and the last one for one year. Now the attacks were more frequent and the pain was worse.

Treated with 10 mgm. of B_1 given intramuscularly every day. There was complete relief after the sixth injection but the pain recurred by 25 per cent after the ninth injection. Vitamin treatment was stopped and he was given potassium bromide gr. 5 and luminal gr. ½ twice daily instead. After one week he again got complete relief and has remained well since. Total dosage = 90 mgm.

Case 7.—N. A., aged 25 years. Six years' history of neuralgic pain confined to the distribution of the right 5th nerve. Stated that he had suffered from gonorrhœa and syphilis seven years before but the Wassermann reaction was negative. Examination showed fair nutrition, all the three branches of the 5th nerve were involved and there was watering of the right eye and right side of the nose. There was very slight wasting of the right side of the face but the sensations were intact. Was given an alcohol injection one year before which gave him complete relief for nearly eleven months. Teeth normal. Given B_1 by intramuscular injections in doses of 10 mgm. daily for seven days but there was no relief. Total dosage = 70 mgm.

Discussion

The above account of seven cases of trigeminal neuralgia shows that only one case did not respond to vitamin-B_1 therapy. This patient gave a history of syphilis and although the Wassermann reaction was negative he was given a course of mercury and iodides by mouth without any relief. Of the six cases which responded to treatment four got 100 per cent relief, one about 50 per cent and one about 30 per cent. Case 3, who obtained about 50 per cent relief, received 84 mgm. of B_1 and case 5 who improved by about 30 per cent received 120 mgm. The four cases which were completely relieved received 160, 210, 84 and 90 mgm. each and in all of them improvement commenced promptly and in two cases was complete when only 50 mgm. of the vitamin had been given, although treatment was continued for a few days more. It is difficult to say whether prolonged treatment with perhaps bigger doses would have benefited cases 3 and 5 any more.

It is generally believed that vitamin B_1 even when given in enormous doses does not cause any toxic symptoms and Weiss and Wilkins (1937) have given 100 mgm. of crystalline B_1 intravenously without any ill effects. However, recently Steinberg (1938) has reported untoward effects from using large doses of vitamin B_1. In three of his patients herpes zoster occurred after large doses and in one case he was able to produce herpes on two successive occasions. Steinberg believes that vitamin B_1 when given in large doses is capable of irritating the peripheral nerve plates. In the case of diabetic polyneuritis above referred to there was definite worsening of burning and tingling sensations in the hands and feet after continued use of moderate doses of vitamin B_1. In case 6 the recurrence of neuralgic pains might be due to the irritant action of B_1 on the sensory nerve endings as the patient was relieved when the

(*Continued at foot of next column*)

INFECTION WITH *GIARDIA LAMBLIA*—ITS PATHOGENICITY AND TREATMENT

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Giardia lamblia is a common parasitic intestinal flagellate. With regard to its geographical distribution, this is now known to be world-wide.

(*Continued from previous column*)

injections were stopped and bromides and luminal were given instead.

Conclusions

Vitamin B_1 is proving to be of great therapeutic value in many diseases of the nervous system for which there was no satisfactory remedy before. The clinical data are too scanty to evaluate its efficacy in all the diseases for which it is advocated but it seems to be of particular value in many forms of polyneuritis. Whether the action of vitamin B_1 is due to its replacing any deficiency or to some other action is not quite clear yet.

In a short series of seven cases of trigeminal neuralgia injections of B_1 have given complete relief in four and partial relief in the other two, while one was unaffected. The relief obtained was dramatic in all the four cases and considering that trigeminal neuralgia is a difficult disease to treat without operation, which in itself is a definite surgical risk, vitamin B_1 promises to be of considerable therapeutic value and should be given a trial in all cases of trigeminal neuralgia.

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The incidence in the tropics is certainly higher than in the temperate zones. The following table gives the incidence of infection with *Giardia lamblia* among the patients treated for various diseases at the Carmichael Hospital for Tropical Diseases and in the out-patient department of the School of Tropical Medicine, for four years.

Giardia lamblia inhabits the lumen of the small intestine, the duodenum being the commonest site of infection. On this account the

TABLE

	Total number of stools examined	Number showing infection with *Giardia lamblia*	Incidence, per cent
1934 ..	4,302	246	*5.8*
1936 ..	5,498	380	*6.8*
1937 ..	4,766	226	*4.7*
1938 ..	4,710	357	*7.6*

motile forms are not usually seen in the stool; but when the patient has diarrhœa, the contents of the small intestine are passed down rapidly and it is then that the active phase of the parasite is encountered in the stool. Encystation takes place in the large bowel and in most cases diagnosis of the infection with *Giardia* is made by finding the cysts in the stool. Excretion of the cysts in the fæces is markedly intermittent so that care should be taken in drawing conclusions as to the effectiveness of any drug administered.

