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Fascioliasis—A Large Outbreak

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Summary: Forty-four cases of liver fluke infestation (fascioliasis hepatica) were diagnosed near Chepstow, Monmouthshire, in 1968. Intramuscular emetine hydrochloride and oral chloroquine given to the adults and children, respectively, were well tolerated. Assessment by repeated stool examination, complement fixation and liver function tests, and full blood counts indicated that treatment had been effective in most cases. It is recommended that both the growth and the sale of watercress should be strictly controlled.

Introduction

The outbreak reported here is by far the largest to have occurred in Britain. Facey and Marsden (1960) described six cases in Hampshire in 1959. Apart from this outbreak, human generalized fascioliasis has been described only in isolated cases in the United Kingdom. Two cases have been reported in Kent (Taylor, 1961) and one in a farm worker from Scotland (Jones and Smith, 1963). The disease is much more common abroad, a well-documented outbreak of 53 cases having occurred in France (Pautrizel *et al.*, 1964), as well as 12 cases in Algeria (Coumbaris, 1966). One interesting case was that of an 8-year-old boy who was treated with intravenous emetine with apparently good results (Quaiser, 1956).

Adult flukes may be found in widespread sites—for example, subcutaneous tissue, brain, and bladder—and several cases of ectopic fascioliasis have been described (Bürgi, 1936; Catchpole and Snow, 1952); one of the cases in this present outbreak may have been a further example. Furthermore, adult liver flukes have been found in the common bile duct and removed during surgery for obstructive jaundice (O'Donnell, 1949; Murphy and Pascall, 1950; Ramage, 1951; Sagar, 1962; Munroe, 1965).

The Outbreak

All 44 patients admitted to having eaten wild watercress from a bed, which was near infected cattle and sheep, during September and October 1968, some two to three months before the onset of their symptoms. The intermediate host, the snail *Limnaea truncatula*, was found in the watercress bed concerned (Figs. 1 and 2). The degree of severe liver damage suffered by cattle is illustrated in a section of a calf's liver, which shows the gross macroscopic disorganization with thick cyst formation (Fig. 3); in one cyst a fluke can be clearly seen. An adult form of the liver fluke is shown in Fig. 4.

The large number of cases discovered has given us an opportunity to assess the difficulties in establishing an exact diagnosis at the onset of the outbreak. Even when the possibility of the correct diagnosis was considered, the typical diagnostic criteria were not always present in subsequently proved cases. Moreover, several completely asymptomatic cases were discovered solely by routine checking of possibly infected patients.

Symptomatology.—Manifestations of the illness were malaise, intermittent fever, night sweats, weight loss, and pain under the right costal margin. Urticaria with dermatographia was a distinctive feature in some of the cases. Coughing was an occasional symptom, and was sometimes severe and persistent though non-productive. Clinical jaundice was not generally noticed, and in several patients erroneous initial diagnoses were made early in the outbreak (see Table).

Investigations.—Laboratory investigations included full haematological examination, liver function and complement

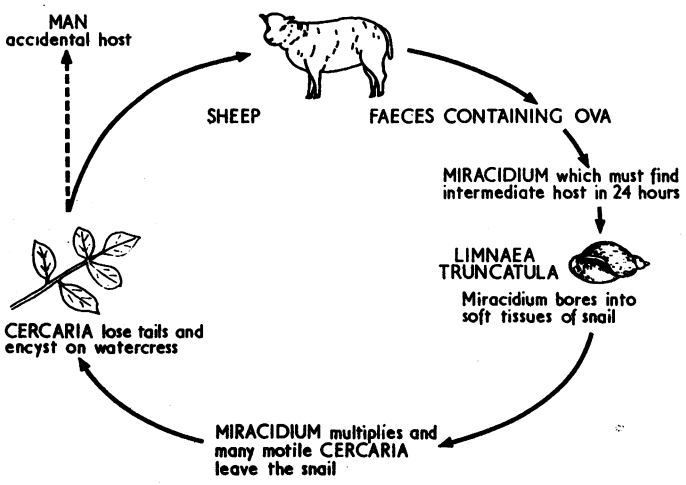

FIG. 1.—Life cycle of the liver fluke (*Fasciola hepatica*).

