DIFFICULTIES IN THE DIAGNOSIS OF SUBACUTE AMOEBIASIS AND THE VALUE OF EMETINE AS A DIAGNOSTIC AGENT.

By Major J. Huston,
Royal Army Medical Corps.

"Try him on a little emetine!" This sage advice was often given by our elders with regard to obscure fevers and other mysterious disease phenomena which had resisted many forms of treatment. It was good advice. My impression is that it is now less frequently acted upon than formerly. Perhaps we are too engrossed with the types and strains of the great bacillary group of dysenteries to dwell long upon the activities of that simple creature, the Entamoeba histolytica.

The subacute and chronic forms of amoebiasis are known to be difficult to recognize. Among other obstacles, the following, either singly or in combination, are found: (a) The previous medical history is often negative or misleading; (b) An insidious onset of symptoms and signs; (c) Unusual manifestations; (d) Amoebiasis may occur in the course of another disease; (e) Negative laboratory findings.

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CHART CASE I.

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Among cases encountered within the past two years in the United Provinces, India, the following are reported to illustrate these points:—

*Case I.—Previous history misleading and negative.*

A private, aged 22, seen on December 11, 1936. History: Two months previously received a severe kick in the right loin while playing rugger. There was acute pain at the time but he was able to finish the game. There had been no obvious haematuria. From the date of injury he suffered from malaise, pain in the injured side and constipation, but managed to carry out his duties which were technical. He reported sick on November 7, 1936, and was admitted to hospital. He had an intermittent temperature, maximum 102° F., for the next four weeks. There were slight night sweats and fairly constant pain in the right lumbar region. Maximum leucocyte count was 10,000 with 65 per cent polymorphs. Arneth count—no change. Red cells: 4,500,000. His medical attendants considered a right perinephritic haematoma or abscess was probable.

Palpation of the right kidney area disclosed nothing, but in the right hypochondrium a three fingers' breadth downward enlargement of the
liver was found. A radiogram showed raising of the right cupola of the diaphragm. There was no history of dysentery or bowel disturbance.

Subacute hepatitis was diagnosed and an injection of one grain of emetine hydrochloride given daily for twelve days. The symptoms abated and the temperature reached normal and remained so after five injections. Seven consecutive examinations of the stools failed to reveal *E. histolytica* cysts.

Comment.—In this case a common mistake occurred in associating the illness with the apparently related history of injury. We all make similar slips and it is in such cases that another opinion is of value in reassessing the whole case.

Case II.—Insidious onset in the course of another disease.

An officer, aged 49, was seen on November 2, 1935, complaining of pain in the right iliac fossa of four days' duration. He stated he had had a similar illness six months previously. The abdomen was soft, but there was definite deep tenderness near McBurney's point, and Rovsing's sign was positive. There had been no vomiting and the bowels were constipated. He had some gastric flatulence, but had suffered from it for some years. The pulse and temperature were normal. The leucocyte count was 10,000; polymorphs 68 per cent.

Subacute appendicitis was diagnosed. His condition gave rise to no anxiety, but as he was going on leave soon, operation was advised. On November 28 a small friable subacutely inflamed appendix, adherent to the right leaf of the mesentery, was removed without difficulty through a gridiron incision and the abdomen closed. Apart from one bout of post-anæsthetic vomiting, the next forty-eight hours passed normally. On the third day the evening temperature was 100°F. and the pulse 80; there was a little fulness in the abdomen, although he was passing flatus. On the fourth day the temperature was 101°F., pulse 84; the bowels were well opened with an enema; examination of abdomen and rectum was negative. On the fifth day after operation the maximum temperature was 101.8°F.; the patient was haggard looking and restless, the abdomen was a little distended and the bowels were acting. On the morning of the sixth day the temperature was 101°F. Rectal and abdominal examinations were again negative, except for a slight fulness, with discomfort in the epigastrium. The evening temperature was 102°F. Total leucocytes—10,000; polymorphs 68 per cent, lymphocytes 26 per cent, large mononuclears 2 per cent, eosinophils 4 per cent.

His condition remained much the same for the next three days, and the temperature about the same level. Blood films taken daily were negative for malaria parasites. Blood culture, Widal tests, urine and faeces examination gave no information. By the ninth day it was noticed that the fulness, previously noted in the epigastric area, was a shade more definite.

Emetine injections were tried. The temperature came to the normal
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level in six days of gradual lysis. The patient felt a little better each day and his feeling of fulness in the epigastrium disappeared.

No dysentery organisms were isolated in seven specimens of feces.

The patient reported by letter, fourteen months after the illness, that he had had no further trouble and felt fitter than he had done for years.

