 1887, 360, Zur klinischen Diagnostik der Chlorose.

⁷⁸ *Ztschr. f. physiol. Chemie*, vii, 315, 1883.

⁷⁹ *Ztschr. f. physiol. Chemie*, x, 453, 1886, Studien über die Leber.

She had 150 grs. hæmol and 120 grs. hæmogalol in a fortnight without the slightest benefit, while reduced iron improved her condition at once.

CASE XIX.—Housemaid, aged 18, ill for some months.

Date.	Medicines.	Red Corpuscles.	Hæmoglobin. Per Cent.
May 2.....	Hæmol, 10 grs. thrice daily.....	3,700,000	40
" 18.....	Ferrum redactum, 2 grs. thrice daily	3,800,000	44
" 25.....	4,200,000	54
June 13.....	4,930,000	72
" 29.....	4,500,000	80
" 9.....	5,100,000	82

In this case 480 grs. hæmol were taken in sixteen days, but the benefit was very trifling.

One of the great problems in the study of chlorosis is to determine why the patient should not be able to renew the iron of the blood from the abundant iron of the food. Cases of acute hæmorrhage are generally able to do so, a few cases of chlorosis do so, but the great bulk of the latter only recover when inorganic iron is given. I have already stated my opinion that (for some as yet unknown reason) inorganic iron is much more helpful towards recovery than organic iron, although in health the latter serves perfectly for the manufacture of hæmoglobin, and is the only form in which iron is ordinarily taken by mankind.

Another point of great interest is to determine the reason why inorganic iron administered to the healthy in no way affects the number of red blood corpuscles or the amount of hæmoglobin. We have absolutely no knowledge as to how the use of iron by the organism is regulated, but it seems impossible to increase the number of corpuscles or the amount of hæmoglobin above a certain fixed normal. These and other matters must be left for future research.

In conclusion, I wish to touch on one other matter. It has been often stated that in chlorotics the amount of hæmoglobin is small and that it is impossible to raise it above a certain point, which is lower than the normal average; and it is pointed out that cases of chlorosis after treatment have seldom more than 70-80 per cent. hæmoglobin (Gowers's hæmoglobinometer). The following explanation of this has been given, and seems to me the true one. During an attack of chlorosis a large number of pale red blood corpuscles are formed, very deficient in iron. These die out only slowly, and it takes weeks, or even months, before they are quite replaced by the newly-formed corpuscles rich in iron. As the pale corpuscles become less and less numerous the hæmoglobin percentage gradually goes up to the normal. In women, however, its normal is only about from 82 to 88 per cent. on Gowers's hæmoglobinometer, and, so far as my experience goes, 100 per cent. hæmoglobin is not very common even in healthy men. Leichtenstein⁶⁶ states that women from 11 to 50 years of age average 8 per cent. less hæmoglobin than men. By the use of iron, therefore, we can scarcely hope to bring the blood of chlorotic women up to 100 per cent. of hæmoglobin, but by a little persistence in treatment we can readily bring it up to between 80 and 90 per cent., which is the average for healthy young women.

These observations were made in Chalmers' Hospital, and my best thanks are due to Dr. George W. Balfour, not only for his kindness in placing beds at my disposal for the treatment of patients, but also for continually affording me the great benefit of his own exceptionally large knowledge and experience of anæmic conditions. To Drs. Basil Orr, Ronald Mackenzie, and Harry Rainy, who, as house-surgeons of the hospital, gave themselves a great deal of trouble on my behalf, I am also much indebted.

A CASE OF PERFORATED GASTRIC ULCER FOR WHICH GASTRORRHAPHY WAS PERFORMED: DEATH ON THE THIRTY-FIRST DAY.¹

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THE following is the report of a case in which a girl, aged 20, passed successively through the shock of the perforation of a gastric ulcer, followed by abdominal section and gastrorrhaphy,

then through slight creolin poisoning, double parotitis, the operation of gastrotomy, septic pneumonia and diarrhoea, and ultimately died of septicæmia, which supervened upon a final operation for closure of the wound.

