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BONE-MARROW IN THE TREATMENT OF PERNICIOUS ANÆMIA.¹

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ALTHOUGH this communication deals with only one case of pernicious anæmia treated with bone-marrow, the curative effect seems sufficiently evident to justify the publication of the case, especially as an opportunity occurred for testing in it the value of the chief remedies hitherto used in the treatment of this disease.

The patient, A. R., a gardener, 60 years of age, entered the Royal Infirmary on September 30th, 1893. His symptoms were frequent vomiting and diarrhœa, œdema of the feet and ankles, moderate and irregular pyrexia, dimness of vision, retinal hæmorrhages, anorexia, dyspnœa, and, latterly, complete prostration. The illness had existed for about four months.

Although I was desirous at once to treat this patient with bone-marrow, the condition was so serious a one that, in the absence of experience regarding the therapeutic value of bone-marrow, I considered it advisable to administer, in the first instance, some of the remedies usually employed in pernicious anæmia. Only after they had failed in producing benefit was bone-marrow given.

For the sake of brevity, I shall divide the history of the patient into eight periods, which correspond with the treatment adopted in each period (see Diagram).

First Period, two weeks, no medicinal treatment. During this period, the hæmocytes of the blood varied from 1,860,000 to 1,460,000 per cub. mill., and the hæmoglobin from 28 to 30 per cent., the specific gravity being 1038. There was great distortion in the shape and variation in the size of the hæmocytes, which did not form rouleaux. Retinal hæmorrhages were present in both eyes.

Second Period, two weeks and a-half; ferrous chloride, 6 to 12 grains daily. The hæmocytes and hæmoglobin steadily fell to 900,000 per cub. mill. and 20 per cent., respectively, and the specific gravity to 1036.

¹ Abstract of a communication to the Eleventh International Medical Congress, held in Rome, April, 1894

Third Period, eight days; arsenic (15 to 30 min. of liquor arsenicalis daily) was given in addition to 12 grains of ferrous chloride daily. Still further deterioration occurred in the hæmocytes and hæmoglobin, the former falling to only 843,000, and the latter to 18 per cent.; but the specific gravity remained at 1036.

Fourth Period, three weeks; arsenic and iron were continued in the above doses, but ox bone-marrow was now also given by the mouth, uncooked, and in the quantity of 3 ounces, daily.

An almost immediate improvement occurred, so that at the end of this period the hæmocytes numbered 1,800,000, the hæmoglobin amounted to 35 per cent., and the specific gravity was 1042. The patient now began to recover strength; he could remain out of bed for several hours each day, and the appetite was improved.

Fifth Period, twenty-six days; ox bone-marrow, arsenic, and salol (15 to 30 grains daily). The improvement was continued. The hæmocytes rose to 2,470,000, the hæmoglobin to 55 per cent., and the specific gravity to 1047. The patient felt much stronger, and his complexion was distinctly pink, and had almost entirely lost its original yellow hue. He had also gained in weight.

Sixth Period, thirty-two days; ox and calf bone-marrow and salol (30 grains daily).

The improvement was still further continued, so that the hæmocytes reached an absolute maximum of 4,130,000, though they afterwards fell to 3,400,000; the hæmoglobin rose with the hæmocytes to 75 per cent. and also fell to 70 per cent., and the specific gravity became 1058. The blood had now a healthy appearance. It could flow readily from a small puncture, it formed fairly good rouleaux, and the red cells were more uniform in size and fewer of them were distorted.

