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# THE DIAGNOSIS OF AMOEBIASIS

BY

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Amoebiasis is one of the major problems confronting the Medical Services in the Far East. The incidence is surprisingly high, the diagnosis often difficult and elusive, the treatment unsatisfactory, and the relapse rate disappointing (Payne, 1945). In addition to those whose symptoms are sufficiently incapacitating to lead to admission to hospital, there are probably a greater number of individuals who, after infection, become cyst-passers, unaware of their condition and of their gradual deterioration in health and fitness. On final demobilization difficulties will arise in temperate climates not only among those returning from the East but among others who will be infected by them.

The disease is so protean in its manifestations that it is important not only to confirm the clinical diagnosis but, if possible, to eliminate the suspicion of amoebic infection in other conditions which may simulate amoebiasis. Moreover, the identification of cyst-passers is of the greatest assistance in preventing its spread. After four years' service in the East one cannot but arrive at the conclusion that the seriousness of amoebiasis has not been fully appreciated in the United Kingdom; nor have the majority of residents in the East been sufficiently alive to the risk of infection to which they may be constantly exposed. It is well known that over 90% of the indigenous population suffer from worm infestation, and the examination of 600 cooks, ward boys, and others handling food in establishments near this hospital showed that 12% were passers of the cysts of the *Entamoeba histolytica*. The danger of infection to which Europeans are exposed is thus considerable. It is possible in the majority of cases to be ignorant of the infection and, even if it be suspected, to experience but little interference with normal life. That health has been below normal is volunteered by all cyst-passers—even though they may have been entirely symptom-free—after the completion of treatment. The danger lies not so much in the more dramatic accidents of hepatitis, haemorrhage, or perforation as in the general lowering of health and efficiency.

It is suspected that amoebiasis is a much more common condition among Europeans than is generally realized, and that the failure to appreciate its incidence is due largely to the lack of symptoms distressing enough to cause the patient to seek advice, and partly to the tendency to arrive at a premature negative diagnosis on the results of too few investigations.

## Material

These conclusions have been drawn from a series of 300 cases seen in Ceylon in which the *Entamoeba histolytica* has been identified in its vegetative or cystic form. During these investigations some 40,000 stool examinations have been made.

The incidence of amoebiasis in intestinal complaints is surprising, as it forms 46% of the total cases admitted to this hospital.

*Cases Admitted with Bowel Disorders*

| | Per cent. |
|---|---|
| Enteritis | 46 |
| Bacillary dysentery: | |
| Proved | 7 |
| Clinical | 1 |
| Amoebiasis | 46 |

Though the incidence may appear to be high, it can be explained in part by the fact that the majority of cases admitted to this hospital are referred from other establishments, and thus the acute cases of gastro-enteritis which normally recover within a week or so are not seen, the greater proportion consisting of ambulatory cases of old-standing diarrhoea and abdominal pain.

The number of examinations required to arrive at a diagnosis differs from case to case.

| Number of Stools | Percentage of Cases Diagnosed |
|---|---|
| 1 | 30 |
| 2 | 12 |
| 3 | 8 |
| 4 | 8 |
| 5 | 7 |
| 6 | 2 |
| 7 | 3 |
| 8 | 3 |
| 9 | 3 |
| 10 | 6 |
| 11 | 3 |
| 12 | 4 |
| Over 12 | 11 |

Two large groups occur. One-half are diagnosed on the first 3 examinations, and half of the remainder after 8 or 12. The diagnosis of the few remaining usually requires between 16 and 20 examinations. The first group represents cases which show obvious blood and mucus with diarrhoea (25%), and three-quarters of the cyst-passers (25%); the second group those with vague abdominal symptoms, whose clinical relapses and admission to hospital are followed by an exacerbation of the pathological findings. If the examination of stools is limited to three specimens (Manson-Bahr, 1943) a considerable proportion will remain undiagnosed. Even 10 specimens (Svensson and Linders, 1938) cannot be considered to be adequate. Each case should be judged on its merits, though for routine purposes nine-tenths of those in which the *Entamoeba histolytica* may be found will be diagnosed if 12 specimens are examined. Caution similarly should be exercised in assessing the results of treatment.