CHART CASE II.

DISEASE. APPENDICITIS SUB-ACUTE. AGE 49.

DATES OF OBSERVATION
DAYS OF DISEASE.

TEMP. °F

PULSE PER MINUTE.

MOTIONS PER 24 HOURS.

Case III.—Unusual manifestation in the course of another disease.

An officer's wife, aged 26, was referred to me as a case of recurrent appendicitis. She gave a history of dyspepsia of several years duration and of attacks of colicky pain in the abdomen with tenderness in the right iliac fossa during the past eight months. On examining her the abdomen was found to be soft but there was definite deep tenderness near McBurney's point. Bimanual examination disclosed nothing abnormal. A barium meal showed no abnormality in the stomach or duodenum; there was, however, a positive gastro-ileal reflex and beaded residue in the appendix for forty-eight hours.

On February 25, 1935, a large swollen fleshy appendix, which adhered by a band to the posterior wall of the cæcum, was removed without difficulty through a right paramedian incision. There followed four days of ordinary convalescence with a normal temperature and pulse. The
bowels were opened once with an enema on the third evening as a small dose of cascara had been ineffective. On the fourth evening a further dose of cascara with liquid paraffin was given. On the following afternoon I received an urgent message to see the patient. While on the bedpan, a large bowel haemorrhage had occurred. I was shown two bedpans full of recently clotted blood mixed with a few tarry scybala. A blanched patient lay on a bed swamped with blood. The pulse was 130, fluttering and barely perceptible. Suitable treatment was instituted and a blood donor was crossmatched and stood by. There remained the diagnosis of the exact cause of this unfortunate state of affairs.

The abdomen was soft. There was no pain and no vomiting. Digital examination of the rectum was negative. A purpura of Henoch's type or a mesenteric occlusion seemed unlikely on account of the absence of pain and the softness of the abdomen. Haemorrhage from a peptic ulcer or from a neoplasm (e.g. adenoma or polypus) appeared more probable. The case was discussed with the Specialist in Medicine, Major J. Bennet, R.A.M.C., whose advice is gratefully acknowledged. He informed me that he had seen a similar case, though unrelated to recent operation, and suggested a bleeding amoebic ulcer as the cause.

A course of emetine injections was commenced the same evening. No further melena occurred and her recovery was uneventful.

On the day following the haemorrhage the blood showed:

Red blood cells 3,000,000 per cubic millimetre. Haemoglobin 40 per cent. Blood platelets 95,000 per cubic millimetre. Leucocytes 15,400 per cubic millimetre.

Sigmoidoscopy at the end of twelve days' treatment showed a normal distal colon.

Pathologist's report on the vermiform appendix was: "Acute catarrh is present, the mucosa being eroded, congested, and infiltrated with leucocytes. The muscular coat is unaffected."

On further interrogation of the patient, she stated that she had blood and mucus in the stools when on her way to India two years previously. On one occasion then, she passed a quantity of blood but it was in no way comparable to the present attack. At the time she had been given stovarsol.

This patient was given a course of eighteen one grain emetine injections, with a fourteen day interval at the end of ten. She reported in January, 1937, that she had had no further trouble with the bowels. Her dyspepsia cleared up three months after operation. That she feels very fit and had had a baby since the illness reported.

Comment.—Intestinal haemorrhage is mentioned as a complication of amoebic dysentery in the textbooks, but on perusing the subject in four of the most popular of them, one finds that "severe intestinal haemorrhage sometimes occurs, and unless quickly controlled may be serious" (Byam and Archibald, 1922), is the most illuminating remark in any of them.
DISCUSSION.

One is well aware that the diagnosis of a primary appendicitis in the two foregoing cases (II and III) is open to criticism.

In Case II it is unfortunate that the appendix was not submitted to a pathologist for section and report. Macroscopically, the appendix presented one of the most usual appearances seen in patients who have been victims of repeated mild attacks of catarrhal appendicitis—the sclerosed appendix.

In Case III the appearances of the appendix are described.

In both cases the lumen was disturbed by the traction of adhesions to adjacent structures. In neither case was the cecum thickened, as one might expect if amoebic invasion were present. In both cases, also, there had been repeated attacks, pointing to an appendicitis which had resolved to some degree. Had the infection in the organ been amoebic in the first instance, would the condition settle down speedily without specific treatment?

An authority (Rogers, 1930) emphasizes the importance of not mistaking thickening of the cecum in chronic and latent amoebic bowel affection for appendicitis and the need, where the symptoms are not of an urgent nature, of a short course of emetine, before submitting a patient coming from an area where amoebiasis is endemic to what may be a needless operation.

