BILHARZIASIS IN TROPICAL AFRICA

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BILHARZIASIS can be listed as one of the most common diseases encountered in Africa and possibly, perhaps, one of the most serious. It is responsible for much ill health, mostly of a chronic nature, and on occasions leads to death. It is difficult to estimate the mortality rate of the disease in an endemic zone, as such a figure would depend largely on what one accepts as being complications of the disease (e.g. cirrhosis of the liver, bladder cancer and cor pulmonale). From my experience, I would estimate that it is responsible for about 1% of deaths in an adult medical ward.

The disease attacks both Europeans and Africans, but as the African comes into contact with the natural waters far more often than the European, who is only exposed to them occasionally for pleasure, as when fishing or picnicking or, very rarely, because of his occupation, the disease naturally assumes a far more serious aspect in the African. There is thus good reason to designate the diseases separately in the two races as European and as African bilharziasis.

African bilharziasis is seen at any age, as no age is immune, but for practical purposes it is a disease of childhood. Yet the infant from birth up to the age of two or three rarely contracts it. This may be because the baby is kept away from infected streams for fear of accidents or because the infant has a natural resistance to the infection. From three to 15 years of age practically every African child in an endemic region may be regarded as having the disease. Thereafter its frequency becomes less and the disease affects 30 to 50% of the adult African population. It is true that, just as there are people living in a badly infected region who do not contract malaria, some Europeans who regularly expose themselves to infected streams do not contract bilharziasis, although their families or friends who have been exposed at the same time succumb to it. Possibly the integument of some humans differs from others, so that it is difficult for the cercariae to penetrate their skins. But there are not many such people and the great majority are easily infected.

Bilharziasis is a self-limiting disease and after about eight years the infection dies out automatically, but, of course, there are the usual exceptions,

and cases are recorded in which living worms were found even as long as 20 years after possible exposure. One not uncommonly meets people who remember having had a terminal hæmaturia, of which no notice was taken, when they were children and years later all efforts to prove the presence of the disease are fruitless. In such cases it is assumed that the infection has died and little trace has been left.

It generally takes about six weeks from the time of exposure until ova appear in the stool or urine, but one cannot state a precise time when this will occur. Often it is difficult for a patient to remember exactly when exposure took place or even when symptoms first appeared.

In Rhodesia we rarely meet a person who can recall having contracted the local irritation with papular eruption where the cercariae have penetrated the skin and careful questioning of many reliable witnesses has revealed that in very few instances there is such a history. In Egypt this very early phase is given the special name of Kabure Itch. It is just possible that some of these local reactions at the time of penetration are due to non-human schistosomes rather like those occurring in 'swimmer's itch'. Little mention of the existence of these forms in Africa is made in the literature, but it is possible that they are more common than is generally believed.

When interrogating a patient as to where he was exposed it is of the greatest importance to know the exact site of exposure and how he exposed himself. For instance, not all natural waters harbour the infection, although the reason for this is not altogether clear. For example, people can bathe with apparent impunity in Lake Nyasa itself yet the rivers flowing into this lake are heavily infected. There is good evidence that the Zambesi River (at least along certain long stretches) is free. At altitudes above 6,000 ft. infection is rare, although it should be mentioned that Schwetzer (1951) has recorded the existence of *S. mansoni* at high levels in the Congo. It is probable that with the intense cold prevailing at these heights the snail does not flourish. In Southern Rhodesia it is commonly held that in the Inyanga mountains, over 5,000 ft. high, bilharzial infection cannot be

contracted. This is not altogether true, for recently we have found a few instances where the disease was contracted in a particular stream. As a general rule, in high African altitudes bilharziasis is rarely encountered.

It is also probable that the cercariæ do not survive in swiftly running water and so exposure in such rivers is unlikely to result in infestation. I have often been told by people who have exposed themselves that the stream was fast-flowing. I must admit that this has been the only kind of exposure in which the disease has rarely been contracted. The same applies to water that has been pumped up from a river to farm lands. I have not as yet met a patient who has contracted the disease from such water, but I must admit I have been told of such occurrences.

It is possible to contract the disease drinking infected water if the cercariæ can gain a foothold, but this is very unusual. I also believe that if the integument is thick or covered by some protective element penetration is difficult. I have noticed that true fishermen who confine their sport to the rod and line and refrain from actually immersing their hands or limbs in the water practically never, in my experience, contract the disease. When a fisherman has bilharziasis it usually means that he has dipped at least a limb into the water. It is possible that the integument of the palm is too thick for the cercariæ to penetrate and pass into the circulation.

The Main Clinical Features of Bilharziasis

It might assist in the recognition of the disease if its clinical features are grouped into three main categories.