Attacks of bacillary dysentery and acute enteritis have often brought to light an underlying amoebiasis. It is therefore of as much importance to be able to eliminate the possibility of an amoebic infection as it is to establish the diagnosis. In all cases complaining of diarrhoea, whether the exudate suggests an amoebic, a bacillary, or a mixed origin, examinations have been carried out throughout treatment and convalescence in order to eliminate latent amoebiasis and to determine whether any reliable diagnostic criteria could be established. It has been found that in cases of acute bacillary dysentery (Sonne and Flexner) which recover clinically the excretion of red blood cells and leucocytes does not persist for more than two weeks after the onset of the original attack. (An insufficient number of Shiga infections have been encountered to afford any conclusion.) No reliable characteristics have been found to differentiate macrophages from pre-cystic forms of the *Entamoeba histolytica* in unstained films. As the infection progresses, however, it becomes evident that cases fall into two groups: those which subsequently excrete less degenerate and later vegetative entamoebae and which, with their remission, pass pre-cystic forms; and those in which the pathological features disappear gradually, with the entire absence of cysts. It is on this last feature—the disappearance of the red cells,

leucocytes, and macrophages, and the non-appearance of cysts —that underlying amoebiasis may be eliminated.

It has been possible to follow for over a year the progress of some 30 patients, in addition to others exposed to exactly the same risk of infection. An opportunity has thus been provided to compare the findings over a long period with the subsequent clinical history. It is found that no contact whose stools do not contain red blood cells and leucocytes for 10 or 15 specimens shows further pathological features; nor do clinical symptoms develop. Those cases in whose stools red blood cells and leucocytes have appeared after having been absent, perhaps, on three or four examinations have been considered as potential hosts of the *Entamoeba histolytica*, for after purging or on more prolonged examination this infection becomes evident. Twenty-five cases with no clinical symptoms have been diagnosed in this manner.

### Identification of the Entamoeba histolytica

The pathological diagnosis of intestinal amoebiasis may be considered from two aspects: (1) the recognition of the *Entamoeba histolytica* and its differentiation from other protozoa; (2) the measures which provide the best opportunity for its recognition.

Little need be added to the accepted features; for if the three criteria of size, the ingestion of red blood cells, and purposive movement with the explosive extrusion of pseudopodia are observed, the possibility of confusion with other intestinal protozoa is remote. Although it may be tempting to predict the subsequent development of one of these features which may be absent for the moment, it has been found in this series of cases that to hazard a diagnosis on sluggishly moving or immobile precystic forms is unnecessary; for sooner or later, usually in the three or four subsequent specimens, a definite diagnosis can be made.

### Methods for Rendering Discovery Easier

The recognition of cysts has proved to be more difficult than is usually assumed, as the majority have ill-defined characteristics. In direct smears the recognition of chromatoid bodies is no easy matter, and in those stained by Weigert's haematoxylin after fixation in Schaudinn's fluid considerable care should be exercised in the elimination of artifacts. Organisms adhering to the surface of the cyst and plications of the wall from enfolding during fixation may closely resemble the internal structures. To overcome this difficulty a modification of Faust's method of concentrating cysts (Faust *et al.*, 1939) has been used, employing copper sulphate.

A piece of faeces about 4 cm. in diameter is macerated with distilled water in a urine glass and allowed to sediment and filter overnight through six layers of surgical gauze. The supernatant fluid is poured off and the faecal mud is mixed with a saturated solution of copper sulphate and centrifuged at high speed for ten minutes. Films are made from the upper surface.

The advantage of this method lies not so much in bringing to light cysts which would not have been seen in direct smears as in that the washed cysts can be seen clearly, for the only bodies which appear with them after concentration are helminth ova and occasional vegetable cells. No confusion of intracellular detail with artifacts can thus arise. The copper sulphate stains the majority of vegetable cells blue and precipitates protein matter. This method of concentration reveals cysts in twice the number discovered by the examination of direct films.