A host of drugs, *e.g.*, treparsol, stovarsol, carbarsone, bistovol, bismuth subgallate, neosalvarsan, yatren, etc., have been used by various workers in cases of infection with *Giardia* but without any appreciable success. We have tried stovarsol, carbarsone and yatren in many cases, the majority of which did not respond to the treatments. In a few instances, however, the parasites disappeared after the treatment. But as the patients were not kept under observation for a reasonable period after the treatment had been discontinued, it is difficult to state with certainty that the infection was completely eradicated, for *Giardia*, as we have said before, reappears in the stool after absence for several days. Recently, Brumpt (1937) conducted experiments on lamblia-infected mice and has noted that, of all the treatments tested, oral administration of one per cent solution of quinacrine (a French equivalent of atebrin) for 5 days was able to bring about a cure in 80 per cent of the animals to which it was administered. Martin (1937) claims that atebrin in the doses employed for the treatment of malaria will rid the majority of patients of lambliasis of their flagellates. In a few cases it may be necessary to repeat the course. In view of the striking results obtained with atebrin, as reported above, we have tried this drug on a number of cases using the same dose as for the treatment of malaria but have considered in this paper only those few cases which could be kept under observation for at least six weeks after the completion of treatment.

Case notes

Case 1.—Mrs. B. has been suffering from looseness of bowels and flatulence for the past two years. Stools examined in January last showed a heavy infection with *Giardia lamblia* (trophozoites and cysts) and *Trichomonas*. She was then treated with stovarsol and bismuth. There was a temporary amelioration of symptoms. No further examinations were possible at the time. On 2nd April, 1939, the symptoms recurred and the stools were full of *Giardia* cysts, *Trichomonas*, *Chilomastix* and a few *Enteromonas*. Besides, there were scanty *E. histolytica* and *E. coli* cysts. She was immediately put on to atebrin (one tablet three times a day for 5 days). Stools were examined daily during treatment and on the 7th, 11th, 15th, 18th, 24th, 30th and 36th day after the treatment had been completed. *Giardia* disappeared after 6 doses of atebrin and were not found any time during these examinations. But all the other flagellates and the amœbæ remained unaffected. A course of emetine injections, however, brought about the disappearance of *E. histolytica* from the stool.

Case 2.—D. C. complained of long-standing diarrhœa alternating with constipation and abdominal discomfort, especially after food. Stools positive for *Giardia* cysts (heavy infection). Put on to atebrin. Stools were examined daily during treatment and on the 7th, 13th, 20th, 29th and 32nd day after treatment. Administration of 5 tablets only, caused the disappearance of the flagellate from the stool. Stools were also plated on McConkey's lactose neutral-red agar but no non-lactose fermenters were isolated. Diarrhœa stopped and the patient's health gradually improved.

Case 3.—M. B. A child of 8 years. There is a history of the passage of voluminous stools containing large quantities of mucus for nearly 4 months. Marked emaciation and tumidity of abdomen. Stools showing large number of *Giardia lamblia* (chiefly trophozoites). Atebrin was given in proportionate doses. There was rapid disappearance of the parasite. After 3 doses very scanty parasites were found and after the 4th not a single flagellate could be discovered in spite of prolonged search. Repeated examinations during and after treatment for two months failed to show the flagellate in the stools. Symptoms disappeared and the patient's general condition greatly improved. Three samples of stools were plated for pathogenic bacteria, one gave a culture of *B. pseudocarolinus*. But no importance was attached to this finding as the patient showed marked improvement on atebrin.

Case 4.—A. R. A case of oriental sore. There is no history of any intestinal disturbance. Stools positive for *Giardia* and *E. coli* cysts. Put on atebrin. Stools were examined every day during treatment and on the 4th, 15th, 22nd and the 30th day after treatment. *Giardia* disappeared after 9 tablets had been taken. The drug had no effect on *E. coli*.

Case 5.—M. D. A long-standing case of *Giardia* infection. Occasional attacks of diarrhœa accompanied by pain about the umbilicus. There is marked flatulence; stools showed a good number of the encysted flagellates. Proved refractory to stovarsol and bismuth. Put on to atebrin which brought about a rapid disappearance of the parasites from the stool. Repeated examinations (three times during and nine times after treatment) failed to reveal the parasites. There was definite improvement of the patient's condition with the eradication of the parasites.

Case 6.—B. D. A girl of 18, suffering from asthma associated with abdominal symptoms. Stools showed the cysts of *Giardia lamblia* and *Entamœba histolytica*, was treated with atebrin, followed by a course of carbarsone. Both the infections were eradicated. Six consecutive examinations after the completion of atebrin and carbarsone treatments were negative for both *Giardia* and amœba. Although the patient's general health improved and abdominal symptoms passed off, she was not cured of asthma.