Group 1

Patients of this group are seen because of a constitutional or general upset or with symptoms pointing to some other disease. Amongst the better-known symptoms are tiredness, dyspepsia, loss of weight, lack of interest, poor concentration and vague headaches. Very often these patients are labelled as suffering from 'nerves' or are considered to be making a deliberate attempt to avoid attending school. In this group should be included the early toxæmic phase of the disease, which has been called Katayama disease, although objections have been raised against the use of this term, as, strictly speaking, it applies to a district in the Far East and to the early stages of japonicum infection. Another name that has been suggested is 'bilharzial fever'. It affects both sexes and mostly children or youths, and is characterized by a varying degree of fever, urticaria, lassitude and high eosinophilia. It generally appears about six weeks

after exposure and many of these cases are mistaken for typhoid fever or food poisoning.

For reasons already given, cases in this group can best be recognized in the European. In the African one should be hesitant to accept symptoms such as tiredness as being due to bilharziasis, because, as a rule, other causes for it may be present at the same time, such as malarial infection, hook-worm disease or an inadequate diet. But it would be safe to assume that the African child is affected in a similar way to the European one, except that the Katayama syndrome has not as yet been described in an African.

Group 2

In this group patients of both races have a history of hæmaturia, whether slight or marked, and characteristically terminal. The manifestation is found in about 30 to 40% of cases. Some patients may complain of hypogastric discomfort or perhaps frequency of micturition. About two-thirds of them do not complain of any symptoms referable to the urinary tract.

Group 3

This group is very important, but it must be stressed that there is no definite proof that many of the complications attributed to the disease are definitely related to it, except those of the urinary tract. We have not yet been able to demonstrate that cirrhosis of the liver, pulmonary hypertension, acute appendicitis, gynæcological disorders and anæmia are, indeed, the result of bilharziasis, although they are said to be due to it.

It is not known for certain whether bilharziasis is indirectly responsible for the poor nutritional states we meet in the African living in tropical endemic regions. Is a person on a poor diet suffering from bilharziasis more likely to develop pellagra than one not so afflicted? Unfortunately, there is no proof as to whether this is so or not. Some workers believe that bilharziasis affects the appetite besides resulting in blood loss, and all these effects must predispose the sufferer to pellagra and other disorders of nutrition.

The Diagnosis

The sole criterion for diagnosing the presence of bilharzial infestation is the demonstration of ova in either the urine or stool or occasionally in various organs of the body. They are very rarely found in liver biopsy material. At laparotomy a piece of specific granulomatous tissue, or ova, may be revealed in an appendix, ovary, fallopian tube or mesentery, uterus, gall bladder or ileum.

Although in the majority of cases the ova can be discovered in specimens of urine or stool, we are not infrequently confronted with a case in which,

despite strong suggestive evidence, actual proof of the presence of the disease is lacking. What should be done to establish the diagnosis? It goes without saying that at least four to six urine and stool specimens should be examined. It is sometimes helpful if the patient performs some mild exercise before collecting the urine, as this tends to encourage the discharge of ova. Another useful procedure is for the patient to collect a 24-hour sample of urine in a Winchester bottle. The total is then spun down and examined for ova. This sometimes reveals their presence when other procedures have failed.

Should all search for ova in the urine and stool specimens prove unsuccessful a rectal biopsy should be performed. Not only is it useful for the recognition of intestinal bilharziasis (*S. mansoni*), but also for urinary bilharziasis, since ova deposited in the inferior or middle hæmorrhoidal plexuses are widely showered and deposited in the rectal mucosa. As this site is an abnormal focus and not the *via naturalis* for this species, the ova deposited there soon die and do not (or very exceptionally) escape into the fæces. Their discovery in the rectal mucosa at rectal biopsy is an important aid to the diagnosis of bilharziasis.

The technique for carrying out a rectal biopsy is an easy one provided snippings are taken in a good light. It is dangerous to snip blindly, as there is a distinct risk of tearing a vein and so producing a serious loss of blood. The patient needs very little preparation and the whole operation lasts a few minutes. After the procedure has been explained to the patient he is placed in knee-elbow or left-lateral position and a sigmoidoscope is inserted under a good light as far as the valves of Houston. A snipper or biopsy forceps is inserted and a sample about 4 mm. square removed. It is best to take three snips from different sites, separated from one another by 1 cm. I do not think it matters whether the snips are taken from the anterior or posterior part of the rectal wall, but I usually prefer the anterior, as it is more closely related anatomically to the bladder. The snips are placed in the centre of an ordinary microscopic glass-slide and pressed firmly with another slide placed on top of it. They are thus squeezed flat and the slide can be examined for ova at once under a low-power lens.