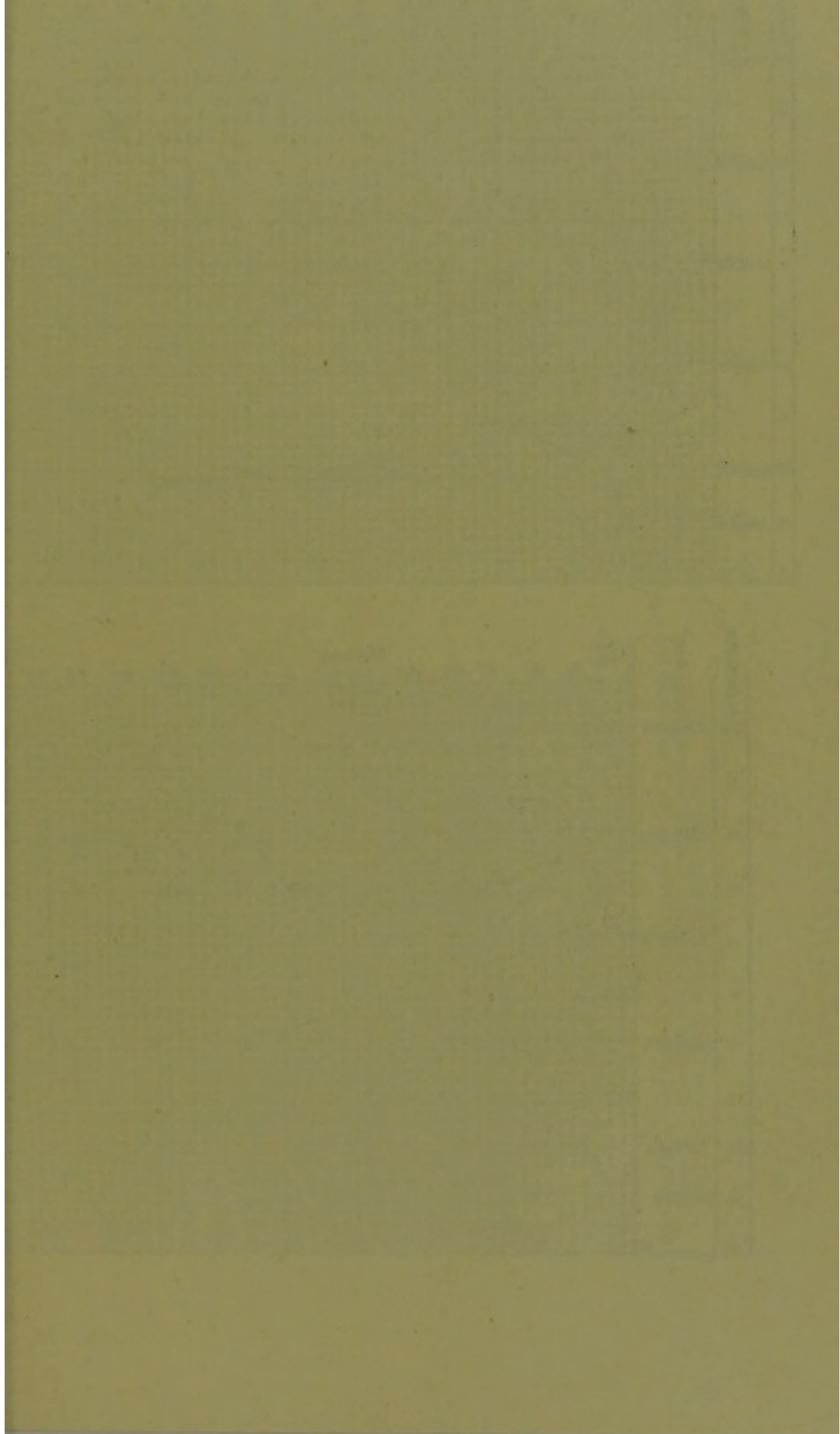
The patient was now able to do light work in the ward without fatigue; the alimentary system was perfectly healthy; œdema, pains, headache, pyrexia, and the venous *bruits* in the neck had disappeared; and the skin had a healthy appearance.