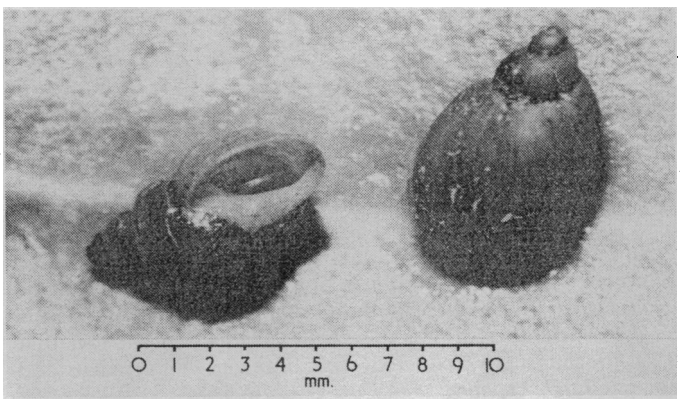

FIG. 2.—Intermediate host, the *Limnaea truncatula*.

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fixation tests, and examination of the stools for ova. In some cases abnormal findings in the blood—for example, a raised erythrocyte sedimentation rate (E.S.R.) and eosinophilia—were not always present, even though ova were subsequently found in the patients' stools (see Table). Since at one stage of our screening we were using the E.S.R. and eosinophil count alone as a diagnostic check, we soon realized that cases would be missed unless further investigations were done.

Treatment.—When a firm diagnosis had been made the patients were admitted to hospital. Intramuscular injections of emetine hydrochloride were given to adult patients, and oral chloroquine to the children. Emetine hydrochloride in 30-mg. doses was given daily for 18 days. No untoward effects were noted on the blood pressure or urine. The patients were discharged after three weeks, no repeat treatment being necessary in any of these patients. Oral chloroquine in 150-mg. doses was given to the children, twice daily in the form of Avloclor suspension, the dose being based on a dose level of 5 mg./kg. body weight/day. Initially, this regimen was given for three weeks. One child, however, required a prolonged course of two months before responding clinically. This patient also suffered depigmentation of the hair, which was reversible, but no other ill effects were noticed.

Discussion

This outbreak has provided a challenging and clinically exacting problem from a general practitioner's point of view. Before the diagnosis was apparent, various differential diagnoses were considered, both within the practice and in