It has been accepted in the past that chance plays a large part in the diagnosis of intestinal amoebiasis. This, however, is not borne out by the findings in this series. The stools are passed and examined under optimum conditions, the bed-pan being dispatched immediately after use and the contents not transferred to a smaller receptacle. The blood and the mucus which may be adherent to the outer surface of the stool are thus retained in this position, and in those cases in which a pultaceous stool is excreted the mucus passed at the end of defaecation is easy to recognize. The delivery of a specimen in a second container, though possibly convenient to a ward, interferes with the easy selection of material for examination. It has been our practice to make four separate slides from each stool, in order to reduce the possibility of error due to random sampling. The appearance of pathological features can be hastened by a purgative. A saline cathartic is preferable, as oily laxatives leave droplets which obscure the microscopical field. It is important to avoid this measure in the quiescent stage before the undisturbed state of the colon has been ascertained, as it is sufficiently irritant to produce red blood cells and leucocytes.

Each case shows a regular evolution. There is a gradual change in a relapse from normal stools with a very occasional leucocyte to the appearance of red blood cells and leucocytes in greater profusion. Cysts then develop. Later mucus, with more leucocytes and pre-cystic forms, is found, with frank blood. This stage is followed by the appearance of vegetative forms, or the condition subsides in the reverse order after a variable interval. This tide is more or less symmetrical, and if, after the pre-cystic and immobile forms have been found, cysts begin to reappear, the vegetative forms are not to be expected, and a further exacerbation must be awaited or a diagnosis made on the identification of the cysts. This cycle is longer in duration and more gradual in its progress in cases associated with vague abdominal symptoms and is more precipitate in those with diarrhoea. Several volunteers whose course could be followed closely confirmed this conclusion. A graphic representation recording the features of consistency, the presence of macroscopic blood and mucus, and the finding of red blood cells, leucocytes, vegetative, pre-cystic, and cystic forms of the *Entamoeba histolytica* made this contrast between the acute and chronic cases evident. So far as is possible every stool has been examined, but in the acute cases those passed at night have been discarded. In the chronic cases, however, as cysts and not vegetative forms are to be expected, these stools are retained for examination the next day.

The regularity of this rhythm suggests that it represents the pathological activity of one lesion—or, alternatively, that the diseased colon undergoes its relapses and remissions as a whole —rather than the existence of separate lesions with uncorrelated cycles. This is confirmed by the general increase in activity accelerated by an attack of gastro-enteritis or by the use of a purgative.

There is a close correlation between the pathological findings and the site of the disease as assessed on clinical and radiological evidence. In rectal disease—when the chief complaints are diarrhoea, tenesmus, and the passage of frank blood and mucus—red blood cells, leucocytes, and vegetative pre-cystic forms are found, but cysts rarely appear. The vegetative forms, though perhaps immobile when examined at first, may become quite active after half an hour on a warm stage, even after the mucus has been previously immersed in broth at room temperature for the purpose of culture. This suggests that, though care should be taken to ensure that examination is made immediately after evacuation, the interval between the shedding of the amoeba from the ulcer and its discharge per anum is of importance. This factor may be reduced by encouraging the patient not to delay in defaecation or by purgation.

When the caecum and ascending colon are involved, with the production of vague pain and constitutional symptoms, there are no active forms; but cysts, leucocytes, and red blood cells are found more or less uniformly distributed throughout the faeces. Perhaps the reason for this is not so much the differing type of lesion as that in their passage down the colon the more active forms degenerate into cells which may not be recognizable as having been derived from protozoa. The "showering" of cysts does not seem to occur when four specimens are examined from each stool.