Another writer (Manson-Bahr, 1935) has the impression that certain intestinal conditions occur frequently as an aftermath of amoebiasis—among them "certainly appendicitis (not necessarily caused by amoebic ulceration)."

There are certainly a number of cases of amoebic dysentery which do not clear up completely with repeated courses of the orthodox medical treatment, who eventually present symptoms of appendicitis of a subacute type, and finally are submitted to operation. In these amoebic ulceration is commonly present.

Case IV.—Unusual manifestation.

An officer, aged 52, was examined on December 26, 1935, for a tumour in the right side of the abdomen. For the previous two weeks he had been treated in his quarters for "gastritis," and during the last two days there had been fever. Two blood-films had shown no malaria parasites.

He was a heavy, pale-faced man complaining of an irritating cough and of pain and distension in the abdomen. Temperature was 102° F. Pulse regular, 88. The abdomen was moderately distended. On the right side a hard smooth mass could be felt, extending from the 10th and 11th costal cartilages at the costal margin to the right iliac fossa where its lower limit was indefinite. Seven inches broad at its widest, the mass had a hard, smooth, well-defined medial border, and the lateral border was lost in the fat and muscles of the flank. The whole tumour was dull to percussion, tender to pressure, with a maximum intensity three inches to the right of the umbilicus. It did not move with respiration. There appeared to be some fulness, but no tenderness in the right costovertebral angle.
liver dulness was normal except at the 10th and 11th costal cartilages, where it was continuous with the dulness over the tumour. Radiograms showed a normal-sized liver. A few scattered rhonchi were noted in each lung.

Clinically the case suggested a right perinephritic abscess; diverticulitis of the ascending colon; malignancy of the ascending colon with fecal accumulation; appendiceal abscess; amoebiasis of the hypertropic type.

On more detailed interrogation, the patient disclosed that he had lost some weight in the last month. He had had "a touch of dysestera in Mesopotamia" in 1916 and again in September, 1934; for the latter, two emetine injections had been given. The centrifugalized urine showed no pus cells. Blood examination showed: Leucocytes, 14,000 per cubic millimetre. Arneth count a marked shift to the left. Differential count: Polymorphs 84 per cent, lymphocytes 14 per cent, large mononuclears 2 per cent. After a barium meal there was normal emptying of stomach and bowel. The ascending colon showed a little more haustration than usual. Part of the transverse colon showed a "mouse-eaten" appearance.

Feces: No blood or mucus. No E. histolytica or cysts.

Amoebiasis of the caecum and ascending colon seemed the probable diagnosis.

Daily emetine injections were commenced. The temperature fell to normal within three days and the tumour in the abdomen became smaller day by day in the most remarkable way. At the end of a week's treatment it felt like an ordinary thickened colon, such as one commonly finds in cases of chronic dysentery. At the end of twelve injections (twelve grains of emetine hydrochloride) the patient left hospital and soon returned to duty. A further short course was given later. When seen at the end of six months he was fit. The ascending colon remained somewhat thickened on palpation. There had been no recurrence at the end of fourteen months.

Twelve consecutive examinations of the feces, in this case, failed to disclose vegetative or cyst forms of E. histolytica.

Comment.—The hypertropic form of intestinal amoebiasis does not appear to be very common among Service patients. I have seen three cases in India in nine years. The others were less well marked than the case quoted.

Referring to this amoebic granuloma, an authority (Manson-Bahr, 1935) describes the process as "an isolated ulcer, with progressive erosion of the bowel wall in response to long continued secondary infection. Large amounts of edematous granulation tissue appear, and the process may affect the entire bowel wall and the neighbouring mesocolic fat."

Case V.—Medical history negative. Unusual manifestation.

A private, aged 21, reported sick on January 20, 1936, complaining of a lump in the pit of the stomach. He was admitted the same day for investigation.
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He had never been abroad before coming to India eighteen months ago. He stated he had not had diarrhoea or dysenteric symptoms at any time. He had an attack of lobar pneumonia (both bases) in November, 1935, and appeared to have fully recovered. On Christmas Day he felt pain in the lower part of the chest on deep inspiration. About January 8 he "felt full and heavy in the stomach" and he noticed the lump. There was no history of trauma or of vomiting.

He was a fresh-complexioned, fit looking young man. Temperature 100° F. Pulse 87. Respiration 18. In the abdomen a swelling the size of a large fist could be seen and felt in the left epigastric area. It felt tense and smoothly rounded. Dull to percussion with the tympanitic stomach note distal to it, the tumour moved with respiration. It appeared to be attached deeply in the left hypochondrium and superficially to the parietes beneath the upper third of the left rectus. Its appearance closely resembled a pseudocyst of the pancreas such as often follows trauma, except that it moved with respiration. Leucocyte count was 16,000 per cubic millimetre. Differential count was not recorded. Arnetth count, slight shift to left. Radiograms showed a generalized enlargement of the liver. The lower border of the left lobe was not clearly defined.

