CHRONIC AMŒBIASIS IN SOLDIERS.

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[*Received July* 18, 1944.]

With the return of troops from tropical and sub-tropical countries, cases of amœbiasis will be seen in increasing numbers by doctors who have relatively little previous experience of the condition. The object of this paper is to describe briefly the methods used in diagnosis and treatment of a series of cases admitted to a Military Centre for Tropical Diseases in England between November, 1942, and January, 1944 ; and, in so doing, to call attention to the necessity of looking for amœbiasis in many cases where the principal symptom is something other than diarrhœa; to the ill-effects of haphazard treatment and to the need for thoroughness and routine method in both diagnosis and treatment. While there is nothing in the paper that is new, there is a great deal which appears often to be neglected in practice and is presumably therefore unfamiliar. No attempt will be made to review the literature as this has recently been done most adequately by Manson-Bahr (1943) in a book to which all students of the dysenteries must be greatly indebted.

In the period mentioned, 112 patients were admitted diagnosed provisionally as suffering from dysentery or the effects of dysentery. Of these, 28 gave what was considered to be a reliable history of dysentery but no pathogenic organisms or protozoa were found in the stools and the symptoms were attributed to the effects of a previous dysentery ; 51 were found to have bacillary dysentery (including acute Sonne dysentery) as shown by the isolation of pathogenic organisms from the stools and 33 were considered to be suffering from amœbiasis. It is with these 33 cases that the remainder of this paper is concerned. Seventeen were officers, including nursing officers, and sixteen were other ranks. While cases from West Africa predominated there were others from North Africa, the Middle East, the Sudan, India, Burma and Ceylon. One patient had never been out of the United Kingdom and he appeared to have become infected in Northern Ireland. The length of the history was often difficult to determine with accuracy but varied from two months up to ten years.

Presenting Symptoms.

Of the 33 patients in 7 only was recent diarrhœa the principal symptom. In a few more occasional diarrhœa was complained of but, in 14 cases, there was no history of recent diarrhœa and diarrhœa had never been a prominent symptom. Some of the patients with diarrhœa had noticed the presence of blood and mucus but others described their stools simply as watery or unformed. Other presenting symptoms were abdominal pain and discomfort, usually situated over the course of the colon or over the liver, " continuous aching abdominal pain," " stomach never really settled," " poor general health," slight fever, loss of weight, and in one case " loss of weight, ill-health and constipation." Four cases presented as a hepatitis, two with diarrhœa and two without.

Diagnosis.

The diagnosis was suggested by: (1) A history of previous dysentery. (2) Previous residence in the tropics or sub-tropics with one or more of the symptoms mentioned above. (3) The presence of tenderness over the colon or liver. (4) The naked eye appearance of the stools which were occasionally characteristic, with blood, mucus and a typical odour, but more often simply watery or unformed.

The picture in chronic cases is therefore variable and may differ considerably from the usual clinical description of amœbic dysentery. The diagnosis was confirmed by :—

(1) *Microscopical Examination of the Stools.*—Vegetative *Entamœbæ histolytica* were found in 6 cases and cysts in 24. In looking for the latter much help was obtained from the use of a modification of the Faust (1939) zinc sulphate concentration method, details of which have, unfortunately, never been published. Not only is the detection of cysts made easier by its use but the fact that a large number of them can usually be examined in a clean field greatly facilitates their identification. At least three stools were examined by ordinary methods and three by the concentration method. In some cases many more were examined and in a few cases positive results were only obtained after repeated examinations. Since symptomless cyst carriers are not uncommon the finding of cysts in the stools does not necessarily mean that the symptoms are due to active amœbiasis nor is it necessarily an indication for treatment. In most of our cases, however, the satisfactory response to specific treatment seemed to show that the symptoms had been due to this cause.