At 1.30 A.M. on October 19th, 1892, I was asked to attend a girl who had been seized suddenly with intense abdominal pain. I found her in great agony, with shrunken features, cold and clammy skin, and a small, hard, frequent pulse. The pain was referred to the left epigastric and hypochondriac regions, and was accompanied by tenderness and muscular rigidity. The abdomen was rather contracted than full, and was resonant everywhere. There was nausea, but she had not vomited, though she made occasional gulps like those which precede vomiting, and belched a little wind. The bowels were regular. Respirations were frequent, shallow, and entirely costal.

At 9 P.M. she had eaten a hearty supper of bread and cheese, cabbage, and potatoes, and at 12 had been awakened from sleep by the onset of the pain. I elicited the facts that she had vomited on a few occasions about a month before, and that there had then been slight pain in the region of the stomach. I gave her two hypodermic injections of sedative solution of opium, and the pain was soon greatly relieved, but as it disappeared a desire for air, of which she had previously complained, became urgent. As the abdomen had now become distended, I had her raised in bed, to her great relief. Two hours afterwards the opiate had to be repeated, and she then vomited half a pint of partially digested food. Meanwhile I made hasty preparations for an early laparotomy, but, finding she was rallying from the shock, I delayed operation until a more convenient season.

At 10.30 A.M. the temperature was 101.6°; the pulse small, hard, 140; the abdomen slightly distended, and tender to pressure in every part. She had not micturated for twelve hours, and there was no hypogastric dulness. The knees were flexed, and any attempt to straighten them caused pain. Dr. Moody-Ward now saw her, advised laparotomy, and kindly gave chloroform.

An incision was made 3 inches long, 1 inch to the left of, and parallel with, the linea alba, starting half an inch from the margin of the ribs. A quantity of peritoneal fluid gushed out, which on close inspection was found to have oil globules floating on its surface. After flowing a few seconds a few particles of half-digested food began to make their appearance. The blood vessels of the anterior wall of the stomach were very full, the congestion increasing as the lesser curvature was approached. A rough, irregular surface was now felt on the lesser curvature near its middle, and on bringing this into view a quantity of granulation tissue was seen, together with lymph of more recent date, while above it, on the adjacent surface of the liver, were corresponding marks of a previous adhesion. It was thought that the ulcer would be found at this spot, and time was spent in searching for it, but without result. After carefully breaking down some adhesions, and watching the direction of the current which was continuously oozing from the stomach, it became evident that the stream came from a direction nearer the cardiac end. The finger was therefore insinuated among the adhesions of this part, and there the aperture was found. It was situated rather on the posterior than on the anterior aspect, and could not be brought into view at this stage. It was large enough to permit of the introduction of the finger for the exploration of the stomach for other ulcers, but with a negative result. Four silk sutures were passed through the stomach walls half an inch from the edge of the ulcer, and tied so as to invert it towards the interior. The abdominal cavity was afterwards irrigated with boiled water, to which, as it was not sufficiently cool, a little creolin (which is said to be an un-irritating, non-poisonous antiseptic) was added, the Reading tap water being on that day much too foul to be safely used without some such precaution. A glass drainage tube was then pushed up so that its extremity rested on the site of the sutured ulcer, and the external wound was closed.

For two days after the operation the patient was delirious at times, and had occasional twitchings of the muscles of the face, with upward turning of the eyeballs and spasmodic clenching of the hands. Urine was passed twenty-four hours after the operation, and was of a dark colour, but contained no albumen; specific gravity 1035. The tube was syringed with weak Condy's fluid in boiled water four times a day

⁶⁶ Untersuchungen über den Hæmoglobingehalt des Blutes, Leipzig, 1878.

¹ Read before the Reading Pathological Society.