THE LETTSOMIAN LECTURES

ON

ANÆMIA:

ITS PATHOLOGY, SYMPTOMS, AND TREATMENT.

Delivered before the Medical Society of London.

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LECTURE III.

Scorbutic Anæmia.—Relapsing Pernicious Anæmia.—The Diagnosis of Anæmia.—The Treatment of Anæmia.—Of Defective Hemogenesis.—Iron.—Of Excessive Hemolysis.—Arsenic.—Concluding Remarks.

MR. PRESIDENT AND GENTLEMEN,—I have already mentioned that there are cases of idiopathic anæmia which differ from cases of chlorosis and the general type of pernicious anæmia. To these I must now direct your attention; and first to cases of

Scorbutic Anæmia.—I have published¹ a case of a man, aged 18, who, one week before he came under observation, was attacked with headache and cough, followed by swelling of, and bleeding from, the gums. When admitted to the hospital, the gums were much swollen, bleeding, and ulcerated; petechial hæmorrhages existed nearly all over the body; no subcutaneous hæmorrhages or synovitis. Urine free from blood and albumen. Examination of the blood showed C. 51, H. 27, W. 0.52.² In the last two years he had had meat and potatoes every day, and green vegetables once a week. I was, nevertheless, inclined to regard the case as scorbutic at first, but in spite of all treatment, including antiscorbutics, he became more and more anæmic, but did not lose flesh; retinal hæmorrhages, more profuse than in any other case I have ever seen, developed, and ultimately general retinal œdema. The cutaneous hæmorrhages disappeared, but the gums remained spongy, and the bleeding from them considerable. Frequent and distressing vomiting set in, murmurs developed over the heart, and the pulse became exceedingly feeble. The urine contained a trace of albumen throughout after the first examination, but no œdema occurred. The red corpuscles sank to 13 per cent.; they varied much in size, some presenting cracks and fissures. The disease lasted a little over two months. The necropsy showed some thin hæmorrhagic extravasations beneath the pia mater; brain exceedingly white; lungs œdematous, with a few hæmorrhages. Numerous ecchymoses on surface of heart; muscle of left ventricle pale and mottled; liver and spleen anæmic; stomach very anæmic, ecchymosed; solitary glands, especially of large intestine, prominent; mucous membrane pigmented. Two small ulcers in large intestine, with deeply pigmented borders. Mesenteric glands mostly healthy, but several enlarged, and filled with calcareous matter. Micrococci were found in the capillaries of the kidneys, liver, and heart. They were only in small colonies, and there were no important changes in the tissues around them. It would, therefore, appear probable that they gained admission to the blood only shortly before death, increasing probably after death. The patient had suffered recently from primary syphilis, but no signs of visceral syphilis were found in the body. I have also recorded³ another case somewhat resembling it, but running a more acute course. Dr. Gowers has recorded⁴ two cases (one fatal) of a similar nature, in which the patients had plenty of vegetables, but had abstained more or less from animal food. He has suggested the very appropriate name of "scorbutic anæmia" for such cases.

I next wish briefly to relate a couple of cases which do not conform in all respects to the type which some recent writers have given of pernicious anæmia, particularly as regards the

¹ *Ophthal. Soc. Trans.*, vol. i, p. 51.² For brevity the following signs are used: C. = red corpuscles per cent; H. = hæmoglobin per cent.; W. = worth or value of individual corpuscle.³ *Ophthal. Soc. Trans.*, vol. ii, p. 34.⁴ *Medical Ophthalmoscopy*, 3rd ed., p. 246.

urine, and which show the marked tendency of this form to relapse.

Relapsing Pernicious Anæmia.—CASE I.⁵—S. F., first admitted under my care on July 9th, 1884. He was an engineer, aged 39, employed sometimes on ships and sometimes on land on stationary engines. He never had ague or syphilis. In 1879 he went to work in the Severn Tunnel. There he suffered much from the defective ventilation and the fumes of dynamite used for blasting purposes. He stated that there were as many as fourteen deaths from these causes. After remaining there nine months he returned to Newport, where he did a great deal of "overtime" work, often working for four nights in succession, besides doing his day's work. In December, 1880, he noticed he was losing colour, and this was followed by loss of appetite, and some wasting. He went into the Newport Infirmary, and after three months' treatment was able to resume work. He had a succession of break-downs and recoveries from that time, and his case excited a great deal of interest; a number of doctors visited him on account of the peculiarity of his case, and he was not expected to recover. He was sent to me by Dr. W. F. Edwards. He was temperate in everything except work. His attacks appear to have come on rapidly, in varying circumstances, and, after lasting an indefinite period, to have comparatively rapidly passed off. To use his own words, "When I begin to get well I get well quickly."

