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The Use of Oxygen in the Treatment of Leukæmia and Grave Anæmias.

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FROM

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES,

NOVEMBER, 1889.

Extracted from the
American Journal of the Medical Sciences for November, 1889.

THE USE OF OXYGEN IN THE TREATMENT OF LEUKÆMIA AND GRAVE ANÆMIAS.

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The treatment of the more serious forms of blood diseases is still so unsatisfactory that any addition to our means of counteracting them is deserving of record and careful scrutiny, and we offer these observations in the hope that others will be induced to try what we have found to be a potent agent. The changes in the blood in the cases observed were followed out in every detail, and the conclusions rest, therefore, not on impressions, but on actual minute inspection of the blood corpuscles.

Case I.—G. B., æt. thirteen, had been subject to attacks of jaundice from infancy; the mother states that she believes the child had a number of malarial seizures, but was not certain. When first seen (February 5, 1889), the patient was pale, the conjunctivæ pearly and somewhat jaundiced. The spleen was enlarged, extending from the eighth rib to four finger-breadths below the margin of the ribs. The tumor had been noticeable for a year previous. For nearly two years the patient had spells of weakness, extending over a period of three weeks, and at intervals of two to three months. Occasionally hemorrhages from the nose occurred during this time, but never sufficient to cause alarm. His strength gradually failed, and he was discharged from his position as cash boy in a dry goods house, being unable to stand the work.

When first seen, the blood was examined and found to contain a sufficient excess of white corpuscles to warrant the diagnosis of splenic leukæmia. This view was substantiated by the fact of the white corpuscles steadily increasing in number, while the red diminished. February 5, 1889: The red numbered 2,350,000, the white 105,000 to the c.mm.; by May 20th the white corpuscles had increased to 320,000.

Having been on arsenic sometime previous to his first visit, the patient was given Basham's mixture and three grains of the extract of ergot three times daily, without, however, producing any effect upon the spleen. Galvanism was tried over the splenic region for two months without any improvement. Trinitrine was given at the same time, but the patient grew weaker under this treatment, and arsenic was again resorted to, though without amelioration.

On June 1st he began to inhale oxygen, and he improved rapidly under the treatment. He was given daily from twenty to thirty litres of oxygen, which was continued until August 5th. At this time the

boy returned to work, much better than when he had left it. The blood was again examined September 2d, and found to be so near the normal that a count of the white corpuscles was considered unnecessary, the red being increased to 4,850,000, and one white found to about every four hundred red. The oxygen treatment was stopped.

Unfortunately, in this case, the early history could not be accurately determined; the mother's statements being very conflicting. But the great improvement spoke for itself—the boy is now steadily at work, and there is reduction even in the size of the spleen. The area of dulness begins fully one inch lower and one inch further to the left of the median line than when first seen.

The following case gives us a clear history; the patient being a man of intelligence and one who takes as much interest in the details of his case as those attending him:

Case II.—S. L., æt. thirty-five; a man largely engaged in mining operations. Up to fifteen years of age he had enjoyed good health. The family history is excellent. In 1869, he lived in Iowa on the banks of the Mississippi River, a highly miasmatic region. Three years later, at the age of eighteen, he had an attack of malaria; the case was a severe one, lasting over a period of two years, during which time he was seldom free from the symptoms of the disease, and never escaped longer than one month without being confined to his bed. In 1874, he moved to a district among the Rocky Mountains, where he was entirely free from the outbreaks. Two years later, he had typhoid fever which confined him to his house for nine weeks. The convalescence was slow. In 1879, he had an attack of erysipelas lasting six weeks; convalescence here, too, was slow. Up to this time the patient had never weighed more than one hundred and fifty pounds; in the spring of 1880 he began rapidly increasing in weight, reaching, in a period of six months, two hundred and twenty pounds.

Although, for two years, at this period of life, the patient claims to have been in the best of health, a slight pallor of the skin was always present. He enjoyed, however, but two years of absolute freedom from ailment; for, in the spring of 1883, while suffering from jaundice, he began to lose flesh rapidly; in one month his weight was reduced to one hundred and ninety pounds. In the summer of the same year he had hemorrhages from the nose, the attacks lasting twenty-one days. The hemorrhages occurred daily, and were uncontrollable by any means other than plugging the nostrils; large doses of ergot and gallic acid were administered. After the hemorrhages ceased, his weight had diminished to one hundred and forty-four pounds.