Details of Cases

Case No.	Age and Sex	Signs and Symptoms at Time of Diagnosis	Investigations at Time of Diagnosis	Treatment	Final Investigations	Comment
1	36 F.	Cough. Pain in right lower chest. Nocturnal rash. Night sweats. Anorexia. Fever. Weight loss. Mild diarrhoea	Stool Positive Eosinophils(%) 35 E.S.R.(mm./hr.)75 C.F.T. 1 in 20 L.F.T. Abnormal	30 mg. emetine hydrochloride for 18 days	Stool Negative Eosinophils 9 E.S.R. 7 C.F.T. Negative L.F.T. Normal	Infestation occurred during pregnancy. Symptoms occurred in puerperium. Fetus normal. Good response to treatment
2	64 F.	Anorexia. Generalized aching pains. Pain in right costal margin. Pain in right loin. Nausea. Night sweats. Loss of weight. Pyrexia	Stool Positive Eosinophils 12 E.S.R. 42 C.F.T. Positive L.F.T. Abnormal	Emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 7 C.F.T. Positive L.F.T. Normal	C.F.T. remains 1 in 10. Still being investigated
3	24 F.	Epigastric pain. Left-sided chest pain. Night sweats. Pyrexia. Loss of weight	Stool Positive Eosinophils 38 E.S.R. 11 C.F.T. Negative L.F.T. Abnormal	Emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 2 E.S.R. 10 C.F.T. Negative L.F.T. Abnormal	L.F.T. has been persistently high and C.F.T. has been negative throughout. Still being investigated
4	33 M.	Night sweats. Epigastric pain. Urticaria. Cough. Vomiting. Pain right costal margin. Pyrexia. Loss of weight	Stool Positive Eosinophils 59 E.S.R. 81 C.F.T. Negative L.F.T. Abnormal	I.M. emetine hydrochloride 60 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 10 C.F.T. Positive L.F.T. Abnormal	First case diagnosed. Severe loss of weight and night sweats most pronounced feature. C.F.T. remain 1 in 20. Still being investigated
5	51 M.	Anorexia. Loss of weight	Stool Negative Eosinophils 26 E.S.R. 15 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 20 E.S.R. 14 C.F.T. Negative L.F.T. Normal	This patient had a negative stool throughout in spite of an eosinophilia and positive C.F.T.
6	46 F.	Urticaria. Pain in right shoulder and right costal margin. Cough. Epigastric tenderness Weight loss. Anorexia	Stool Negative Eosinophils 50 E.S.R. 12 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 9 C.F.T. Negative L.F.T. Normal	Typical history with satisfactory response to treatment
7	75 F.	Anorexia. Epigastric pain. Night sweats. Pyrexia. Weight loss	Stool Positive Eosinophils 35 E.S.R. 74 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 12 E.S.R. 2 C.F.T. Positive L.F.T. Normal	C.F.T. remain 1 in 20. Still being investigated
8	54 F.	Pyrexia. Anorexia. Loss of weight. Pain right costal margin	Stool Positive Eosinophils 8 E.S.R. 10 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 14 C.F.T. Negative L.F.T. Normal	No eosinophilia. Pain was a prominent feature in the early stage
9	72 F.	Pyrexia. Anorexia. Loss of weight. Epigastric pain radiating Right costal margin	Stool Positive Eosinophils 42 E.S.R. 50 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 5 E.S.R. 20 C.F.T. Negative L.F.T. Normal	Typical response to treatment in an elderly person. No side effects. Now perfectly fit
10	64 F.	Anorexia. Pyrexia. Nausea. Abdominal pain. Loss of weight	Stool Positive Eosinophils 2 E.S.R. 7 C.F.T. Negative L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 1 E.S.R. 10 C.F.T. Negative L.F.T. Normal	E.S.R., eosinophils, C.F.T., and L.F.T. normal throughout in spite of positive stools
11	75 F.	Anorexia. Pyrexia. No rash. Pain right costal margin	Stool Positive Eosinophils 14 E.S.R. 11 C.F.T. Positive L.F.T. Normal, became abnormal later	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 1 E.S.R. 17 C.F.T. Negative L.F.T. Normal	L.F.T. initially normal; became abnormal during treatment and then returned to normal after treatment
12	30 F.	Pain right costal margin. Anorexia. Pyrexia. No rash. Loss of weight	Stool Positive Eosinophils 2 E.S.R. 5 C.F.T. Negative L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 3 E.S.R. 6 C.F.T. Negative L.F.T. Normal	Positive stool was the only diagnostic feature of the case
13	72 F.	Upper abdominal discomfort. Sweating ++. Pyrexia. Diarrhoea. Weakness ++ pain left costal margin. Jaundice	Stool Positive Eosinophils 83 E.S.R. 30 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 8 E.S.R. 24 C.F.T. Negative L.F.T. Normal	Weakness and jaundice a pronounced feature of the case. The jaundice developed very early in the illness