On admission he complained of great weakness and depression. There was extreme pallor, and a faint yellow tint of the skin. His pulse was 96, tension not increased; systolic murmur over third left rib, conducted to apex; no dilatation, no retinal hæmorrhages, no œdema. His blood, on admission, showed C. 13, H. 20, W. 1.5. His urine had specific gravity 1021, and was of amber colour. His history of working in a tunnel led me to prescribe anthelmintics, and to examine the stools microscopically, but with negative results. He was troubled with constant nausea and occasional vomiting at first, but there was at no time diarrhœa. He was put on Bland's pills, which he took for some time without benefit. Arsenic was then substituted at first in 4-minim doses, increased later to 6, three times a day. The improvement, as shown by the chart, was immediate and progressive from the time he took arsenic, and when discharged, on September 2nd, examination showed C. 95, H. 90, W. 0.94. His urine was examined every few days throughout his residence in the hospital. It was "straw" or "amber"-coloured, except on three occasions, when it was "orange." These were, when he was rapidly improving, C. 55, H. 33, W. 0.6. The average quantity was 65 ounces, and the specific gravity varied from 1010 to 1018. His temperature never exceeded one degree above the normal. He was admitted a second time in the early part of 1885, under Dr. Fenwick, and recovered under arsenic.

Third admission, November 14th, 1885. This relapse began with nausea, anorexia, and rapid loss of colour and strength two months before. He had vertigo, faintness, and palpitation on the least exertion. He had been under medical treatment six weeks, but the only result, he said, was constant diarrhœa the whole time. He had complete anorexia, discomfort after what he took, and looseness of the bowels. No *bruit* over heart, venous hum in neck. Defect of vision in right eye, with some atrophy of papilla. Loss of smell. No œdema. Blood on admission C. 20, H. 38, W. 1.9. It was later C. 25, H. 24, W. 0.96; and then steadily rose, when taking arsenic and iron, to C. 73, H. 86, W. 1.17. His urine, on admission, was of deep colour, 1018, alkaline; with this exception it was "amber" or "deep amber" on each occasion. It was deep amber most frequently when he was recovering. It contained a trace of albumen on four occasions. He left on January 12th, 1886, feeling well, and with a good colour. His temperature was 100° F. several times, and once rose to 102.5°. It will be observed that the recovery, as indicated by the condition of the blood (C. 73, H. 86, W. 1.17), was not so complete on this as on other occasions. This I attribute to arsenic not being used so freely. He took mist. ferri arsenicalis, which contains 5 minims of Fowler's solution, and pil. ferri co. three times a day.

Fourth admission, March 31st, 1887. This relapse had existed about one month. It was apparently induced by a cold,

⁵ Compiled from notes by Messrs. Owen and Kenneth Morell Mackenzie and Drs. Taylor and Robb.

following which he had the usual train of symptoms—nausea, anorexia, anemia, and some wasting; he was very pale; there was anorexia, breathlessness and palpitation on the least exertion. No murmur. His blood, on admission, showed C. 45, H. 40, W. 0.88; on April 5th, C. 34, H. 45, W. 1.35. It improved under arsenic a little irregularly to C. 95, H. 80, W. 0.84. On the last two examinations the corpuscles exceeded the hæmoglobin. The urine averaged 56 ounces; the specific gravity varied from 1012 to 1020. The colour was "pale," "yellow," or "amber" on every occasion except one, when it was "dark sherry." This was when he was improving (C. 58, H. 65, W. 1.1). There were occasional traces of peptones and albumen; slight deposits at times of uric acid and phosphates, and indican was present twice. His temperature never exceeded 100° F. He was treated with Fowler's solution, beginning with 5 minims, and increasing gradually to 10 minims three times a day. He died at home in a later attack.

Fifth admission, May 31st, 1888. The attack had lasted one month, came on in the usual manner, and had the same general characters. He was at once put on arsenic, beginning with 5 minims and increasing to 12, three times a day. The corpuscles, which alone were measured, were 37.6 per cent., fell to 21 and 15 per cent. later, and only reached 41 per cent., when discharged on September 4th. He remained weak for one month and then became worse, and died in a week with delirium and vomiting.

CASE II.—I have another very similar case under my care at the present time—D. M., boiler maker, aged 48. He had increasing pallor, weakness, with loss of flesh for many months before admission on December 6th, 1889. There was great pallor, anorexia, and costiveness; pulse 84, small and soft; no murmur, but venous hum in neck. Hæmorrhages in both retinae.