In the autumn of 1883, a physician in Denver found that the spleen was enlarged; no examination of the blood, however, was made, and he was treated for "ague cake." Soon after this the patient went to Boston, where he had another attack of hemorrhage, lasting ten days. Up to this time he had gained ten pounds, but was soon reduced to one hundred and forty pounds. A trip to Europe was recommended, and there the patient in four months' time gained forty-four pounds. After leaving Europe he gradually lost weight. No hemorrhages have since occurred.

Since 1883 he had always suffered the inconvenience of an unquenchable thirst, the amount of liquids drunk being enormous—as high as twenty pitchers of ice water in the twenty-four hours; besides this, he imbibed a large amount of champagne, brandy, and other drinks. Concerning the early habits of the patient, they were anything but favorable to the success of any treatment. From the age of eighteen he had been a heavy drinker, though never to intoxication; by his own statement he has taken in a day, without any effect other than exhilaration, two quarts of brandy, besides beer and wine. He has always been an inveterate smoker, and even at the present time does not find it easy to smoke less than nine cigars a day. Though a specific history in the case cannot be positively asserted as being negative, yet there have never been any symptoms of secondary infection.

Early in September the patient came to Philadelphia for treatment. When first seen he suffered from intense thirst and frequent micturition, passing large quantities of water, containing neither albumin nor sugar. The spleen was enormous; it passed nearly two inches beyond the umbilicus. There were profuse diarrhœa and great emaciation. Ergotine gr. ij t. d. was prescribed, followed by tartrate of iron and potassium, and that by the sulphate of iron. The ergot was continued more or less throughout the month of September, and, obeying strict directions, the stimulus was reduced to very moderate amounts. During this time the diabetes insipidus disappeared, and the patient drank but a pint of water in the twenty-four hours; the diarrhœa was arrested.

September 24th. Arsenite of soda, in gr. $\frac{1}{40}$ doses, was prescribed. Soon after this the patient went of his own accord to Hot Springs, Arkansas, but was advised there to return to Philadelphia, his case being considered non-specific. While at the Hot Springs he took the iodide of potassium gr. xv, t. d. This was continued until December 9th, being stopped on account of gastric irritation. At this time the spleen was outlined and found to extend an inch and a half to the right of the median line, and to fill completely the left abdominal cavity—from the lower border of the seventh rib above to the lower border in a line with Poupart's ligament. The blood contained 3,400,000 red and 62,000 white corpuscles to the c. mm.; hæmoglobin 60 per cent.

There was some improvement under the use of arsenic and Basham's mixture. But January 10th the patient was worse. Arsenite of soda, in doses from $\frac{1}{30}$ to $\frac{1}{25}$ of a grain, was taken at irregular intervals until June 27th, when it was discontinued, and the oxygen treatment begun. An examination of the blood at this time showed that the red corpuscles had diminished to 1,440,000, the leucocytes had increased to 1,120,000, a proportion of as $1 : 1\frac{1}{5}$. The patient had been in the West three months previous to this time. When he returned to Philadelphia it was found that the character of the disease had assumed a most serious type. His appearance was striking. The veins of the forehead were largely distended, and the capillaries plainly visible in many parts of the face, most prominent on the nose. The spleen was as large as ever, the abdomen greatly distended and tense, assuming a spherical shape. The knees were shaky; the feet were swollen, the swelling extending up as far as the knees. Shortness of breath was produced upon the slightest exertion; he always felt extreme fatigue. The spinal column was tender to the touch; the sitting posture produced severe pain in the bones of the ilium. A distinct anæmic