Case No.	Age and Sex	Signs and Symptoms at Time of Diagnosis	Investigations at Time of Diagnosis	Treatment	Final Investigations	Comment
14	74 M.	Symptomless	Stool Negative Eosinophils 28 E.S.R. 52 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 8 E.S.R. 37 C.F.T. Negative L.F.T. Normal	This man would not admit to any symptoms and has declined further investigation
15	52 M.	Upper abdominal pain. Urticarial rash. Weight loss. Night sweats. No fever. No jaundice	Stool Negative Eosinophils 30 E.S.R. 14 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 11 E.S.R. 5 C.F.T. Negative L.F.T. Normal	Typical case with classic symptoms. Positive C.F.T. has persisted
16	15 F.	Only complaint was of slight tiredness	Stool Positive Eosinophils 6 E.S.R. 6 C.F.T. Negative L.F.T. Normal, became abnormal later	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Positive Eosinophils 3 E.S.R. 4 C.F.T. Negative L.F.T. Normal	Mild case with minimal symptoms. Daughter of Case 15
17	8 M.	Urticaria. Loss of weight. Malaise. Cough. Night sweats.	Stool Positive Eosinophils 1 E.S.R. 8 C.F.T. Positive L.F.T. Abnormal	Chloroquine (Avloclor suspension) 150 mg. twice a day. Initially for 3 weeks but as positive stool persisted, course of 2 months given	Stool Negative Eosinophils 3 E.S.R. 7 C.F.T. Negative L.F.T. Abnormal	An interesting case in a child with normal blood picture. He had persistent ova in stools needing prolonged treatment. Complete depigmentation of hair during treatment with chloroquine, which was not entirely satisfactory. Further investigations proceeding
18	21 M.	Weight loss. No other symptoms (brother of Case 17)	Stool Negative Eosinophils 8 E.S.R. 3 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 3 E.S.R. 1 C.F.T. Negative L.F.T. Normal	Mild case. Responded well to treatment
19	46 M.	Generalized aching. Febrile attacks. Night sweats	Stool Negative Eosinophils 48 E.S.R. 28 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 2 E.S.R. 5 C.F.T. Negative L.F.T. Normal	Mild case. Responded quickly to treatment
20	46 F.	Weakness. Upper abdominal pain	Stool Positive Eosinophils 4 E.S.R. 12 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 6 C.F.T. Negative L.F.T. Normal	Wife of Case 19. Moderate case. Responded quickly to treatment
21	47 F.	Upper abdominal pain. Night sweats. Urticaria	Stool Positive Eosinophils 2 E.S.R. 3 C.F.T. Negative L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 4 C.F.T. Negative L.F.T. Normal	Typical mild case
22	31 F.	Upper abdominal pain. Nausea. Slight urticaria. Night sweats	Stool Negative Eosinophils 40 E.S.R. 44 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 3 E.S.R. 11 C.F.T. Negative L.F.T. Normal	Moderately severe case with no ova detected in stool. Responded well
23	25 F.	Weight loss. Urticaria. Upper abdominal pain. Pregnant while infected	Stool Positive Eosinophils 10 E.S.R. 7 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 4 E.S.R. 5 C.F.T. Negative L.F.T. Normal	A moderate case with the interesting feature that she was pregnant in the acute phase and was delivered of a healthy baby before treatment was started
24	24 F.	Weakness. Upper abdominal pain. No sweats	Stool Positive Eosinophils 5 E.S.R. 2 C.F.T. Positive L.F.T. Normal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 2 E.S.R. 5 C.F.T. Negative L.F.T. Normal	Mild case. Responded to treatment
25	35 F.	Malaise + + pain right costal margin radiating to right shoulder and left costal margin. Anorexia. Hepatosplenomegaly. Night sweats. No urticaria	Stool Negative Eosinophils 52 E.S.R. 90 C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Emigrated to Australia. Clinically well. No further investigations performed	Typical severe case with no ova in stool.
26	9 M.	Sharp pain in right costal margin. Pyrexia. Anorexia	Stool Positive Eosinophils 4 E.S.R. — C.F.T. Positive L.F.T. Abnormal	Chloroquine 150 mg. twice a day for 21 days	Stool Negative Eosinophils — E.S.R. — C.F.T. — L.F.T. —	Son of Case 25. Emigrated to Australia. Moderately severe case in child. Final investigations not completed. Clinically well
27	6 M.	Completely symptom-free. Routine screening	Stool Positive Eosinophils 45 E.S.R. — C.F.T. Positive L.F.T. Abnormal	Chloroquine 150 mg. twice a day for 21 days	Stool Negative Eosinophils — E.S.R. — C.F.T. — L.F.T. Normal	During treatment a tender ill-defined swelling developed in muscle of right side of abdomen. We thought this was probably due to an ectopic fluke. It resolved after one week. He emigrated to Australia. Follow-up incomplete
28	35 M.	Completely symptom-free. Routine screening	Stool Positive Eosinophils 29 E.S.R. — C.F.T. Positive L.F.T. Abnormal	I.M. emetine hydrochloride 30 mg./day for 18 days	Stool Negative Eosinophils 22 E.S.R. 8 C.F.T. — L.F.T. —	This man did a commando training course during the acute period of the infection with no ill effect. Emigrated to Australia

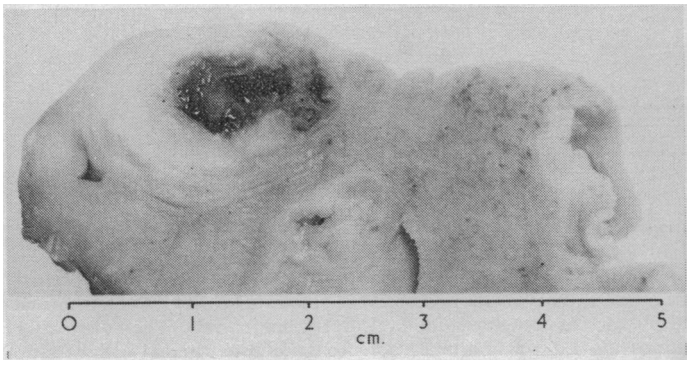

FIG. 3.—Section of calf's liver showing gross macroscopic disorganization with thick cyst formation.