On admission, C. 30, H. 25, W. 0.83. He was put on arsenic, beginning with 5 minims, and increasing to 13 for a dose three times a day. He rapidly gained colour, strength, and flesh, and the retinal hæmorrhages, disappeared, and on discharge he had C. 82, H. 68, W. 0.82. His urine was amber, pale amber, and straw coloured throughout; its density varied from 1014 to 1023, and was always free from albumen. His temperature was never above 99° F. His weight increased from 9 stone to 10 stone 5½ lbs.

Second admission, November 28th, 1890. His appetite had been bad all through the summer, and he had consequently lost flesh. In the last five weeks appetite almost entirely left him, he became very pale and weak, and suffered from constipation and headache. He was very pale on admission, and his skin and conjunctivæ had a yellowish tint. First sound of heart feeble and distant, second reduplicated; dyspnoea on the least exertion; no hæmorrhages in retina; C. 46, H. 30, W. 0.65. He was put on arsenic solution, beginning with 5 minims and increased by degrees to 12 three times a day, with a morning saline aperient. He has steadily improved, and his blood on January 15th was C. 75, H. 60, W. 0.8. His urine has been examined daily. It has averaged 58 ounces, specific gravity from 1018 to 1030. It has never contained sugar, albumen, or bile pigment. Particular attention has been paid to its colour. It has been "amber," "yellow," or "pale straw" on most occasions, "darkish straw" or "pale brown" on several. It has never contained any excess of normal urobilin, nor any pathological urobilin, though examined daily for these. He has had one febrile attack, in which his temperature reached 102.5°, lasting two days.

These two cases present many points of interest, two only of which I must dwell upon. First, the character of the urine. In Case I it will be observed that it was always pale, except when he was recovering, that is, when the pathological process causing the anemia was least active, at a time when he was taking arsenic. I believe I have observed the same effect in some other cases, the urine becoming dark when the patient was being treated by arsenic. Arsenic, as well known, is eliminated by the kidneys.

In Case II the urine has been examined most carefully daily by my house physician, Dr. David Brown, who is a very good chemist; and though it has been darker on some occasions than others, there has been no pathological urobilin, and no excess of normal urobilin.

⁶ From notes by Messrs. Turrell, Lea, and Stanton.

The second point to which I must refer is the prognosis in such cases. In Case I, repeated recoveries under arsenic were followed by repeated relapses over a period of about nine or ten years, and at the earlier part of the illness he was given over as irrecoverable. Change of locality, change of occupation were tried without avail in warding off the fatal termination. Though Case II is now nearly convalescent, I have little doubt he will have a return of his disease with the same ending.

Dr. Hale White, in a paper in the forthcoming vol. 47 of *Guy's Hospital Reports*, of which he has allowed me to see a proof, has gone very carefully into the prognosis of cases of pernicious anemia, and shown that though a small number of cases left Guy's Hospital relieved, several relapsed and died of the disease in the same hospital. Moreover, during the ten years 1879 to 1889, there were nine patients believed to be suffering from pernicious anemia who recovered sufficiently to leave the hospital. Of these two are known to have died, and, from reasons given in the paper, there is a presumption that six more died. One case under Dr. Hale White's care recovered and remained well at the end of nearly four years. A previously published case of Dr. Pye-Smith's was well at the end of two years. These are the only two in which a real recovery can be stated to have occurred in Guy's Hospital since the time of Addison. Both were treated with arsenic. Dr. Tyrrell Brooks has recorded a case⁷ of apparent recovery, but with a fatal relapse a year later. I can endorse Dr. Hale White's statement that a subsequent report of cases published as cured by arsenic is much to be desired.

Diagnosis.—The diagnosis of anemia presents no difficulty if we make this reservation that pallor is not always indicative of the presence of anemia. The colour of the mucous membranes is a more trustworthy guide than that of the skin. In Bright's disease, for instance, patients look much more anæmic than is proved to be the case. Having established, by actual examination of the blood, that anemia exists, we have next to determine on what this depends; in other words, whether it is a secondary and symptomatic, or a primary and idiopathic anemia. To exclude the former we have to consider the history of the case, and to make a careful and complete physical examination. There are in this country two diseases of which anemia is symptomatic, and in which the signs of local disease may be wanting for some time; these are tuberculosis and cancer. Anemia may be one of the earliest indications of pulmonary and other forms of tuberculosis. It is usually, but not invariably, accompanied by wasting. The occurrence of anemia and wasting in a young person should excite a suspicion of incipient tuberculous disease, and lead to repeated examination of the lungs and other organs. Wasting is not characteristic of chlorosis, but may accompany it, and be carried to an extreme degree, as in a case of chlorotic hysteria sent to me by Dr. Heywood Smith in 1882. The patient was emaciated to an extreme degree. When first seen she had C. 50, H. 30, W. 0.6; later, C. 48, H. 20, W. 0.42, and ultimately rose to C. 96, H. 60, W. 0.62. Her weight when she first came under my care was 4 stone 2 lbs., and it rose to 6 stone 7 lbs. She has remained well ever since, but has entire suppression of menses, and has become exceedingly stout. I was once present at a *post-mortem* examination of a case believed, during life, to be pernicious anemia, but which was proved to be cancer of the stomach. In this case the diagnosis was rendered peculiarly difficult by the entire absence of gastric pain and vomiting. This case shows the caution necessary in diagnosis, and in accepting as pernicious anemia cases not proved by necropsy. Whilst indeed it was necessary at one time to reject all cases not proved by *post-mortem* examination, so as to get a clear picture of the disease, yet we are not justified now in rejecting cases which have the characters I have described. It must be remembered that neither variations in the size, nor alterations in the shape of the red corpuscles is peculiar to idiopathic anemia. Still the careful examination of the blood will go far towards the diagnosis of the variety of anemia. Thus the reduction of the red corpuscles to, or