(2) *Microscopical Examinations of Specimens Obtained at Sigmoidoscopy.*—Scrapings were taken with a Volkmann's spoon through the sigmoidoscope, mounted in normal saline under a cover slip and examined unstained. For this purpose the sigmoidoscope should be lubricated with mucilage as the presence of oil droplets, which will appear if any grease is used, makes the scrapings almost useless for microscopic examination. In this series of cases amœbæ were never found in scrapings of mucous membrane taken from a completely unbroken surface. They were however found in smears of bloody mucus seen coming down the sigmoid colon when no ulceration was visible ; and the particular importance of this method is shown by the fact that numerous active vegetative amœbæ were found in scrapings from two cases with ulceration after repeated examination of stools had failed to demonstrate amœbæ or cysts. One of these patients had not been abroad since 1932, when he had been in the tropics as a merchant seaman, but had suffered from diarrhœa almost continually for the last three years. His symptoms cleared up completely with specific therapy.

(3) *Sigmoidoscopic Appearances.*—One case only was diagnosed on sigmoidoscopic appearances when neither amœbæ nor cysts were found in direct films, concentrated specimens or scrapings. This patient had a history of previous amœbic dysentery followed by mild diarrhœa, aching abdominal pain and loss of weight, and he had a leucocytosis. The colon showed two ragged ulcers and elsewhere a hard leathery surface over which the end of the sigmoidoscope grated. With specific treatment the symptoms were relieved and the colon as seen through the sigmoidoscope returned almost to normal.

(4) *Response to Therapy given Empirically.*—With the exception of the case mentioned in the preceding paragraph, patients complaining of diarrhœa or colonic symptoms, in whose fæces no *E. histolytica* were found when direct films, concentrated specimens and scrapings of the mucous membranes had been systematically examined, rarely, if ever, in our experience, derived benefit from specific treatment for amœbiasis given empirically. The same statement does not of course apply to cases of hepatitis.

From what has been said it is evident that *E. histolytica* must be looked for in patients with many symptoms other than diarrhœa ; and that, though the common practice of examining one or two fresh specimens of stool may reveal them, many cases of chronic amœbiasis will be missed unless a routine procedure including repeated examinations of the stools, sigmoidoscopy and the examination of scrapings is employed.

Treatment.

Of the 30 cases in which this was recorded, 20 had been treated previously for amœbiasis and 10 had not. Of the 20 treated, 7 had received only injections of emetine hydrochloride, sometimes on several occasions. In almost every case this had produced temporary relief but the symptoms had soon returned. Only 7 of the 20 appeared to have been given an efficient course of E.B.I. and chiniofon retention enemata. A number more had been treated at different times with emetine, stovarsol and a few odd doses of emetine-bismuth-iodide or a

few odd enemata, sometimes of chiniofon and sometimes of other fluids not usually considered to be amœbicidal. It is probable that the chronic cases that reached us were not a fair sample of treated cases of amœbiasis and that the records of previous treatment were incomplete but, even so, they suggest that the treatment of this condition at the present time is often somewhat haphazard and casual. This is unfortunate, since chronic amœbiasis is a trying and disabling condition but one which is usually curable by thorough treatment at a reasonably early stage.

Of the standard drugs generally available—emetine, emetine-bismuth-iodide, auremetine, chiniofon (quinoxyl) and stovarsol or carbasone—it is generally agreed in England now that, whereas emetine hydrochloride by injection usually abolishes symptoms most satisfactorily, its effects are rarely permanent; that emetine-bismuth-iodide or auremetine given by mouth is the most effective single drug, and that the simultaneous administration of emetine-bismuth-iodide or auremetine and chiniofon retention enemata probably gives the highest proportion of permanent cures. Manson-Bahr (1941) claimed almost 100 per cent successful results in 535 cases treated by him, mostly with combined emetine-bismuth-iodide and chiniofon; others have not been so fortunate but there seems to be no doubt that a high proportion of cures can be obtained by this form of treatment particularly if the adminstration is carefully supervised and due attention is paid to details.

