a mobile cecum, a long colon with ptosis of splenic flexure. The splenic flexure is tangled, usually shows retention with intermittent obstruction. There is evidence of small intestine obstruction, disappearing in two hours; this is probably in the jejunum near the beginning of the ileum. April 26, patient operated by Dr. John S. Irvin, at which time there was found two lesions in the first part of the jejunum, separated by ten inches of normal intestine. A resection was done with the resected portion including both neoplasms. These growths had narrowed the lumen until only a small opening remained. At this operation there could be seen a larger growth involving the descending colon.

On May 1st, the patient came under the care of the writer. After prolonged preparation that included numerous blood transfusions the patient was again submitted to laparotomy for the purpose of removing that portion of the colon containing the mass palpated and seen during the first operation. The neoplasm was matted down rather badly as results of previous operation and manipulation, with adhesions to small intestine and omentum. The growth was attached to a lower segment of descending colon so that a knuckle of colon was posterior to the neoplasm. Distal to this growth was a second tumor, in the sigmoid, four inches below where the tumor was adherent to the knuckle of bowel. The whole mass, splenic flexure and descending colon, freely mobilized and then the tumor-bearing portion brought through the wound and an obstructive type of resection was done.

The laboratory report on the two growths removed from the jejunum show there was a marked proliferation of the mucosal glands, which in places was grossly enlarged and distended. In other areas they are transformed into plugs and cords of infiltrating cells. The picture is that of an adenocarcinoma. The microscopic examination of the two growths removed from the colon showed an extensive adenocarcinoma.

There has been reported a young man 26 years of age, in which there appeared simultaneously in his intestines, four neoplasms, all adenocarcinoma.

It would seem that the involvement in the jejunum and the involvement in the colon were primary growths. They occurred in widely separated structures and while the large growth in the colon showed glandular involvement with size of glandular enlargement no larger than size of a pea, there was no glandular enlargement of the mesentery of the small gut.

A close examination of the sections of both large and small intestines, did not show any polyps or adenomas on the mucosal surface nor did the mucosa of the rectum show any adenomas. Hence, the carcinomatous did not, apparently, grow from a pre-existing multiple polyposis.

Because of the fact that the tumors in the small bowel were separated by a considerable amount of normal mucosa and that there was no glandular involvement, it would seem that these growths did not depend upon metastasis.

In the double growth in the large bowel the origin is not so clear. We feel that the larger growth represents a third primary growth and because the fourth growth was quite some distance removed and without visible metastasis, that it was very possible for it to represent a fourth primary malignancy.

REFERENCES


A Critical Appraisal of the Newer Amebicides and the Results of Treatment of Amebiasis with Di-iodo-hydroxyquinoline* (Diodoquin)

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O
ne of the every day problems, confronting the physician, is the appearance of a new drug which is recommended to the profession for the cure of disease. During the past two decades many compounds have been suggested and used for the relief of amebic colitis which were often based on insufficient experimental and clinical data. Some of these drugs have been praised, while others have been condemned with the result that the bewildered practitioner is at a loss to know which preparation to choose for his patient.

With the advent of each new amebicide many clinicians who have treated patients suffering from amebiasis have experienced a keen hope that a cure for this prevalent malady finally has been found, only to be disappointed sooner or later, when relapses occurred. This is particularly true in those patients whose infection has not been diagnosed early enough and is, therefore, of long standing. Deep seated infections of the submucosa and muscularis and sometimes secondary pyogenic infection, leading to stricture of the rectum (as was observed recently in two patients), is the rule and complicated the clinical picture, thus preventing rapid cure. On the other hand, early amebiasis, especially if the symptom-complex is ushered in by diarrhea or dysentery, can be recognized in time and responds, as a rule readily to our modern amebicides, because, in these patients, the deeper tissues have not been invaded and the lumen-dwelling amebae,
lining the mucosa, are more vulnerable and, therefore, are more easily eradicated.

In general, the prognosis of any infection depends on four factors: 1, the extensiveness of the pathological process. 2, the associated and secondary pathological changes produced in the host. 3, the efficiency and potency of the therapeutic principle applied. 4, the vis medicatrix naturae or healing power of nature. Treatment of amebiasis must, therefore be based on knowledge of its pathology. Amebae are found in the colonic contents and on the surface of the mucosa as lumen-dwelling amebae. However, they rapidly invade the interglandular septa, the muscularis mucosae and submucosae, tissue amebae. Since the latter condition probably prevails in the majority of individuals infected, it is possible for us by means of sigmoidoscopy and the help of roentgen visualization of the colon to plan a rational therapeutic attack. Eradication of the parasites is, therefore, only possible by exposing both lumen-dwelling and tissue amebae to lethal concentration of a potent amebicide. Craig (1) states that in his experience every chronic infection with the E. histolytica is a separate medical problem, and the longer the infection has lasted, especially if active symptoms have been present, the more doubtful is the prognosis as to cure, so that early recognition and proper treatment are of greatest importance in amebiasis.