⁷ Reprint from *Lancet*, 1887, vol. ii, 859.

⁸ Laache, at the International Congress, 1890, narrated a case in which under arsenic rapid improvement took place, an increase of about 211,000 per cubic millimetre taking place daily, and the patient appeared to recover completely; after some months he relapsed and died.

below, 30 per cent., especially if the hæmoglobin is relatively high, is in favour of pernicious anæmia. The other diseases in which such great reduction in the number of corpuscles occurs are hæmorrhage, in which the corpuscles and hæmoglobin usually have their normal relationship, and the history of loss of blood is rarely wanting; and cancer, in which as in some cases I have mentioned the hæmoglobin is sometimes greatly below the corpuscular richness. In chlorosis the marked characteristic is the deficiency of hæmoglobin. It should be further remembered that retinal and other hæmorrhages, whilst characteristic of pernicious anæmia, are not pathognomonic of it. They indicate a severe degree of oligocythæmia—usually less than 50 per cent. of red corpuscles. A rough but serviceable guide to the recognition of this degree of anæmia is furnished by the colour of the nail bed of the fingers. As long as any pink colour can be seen, then it may be assumed that there is at least 50 per cent. of red corpuscles. When the pink colour entirely disappears from the nail bed, the corpuscles will be found to be below 50 per cent. The recognition of this degree of anæmia is a warning that the grave consequences of anæmia may be expected.

THE TREATMENT OF ANÆMIA.

The use of pathology is to guide us in the prevention and cure of disease, and treatment, to be scientific, must rest upon pathology. We have endeavoured to work out the pathology of anæmia, and have shown that anæmia depends upon either defective hæmogenesis or excessive hæmolysis, or upon the two combined. The principles of the treatment of anæmia must therefore follow upon these lines. It will be convenient to consider treatment under three heads—dietetic, hygienic, and medicinal.

In *defective hæmogenesis*, whether the anæmia is idiopathic or symptomatic, it is essential that the diet should be ample to supply the pabulum from which the corpuscles and their hæmoglobin are prepared. It must be remembered that the food of ordinary life, in sufficient quantities, contains all the elements, including iron, that are necessary for blood formation. We must be careful to see to the condition of the teeth that mastication may be properly performed. A good amount of meat is desirable—as much as the patient can comfortably and perfectly digest. A small amount of stimulants—especially red wines, such as burgundy, claret, or port; or malt liquors, such as stout or light bitter beer, is often of service. The hygiene consists in securing the patient as much light—especially direct sunshine—and fresh air as is possible. The bleaching effects of darkness are seen throughout organic life. Gentle exercise in the open air, or driving, when the strength permits, is of importance, but, in severe degrees of anæmia, absolute rest is imperative and of the greatest service. In less severe degrees of anæmia longer hours than usual in bed, and the recumbent position for some hours in the day time, to save the enfeebled heart, are important matters in practice. A morning tepid sponge bath should be used. Suitable and sufficient, but not excessive or tight, clothing should be worn. Anæmic persons are usually sensitive to cold.

We come now to the *medicinal* treatment. The following are the remedies which increase the rapidity of, or perfect, blood formation: Iron, phosphorus, potash, manganese, arsenic (?), hydrochloric acid (indirectly), and oxygen.