In the treatment of our cases emetine hydrochloride was used for two purposes only; for the treatment of hepatitis in which 12 daily injections of gr. 1 were given intramuscularly and, secondly, to control diarrhœa in patients with active dysentery, before other treatment was begun, for which purpose 3 or 4 injections were usually sufficient. All patients were treated with a course of emetine-bismuth-iodide by mouth and chiniofon retention enemata for twelve days followed by stovarsol for ten days. The minimum dosage, usually given to nursing officers who had not had this treatment previously, was emetine-bismuth-iodide, gr. 2 nightly, with 300 c.c. 2½ per cent chiniofon every morning as an enema to be retained for at least six hours. The maximum dosage, given to men in whom this treatment had failed before, was emetine-bismuth-iodide gr. 3 nightly and 300 c.c. of 5 per cent chiniofon. Most of the patients had six days of the lower dosage followed by six days of the higher. Stovarsol was given in doses of gr. 4 twice daily. In our experience this treatment was rarely depressing. In a few cases it failed completely. In the remainder there was a noticeable improvement in the patient's colour and general condition with a relief of symptoms during the course and, at the end of it, some patients stated that they felt better than they had done for months or even years. A few had difficulty in retaining their enemata for the required six hours on account of abdominal discomfort and diarrhœa. If this became distressing it was generally relieved by reducing the dose of emetine-bismuth-iodide. A few complained of soreness of the anus. One developed a severe generalized maculo-papular rash while taking stovarsol but this cleared up in a few days when the drug was discontinued. In one case the full course could not be given, as the patient was found to have serious delusions about the nature and purpose of the treatment.

It is unfortunately impracticable, under present conditions, to follow up these patients satisfactorily since some of them are already abroad again. The immediate results, for what they are worth, were on the whole satisfactory in the case of officers and unsatisfactory in the case of other ranks. Of the seventeen officers all had at least three negative stools after treatment, all were relieved of their main symptoms and all were considered fit to remain in the Service and continue duty. Of the sixteen other ranks, the treatment failed completely in three, that is to say cysts were still present and symptoms for all practical purposes unaltered after two complete courses of emetine-bismuth-iodide, chiniofon and stovarsol, and in the case of two of them an additional course of auremetine gr. 1 four times a day for ten days. Two were also given chiniofon by mouth for ten days without any effect. In three more the stools were cleared of cysts for the time being but the symptoms remained and the patients were in a poor mental and physical state. All these six patients were discharged from the Service. The remaining ten had at least three negative stools after treatment and

were considered fit to return to duty, mostly in Category " C " for home service. In about half of them the symptoms were substantially relieved. The remainder continued to have some symptoms but these were not considered disabling.

Cause of Failure in Treatment.

A most striking feature of this series of cases was the difference in the immediate results of treatment in the case of officers and nursing officers from other ranks. This is probably due mainly to the fact that the type of case was different in the two instances. Of the seventeen officers nine had had no previous treatment and, of the remainder, in only a very few had treatment been unsuccessful on more than one previous occasion. Of the troops only one had had no previous treatment. The majority had been treated unsuccessfully on many occasions abroad, had again been treated unsuccessfully in England and had only then as a last resort been transferred to the Centre for Tropical Diseases. The troops were therefore a selected sample of peculiarly intractable cases.

The reasons for failure in treatment are not fully understood but several possibilities are worth considering :—

(1) *Failure of Co-operation on the Part of the Patient.*—Of the troops a number had been under treatment abroad, in the process of evacuation to the United Kingdom, and under treatment at home with continuous diarrhœa and other symptoms for twelve months. They were a sorry crowd who, not unnaturally, had lost all faith in treatment and often only wanted to get out of the Army. Further, it was noticed that those in whom treatment failed completely were among the most difficult and disgruntled. The possibility that some of them were evading treatment by not swallowing their capsules or by surreptitiously passing their enemata had to be considered. Although these patients were kept under as close an observation as was possible in a big ward, no instance of attempted evasion of treatment was discovered.

(2) *Failure of the Coating of Emetine-bismuth-iodide Capsules to Dissolve.*—This danger has often been stressed and should be well known. It is probably greatest in warm climates and I have myself recovered undissolved orange coloured keratin-coated capsules from the stools of patients in this war.