In a previous paper I (2) have stressed the fact that recurrences are frequent and that the prospect of complete cure of chronic amebic colitis, at the present time, with any known method of treatments is uncertain. Space does not permit me to enumerate the many optimistic and pessimistic reports about the various amebicides, in use today. Mention must be made, however, of the outstanding contribution to the chemotherapy of amebiasis by C. D. Leake (3) and Reed, Anderson, David and Leake (4), who critically studied the drugs employed in the treatment of this disease. These investigators quantitatively estimated the amebicidal action of the compounds under consideration in vitro and carefully observed their curative range and toxicity in laboratory animals and human volunteers. They furthermore stressed the possibility of developing new and better drugs. Leake pointed out the chemical groups which offer the possibility of developing new and better drugs. Leake pointed out the chemical groups which offer the greatest hope of giving us the ideal amebicide and stated that the organic arsenicals and the oxyquinoline derivatives offer the greatest possibility.

The ideal amebicide should: 1, promptly and lasting rid the host of the parasite; 2, it should promptly relieve the clinical symptoms of amebiasis; 3, it should be non-irritating; 4, it should be of such low toxicity that it causes no damage to the vital tissues and organs; 5, it should be readily absorbed and promptly eliminated; 6, it should destroy both lumen-dwelling and tissue amebae and cysts; 7, it should be easily administered (orally); 8, it should not interfere with the usual activity of the patient; 9, it should be effective at low dosage, relative both to the single or total amount administered; 10, it should be reasonable in price. At the present time no drug meets all these criteria.

It might be timely, briefly to point out the disadvantages of the commonly employed drugs. Most workers in this field have agreed that emetine in safe amounts fails to cure more than half the cases of amebiasis. Furthermore, it is cumulatively toxic and it has no effect on the cysts of the E. histolytica. Its therapeutic range is limited, as it cures very few infections and it should be used only to control symptoms of diarrhea and dysentery. Its indiscriminate use, unfortunately still prevalent, is one of the most important causes of relapse. It has its greatest usefulness in amebic hepatitis and amebic abscess of the lung and liver.

Next to emetine the halogenated oxyquinoline chiniwoffen (N.N.R.) has been most widely used in the treatment of this disease. Originally introduced as Yatren by the Germans in 1921, chiniofon contains about 28% of iodine. The early reports of Muehlens (5), Menk (6), Olpp (7), Huppenbauer (8) and many others were most enthusiastic, but the drug has not fulfilled the original expectations and claims which were made for it as an amebicide. My own experience with chiniofon has been extensive and, when used alone, it has failed to cure in about 25% of my cases. It exhibits little, if any toxicity, and no untoward symptoms from its continued oral or rectal administration are observed, with the exception of diarrhea, which is usually of short duration, but some times may be annoying to the patient.

During the last few years another oxyquinoline has been advocated for the treatment of amebiasis, as iodochlorhydroxyquinoline (vioform N.N.R.), containing between 37.8 and 41.5% of iodine. This drug is less irritating, when administered orally, than chiniofon, and no untoward symptoms are observed from its prolonged administration. There are very few authentic reports as to the results of vioform in a controlled large series of cases encountered in the literature. Experimentally it was shown to be very effective in monkey-amebiasis by David, Johnston, Reed and Leake (11) who found that the drug eradicated amebae promptly and consistently. These results have, however, not been obtained in human amebiasis. Brown (9) in a comparative survey of amebicides at the Mayo Clinic during the past fifteen years has employed it and states that it failed to cure, when used alone. David, Johnston, Reed and Leake (11) report that in forty-seven unselected cases of human amebiasis, cure resulted in thirty-eight cases or 84.4%. This has been my experience in thirty-three relapsing cases of amebic colitis, where it was administered, when other drugs had failed. To effect cure, it had to be alternated with the organic arsenical carbarsone. Most recently a third oxyquinoline derivative has been recommended for treatment, a diiodo-hydroxyquinoline (diodoquin) containing 64% of iodine concerning which more will be said in the second part of this paper.

The organic arsenical compounds which have been employed are acetarsone, treparsol and carbarsone. In effective dosage acetarsone and treparsol are cumulatively toxic and frequently produce gastro-intestinal upsets, such as abdominal pain or cramps, diarrhea and flatulence, and also toxic dermatitis. Therefore, one should always keep in mind that these arsenical preparations are potent drugs. They have not come in general use as amebicides on account of their toxicity.

The arsenical compound most widely used in the treatment of amebic infection is carbarsone, a 4 carbamino-phenyl, arsenic acid, first elaborated by Ehrlich, and introduced by Reed, Anderson, David and Leake (11) as an amebicide. These investigators have studied this drug extensively from an experimental,