Iron is proved by every day clinical experience to be of the greatest value in anæmia, though objectors are still found to its being absorbed and acting on the blood. They believe that its good effects are due to its local tonic action on the stomach and intestine. That it is, in some part, absorbed has been proved by Rabuteau and many other observers. Much that is taken is undoubtedly not absorbed, and passes into the intestine, where it is converted into the sulphide or tannate, which cause the black stools of patients taking iron, and it is probable that much that is absorbed into the portal vein returns to the intestine with the bile. In the stomach and intestine, if not given in these forms, it becomes converted into a chloride or albuminate. It soon becomes incorporated with the red corpuscles, as it cannot be detected in the plasma elsewhere than in the portal system. I cannot refrain from quoting an interesting remark of Dr. Mitchell Bruce's:⁹ "The action of iron on the blood is almost unique

of its kind: First, because its specific action is exerted, not upon the plasma, but upon the red corpuscle, and on this alone, not on any other tissue or organ. Secondly, because the action appears to be nothing more than the combination of iron, as one of the constituent elements of the corpuscles with the others. In the case of no other metal can we speak so definitely of its *modus operandi*." It being accepted, as all clinical experience teaches, that iron does improve the character of the blood, we must next examine into how it accomplishes its effect. Systematic examinations of the blood in chlorotics and other subjects of anæmia show that usually its immediate effect is to increase the number of corpuscles without a corresponding increase in the amount of hæmoglobin, so that the first result may be a lowering of the worth of the individual corpuscle. By degrees, however, the corpuscles become more deeply impregnated with hæmoglobin, and ultimately they reach their normal value. It would thus appear that the influence of iron is first to stimulate the production of new or young corpuscles, and only secondarily does it add to the amount of hæmoglobin in the corpuscles. The practical matter that concerns us most is the determination of the best manner of administering it. Probably all forms are useful, and possibly the form makes no difference if enough can be given. The bland and non-astringent forms are tolerated in larger doses and for a longer time than the astringent forms. It is, again, a question whether ferrous or ferric salts are the most useful as hæmatinics. This is, in a measure, answered in the preceding paragraph, and, speaking generally, my experience leads me to the conclusion that the ferrous salts are to be preferred.

A few words on the method of conducting an iron treatment will not be out of place. I would remark it is exceedingly rare for patients to be unable to take iron in some form when it is really needed. Next, the pill form is the most convenient in the usual way. It does not blacken the teeth, is tasteless, the dose is easily augmented without modification of the formula, and is proved by experience to be thoroughly efficient. In cases where there are reasons for not giving it in pill, albuminate of iron, dialysed iron, Griffith's mixture, or one of the scaly preparations may be employed. Where there is much gastric disturbance this must be treated at the same time, but is no bar to the administration of iron. When the tongue is coated, flabby, and indented by the teeth, it is my practice to give an alkali and bitter mixture between meals, and iron in pills immediately after or with food. We may combine the iron with the citrate or bicarbonate of potash, and give the two together, but it is not in this way so convenient to regulate and augment the dose of iron. Dr. Lauder Brunton recommends the astringent preparations of iron when the tongue is pale and flabby. Where constipation co-exists, as it often does, there are several ways of dealing with it, dependent on its cause. Dietetic measures should always be employed; but failing these we may combine the iron with an aperient in the form of a mixture, as the sulphate of iron and sulphate of magnesium, or the iron may be combined in a pill with aloes and myrrh. My own plan is, however, usually to give a saline aperient in the morning on rising. One of the natural purgative waters may be employed, or a drachm (or thereabouts) each of sulphate of sodium and sulphate of magnesium (with or without a drachm of chloride of sodium) in half a tumblerful of warm water. My distinguished colleague and friend, Sir Andrew Clark,¹⁰ has particularly emphasised the importance of aperients in the treatment of chlorosis, and states: "If in the treatment of this malady I were perforce limited to the employment of one sort of drug, the drug which I should choose for use would be an aperient." Nevertheless, he usually advises the employment of an acid or alkaline ferruginous cathartic mixture, or sulphate of iron in pill, and a saline aperient in the morning, as recommended above.

Fashion no doubt influences our choice of the particular preparation, and so one salt or combination of iron after another is for a time the popular medical remedy. The teaching of Niemeyer and the pushing of advertising pillmongers have made Blaud's pill the general favourite at the present time, and it is undoubtedly one of the most valuable. I have used this preparation for the last twenty years with excellent results. The slight pharmacological knowledge I possessed

⁹ *Materia Medica and Therapeutics*, 4th ed., p. 85.

¹⁰ *Lancet*, vol. ii, 1887, p. 105.

told me that the amount of carbonate of potassium was in excess, and for years I have prescribed the pills in the following formula: Ferri sulph. exsic. gr.ij; potas. carb. gr.j; glycerin. of tragacanth. q.s. Blaud's pill being so much in use, it is interesting to learn what we can about it. A good deal has been written on the exact condition of the iron in these pills. Mr. Martindale has been good enough to supply me with some interesting information. "The following formula represents the decomposition in making Blaud's pills:

By exposure in the moist condition $FeCO_3$ evolves CO_2 , and absorbs oxygen, becoming converted into ferric oxide as ferric hydrate. Thus:

Mr. Martindale suggests that "instead of equal quantities of carbonate of potassium and sulphate of iron (crystals), about three of the former and five of the latter should be used, so as not to have an excess of the potash salts, which makes the pill become damp; or equal weights of dried sulphate of iron and carbonate of potassium nearly exactly neutralise each other. A five-grain Blaud's pill, according to the *Addendum* to the *British Pharmacopœia*, 1890, should contain about 1 grain of true carbonate of iron, as ferrous carbonate; but it is found that before the pills can be dried and coated, quite one-half of this has been converted into ferric oxide."