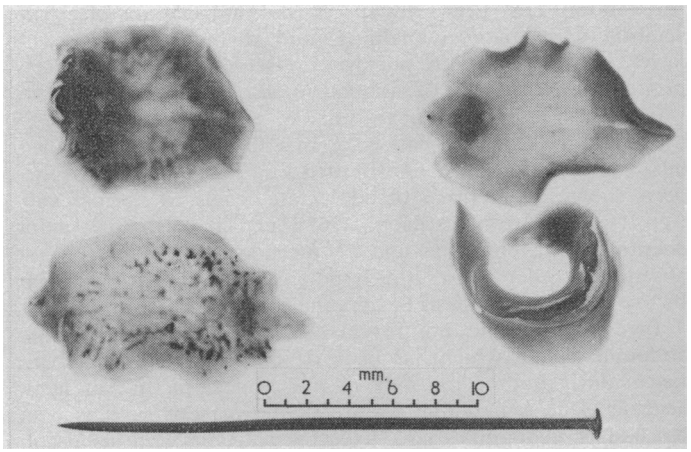

FIG. 4.—Adult form of liver fluke.

patients referred to hospital. Because of the latent period of rather vague symptoms without, initially, the common factor of the ingestion of watercress, the diagnosis was delayed in some cases.

Typical differential diagnoses in the early stages of the outbreak were diaphragmatic pleurisy, cholecystitis (one of the early patients having been jaundiced), peptic ulcer, amoebiasis, hydatid cyst, and follicular lymphoma. When it was discovered on repeated stool examinations that one patient (Case 4) was producing ova of *Fasciola hepatica* we realized that each of us was currently investigating patients who had many of the diagnostic features of the initial case of fascioliasis. Thus we requested further, more specific, investigations, and it soon became apparent that a large outbreak of this rare disease was present in the community.

Though most cases followed a basic pattern, in which the clinical signs and symptoms could be reconciled with the laboratory findings, this was by no means always true. For instance one patient (Case 10), who presented with pronounced anorexia, nausea, abdominal pain, and weight loss, had a normal blood picture, and the only abnormal finding was ova in the stools. This, we considered, might be the sort of case which could easily be misdiagnosed if no generalized outbreak was apparent. On the other hand, both Cases 14 and 28 were completely symptom-free, but were investigated further because other members of the family were proved cases. Laboratory results indicated that they were severely infected. These patients would probably not have consulted a doctor if the disease had not been confirmed in the family.

Between these extremes a variety of clinical signs and symptoms had to be correlated with a similar variation in the results of laboratory investigations. We still consider, from knowing the method by which the watercress was distributed, that more cases may have occurred in this area at the time of the outbreak, but the people concerned did not seek advice.

Treatment with emetine was successful in all but three cases. An assessment of chloroquine was difficult, however, as two of the three children treated emigrated to Australia; though these children were clinically well, final laboratory investigations could not be done.

We hope that the necessity for strict control of both growth and sale of watercress has been underlined by the magnitude and severity of this outbreak. We have often wondered why the disease is so uncommon; we consider that in rural areas where liver fluke is endemic in the cattle the possibility of its presence should be borne in mind in cases with difficult diagnostic problems.

We would like to record our thanks for the help and advice of Professor B. G. Maegraith, of the Liverpool School of Tropical Medicine, and of Dr. R. D. Gray and his staff at the Public Health Laboratory, Newport, particularly Mr. Lowe, who first observed the ova in a stool specimen. We thank Mr. Peter Sladen for the photographs and Dr. Verrier Jones, of Bristol, for his general advice. We are also grateful to Dr. D. S. Ridley and his staff at the School for Tropical Diseases, London, who performed the complement fixation tests, and the staff of the Commonwealth Institute of Helminthology for providing many useful references.

ADDENDUM: In view of the slight but persistent abnormality of the liver function tests in Case 17, a course of metronidazole 200 mg. three times daily was given for 10 days. A liver biopsy was performed three weeks after treatment and was found to be quite normal.

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