

"As soon as she became pregnant she became sick, not only in the morning, but very often all day, vomiting everything she took. She also began to suffer from breathlessness and palpitation. During the second month of pregnancy she began to complain of her eyes; they seemed to have something before them; she tried to rub it off, but it always remained the same.

"From the second month onwards she gradually became worse, with no additional symptoms until the fourth month.

"At this period she occasionally complained of peculiar numb feelings in her fingers, which passed up her arm (right). These feelings came over her twice and sometimes three times a day, and remained for a quarter of an hour at first, but were more severe and remained longer as time went on. She compared the sensation to a feeling of lightness coming over her arm, followed by a heavy one.

"About the fifth month the sensations went to the left arm. By this time her eyesight became so bad that she had to be led about, and she could distinguish little more than light and dark. She first consulted me at the fifth month, when I found the urine loaded with albumen. Her feet and hands were very cold and swollen. I recommended her to go into the Sheffield General Infirmary at once. At the sixth month she had what appeared like a paralytic stroke; she lost the feeling and power of her right side and could not speak. This lasted half an hour. The same day week she had a similar attack. In the interval there were still the minor attacks in the right arm. She now suffered very much from palpitation and breathlessness; her pulse was 140 and breathing 36. The third day after the stroke she became so bad that I induced labour by dilating the os and puncturing the membranes. At this time she was quite blind. The third day after labour her eyesight began to return. On the fifth day she took pneumonia, which retarded her recovery for some weeks."

It will have been noticed from Dr. Baker's account that, during the short interval that elapsed from the time of my seeing her in December to the induction of labour that vision had become materially worse, and the gratifying fact will have been observed that from the third day after the labour her eyesight began to improve.

She did not come to see me again until February 27th, when there was a small quantity of albumen still present; specific gravity 1010. The condition of the fundi was distinctly improved and the patches were clearing.

March 13th. Still further clearing, leaving the discs white. Vision in the left eye  $\frac{1}{6}$  and right  $\frac{1}{6}$ .

September 14th. Left  $\frac{1}{8}$ , right  $\frac{1}{8}$ . The urine never became free from albumen. It was examined on November 23rd; specific gravity 1010; albumen present.

On January 5th of the present year she informed me she was again pregnant, and had missed two periods. She was anxious to know if abortion should not be induced. Dr. Baker at the same time wrote asking me if it should not be done, and if so whether the present was not a favourable time. There was no further deterioration of vision, but, as had been previously mentioned, the albumen had never been absent from the urine. I saw no reason why Dr. Baker should not act upon his suggestion, which he accordingly did; and he reported as follows:

"Last November (1894) she became pregnant again. The former symptoms began to return. The eyesight was getting worse, so I thought it advisable to produce abortion.

"At the second month I introduced a sound into the uterus, and rotated it freely but gently. Two days after the operation she aborted, and since then she had been improving.

"Five days after the abortion she had the peculiar sensation in her right arm which she had experienced in her first pregnancy."

A few days ago I examined Mrs. S. again. Vision remained the same as at the last entry. The optic discs are white, and vessels attenuated; there is pigmentation and development of connective tissue round the papillae. Albumen is still present, but no casts were found.

I do not think there can be much question as to the propriety of inducing labour in such a case as this. To have permitted gestation to continue to the normal period would have been fraught with considerable danger to life, and with more certainty it may be asserted that blindness would have resulted. The second pregnancy was treated early. A recurrence of the retinitis would have destroyed in all probability the vision preserved from the previous pregnancy.

A matter of consideration in these, as in all cases in which induction of labour is indicated, is the desire for a living child, but is it not often or generally the case that even if gestation proceeds the foetus perishes?

It seems to me that in these cases we may draw a distinction between those in which the retinal affection shows itself in the early months, and those in which it only appears towards the end of pregnancy. In the latter case the period during which the affection would become worse is more limited, and as a rule it is probably true that vision is less seriously injured than in those in which the retinitis has appeared early. I would therefore say:

1. For retinitis appearing before or about the sixth month induction of labour should be recommended.

2. That when it shows itself only in the last few weeks it may often be unnecessary, but that each case must be judged by the severity of the affection.