Of course it may be maintained that there is a great difference between pharmaceutical elegance and practical results, and that the excess of alkali in Blaud's pill, as prescribed by Niemeyer (modified from Blaud's original formula), increases their efficiency, if it gives the dispenser more trouble. I have not found, however, that the diminished quantity of alkali in any way impairs the utility of the pill. Potash is the principal base of the red corpuscles, and potash is found in the urine in excess in some forms of anæmia, so that the blood may be poor in it. The latter, however, is the case when the anæmia is hæmolytic, and when iron is, as a rule, not indicated; whilst in anæmia due to defective hæmogenesis there is no loss of potassium. Moreover, the potassium is so abundantly supplied by the food that the amount given in the pill is a mere drop in the ocean. Two other pill preparations containing iron deserve mention. The pil. ferri carb., *B.P.*, made with saccharated carbonate of iron and *syrup* instead of conf. rosæ, as suggested by Mr. Martindale, is an excellent one which I have been using lately. A 5-grain pill will contain $\frac{1}{2}$ grain of ferrous carbonate—three times as much as Blaud's pill—and is much more stable. Five grains of dried sulphate of iron made into a pill with *syrup*—a favourite of Dr. Ringer's—also contains three times as much iron as Blaud's pill.

In treating primary, especially chlorotic, anæmia, the best results appear to be obtained by pushing the iron in large doses, and it is on this account that the pill form is so convenient. We can begin with one pill three times a day, soon give two pills three times daily, and later in some cases give three pills for a dose. More than this is not usually necessary. No doubt much of this is squandered, not being absorbed from the digestive tract. Whether in these circumstances more is actually absorbed than when it is given in smaller doses, or whether it acts indirectly on the gastrointestinal tract, as maintained by Buchheim, Kobert, and Reini, is uncertain; but the fact that large doses act more promptly and efficiently is established by experience.

One more point of great importance which is often lost sight of. The iron treatment, in cases of chlorosis especially, should be persevered in for two or three months after the patient feels herself well, and often has a good colour. We have seen that the hæmoglobin remains deficient after the corpuscles have returned to about their normal number, and it is only slowly that the corpuscles arrive at their normal amount of hæmoglobin. Relapses in such cases are exceedingly common if the iron is prematurely discontinued. Laache, in a recent communication,¹¹ has emphasised this fact, and pointed out that Niemeyer's statement, that three boxes of 96 Blaud's pills suffice to cure the most obstinate chlorosis, is very misleading.

Phosphorus, in my experience, is of greatly less value than iron in chlorosis and other forms of defective hæmogenesis.

¹¹ Sep-Abdr. aus d. *Wiener klin. Wochenschr.*, 1890, No. 33.

It is, however, sometimes serviceable, as in cases recorded by Gowers¹² and others. When given it should be in pill made with ol. theobromæ, and recently prepared.¹³ It has been maintained by some recent writers that dilute hydrochloric acid is more useful than iron (Zander). It may do good by increasing the digestive power, and thus enable the patient to gain more iron from the food. Manganese appears of doubtful value. Arsenic has been proved to be useful in some cases of chlorosis, but iron is usually much more efficacious. Oxygen, administered by inhalations, has been used in some cases with apparently good results, but I have no personal experience of this method of treatment. We occasionally meet with cases of chlorosis which improve time after time with iron and other remedies, but which ultimately die of this disease.

We now pass on to the treatment of *Hæmolytic Anæmia*. Here theoretical considerations suggest that animal food should be sparingly given, since it has been pointed out in the first lecture that it is asserted that a diet rich in animal food increases active destruction of red corpuscles. Dr. Hunter¹⁴ has suggested a trial of a purely milk diet, or of a farinaceous and milk diet, and in the case in which he tried these, though the disease was in an advanced stage, a certain amount of improvement took place—the blood pigment disappeared from the urine, and the amount of aromatic sulphates was diminished. I shall certainly give a purely milk, and a farinaceous and milk, diet a trial. Alcohol does not, as a rule, benefit such cases, and, if given, weak spirit and water is the best form. As long as patients with pernicious anæmia have the strength, they should get into the open air and sunshine, but should not tax their powers by exercise. They should adopt the recumbent position as much as possible, so as to conserve their powers, and put as little tax as possible on the fatty and weakened heart. We must remember, however, whilst combating the hæmolytic, not to neglect hæmogenesis, which is often struggling to maintain the balance. Sitting in the open air and sunshine in suitable weather, and carriage exercise, are therefore to be encouraged, the patient, of course, being suitably clothed.