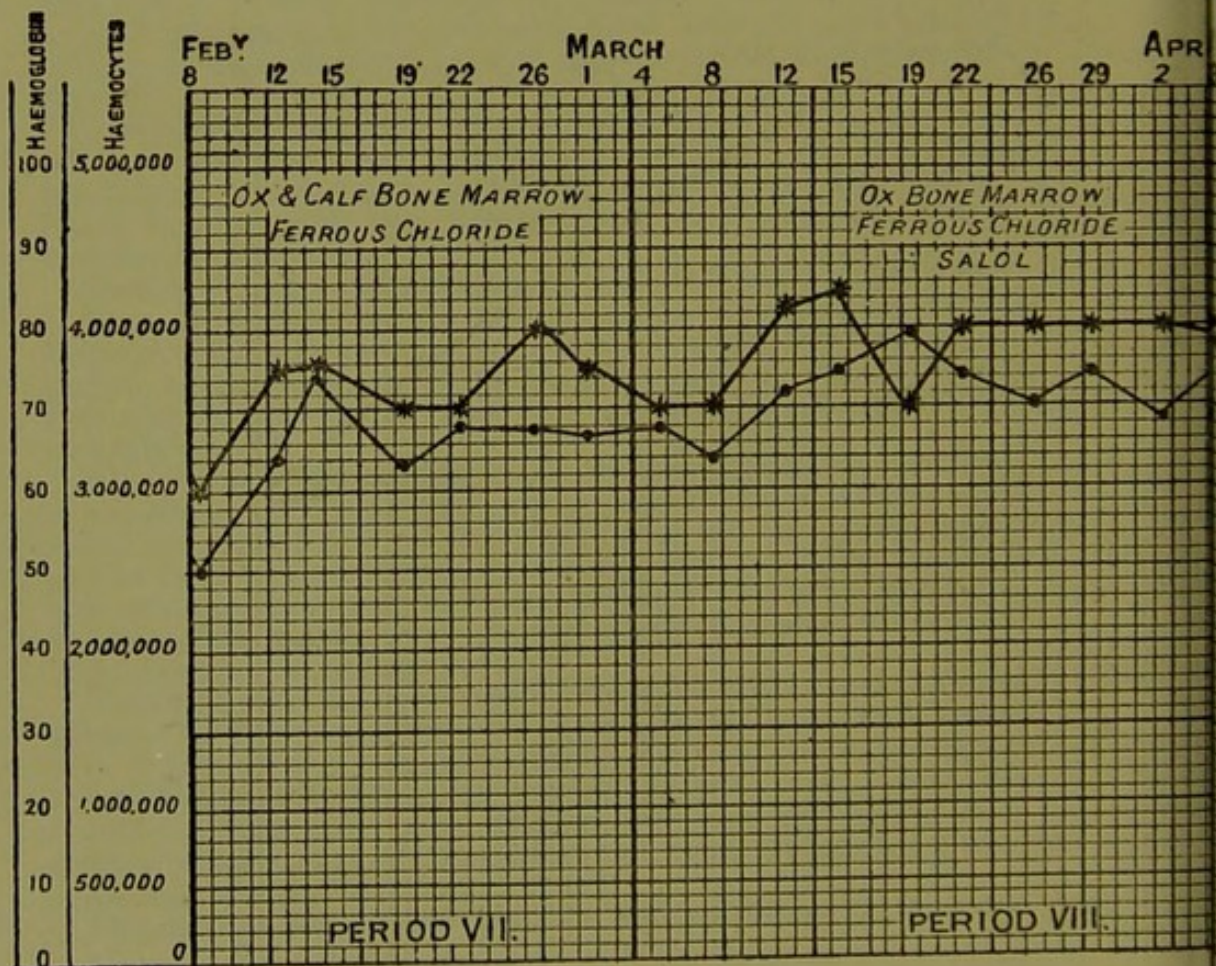
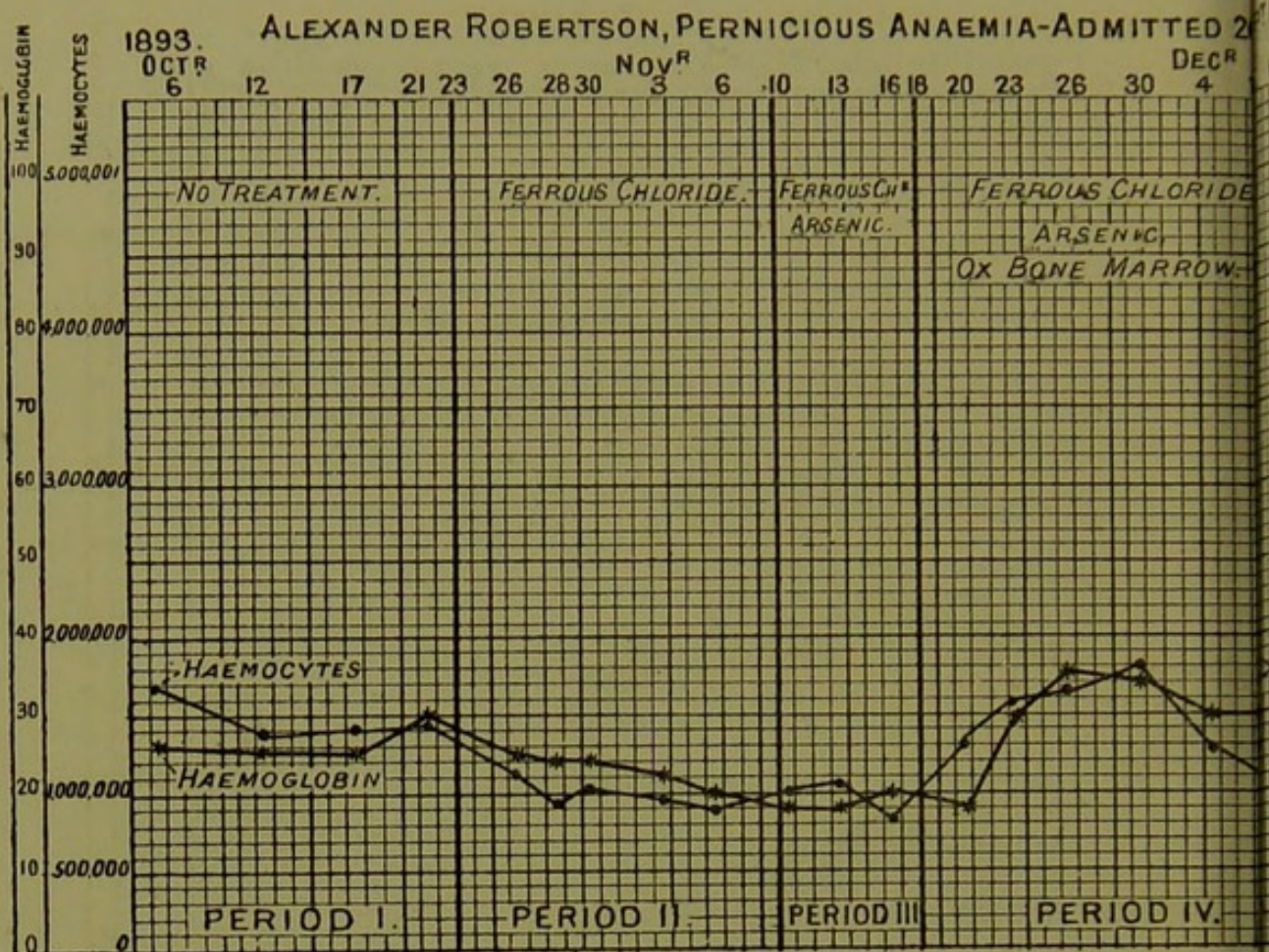
Seventh Period, one month; ox and calf bone-marrow and ferrous chloride (6 to 12 grains daily). The hæmocytes remained, with some oscillations, at about 3,400,000; the hæmoglobin averaged from 70 to 75 per cent., on one occasion reaching 80 per cent., and the specific gravity remained steadily at 1059.