3. That a case in which retinitis has shown itself in one pregnancy should be carefully watched both as to the presence of albumen in the urine and as to the eye affection, and treatment adopted accordingly.

The importance of this is often demonstrated. An instance of a lady occurs to me as I write, whom I saw after confinement at term with a medical friend, and who recovered then from retinitis with fair vision, but in a subsequent pregnancy, eighteen months after this one, going on to full time, and attended with eclampsia, absolute blindness resulted. This very day also a woman presented herself with total blindness. Partial recovery had occurred after confinement fifteen months ago, but another pregnancy twelve months later (three months since) had led to the result mentioned.

Whilst then recognising fully the advisability and propriety of induction of labour in these cases, a further question presents itself—How often is it justifiable to recommend hastening of labour in these cases?

The woman whose case has been related has required it twice in scarcely over twelve months. She is only 21, and in the natural course of events other pregnancies will occur, and the question of inducing labour, as it was recently, will again be presented by the patient or her friends.<sup>1</sup> On the one side it is clear that, should a return of the retinitis take place, which in her case it would appear specially prone to do owing to the albumen having never disappeared, blindness would result, and this quite apart from the danger to life from the kidney affection. On the other side is the disagreeable position of the medical man being again and again called upon to interfere with the natural course of gestation.

Should such a case be treated in a more radical manner by the removal of the ovaries, and would the condition of such a patient be sufficiently favourable to allow of such a proceeding being recommended?

## THE NEW ANTIDOTE FOR OPIUM POISONING.

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THE number of deaths caused annually by opium poisoning is so great that the knowledge of a prompt, efficient, and safe antidote to opium is a matter of importance. Special studies and experiments extending over a period of two years have convinced me that permanganate of potassium is the true antidote to opium and its alkaloids, especially morphine. While it was known long ago that morphine is readily oxidised by this salt of potassium, the latter being reduced to hydrated manganese dioxide, yet it has not been shown that the oxidation of morphine renders it perfectly innocuous, entirely void of any toxic properties. Furthermore, it may have been thought that the contents of the stomach would reduce the permanganate so quickly as to render the latter useless for antidotal purposes. I have shown<sup>2</sup> that a solution of permanganate of potassium will decompose sulphate of morphine infinitely more rapidly than it would decompose albuminous matter. A striking demonstration of the astonishing selective faculty of permanganate of potassium for morphine can be shown by mixing 250 grains of the white of an egg with 1 ounce of water, dissolving in this mixture 1 grain of sulphate of morphine, and adding rapidly to the whole just 1 grain of the permanganate dissolved in 1 ounce of water. After thoroughly mixing, not a trace of morphine can be detected, which conclusively proves that the molecules of the antidote instantaneously selected the molecules of morphine without being interfered with by albumen, though the quantity of the latter so greatly exceeded the quantity of morphine. I should state here that 1 grain of permanganate oxidises exactly 1 grain of morphine.

My experiments with the new antidote were made chiefly upon myself. This should not be deemed an unnecessary procedure when we consider how unsatisfactory is experimentation on animals with opium or morphine. It is well known what enormous quantities of this poison the lower animals can ingest with impunity. H. C. Wood and David Cerna have given to a dog, weighing 15½ kilogrammes, 2.4 grammes (37 grains) of morphine; yet at the end of the experiment the air movement and the rate of respiration were practically what they had been in the beginning.<sup>3</sup>

<sup>1</sup> The patient fell down dead on June 8th.

<sup>2</sup> New York Medical Record, February 17th, 1894.

<sup>3</sup> See Journal of Physiology, Cambridge, England, page 870, 1892.