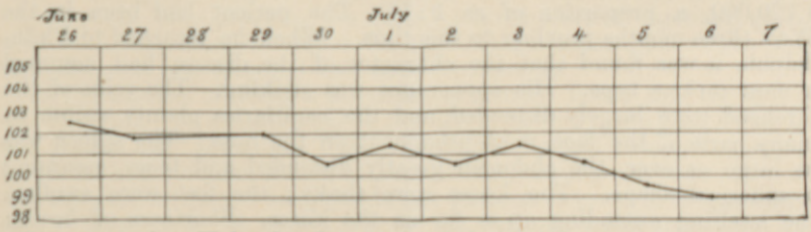
murmur was heard over the base of the heart. Profuse watery discharges from the bowels had set in four days before his return, and still continued. He reported that he had been feverish for weeks, his temperature at that time (June 26th) being 102.3°; he was much depressed in spirits. ate stated that, having himself made a careful study of the disease, he Hew there was not the slightest hope for him. He was willing and anxious that an experienced surgeon should attempt to remove the spleen, knowing that his chances were of the very slightest.

Beside the condition of the blood in regard to the relation of the corpuscles, it might be of interest to add that its color was opaque, it flowed freely from the puncture made by the lancet, and coagulated very slowly. Microscopically, the red blood-corpuscles were found to be widely separated, extremely pale, and at no time formed in rouleaux. The leucocytes varied in size and shape; some were small, others of enormous size, fully the one-five-hundredth of an inch in diameter; many were crescent-shaped as well as large, while others were shapeless.

After two days' inhalations of oxygen, the character of the blood was entirely changed; observed on the glass slide, the large and misshapen leucocytes had entirely disappeared, the red corpuscles formed rapidly in rouleaux, and the blood showed no abnormal character other than the relation of the white and red corpuscles.

From June 27th to July 3d the patient took nothing beside the oxygen, except a mild hypnotic upon retiring. Ten litres, three times a day, were inhaled. The oxygen was perfectly pure, and was allowed to pass through water, to prevent dryness of the throat. The effect at the end of the week was marked; the swelling of the feet was scarcely perceptible; the appetite was good; the bone pains had almost entirely disappeared; the temperature had steadily fallen, and the patient walked about with comparative ease. The number of white corpuscles had diminished nearly one-half, while the red had gained a million. During the second week the patient was given Basham's mixture, but it did not suit him, and at the end of the week it was discontinued. In the third week of the treatment the most marked improvement took place in the general condition. The fever disappeared entirely; there was no swelling of the feet; the prominent veins on the forehead and the capillaries visible on the face had almost completely passed from view; the appetite increased; there was shortness of breath only on violent exertion, and the patient was but little inconvenienced by walking a mile. By the end of the fourth week he had gained nine pounds.

CHART.



Temperature from Wednesday, June 26, to July 7, 1889. Oxygen commenced in the morning of July 27th. Temperature taken 3 P. M. After July 7th the thermometer at no time registered over 100°.

From this time the improvement was steady until August 20th, when, by some indiscretion in diet, aided greatly by a few bottles of champagne, together with the atmosphere of Boston, which did not suit him, he began to fail. The white corpuscles increased in number, the red slightly diminished.

August 26th, he returned to Philadelphia, since which time he has rapidly gained in strength, and is now on a visit in Colorado, having stood the trip very well. Not long before he left, the spleen was carefully percussed, and presented a marked reduction in size, the transverse diameter extending only to three-quarters of an inch of the median line near the umbilicus. A telegram from Denver of September 20th records: spleen going down, blood in excellent condition, hæmoglobin up, appetite excellent.

An ophthalmological examination made August 29th, by Dr. Gould, showed a noteworthy absence of several of the typical signs of leucæmic retinitis as described by Liebreich, Becker, Leber, and others. Dr. Gould regretted that he had no opportunity to make an examination at an earlier stage of the disease when the proportions of the red and white corpuscles were so abnormal. There is in both eyes a grayish haze that suffuses the central part of the fundus, especially about the papilla, in semi-obscurity. This gradually clears until at about 50° the details of the periphery are normally clear. But this discoloration is not yellow, nor has it an orange tint. The veins are highly distended and engorged, but only slightly tortuous; the arteries of subnormal size, often thread-like; the light-streaks of the centre well preserved; the color of the blood is pale, but not excessively so. No white bands of extravasated corpuscles follow the vessels, and the white dots or splotches usually described are not to be seen about the macula or periphery, and no remains of hemorrhages are to be found. The existence of a typical tobacco papilla is very noticeable. The visual acuity is good, full $\frac{20}{xx}$ with either eye, despite a slight hyperopic astigmatism.