We come now to the medical treatment of pernicious and other forms of hæmolytic anæmia. Amongst the remedies which diminish blood destruction—*anti-hæmolytics*—may be enumerated arsenic, quinine, mercury, phosphorus, betanaphthol, iodoform, carbolic acid, sulpho-carbolates, menthol.

Arsenic.—Amongst the great gains we have had in the treatment of anæmia in recent years arsenic stands in the first position. We owe the suggestion of its employment to Dr. Byrom Bramwell,¹⁵ who was the first to use it in pernicious anæmia in 1877. Since then abundant testimony has confirmed its value, and its action, if not specific, is at least very marked where tolerated. Various modes of administration have been adopted, but none is more efficient than Fowler's solution, in which form usually the maximum quantity can be exhibited. The dose, beginning with quite a small one—2 to 4 or 5 minims—freely diluted, and given with or directly after food, can be gradually increased until largish ones are tolerated. I believe the larger doses—10 to 15 minims three times a day—to be the most capable of producing good results. In some cases of pernicious anæmia arsenic is not well borne, though I cannot remember to have had such a case under my own care. In such circumstances I should certainly try its administration subcutaneously. It is not always successful even when tolerated. As regards its mode of action we have no certain knowledge. It was originally tried on account of its undoubted though somewhat capricious efficacy in Hodgkin's disease, which led to the inference that it exercised some, although unknown, action on the blood-forming organs. It has been suggested that it acts locally on the mucous membrane of the stomach and intestine (Hunter)—I presume as a germicide, preventing the development of ptomaines. Its well known action in malarial anæmia is probably due to its germicidal action on the plasmodium malarie in the blood corpuscles. A new

¹² *Practitioner*, July, 1878.

¹³ The *Extra Pharmacopœia*, Martindale and Westcott. Sixth Edition 1890. P. 295.

¹⁴ *Med. Soc. Trans.*, vol. xili, p.

¹⁵ *Edinburgh Med. Journ.*, November, 1877; and *Med. Times and Gaz.*, 1877 vol. li, p. 431.

light has been thrown on its possible action by an interesting observation of Dr. Copeman's.

He writes¹⁶ of pernicious anæmia: "When a drop of blood was removed from the finger and allowed to fall on a glass slide, then when the edge of the drop had dried somewhat a cover glass was gently placed upon it, crystals of hæmoglobin gradually formed in the film of blood in from ten to forty-eight hours without any further preparation. The only exception to this was in the case of patients who had been treated with arsenic for some days, after which crystals could not be obtained, although, if then the arsenic were discontinued for an equal length of time, they again put in an appearance."

It would appear from this important observation that arsenic exercises a direct influence upon the red corpuscles, lessening their vulnerability, which we have seen is one of the characteristics of anæmia, especially of hæmolytic origin. Arsenic has been shown to diminish the glycogenic function of the liver, and it is possible it may exercise some influence in restraining the hæmolytic function of this organ. In poisonous doses arsenic exercises a destructive influence on the red corpuscles, reducing the hæmoglobin and impairing its oxygenating powers. An interesting point in connection with the administration of arsenic is the fact that it sometimes produces bronzing or pigmentation of the skin. How this is brought about is a disputed point; but it is probable that it is by increasing the activity of the pigment-producing tissues. It is probable that the increase of colour of the urine in some cases of pernicious anæmia during the administration of arsenic is in some way connected with this action.

Quinine is sometimes useful in the pyrexial attacks of pernicious anæmia. Phosphorus has proved useful in one case recorded by Dr. Broadbent, but has failed to do good in others. The evidence regarding mercury is conflicting, but Keys has asserted it increases also the number of red corpuscles. Betanaphthol has been suggested by Dr. Hunter, and this drug and the other disinfectants I have named perhaps deserve a trial, but I have no personal experience of their employment in anæmia. Too often in pernicious and other forms of hæmolytic anæmia, all treatment is incapable of preventing the final issue in death. Arsenic may arrest the disease for a time, and in a few cases effect a cure, but more often, as we have seen, its effects are more transitory than is generally believed. Indeed, the position to-day is but little altered since Addison said of it, "The disease presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed after a variable period by the same fatal result."