Caldwell gave in one experiment 1.11 gramme (17 grains) to a dog without producing any serious symptoms. To a number of other dogs 0.78 gramme (12 grains) were given hypodermically with no ill effects.<sup>4</sup> Another disadvantage of experimenting on dogs with morphine, given by the mouth, is that these animals generally vomit after ingestion of the poison. In rabbits I have noticed the peculiar fact that doses of morphine which when given hypodermically will cause profound narcosis have no effect whatsoever if administered by the mouth. In one instance I gave a rabbit 5 grains of the sulphate of morphine by the mouth without noticing the slightest effect. On the other hand, 1 grain of the alkaloid administered hypodermically invariably caused pronounced narcosis. The foregoing proves that the antidotal virtues of a therapeutic agent in regard to opium can be demonstrated satisfactorily only on man, especially if the alkaloid is taken by the mouth.

Being extremely susceptible to the action of narcotics, I consider myself a fair subject for such experiments. I was able to take in one instance (January 9th, 1894), three hours after a light supper, in the presence of several well-known physicians of this city, 3 grains of sulphate of morphine, followed in about thirty seconds by 4 grains of potassium permanganate—for safety's sake 1 grain more than necessary—both in aqueous solution. I was perfectly confident that the antidote possessed such a wonderful affinity for the morphine that it would instantaneously select it from among the contents of the stomach, and thus render harmless that might have easily been a fatal quantity to one so susceptible as I am to even very small doses of this alkaloid. Had only one-eighth of a grain of morphine been absorbed into the circulation I should have felt it undoubtedly. Only a few weeks ago (January 20th) I took, about two hours after breakfast, 5 grains of sulphate of morphine in 1 ounce of water, followed in a few seconds by 8 grains of the antidote dissolved in 8 ounces of water, without experiencing any effect whatsoever from the narcotic.

In cases of poisoning by any of the salts of morphine 8 or 10 grains (0.5 to 0.6 grammes) of the antidote, dissolved in one pint (500 c.cm.) of water, should be administered at once, and repeated at intervals of thirty minutes, once or twice. In case of poisoning by the alkaloid morphine itself (not its salts), or by opium and its preparations, it is advisable to acidulate the antidotal solution with one or two teaspoonsful of diluted sulphuric acid or white vinegar (not red vinegar) by which the insoluble morphine will be at once converted into the soluble sulphate or acetate. Of course the amount of the antidote to be given depends on the amount of the poison ingested. If, for instance, 2 or 3 grains of morphine were taken it is sufficient to give 3 or 4 grains of the antidote in solution by the mouth. In case the patient is unable to swallow I would suggest, in order not to increase by the use of a stomach tube the cerebral congestion already present, to introduce into the patient's œsophagus, through the nose, a hard rubber catheter, which is attached by means of a piece of soft rubber tubing to the end of a glass funnel, and pour into the latter the antidotal solution. This simple method proved very feasible in a case of opium poisoning which occurred in my practice.

A weak solution of the antidote, say 1 grain to a tumblerful of water, should be administered by the mouth from time to time, even after all the opium or morphine in the stomach is supposed to have been rendered inert. I state this for the following reason:

It is now a well-established fact that morphine which is injected subcutaneously is excreted by the mucous membrane of the stomach. Hitzig, of Halle,<sup>5</sup> by washing out the stomachs of animals that had received morphine subcutaneously succeeded in obtaining fully one-half of the injected amount during the first hour after the injection. It is a logical necessity that an antidote which acts instantaneously must destroy in the stomach a certain amount of poison that got into the circulation either through hypodermic injection or through absorption by the stomach, for it is evident that the same circulation which conveys the poison from the peripheral parts of the body to the stomach must also bring back to the latter a part of the poison which previously was

absorbed by it. In connection with this it is of interest to cite a case mentioned in the *American Journal of Medical Sciences*, January, 1895, which, verbatim, is as follows:

Mr. L. P. Hamburger cites the case of a Chinaman who had taken the estimated quantity of 150 grains of opium at 10 A. M. At 5.30 P. M. the stomach was repeatedly washed out until there was reason to believe that there was no longer any opium contained therein. A second lavage was made at 8 P. M. and a third at 11.30 P. M., a quarter of an hour before his death. The second washing came out colourless, although it gave fine alkaloidal reactions, but did not respond to the test for meconic acid; the third, also colourless, gave good reactions. The first washing removed the ingested but unabsorbed opium, but the alkaloids found in the others could only have been detected through their excretion by the gastric mucous membrane. Repeated washings, then, to remove the alkaloids as fast as they are eliminated by the gastric mucous membrane must certainly be a life-saving process, whether the poison has been taken by the mouth or hypodermically.

