

THE RAPID CURE OF AMOEBIC DYSENTERY AND HEPATITIS BY HYPODERMIC INJECTIONS OF SOLUBLE SALTS OF EMETINE.

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IPECACUANHA is a drug with an interesting past and a brilliant future. The Brazilian root was first brought to Europe by Piso in 1658, and was successfully used by Helvetius in the treatment of Louis XIV, and sold as a secret remedy to the French Government. It was given for dysentery, chiefly in small doses, by Twining and many other Anglo-Indian physicians, but it was not until 1858, exactly two centuries after Piso, that Surgeon E. S. Docker, I.M.S., introduced the use of large doses (60 grains two or three times a day) of powdered ipecacuanha in the treatment of severe dysentery in Mauritius, with the remarkable result of reducing the death-rate of the disease from a former annual rate of 10 to 18 per cent. to only 2 per cent. His excellent results were rapidly confirmed by numerous physicians in India, but it was not until 1880 that Docker's great services to humanity was tardily rewarded by the Government with a gratuity of £400! Maclean and Norman Chevers in 1886 advocated the use of ipecacuanha in the treatment of acute hepatitis, but two or three decades later the pendulum again swung in the opposite direction, and the drug was largely replaced by ammonium chloride in hepatitis and by salines in dysentery, chiefly as a result of the success of the latter in very early and mild attacks of colitis. Indeed, only a few years ago a committee of London pharmacologists actually advised the omission of this invaluable drug from the medical panniers to be taken on field service by the army in India, so far had the Brazilian root fallen in the estimation of the medical profession. During the last few years ipecacuanha has once more gained ground, mainly on account of Sir Patrick Manson's advocacy of it in dysentery, and of the writer's success in the treatment of early acute amoebic hepatitis.

Doubtless, the principal cause of the vicissitudes of ipecacuanha is the production of very disagreeable and exhausting nausea and vomiting by the large doses which are essential to obtaining its full curative effects. This serious drawback is only partially overcome by the present methods of giving the drug in salol or keratin coated pills, and the use of opium, chloral hydrate, or tannic acid to check vomiting. Last year Vedder showed that emetine, the principal alkaloid of ipecacuanha, has the power in high dilutions of destroying amoebae in broth cultures, although it is not clear that this was a pathogenic form, which most recent authorities believe has not yet been cultivated. I have, therefore, tested the effect of the soluble emetine hydrochloride on *A. histolytica* in dysenteric stools. I have found that, on placing a piece of mucus containing numerous active amoebae in normal saline solutions of this salt, the pathogenic organism is immediately killed and materially altered in its microscopical appearances by a 1 in 10,000 solution, while after a few minutes they are rendered inactive, and apparently killed, by as weak a solution as 1 in 100,000.

I therefore decided to try if this powerful alkaloid can be safely administered hypodermically in the treatment of amoebic disease, and have obtained such striking results in a few patients that it seems to be advisable to make them known to others before the ensuing rainy season of widely prevalent amoebic disease. The following three cases, which have been selected because in none of them could the patients take ipecacuanha by the mouth, will suffice for this purpose, although much further experience will be necessary before the full value and limitations of the method can be ascertained.

CASE I.—*Acute Haemorrhagic Amoebic Dysentery, in a Patient who could not retain Ipecacuanha, Rapidly Cured by Emetine Hydrochloride Hypodermically.*

A Japanese female, aged 29, was admitted to the cholera ward under my care with a history of diarrhoea and sickness for three days, with four or five black stools daily, and severe epigastric pain. Specific gravity of the blood 1052, pulse fair, transfusion not necessary. A small stool containing blood and mucus was passed soon after admission, but I could find no amoeba in it. Castor oil mixture and bismuth ordered.

Second Day.—Three stools containing black blood passed during the night. Severe epigastric pain and vomiting of glairy mucus, without blood, still present. Calcium chloride given. By the evening four large black haemorrhagic stools had been passed; the pulse was feeble, restlessness and deep sighing respiration were present, as well as severe epigastric pain. Duodenal ulcer was suspected, and 20 minims of tincture of opium ordered.

Third Day.—At 7.30 a.m. the condition was still grave, but there was less restlessness. A large black haemorrhagic stool had just been passed, in which I noticed a few yellow pus-like streaks, and at once suspected amoebic dysentery. The transverse colon could now be felt as a thickened and tender mass in the middle line above the navel. Ten grains of Dover's powder were ordered. On examining the stool microscopically I found numerous large amoebae having the characters of *A. histolytica*. As the Dover's powder had been vomited, 10 grains of ipecacuanha with 5 of tannic acid was given, but this also was vomited, and the position became critical. As I had recently obtained emetine hydrochloride from England, I dissolved some in sterile normal salt solution, and at 3.30 p.m. injected hypodermically one-sixth of a grain, being the equivalent of 15 grains of ipecacuanha. This small dose was used for the first trial. No local irritation was produced, while, to my surprise, neither nausea or vomiting ensued. At 7.30 p.m. one-third of a grain more was injected, which also produced no ill effects, not even temporary depression of the pulse.