If keratin-coated capsules or similar preparations are used it is essential that from time to time the stools should be strained through muslin to see whether undissolved capsules are present. If this does occur and no other preparation is available the capsules should be crushed and given in a spoonful of jam. I have treated a number of cases quite successfully in this manner, without producing undue nausea or vomiting. As orange coloured keratin-coated capsules have been used extensively in the Army in this war, it is possible that they have been one cause of failures in treatment. They were not used in the treatment of cases in this series and have now been withdrawn from general use.

(3) *Possible induced Emetine Fastness.*—Whereas the immediate results of treatment were highly satisfactory in all cases treated for the first or second time, the cases in which treatment was quite unsuccessful were all ones who had had repeated unsuccessful treatments previously. This might be simply explained by supposing that the latter cases had originally been infected with a strain of *E. histolytica* which was resistant to the action of amœbicides. It is however also possible, as suggested by Manson-Bahr (1941), that a state of emetine fastness is induced by repeated ineffective treatment. In the present state of knowledge it seems wise to recommend that emetine injections alone should be used only in an emergency or to tide a patient over for a short period till it is convenient for him to have other treatment. Until a better amœbicide is discovered all patients should be treated, as early as possible in the course of the disease, with a combined course of emetine-bismuth-iodide or auremetine and chiniofon retention enemata. Whenever possible, the effect of such treatment should be checked by further examinations of the fæces and sigmoidoscopy and the course of treatment should be repeated if a cure has not been obtained. Thereafter, ideally, the fæces should be re-examined in, say, three, six and twelve months time.

Organization of Treatment.—The adequate treatment of cases of chronic amœbiasis requires the co-operation of a physician who has some facility in the use of the sigmoidoscope; a pathologist who is skilled in the detection and recognition of parasites of the fæces and nursing staff who understand and are prepared to give attention to the details of treatment. It would be an advantage if the treatment of this condition were only to be undertaken in places where these essentials are available. In any case it is highly desirable that patients whose disease has relapsed once should be transferred to such a place without further delay and before undue physical deterioration and mental hopelessness have supervened.

Summary and Conclusions.

Of the 112 patients admitted to a Military Centre for Tropical Diseases in England, suffering from dysentery or its effects, 33 were found to have amœbiasis. Only 1 had never been abroad.

The diagnosis was made on the finding of vegetative amœbæ in the fæces in 6, cysts in the fæces in 24, vegetative amœbæ in scrapings of mucous membrane taken through the sigmoidoscope in 2 and sigmoidoscope appearances alone in 1.

In 14 cases diarrhœa was not a recent complaint and had never been a prominent symptom. Cases of chronic amœbiasis will therefore be missed unless the condition is suspected in patients whose main symptom is something other than diarrhœa and unless a routine method, including repeated examinations of stools, sigmoidoscopy and examination of specimens taken through the sigmoidoscope, is followed in diagnosis.

The immediate results were, on the whole, satisfactory in the case of officers, all of whom were returned to duty, and unsatisfactory in the case of troops. The difference was probably due to the fact that the former were given efficient treatment earlier in the course of the disease than the latter.

It is suggested that emetine hydrochloride by injection should be used only for the treatment of hepatitis, in temporary emergencies, and to control diarrhœa before other treatment is begun. Until a better amœbicide is discovered all patients should be treated as early in their disease as possible with emetine-bismuth-iodide or auremetine and with chiniofon retention enemata. It is also suggested that vigorous and efficient treatment in the early stages, persisted in till there is laboratory and sigmoidoscopic evidence of cure, might prevent the development of a state of intractable symptoms, physical deterioration and mental hopelessness, which was seen in a few cases in this series.

My thanks are due to Colonel C. F. Anthonisz, Officer Commanding a Military Hospital, for permission to forward this paper; to Colonel O. J. O'Hanlon, Officer Commanding the Hospital in which the observations were made; to Majors J. S. F. Niven, J. Keall, and T. Crawford, Specialists in Pathology, whose willing co-operation alone made the work possible; to the numerous medical officers and sisters who were concerned with the treatment of the cases and to Major-General A. G. Biggam for his advice and encouragement.

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