The patient felt strong, and enjoyed assisting in ward work, such as carrying coals up a long flight of stairs. He remained out of bed all day, there were no subjective symptoms even on considerable exertion, and "hæmic" venous and cardiac *bruits* were no longer audible. Ophthalmoscopic examination of the eyes showed that all traces of retinal hæmorrhage had disappeared.

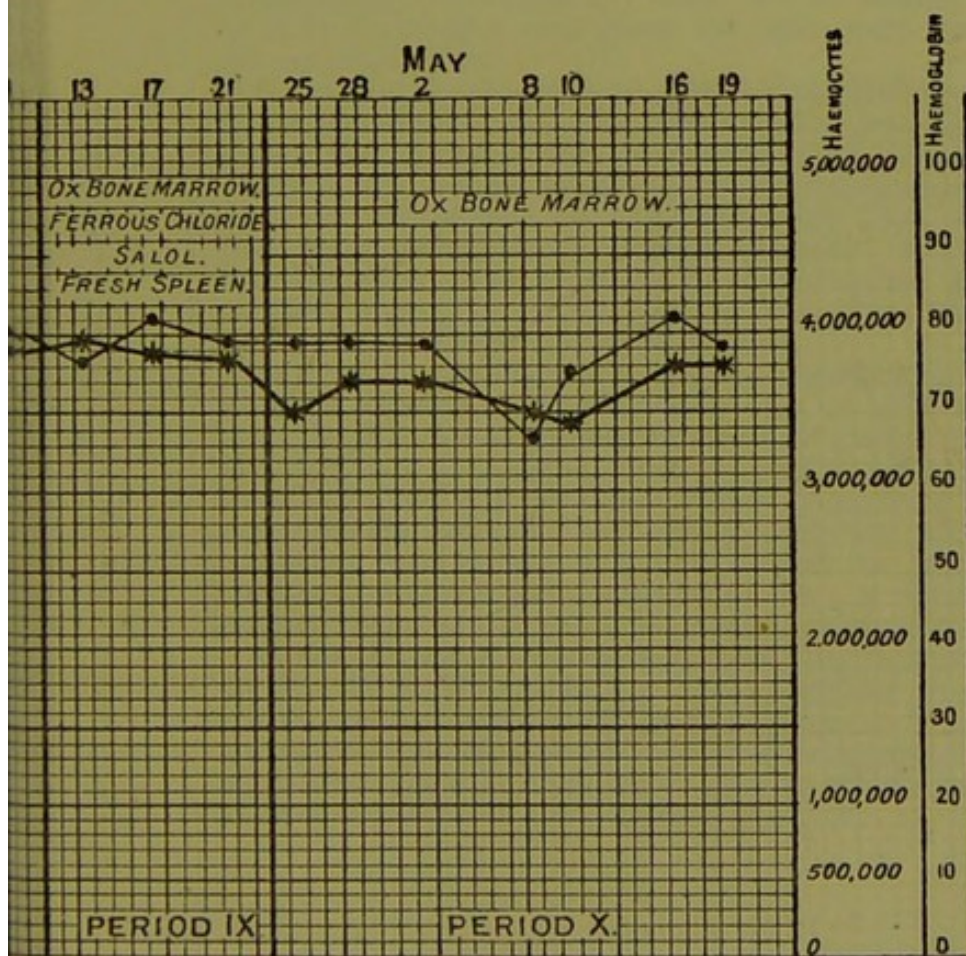