Fourth Day.—Only one small black stool was passed during the night; the general condition much improved. One-third of a grain of emetine hydrochloride was injected at 10 a.m., making the equivalent of 75 grains of ipecacuanha in sixteen and a half hours, without the slightest unpleasant effect on the patient, who had been unable to retain 1 grain when administered by the mouth.

The further progress was uneventful. The next three stools contained steadily decreasing quantities of blood, no further dysenteric motions were passed, and the thickening of the transverse colon could no longer be felt. After another week, during which ipecacuanha was given by the mouth, the patient left hospital, and she sailed for Japan with her husband a few days later in apparently good health.

The remarkably rapid recovery from the very grave haemorrhagic type of amoebic dysentery in this case can, I think, be safely attributed to the hypodermic administration of the active principle of ipecacuanha.

CASE II.—*Severe Chronic Amoebic Dysentery, of Three and a Half Years' Duration, Rapidly Cured by Hypodermic Injection of Emetine Hydrochloride.*

A high class Indian patient, who had suffered from repeated attacks of dysentery for three and a half years, and continuously for six months, during the last four of which he had been bed-ridden, had been variously treated by a number of eminent medical men, and had had a course of dysentery vaccine, but without avail. Recently four very experienced surgeons had advised colotomy as the only chance of getting the extensive ulcers to heal, but his Indian medical adviser did not think he was in a condition to stand the operation. The stools had been sent to me for examination, and I found amoeba having the characters of *A. histolytica*. When I first saw him in consultation he was extremely emaciated, over twenty foul-smelling stools of pure mucus and blood were being passed daily, his pulse was 120 and over and intermittent, and his general condition very bad. As he was quite unable to take ipecacuanha by the mouth, I advised subcutaneous injections of the emetine hydrochloride. The first dose was one-sixth of a grain, which was rapidly increased to one-third twice a day, being equivalent to 60 grains of ipecacuanha.

On the second day the blood had disappeared from the stools, and faecal matter appeared in them; the mucus then became steadily less, and disappeared finally after ten days. Much pain and trouble arose from extensive ulceration of the rectum, for which 10 grains of calcium permanganate in a pint of water was injected daily, with a good effect, an alum solution being later substituted for it.

After ten days he was able to be weighed, and scaled only 80 lb., although a tall man. His diet was now gradually increased, and during the next two weeks he put on 8 lb. in weight. The emetine was gradually reduced until only one-sixth of a grain was being given every other day to guard against a relapse. He was now eating solid food, and able to get out into the verandah morning and evening, and was passing two or three faecal motions daily, being quite free from all dysenteric symptoms.

His relations were much astonished at the result of the treatment, while I can testify that his recovery is by far the most remarkable I have seen in chronic amoebic dysentery, the difficulty in dealing with which is so well known to all workers in the tropics. I have no shadow of doubt that he owes his life and rapid recovery entirely to the new method of administering the active principle of ipecacuanha. He never once vomited during the treatment, while after the first few doses there was also no nausea, although he received the equivalent of 1,000 grains of ipecacuanha within four weeks.

CASE III.—*Acute Hepatitis, in a Patient who could not take Ipecacuanha by the Mouth, Rapidly Cured by Emetine Hydrochloride Hypodermically.*

A European lady who had been suffering from fever and pain over the liver for ten days had had an attack of dysentery some two months before. Widal tests for typhoid and paratyphoid were negative. Ipecacuanha was now given by the mouth for three days, with the result that the hepatic pain became less and the temperature declined to a lower level.

On account of the great nausea and vomiting she now refused to continue the ipecacuanha, and during the next three days the temperature rose steadily to reach 103° F. in the evenings, and the hepatic pain recurred. At this period I was asked to see her in consultation, and injected one-third of a grain of emetine hydrochloride in the afternoon. The temperature fell steadily during the next twenty-four hours to 100° F., and the pain had also disappeared. I now gave a second injection of half a grain, equal to 45 grains of ipecacuanha. No vomiting, and practically no nausea, was caused by these doses, and her medical attendant reported to me that she was much better.

Four days later I was again asked to see her, as the temperature had once more risen to 103° F., and it was feared that liver abscesses would result if the disease was not quickly cured. I repeated the former doses on that and the following day, and the temperature declined steadily, to reach the normal in three days, when two more similar doses were given to guard against any recurrence, and no more fever or other trouble has occurred.

Emetine hydrobromide may also be given subcutaneously, but is not quite so soluble as the hydrochloride.

In view of the strikingly good results obtained in these three cases, which are illustrative of the most important types of amoebic disease, and in each of which the administration of ipecacuanha by the mouth was impracticable, I venture to think that no apology is needed for bringing this method of treatment to the notice of physicians in the tropics without delay. Should further results fulfil the great hopes raised by the successes above recorded, it will be difficult to exaggerate the boon which will be conferred on the numerous sufferers from the intractable and deadly amoebic form of dysentery and its very serious hepatic complication.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

ON THE GENESIS OF THE VENOUS PULSE.