### Adjuncts to Diagnosis

The value of sigmoidoscopy as an adjunct to diagnosis would seem to depend on the experience of the investigator. In the more obvious cases, in which pathological confirmation of an almost certain clinical diagnosis is required, the findings on sigmoidoscopy are usually definite. A preliminary stool examination to eliminate bacillary dysentery and perhaps to identify the *Entamoeba histolytica* might well be followed by sigmoidoscopy or proctoscopy for the easier collection of mucus. In the obscure cases, in which doubt arises in the pathological findings and in which the elimination of amoebiasis may be of importance, the lesions may be high up or minute. Furthermore, in this series of cases few of those presenting

caecal tumours had ulcers in the rectum or the pelvic colon. This experience is in contrast with that of Payne (1945). Sigmoidoscopy would appear to be of great value in effecting a diagnosis in the dysenteric case in the shortest time but to have limitations in latent cases.

### Conclusions and Summary

The prevalent attitude to amoebiasis is concerned with the difficulties of treatment, the liability to infection being regarded as an unavoidable risk. As a feasible and practicable laboratory diagnosis can be made, it is felt that attention should be directed to the prevention of its spread by the removal of cyst-passers from the handling of food, the diagnosis of latent cases in permanent residents in the Tropics, and the elimination of unsuspected infection among members of the Services on repatriation.

The pathological findings of 300 cases of amoebiasis in which the *Entamoeba histolytica* has been identified are described. The difficulties of laboratory diagnosis are discussed. Routine examinations, to reduce the incidence of the disease, are suggested.

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#### REFERENCES

Faust, E. C., Sawitz, W., Tobie, J., Odom, V., Peres, C., and Lincicome, D. R (1939). *J. Parasitol.*, **25**, 241
Manson-Bahr, P. H. (1943). *Dysenteric Disorders*, London.
Payne, A. M. M. (194 ) *Lancet*, **1**, 206.
Svensson and Linders (1938). Cited by Stitt, Clough, and Clough, in *Practica Bacteriology, Haematology, and Animal Parasitology*, p. 416, Philadelphia

# ACROPARAESTHESIA IN THE LOWER LIMBS

## UNEXPLAINED PAINS IN THE LEGS AT NIGHT

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For simplicity I have used the word "pains" in the subtitle of this note, but the sensation which is experienced in the cases I refer to is not actually pain but a peculiar tingling discomfort which, when intense, becomes painful. I believe the sensation is the same as in the condition called acroparaesthesia, which commonly occurs in the arms at night and is of far more frequent incidence in women than in men. Among the early descriptions of it were those of Putnam in 1880 and of Ormerod in 1883, and, following the lead of the former, it is still usual to regard it as a vasomotor neurosis; but Behrman (1945) in his recent paper regarded it as due to slight pressure on the brachial plexus at the thoracic inlet, and, while insisting that it was not necessarily nocturnal, attributed its frequent occurrence at night to the influence of the recumbent posture and the hypotonia of sleep in bringing about such pressure. Walshe (1945) has taken a similar view. Acroparaesthesia in the lower limbs has been mentioned by some of those who have written on the subject, but in recent times its occurrence seems to have been insufficiently recognized. All the sufferers from it whom I have encountered have been in men, but one patient said that his mother had suffered from "pains" in the legs which he thought were similar to his own.

The following cases provide good examples of this condition.

### Case I

An architect aged 68 complained that he had pains in his legs at night, which he had been subject to for more than forty years. They had gradually grown worse as he got older, and now they kept him awake a great deal. The pains used to come on after he had gone to sleep and wakened him up, but recently they had occurred about half an hour after he had got into bed. Formerly he used to move his legs to a cooler part of the bed or put them out from under the blankets, but in recent times these measures have been insufficient, and he has had to get out of bed and walk about the room for a little. He may have to do this several times in one night. If he gets out of bed in this way while the pain is present he may feel "groggy about the ankles," and in the mornings he sometimes feels similarly "groggy." When he came to see me he said he was getting practically no sleep till three or four o'clock in the morning.