An injection of one grain of emetine hydrochloride was ordered, preparatory to aspiration and/or exploration the following day.

In the theatre, two attempts at aspiration failed, and the tumour was exposed through an upper left paramedian incision. The left lobe of the liver was found to be greatly enlarged in a downward direction (within two fingers' breadth of the umbilicus). It contained in its substance an abscess—the size and shape of an egg, with the long axis lying in the sagittal plane. The thick grumous pus which the cavity contained was wiped out with gauze and the cavity packed. Daily injections of emetine were continued, and the temperature came to normal within three days. From the cavity there drained a very small quantity of anchovy-sauce-like material. The liver enlargement disappeared in the course of a week, and an uneventful convalescence followed.

Laboratory investigation of the abscess contents disclosed "a Gram-negative bacillus, not coli group." Eight consecutive examinations of the faces did not reveal E. histolytica cysts.

Comment.—It is a remarkable thing that there is comparatively little constitutional disturbance in some liver abscesses. This case is an illustration. If one had not used a thermometer or seen the swelling the patient might well have been considered fit.

In this patient I was a little uncertain of the pre-operative diagnosis. Puncture is not considered a particularly safe procedure below the left costal margin (Rogers, 1930) and only two attempts were made. The abscess contained, at most, two ounces of debris, and might have been absorbed without active intervention with emetine. And yet it does not do to be over-dogmatic on this point as the following chastening experience
will show. In 1934 I was called to see a man, aged 52. He had been diagnosed acute amœbic hepatitis six days previously, and had received five emetine injections. The physical signs were definitely those of involvement of the upper right lobe. The temperature had fallen gradually and the liver enlargement seemed to be decreasing when he developed a sudden and very acute abdominal pain. A small abscess on the upper surface of the right lobe had leaked and a general peritonitis had resulted. The patient died.

CONCLUSION.

A number of difficulties in the diagnosis of secondary amœbiasis are illustrated by case records. My main interest in the subject is its surgical aspect, but at the risk of indulging in a hackneyed topic, these remarks on aids to the diagnosis are ventured.

A careful, and until the diagnosis is settled, a daily repeated clinical examination of the patient is essential.

The leucocyte count gives very useful information. A moderate leucocytosis of between 10,000 and 20,000 per cubic millimetre is usual in these cases. The polymorphonuclears are present in little over normal proportion, and where invasion by secondary organisms has not occurred, one higher than 85 per cent need not be expected. Where the leucocyte count is low a red cell count should be done. It may reveal a relative leucocytosis. It must be remembered that anaemia is often present (Rogers, 1933). The Arneth index, or one of its modifications, is helpful in association with the other findings. It is of great use in prognosis.

Radiography and examination with the sigmoidoscope yield rapid and often definite information.

Microscopical examination of the stools may shed light on the obscure case. In the cases described the results are disappointing, but this is unusual. The method has its limitations. It is well to recall that though the discovery of E. histolytica, in one or other of its forms, justifies a diagnosis of amoebiasis, this by itself does not imply that the patient is suffering from amoebic dysentery or indeed any other amoebic disease (C. Dobell and G. C. Low, 1922).

When the organism is found in association with an appropriate clinical picture, it clinches the diagnosis.

Let me here diverge for a moment to an aspect of disease in which we, as a Corps, are now mainly interested—Prevention!

Are we doing everything possible to prevent the development of these cases of amœbiasis? It is not uncommon to see a patient with a relapse of dysentery treated several times with salines and starvation. Despite all care his bowel symptoms never quite clear up. His health and morale deteriorate; he may become the wreck of a man. Then one day the glad news spreads through the hospital. The wandering amœba has been found! The "scientific" honour of medicine has been satisfied! And the patient receives his long delayed emetine. In the treatment of recurrent dysenteries.
in ordinary practice, many eminent and experienced men tell me that they give adults a course of emetine as a routine. Let us use our microscopes by all means, and also our common sense. Huxley's definition is relevant—"Science is nothing but trained and organized common sense."

To return to the main theme—in emetine we have a drug of unique value in diagnosis and in treatment. With the ordinary precautions we can do no harm and a great deal of good by using it. It has the merits of rapidity and definiteness in its action. A few doses—at most six—will indicate whether or not we are dealing with a case of amoebic infection.

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