I AM sorry not to have replied earlier to the letters of Dr. Wilkinson and Dr. Verdon which appeared in the JOURNAL of May 4th, but my absence from home prevented my attending to them.

Dr. Wilkinson says that the *a* wave of the venous pulse ought to be greater in the vertical position, if my suggestion that it is an inertia wave be true, "for then the inertia of the column of blood in the vein is augmented by the effects of gravity." He forgets, however, that the amount of blood which comes down from the head depends on the amount which goes up, and gravity opposes its going up in the arteries quite as much as it encourages it to come down by the veins, and consequently has no resultant effect on the flow. The second part of Dr. Wilkinson's letter is probably correct, but I was not discussing in my communication what takes place in abnormal conditions, such as the instance he gives when the auricle and ventricle contract together, where, obviously, if the auricular contraction be forceful enough to effect anything it must be a regurgitation.

Dr. Verdon definitely states that the blood "stream is swifter" in the jugular vein in the upright position than in the recumbent. Whether this statement is based on observation or inference I do not know, neither can I judge whether Dr. Verdon means that more blood comes down the jugulars in the erect than in the horizontal position. A "swifter" flow may go with less blood if the jugulars are contracted. If more blood comes down more must have gone up, and it would seem on this supposition that a fainting person gains nothing by lowering the head, which is contrary to experience.

Whatever the origin of the *a* wave the horizontal position is likely to develop it, since the tone of the vessels relaxes, and oscillations in them are far more easily produced. Moreover, the acclivity and declivity of the *a* wave is not necessarily steep, as Dr. Verdon maintains it would

be if it be caused by inertia and the block be sudden. The steepness depends chiefly on the yield of the jugular, which is gradual, the oncoming blood being stored in it as it arrives.

The jugulars commonly dilate considerably on lying down, and are capable of much bigger oscillations, to which rather than to auricular regurgitation is to be attributed the exaggerated appearance of the *a* wave in the horizontal position.

Clyst St. George, Devon.

D. W. SAMWAYS.

REPEATED BREECH PRESENTATIONS.

I READ with interest Dr. Hott's letter, *re* breech presentation.

Last year I was called in to see a woman in labour (I had never seen her before), and on arrival I found her sitting on the edge of the bed suffering from a great fit of depression. On inquiring the cause, she informed me that her three previous confinements had been breech cases, the children dying immediately after birth; she also said she felt convinced that the coming child would be a breech presentation and would die like the rest, hence her depression.

On examination, I found that there was a breech presentation, and, to cut the story short, I delivered her of a male child, which, after some artificial respiration, took to life with great gusto, and is now as fine a baby as it is possible to find. The patient informed me that her first youngster (now some 8 years old) was a normal head presentation, but that all the others were breech presentations.

Cosham, Hants.

H. TAYLOR MORGAN, M.D.

British Medical Association.

CLINICAL AND SCIENTIFIC PROCEEDINGS.

SOUTH WALES AND MONMOUTHSHIRE BRANCH.

Swansea, April 25th, 1912.

Dr. BIDDLE, President, in the Chair.

Plumbism.

DR. ARBOUR STEPHENS read a paper on plumbism. He said that, as appointed surgeon under the Factory Act for lead processes, he had had considerable opportunities of observing men employed at lead works, their dangers, and the consequences. The symptoms were more or less classical and fairly well known. One symptom he would draw attention to, because it was unreported but had been observed by himself, was a tenderness over the sciatic nerve in its lower third, the upper part being practically free from such tenderness. The difficulty was to decide in a large number of cases what part alcohol had played. *Mode of admission*: (1) *Skin*, said to have occurred by the use of cosmetics; (2) *lungs*, which Dr. Goadby has tried by experiments to prove is the main one, but with which Dr. Arbour Stephens could not agree; (3) *stomach*, into which lead got by eating food with dirty hands, chewing, cigarette smoking, and suchlike methods. The foremen and undermanagers never got plumbism. The test for KCNS in the saliva was interfered with if the man had been eating any sugary material. All persons working before furnaces developed a red line on the gum, and on this red line the lead was readily deposited. What was the origin of this red line? Was it inflammatory? Prevention could be brought about by cleanliness as to food and other habits. Cigarette smoking ought to be stopped, and chewing was most injurious. The rotten teeth should be removed, as they tended to give rise to gastritis. A preliminary gastritis by the accompanying increase of absorbing surface tended to produce absorption of lead, and so hastened an "attack." The plentiful supply of fruit last summer increased the number of cases of lead colic. The blue line was nearly always preceded by a red one, which was always found with furnace men. The best treatment for the early stages of plumbism was by means of the internal administration of calcium permanganate.