The sensation in his legs began as a tingling in the calves, and gradually, as it became worse, it became more like pain. He called it "neuritis." The discomfort was always below the knees. In answer to my inquiry he said he had some burning sensation in his feet, but evidently this was not an important feature in his condition. The "pains" were limited to the night, except that very occasionally in winter, when sitting in front of the fire, he had felt some tingling in his calves. Even when he had to stay in bed because of illness the pains were limited to the night, and they had been very troublesome when he had pneumonia, and also after he had had his prostate removed nine or ten years ago. He did not think that his position in bed made any difference to the occurrence of the pains. As an architect he was in the habit of standing all day at his work, but he did not believe that exercise during the day had any influence on the nocturnal pains, because the latter had occurred as usual when he was kept in bed by illness. He was inclined to think that mental strain had more effect in aggravating them than physical exercise. He said he was not a rheumatic person and had no pains elsewhere.

The patient was a thin man of medium height and generally of light build. I found no abnormal physical signs in any part of his nervous system or elsewhere in his body. In particular the knee-jerks and ankle-jerks were normal and the plantar reflexes "flexor." He had no loss of appreciation of light touch, pain, temperature, position of his toes, or vibration. The muscles of his legs were all of normal size and were not tender. He walked normally, and Romberg's sign was negative. His blood pressure was 140/90 mm. Hg and his arteries felt normal for his age. There was good pulsation in the dorsalis pedis artery in each foot, and his toes showed no cyanosis or pallor. He had no varicose veins. His heart was normal. His spine seemed normal and he stood in a normal posture. There were no signs of arthritis in his knees or hip-joints, or elsewhere. In his abdomen I found no abnormality. His Wassermann reaction had previously been done, and was negative.

He had had various kinds of physiotherapy to his legs and different types of antirheumatic treatment without any benefit resulting. He had also been treated with vitamins $B_1$ and $B_2$ over a long period, and had been given phenobarbitone at bedtime to make him sleep.

I advised that he should cease standing at his work and prescribed a combination of aspirin 10 gr. (0.65 g.) with phenobarbitone 1 gr. (65 mg.) to be taken at bedtime, and these measures brought about a dramatic improvement. After ten days he gave up the phenobarbitone, and he has continued to have restful nights.

### Case II

A doctor of my acquaintance, now aged about 50, has suffered from paraesthesiae and pains in his legs at night off and on for about fifteen years. If mild the sensation is an uncomfortable tingling, but if severe it is painful and is associated with some tenderness in his calves. At first the discomfort occurred only after playing tennis, and in recent years it has usually been associated with other forms of physical exercise such as gardening or driving his car long distances. He has long intervals of freedom from his symptoms, and at other times the pain or discomfort may be troublesome every night for weeks. It has gradually become more frequent; its intensity is very variable; but during the war, when he was working very hard and driving about a great deal, there was a period during which it was worse than he had ever experienced before. The discomfort wakens him up about half an hour after he has gone to sleep, and it may awaken him two or three times in a night. If it is not severe he merely puts his legs in a cooler part of the bed, but ordinarily he puts them out from under the bedclothes, and sometimes he lies on his face and holds his feet up in the air and moves them at the ankles so as to exercise his calf muscles. In recent times he has had a mild burning sensation in his feet associated with the "pains," but this burning sensation also occurs independently of them. So far as he has been able to determine, the posture in which he sleeps does not make any difference to the incidence or severity of the symptoms, which occur every night for a time and then remit for weeks or months. He has not observed any influence of psychological factors on the pains, and has been through periods of mental stress without suffering from them. In contrast to the previous patient, he was free from these pains during a period of illness. He never has any active discomfort in the daytime, but when the pains are troublesome he says that he can feel a little tingling in his calves during the day "if he thinks about it," and there may even be a little deep tenderness in his calves.

His ankle-jerks and knee-jerks are quite normal. There has been no wasting of his calf muscles or other musculature, and no loss of sensation or change in the appearance of the skin. The arteries of his feet seem normal and there is no indication of impaired circulation, but when the burning sensation is present some redness is seen along the outer borders of his feet and outer parts of the soles. He has no varicose veins.