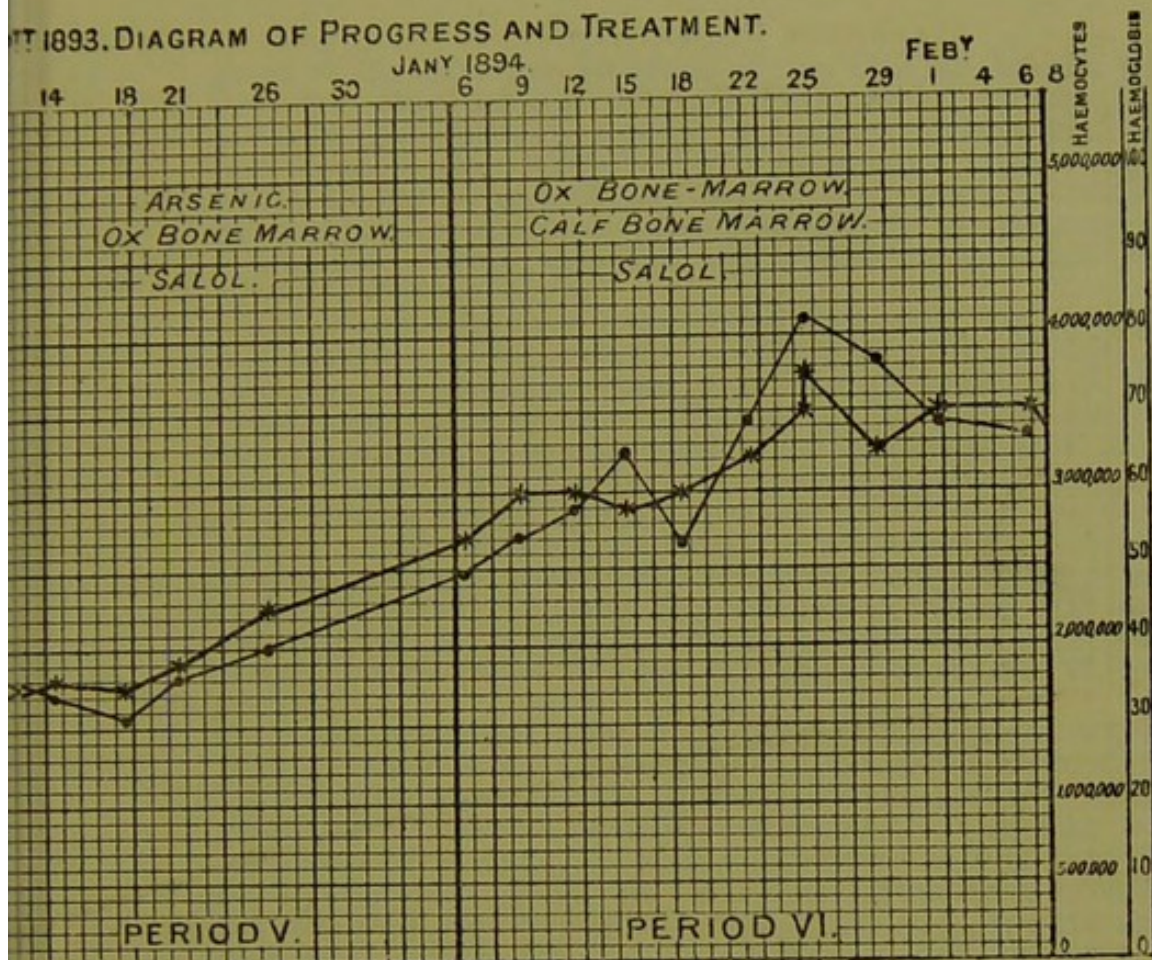
Eighth Period, not concluded (when this paper was communicated to the Congress); ox bone-marrow, iron, and salol. The improvement was maintained, so that the hæmocytes reached 4,000,000, the hæmoglobin 85 per cent., and the specific gravity 1060. The patient was now practically in a normal condition. His appetite was good, and his appearance that of a healthy man.