During the course of treatment the oxygen was steadily increased to sixty litres in the twenty-four hours, and now one hundred litres a day are inhaled; the patient having sent by express nearly a thousand gallons to Colorado. It was at first thought best to administer the oxygen so that it be taken at three sittings, this was changed to two sittings in the twenty-four hours. Throughout the treatment no unpleasant symptoms attended the use of the oxygen. An exhilarating effect, at least, was looked for, and it was expected that such large doses would produce some action upon the heart, but a sense of freedom felt about the chest after the inhalation was the only effect noticed.

During the treatment of these cases of leukæmia, two cases of chlorosis were given inhalations of oxygen, as an adjunct to the use of iron. These are brief records of them.

Case III.—A. M., æt. seventeen, school-girl. In the early spring she began to feel weak, and suffered considerably from headache. Her menses at that time were scant, and disappeared entirely during the

months of April and May. For six months previous to this she had been pale. On June 8th, the patient was extremely pale, the conjunctivæ pearly, there was but little color to the lips. The blood was examined, and found to contain but 25 per cent. of hæmoglobin, the red blood-corpuscles numbering 3,800,000 to the c. mm.; white corpuscles one to every four hundred and eighty red. The sulphate of iron in increasing doses was prescribed, with daily inhalations of from twenty to thirty litres of oxygen. In two weeks time there was marked improvement. June 24th the menses reappeared, though scant.

By July 1st her color had returned. An examination of the blood showed the hæmoglobin to be 90 per cent., the red corpuscles numbering 4,850,000 to the c. mm. White corpuscles one to every six hundred red.

Case IV.—R. E., æt. twenty-three, teacher. Menses irregular and scant for a number of months. She suffered much from headache. For the past three months she has been very pale. There was considerable shortness of breath. A large eczematous patch covered most of the chin. Examination of the blood showed the hæmoglobin to be but 30 per cent. of the normal, the red corpuscles numbering 5,000,000 and the white normal. She was given the sulphate of iron in increasing doses, and inhalations of from twenty to thirty litres of oxygen a day. To the eczema an ointment of ten grains of resorcine to an ounce of ointment of oxide of zinc, was applied at night. July 24th, the general health was much improved, and the hæmoglobin found to be 45 per cent. The iron pills and the oxygen were continued.

August 2d. Menses were about normal, the hæmoglobin 60 per cent. The patient was again seen August 28th. She had discontinued the oxygen on August 8th, and took no medicine after August 12th, the eczematous patch having disappeared. She was still somewhat pale; the hæmoglobin was found to be 75 per cent. The pills were renewed, oxygen was resumed, and pepsine and hydrochloric acid were taken after meals. September 8th, her color was normal and the hæmoglobin found to be 90 per cent., the patient feeling strong and hearty.

Of the value of the oxygen in these severe cases of anæmia there can be no doubt, though they were of a character in which it is likely that other treatment long persisted in would also have been beneficial. But certainly a curative effect would not so soon have been accomplished without the oxygen. With these results in mind, it is natural that we should have been anxiously waiting to observe its effects in a case of undoubted pernicious anæmia. Such a case is now in our hands, in which the first examination showed only 900,000 red corpuscles, and the second, in about a week afterward, 700,000; the hæmoglobin at both being 25 per cent. The patient is weak to the verge of utter exhaustion. We have begun the oxygen treatment, but have not as yet used it long enough to judge of its merits.

But to return to what we have been studying in the first group of cases—to the leukæmic condition and the changes wrought in it. That these were made through altering the blood seems certain. With its alteration, the nervous system recovered from its depressions, the mind improved, flesh and strength were gained, the secretions became healthier,

and all this took place rapidly, and in cases in which iron and arsenic had failed to stay the downward course. The effect on the spleen was less evident, for the organ, though decreased, remained very large in both.