Case 7.—P. B. The patient is a railway doctor. Was suffering from giant urticaria for a month and a half. The stool showed a heavy infection with *Giardia*. There was no history of any intestinal trouble. Five tablets of atebrin caused the disappearance of the flagellate from the stool. The patient felt that after he had received a full course of atebrin treatment the severity of the urticarial eruptions was lessened. Examination of stools were carried out at weekly intervals, the last being done 29 days after the completion of the treatment. All these specimens were negative for *Giardia*.

Case 8.—K., aged 2½ years. History of persistent diarrhœa. Was treated with 'Inteste Phage' (A. F. D.), castor oil emulsion, bismuth with salol, etc., but to no purpose. Stools showed a large number of *Giardia*, chiefly trophozoites. At once put on to atebrin. After 3 days' treatment the parasites disappeared from the stool and diarrhœa stopped. Stools were examined 23 times after treatment, but they were invariably negative.

Case 9.—R. C. A case of chronic malaria (benign tertian) with enlarged spleen. No history of any recent bowel disorders. Stools positive for *Giardia* cysts. A course of atebrin caused the disappearance of the parasites from the stool. As daily specimens were not available it was not possible to state after how many doses of atebrin the parasites had disappeared. Several examinations after treatment failed to show the parasites.

Case 10.—T. M. History of recurrent diarrhœa and pain in the abdomen for two years. All six serial examinations of stools showed the cysts of *Giardia* in large numbers. Atebrin was given. Several examinations after a full course of atebrin had been taken were carried out covering a period of a month and a half. On no occasion was the flagellate ever found. The patient's condition improved very definitely after treatment.

Remarks.—It will appear from the foregoing that the parasites in all cases disappeared after the administration of 9 tablets of atebrin as a maximum. These cases were kept under observation for a minimum period of six weeks after the treatment had been discontinued. During and after this observation period the stools, examined several times, were invariably negative for *Giardia*. In a case of very long duration and showing large numbers of the parasites in the stools the infection was eradicated with remarkable rapidity (case 3). Some cases showed a mixed infection with flagellates of other genera and amœbæ (cases 1, 4 and 6). Atebrin does not seem to affect these flagellates, *e.g.*, *Trichomonas*, *Chilomastix* and *Enteromonas*. Nor has it any action on *Entamœba histolytica* or *Entamœba coli*. The question of pathogenicity or otherwise of *Giardia lamblia* is still awaiting solution. Some observers consider that, like other intestinal flagellates, this parasite is also a harmless organism. Their contention is that the infection—and often a heavy one—is frequently found in perfectly healthy individuals and not associated with any symptoms. Further, *Giardia* infections are very common in animals, *e.g.*, quite a large proportion of rats and mice harbour *Giardia muris* and in such animals no lesions of the gut are to be discovered. It lives in the fluid contents of the gut and does not possess the power of invading tissues. Others who lay claim to its pathogenicity argue that the mere fact that *Giardia* infection can be seen in healthy persons does not prove its non-pathogenicity, for quite a large number of apparently healthy individuals harbour *E. histolytica* infection. As a result of their clinical observations they are inclined to hold that *Giardia* often causes diarrhœa alternating with constipation, abdominal pain, flatulence, etc. Children are the worst sufferers; in them there may be intractable diarrhœa associated with the passage of large quantities of mucus and impairment of growth as a result of chronic indigestion. Some observers even go so far as to incriminate this flagellate as the cause of cholecystitis, although they cannot furnish any satisfactory evidence to show that the flagellate can spread from the duodenum to the gall bladder. In our series of 10 cases 3 had no intestinal disturbance, 2 had associated *E. histolytica* infection, and the abdominal symptoms complained of by them may be attributed to this. In the remaining cases repeated examinations showed no other abnormality than a heavy infection with *Giardia* and their symptoms ameliorated or disappeared with the eradication of the infection. In the circumstances it is not perhaps unreasonable to assume that *Giardia* infection was the cause of the symptoms in these cases.

Summary

Ten cases of infection with *Giardia lamblia* have been treated with atebrin using the same dose as for the treatment of malaria. Administration of 9 tablets as a maximum brought about the disappearance of the parasites from the stool in every case. Repeated examinations of the stools after treatment up to six weeks or more failed to show the parasite. Although atebrin has proved invaluable for the eradication of *Giardia* infection, it does not possess any action on other flagellates of the intestine, *e.g.*, *Chilomastix*, *Trichomonas* and *Enteromonas*. Nor does it affect *Entomœba histolytica* or *Entomœba coli*. The question of the pathogenicity of *Giardia* is discussed and the authors are inclined to the view that in some cases at least infection with *Giardia lamblia* is responsible for intestinal disturbances, especially in children.

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