An examination of the graphic representation of the pro-

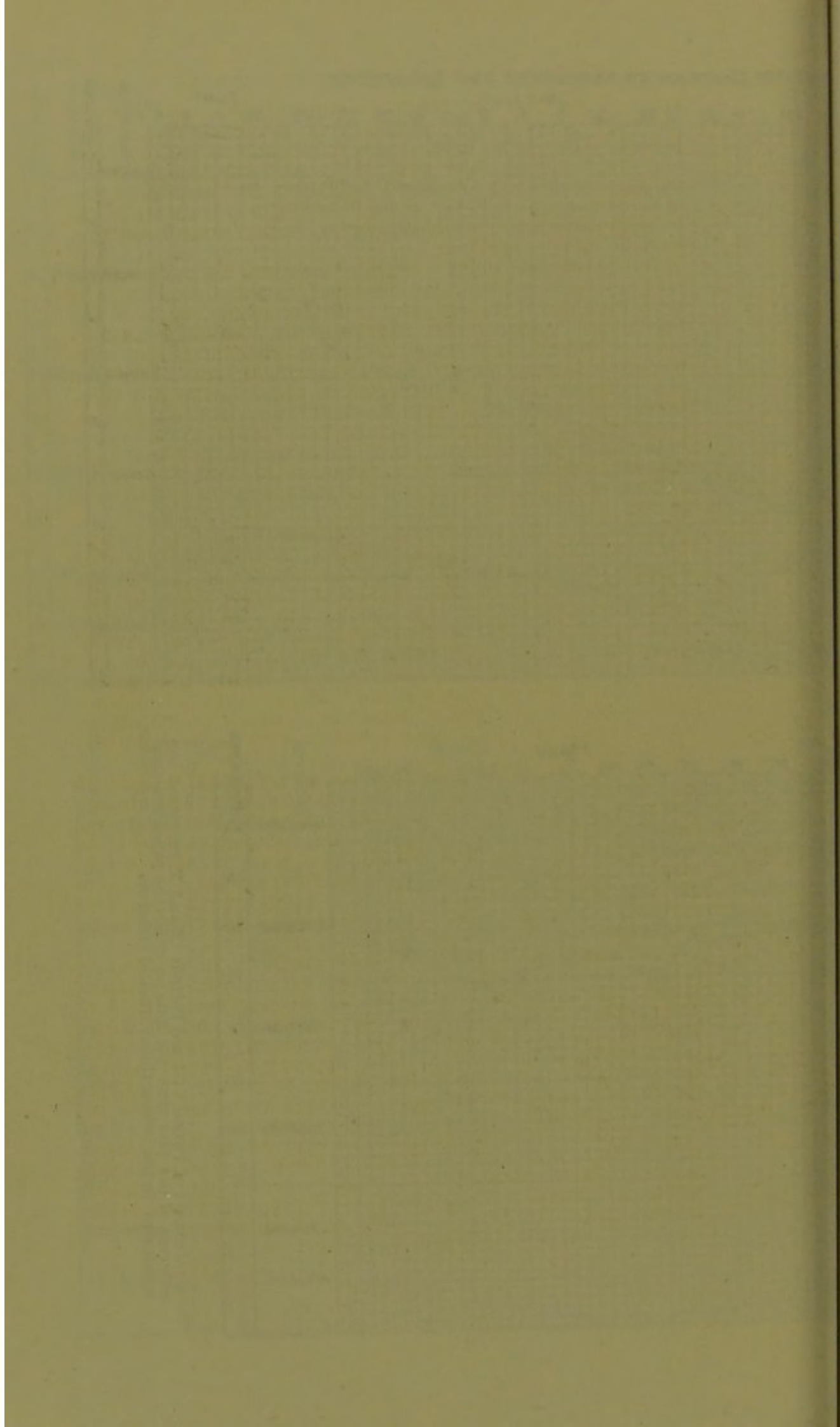




1893. DIAGRAM OF PROGRESS AND TREATMENT.



The greater part of Period VIII and Periods IX and X represent the progress of the case after the date on which the paper was communicated to the International Medical Congress



gress of the case (see Diagram) shows that no benefit was obtained—that, indeed, deterioration occurred—during the prolonged administration of iron and arsenic in both medium and large doses; but that the remarkable improvement which occurred was produced only after the administration of bone-marrow had been commenced, while it continued to be produced during periods in which neither arsenic nor iron were being administered.

The demonstration of a curative influence by bone-marrow may appear to be somewhat obscured by the introduction of salol into the treatment, and a further examination of the therapeutic value of this substance in pernicious anæmia appears, indeed, to be suggested. The introduction of salol was due to the urgency of the case requiring that no description of treatment should be neglected in whose favour any theoretical or experimental evidence had been advanced. Since, however, this communication had been made to the International Medical Congress, the patient was treated with only bone-marrow for a period of twenty-seven days (Period x), and the improvement was well maintained to the end of this period.

He was discharged from the hospital because of his urgent wish to return to work as a gardener, for which he declared himself more able than he had been for the last five or six years; and, to use his own expression, he felt "as if he had been made over again." On the day when he left the hospital (May 19th, 1894), the hæmocytes numbered 3,900,000 per cub. mill., the hæmoglobin was 78 per cent., and the specific gravity 1058; the hæmocytes were nearly uniform in size, only a few of them showed slight "tailing," and no megalocytes were present; there was no excess of leucocytes or of blood plates; and good rouleaux were formed on the microscope slide.

It may be worthy of note that before medicinal treatment had been commenced, and in the earlier periods of treatment when the patient was receiving large doses of iron and arsenic, the blood plates were conspicuously deficient in number; while soon after the administration of bone-marrow had been commenced, a great increase occurred in their number, which was followed by a reduction to a moderate number during the later periods when the blood had been restored to a nearly normal condition.

The frequent failure of therapeutic measures in pernicious anæmia confers an interest upon any remedy which appears capable of controlling this malignant disease, even although the evidence is derived from one case only, and notwithstanding the circumstance that temporary improvement occasionally, though very rarely, appears to occur spontaneously. The facts now stated appear to justify the hope that bone-marrow will be found to have a remedial value in some at least of the cases of pernicious anæmia.

It is with much satisfaction that I express my obligations to Mr. D. A. Welsh, M.B., C.M., resident physician in my wards, for the efficient aid he has given me in conducting the numerous microscopic and other observations that were made in connection with this case, and to which only a general reference has been made in this abstract.