It may be of interest to compare the results of the treatment with some instances of the disease in which blood counts were made while other remedies were employed. In Mr. Barton's well-known case,[1] in which for four months large doses of arsenic were taken, the dose reaching twenty-five minims of the liquor arsenicalis six times a day, there was a most striking improvement. The white corpuscles were greatly reduced, but there was but little increase in the red. We have made blood counts in cases treated with phosphorus, and in cases treated with arsenic. In one with phosphorus persisted in for three weeks in decided doses, two observations on the blood showed no improvement, and the patient was lost sight of. Arsenic we have often employed and made frequent examinations of the blood during its use. We append one followed to the end, drawn up for convenience' sake in tabular form.

THE CASE OF H. R., TREATED MAINLY BY ARSENIC.

	Number of red corpuscles to the c.mm.	Number of white corpuscles to the c.mm.	Per cent. of hæmoglobin.	The proportion of red to white corpuscles.
June 12, 1888.	2,830,000	145,000	40	1 : 20
" 26,	2,800,000	103,200	40	1 : 27
July 9,	2,915,000	108,000	45	1 : 27
" 16,	2,500,000	95,000	30	1 : 25
" 30,	2,405,000	90,000	35	1 : 27
Aug. 12,	2,365,000	205,000	20	1 : 11+
" 21,	2,160,000	300,000	30	1 : 7+
" 30,	2,050,000	368,000	25	1 : 5+
Sept. 15,	1,950,000	400,000	25	1 : 4+
" 25,	1,760,000	950,000	20	1 : 1+
Oct. 18,	1,570,000	1,000,000	20	1 : 1+
" 29,	1,240,000	1,938,000	15	1 : 0.5+
Nov. 5,	1,120,000	2,560,000	10	1 : 0.5

The following shows the line of treatment in the case of H. R.:

June 12th to July 1st. Quinine sulph. grs. v, t. d., ext. of ergot. grs. v, t. d.

July 1st to Sept. 26th. Stomach irritable. Ergot discontinued, liq. Fowleri ♏ iv, increased gradually to ♏ xx, t. d., discontinued only when stomach became irritable.

The patient died November 29, 1888. Post-mortem examination: Spleen weighed eight pounds, the liver six and a half. Kidneys contracted. Inflamed condition of the alimentary canal and peritoneum. Mesenteric glands enlarged. Fatty and dilated heart. Pleural adhesions. Slight broncho-pneumonia. Anasarca.

[1] Year book of Treatment, 1889.

For purposes of comparison we append, at the risk of some repetition, the results in tabular form, with reference to the blood and its change by the oxygen treatment, in the two cases of leukæmia detailed at the beginning of the paper. The increase of red as well as the diminution of the white corpuscles is very obvious.

THE CASE OF G. B., SHOWING THE RELATION OF THE RED AND WHITE CORPUSCLES BEFORE AND AFTER THE INHALATIONS OF OXYGEN.

	Number of red corpuscles to the c.mm.	Number of white corpuscles to the c.mm.	Per cent. of hæmoglobin.	The proportion of red to white corpuscles.
Feb. 5, 1889.	2,350,000	105,000	20	1 : 22
April 10,	2,860,000	120,000	25	1 : 24
May 12,	2,650,000	300,000	20	1 : 8
" 20,	2,550,000	320,000	15	1 : 8
June 10,	3,000,000	165,000	20	1 : 12
" 23,	2,675,000	160,000	—	1 : 16
" 28,	3,500,000	17,500	—	1 : 200
July 5,	3,800,000	17,277	30	1 : 220
" 10,	4,000,000	10,650	—	1 : 380
" 16,	4,300,000	13,300	45	1 : 323
" 29,	4,520,000	14,000	65	1 : 323
Sept. 1,	4,850,000	——	—	1 : 400

The following shows the line of treatment in the case of G. B.:

February 5th to 23d. Basham's mix. ℥ss, t. d.; ext. of ergot. grs. iij, t. d.

February 23d to May 25th. Trinitrine gtt. i–v, t. d.; quinine grs. iij, t. d.; galvanism.

June 1st to July 29th. From 20 to 30 litres of oxygen a day; no other treatment.

During the month of August the sulphate of iron was prescribed.