Thus we see that thirteen hours after the opium was taken its alkaloids could be washed out from the stomach. It seems to me much simpler to give a weak solution of the permanganate from time to time, which is sure to annihilate all the morphine which is excreted by the stomach. That the mucous membrane of the stomach takes part in the excretion of alkaloids and other chemical bodies has also been shown by Kandiodoff,<sup>6</sup> who experimented on young persons with different drugs and found that iodide of potash, bromide of potassium, hydrochlorate of quinine, salicylate of soda, arsenic, and antipyrin introduced into the rectum are discharged by the mucous membrane of the stomach.

I have found that the hypodermic administration of permanganate of potash is of benefit also in cases of opium poisoning. While a part of the potash salt is reduced by the subcutaneous tissues, yet enough remains to find its way to the circulation to select the morphine out of the albuminous constituents of the blood.

Rabbits which had received morphine by hypodermic injection were greatly improved by the hypodermic administration of the antidote.<sup>7</sup> Several cases of opium poisoning were reported to me in which the subcutaneous injection of the antidote was of unmistakable efficacy. Up to this date to my knowledge about 35 cases<sup>8</sup> of opium poisoning have been successfully treated by permanganate of potash.<sup>9</sup> In many cases the antidote was given by the mouth and hypodermically, in some cases only by the mouth, and in others only subcutaneously. In many instances several hours had elapsed before the antidote was administered.

As regards other alkaloids and inorganic poisons, I have found that permanganate of potassium, even after contact of several hours' duration, has no oxidising effect upon atropin, hyoscyamin, hyoscin, cocain, aconitin, veratrin, pilocarpin, muscarin, caffein, and phosphorus.<sup>10</sup> Furthermore, it will give up its oxygen much more quickly to albuminous matter than to strychnine, oxalic acid, colchicum preparations, and hydrocyanic acid.<sup>11</sup> The first condition for permanganate of potassium to act as an antidote to any toxic substance is that it shall act instantaneously upon the poison by oxidising it, else it would be unreasonable to administer it not knowing the amount of organic matter present in the patient's stomach at a given moment. This condition is met with morphine and eserine, the permanganate being capable of selecting instantaneously these two alkaloids amongst other organic matter, like albumen and peptone, which happen to be present in the stomach, and, therefore, the remarkable salt of permanganic acid is a positive antidote to opium and calabar bean.

I conclude by expressing the earnest hope that these lines will aid in diminishing the number of serious and fatal accidents due to opium poison.

<sup>6</sup> *Vratch* (St. Petersburg), No. 13.

<sup>7</sup> *New York Medical Record*, March 2nd, 1895.

<sup>8</sup> *Medical News*, April 7th, 1894; May 6th, May 12th, June 23rd, 1894, Philadelphia. *Medical World*, March, 1894, Philadelphia. *Medical Record*, New York, September 15th, 1894, November 3rd, 1894, March 2nd, 1895, March 9th, 1895. *Texas Courier Record of Medicine*, July, 1894. *Railway Surgeon*, Chicago, August 26th, 1894.

<sup>9</sup> It is fair to assume that many other cases were not reported, or else that I am not cognisant of them.

<sup>10</sup> *New York Medical Journal*, February 2nd, 1895.

<sup>11</sup> While there is hardly any reaction at all between prussic acid and the permanganate, yet the latter at once decomposes cyanide of potassium.

Mrs. Morton, formerly of Bolton, has bequeathed £32,000 to the Bolton Infirmary.

<sup>4</sup> *North American Practitioner*, November, 1892.

<sup>5</sup> *Berliner klinische Wochenschrift*, No. 49, 1892.