I had intended to have dealt with Transfusion in the treatment of anæmia, but my time is exhausted, and I must leave this undiscussed. This is the less to be regretted, as my own experience on the subject is small, and distinctly unfavourable. The literature is voluminous, and the matter a very complex one. Moreover, the subject has been very fully dealt with by M. Hayem, and quite recently by Dr. Hunter,¹⁷ and the outcome of their experiments, and the general medical experience, is against the employment of transfusion, though cases of recovery from pernicious anæmia have been recorded after transfusion. Intraperitoneal and subcutaneous injections of blood have also been tried, especially on the Continent, but such treatment, even in the most skilful hands, has been shown by Cohnheim not to be free from great danger, fatal peritonitis having occurred in several cases after intraperitoneal injections.

But I must now bring my lecture to a close. I am deeply conscious of the imperfect manner in which I have accomplished my task. I feel that, in trying to cover so wide a field, I have dealt in a sketchy and imperfect manner with many parts of the subject.¹⁸ Still, I cannot but believe that it is important that a survey of the whole subject of anæmia should be made, so as to fit the many and detailed observations of the numerous workers into one harmonious whole. The enormous amount of work that has been done in recent

years, and the complexity of the subject, render the office a difficult one, requiring an abler exponent than myself.

In conclusion, I desire to express to you, Sir, and the Council of the Society, my sense of the honour conferred upon me in inviting me to deliver these Lettsomian Lectures, and also to thank the Fellows and gentlemen who have patiently listened to them.

ON THE TREATMENT OF PSOAS, ILIAC, AND OTHER LARGE TUBERCULOUS ABSCESES BY HOT WATER FLUSHING WITHOUT DRAINAGE.

By ARTHUR E. BARKER, F.R.C.S.,
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HITHERTO the usual treatment of large tuberculous abscesses, whether connected with a diseased spine, with broken-down glands, or in the soft parts, has left much to be desired. Whether they were simply allowed to burst, or were opened and dressed antiseptically, or whether they were aspirated with or without subsequent injection of germicidal fluids, the results have often been far from satisfactory. Either the discharge, however sweet, has gone on for an indefinite time through open sinuses, or the abscess has become infected with saprophytic organisms, and only too often with acute septic processes.

Most of us must have always felt, in dealing with these large collections of curdy and often semisolid material, that the great difficulty was their complete evacuation. But I question whether many of us realised what complete evacuation really ought to involve until comparatively recently. Formerly, it simply meant the escape of as much of the liquid contents of such an abscess as would flow freely either through a limited opening or through an aspirator needle. But it is only lately that thorough evacuation of a tuberculous abscess has come to mean not only the removal of its fluid contents, but also of all solid and semisolid, caseous or calcareous, *débris*; and not only this, but of that lining of half organised exudation material which covers the whole inner surface of the abscess, formerly called the "pyogenic membrane." It is in this last structure, if left behind, that we probably have the greatest obstacle to the complete obliteration of simple tuberculous abscesses of soft parts when otherwise emptied by methods hitherto in vogue. So long as it remains behind, we leave the most active part of the tuberculous material undisturbed, and this is capable of continuing indefinitely the process which originally produced the fluid contents of the abscess. Outside of this material is found the firm wall of the cavity, which is nothing else than more or less perfectly organised fibrous tissue. This latter may be regarded as a natural barrier thrown out by the tissues around the tuberculous focus by plastic exudation, and tending to protect the system against the spread of the infective process. In everything that is done to a tuberculous abscess, this natural wall therefore must be respected as far as possible. Further, in evacuating such an abscess, we must guard the freshly-cut surfaces of the healthy tissues through which we have to cut in order to reach the tuberculous matter against inoculation with the latter in the course of its removal. If this precaution is not taken, our scar will often break down weeks after primary union has taken place, and the process of reinfection may again take place over the whole tract of the recently closed abscess cavity.

Now if we adopt this view of the nature of tuberculous abscesses, and the principles of eradication which should be applied to them, the question how to accomplish thorough evacuation forces itself upon us very urgently. It would serve no useful purpose here to review all the various methods of treating the abscesses in question now in practice, but I shall briefly sketch one which has yielded me excellent results of late years, indeed better than any I have ever had by other methods.

Having had considerable experience in the removal of tuberculous material from widely diseased hip-joints by hot

¹⁶ *St. Thomas's Hospital Reports*, vol. xviii, p. 103.

¹⁷ Arris and Gale Lectures, *BRITISH MEDICAL JOURNAL*, 1889, vol. ii.

¹⁸ I regret exceedingly that a very able and important paper by Dr. Edington, "Report on the Morphology and Development of the Blood," *BRITISH MEDICAL JOURNAL*, May 31st, 1890, has entirely escaped my observation until too late to deal with. It should be consulted by the reader.