THE CASE OF S. L., SHOWING THE RELATION OF THE RED AND WHITE CORPUSCLES BEFORE AND AFTER THE INHALATIONS OF OXYGEN.

	Number of red corpuscles to the c.mm.	Number of white corpuscles to the c.mm.	Per cent. of hæmoglobin.	The proportion of red to white corpuscles.
Dec. 9, 1888.	3,600,000	65,000	70	1 : 55
Jan. 5, 1889.	3,200,000	200,000	60	1 : 16
Feb. 5,	2,600,000	450,000	45	1 : 5⅞
June 26,	1,440,000	1,120,000	25	1 : 1¼
July 3,	2,408,000	584,000	35	1 : 4⅛
" 10,	2,140,000	560,000	35	1 : 4
" 17,	2,292,000	358,000	40	1 : 6½
" 24,	2,484,000	320,000	—	1 : 8
" 31,	2,792,680	167,320	—	1 : 17+
Aug. 18,	4,614,200	165,800	60	1 : 30
" 27,	3,440,000	320,000	—	1 : 14
Sept. 1,	4,658,000	142,000	65	1 : 32+

The following is the treatment carried out in the case of S. L.:

Dec. 9, 1888, to Jan. 5, 1889. Potassium iod. grs. xv, t. d.; sulphate of iron.

Jan. 10th to June 26th. Arsenite of soda gr. $\frac{1}{40}$—$\frac{1}{25}$, t. d.; iron discontinued.
June 27th to July 3d. 30 litres oxygen daily.
July 3d to 10th. 45 litres oxygen daily; Basham's mix. ℥ss, t. d.
July 10th to Aug. 14th. 54 litres oxygen daily.
Aug. 14th to 22d. 54 litres oxygen daily; sod. arsenite gr. $\frac{1}{80}$, t. d.
Aug. 22d to Sept. 1st. 60 litres oxygen daily; arsenic discontinued.
After Sept. 1st. 100 litres oxygen daily.

We are not aware that oxygen has been systematically used in serious blood affections. The only case of its employ we can find recorded is the one of leukæmia reported by Sticker.[1] The examination of blood showed the red corpuscles decreased to 30 per cent., the white corpuscles numbering 3,735,000; a proportion of white to red of 1 : 0.5. From May 5th to August 22d the patient took daily inhalations of oxygen, commencing with thirty litres, which was finally increased to sixty litres a day. August 22d the red corpuscles numbered 4,460,000, the white 33,200; the patient, after a relapse in which the administration of oxygen had no effect, died the following January.

The mode of action of oxygen is not fully known. We have here a field in which the therapeutic powers of this gas may be, by continued observation, ascertained. Sticker has suggested that the white corpuscles absorb oxygen, and use it up in the blood, and this at the expense of the red corpuscles, and that the administration of the gas might be expected to restore the normal condition, as well as to aid in the conversion of white into red corpuscles.

In all cases of leukæmia there is always found an impairment of some one or more of the blood-making organs, due at times to a known cause, at others to an unknown one. In Case II. the history is that of decided disease of the spleen, long before the blood became markedly affected. It was not until the functioning power of the spleen was seriously diminished that the blood gave signs of leukæmia, and as it became more and more impaired by the overgrowth and distention of the diseased organ, the red corpuscles diminished and the white increased. We had then, it seems, in the action of oxygen, a substitution for the function of the spleen. We did in both these cases, artificially, what the damaged organ could not perform—we allowed the metamorphosis of the white corpuscles into red to go on. The hope in benefiting the patient is to keep up this substitution until the lesion is influenced by the improved nutrition, aided by other means; or, in appropriate cases, until the system is so far built up to make surgical interference a procedure much more likely to succeed than it does now. Whether permanent effects follow this

[1] Beiträge zur Pathologie und Therapie der Leukæmia. Zeitschr. f. klin. Med., Bd. 14, Heft. 1, 2, 1888.

oxygen treatment, or mere temporary benefit and prolongation of life, we cannot as yet say. In cases in which the structural changes are still slight, we believe the remedy may bring about a permanent change; in more advanced cases this is more doubtful. But, under any circumstances, that it prolongs life and produces results not to be otherwise obtained, our experience enables us to affirm.