If the rectal biopsy is negative, a cystoscopy should be considered. This may be a very useful method of investigation, as almost invariably in the presence of bilharzial disease of the bladder changes can be detected in the vesical mucosa, which reveals whitish lesions like sago grains. In the African these changes are usually much more extensive than in the European, with sandy patches evident as well. They are so typical, as a

rule, that a biopsy need not usually be taken. (I have always been puzzled as to why the rectal mucosa appears normal in *S. mansoni* infestations. I have rarely seen changes such as papillomata or a granulomatous mass in the rectal mucosa as are described in Egypt.) A serious difficulty in the performance of a cystoscopy is that the procedure often requires an anæsthetic. It thus becomes an expensive affair, not without risk, and therefore cannot be adopted as a routine investigation.

An easier but less helpful method is a radiological examination of the urinary tract. Not infrequently in the African (but rarely in the European) some degree of calcification can be found in the bladder and less often in the lower portion of the ureters. The linear calcification of the outline of the bladder is extremely valuable evidence of bilharzial disease and generally denotes an infestation of at least several years' standing.

One of the early signs of urinary bilharziasis follows the deposition of bilharzial ova in the lower portion of the ureter, especially that part close to its opening into the bladder. This is well demonstrated on pyelography as a persistent filling of the lowermost portion of the ureter with dye for about 1 or 2 in.

When the deposition is more marked, especially if some degree of obstruction develops, the affected part of the ureter dilates and becomes tortuous. In more advanced cases, as well as a ureteric dilatation, there may be evidence of a hydronephrosis.

An eosinophilia may be said to be significant when it is over 4%. This is a difficult sign to interpret in the tropics, as many of the intestinal parasites (amœbiasis is an important exception) and also allergic states are capable of producing it. Further, at least half of the bilharzial cases have a very pronounced eosinophilia in the early phases of the disease, but show no signs of it after they have had it for two or more years. I attach great importance to an eosinophilia provided there is a proper history of exposure. We all know of cases in which ova could not be recovered until weeks or months later, when they provided the true explanation for the eosinophilia. In cases showing an eosinophilia where a good account of symptoms suggestive of the presence of bilharziasis is given, provided all other causes have been carefully eliminated, a course of bilharzial treatment should be prescribed. It is worth remembering that one of the forms of filariasis is probably more common than is believed in Africa and that this particular species may not be easy to find. In one such case with a reasonably good history of exposure to bilharziasis the patient failed to improve with antimony and later *A. perstans* was discovered in his blood and he improved on Hetrazan.

Treatment

It is difficult to write about the treatment of bilharziasis, as it depends on so many aspects, such as the patient himself, the duration of the illness, the kind of infestation, whether it is a relatively early or late one and whether it is complicated.

An important factor in the management of any case is whether or not the patient can or is willing to carry out the treatment prescribed. Many Africans refuse prolonged treatment or one that is accompanied by much constitutional upset or is perhaps painful. Frequently many patients are given a full course of treatment and then allowed to return to the environment in which they contracted the disease. As a rule *S. mansoni* is more refractory to treatment than *S. haematobium*; but in the great majority of cases a cure for the active disease can be achieved with antimony. The most effective drug is sodium antimony tartrate. This trivalent antimony preparation is given intravenously, preferably on every alternate day, commencing with $\frac{1}{2}$ gr. (30 mg.) for an average male adult weighing 150 lb. and then increasing to 1 gr. and then $1\frac{1}{2}$ gr. For a bigger man the amount may be increased to as much as 2 gr. The total amount for a man is 25 to 30 gr. (1.6 to 1.95 g.), but for a woman about 20 to 25 gr. (1.3 to 1.6 g.) is sufficient. She should not receive more than $1\frac{1}{2}$ gr. at a time. Whilst undergoing treatment the patient should rest as much as possible. He should not be engaged in manual labour, nor indulge in exercise. School children may attend school, but not participate in games and if not generally fit should be confined to home or even to bed. The patient should have a glucose drink about an hour before treatment and rest on a couch for about half an hour after it. Many doctors argue that these precautions are unnecessary, but I have found that if the patient is kept quiet and not permitted to move about unduly he is often able to take a full course of the drug. If the joints become too painful, or if a fever commences during the course, the injections should be stopped for two or more days and then continued again. It is as well to remember that about 40 to 50% of the cases are cured with only about 10 gr. of sodium antimony tartrate, so if it happens that injections have to be stopped after about that amount has been administered the treatment may not have been in vain. In such a case it would be as well to wait a few weeks and then re-check the specimens or repeat the rectal biopsy. The full course is given because with the additional 15 gr. or so the cure rate with SAT can be increased to 80%. A drawback to this method is that the treatment takes six to eight weeks to complete and this is far too long for many

people. For them the course has to be modified so that the patients can receive daily injections of 1 to 2 gr., depending, of course, on their physical condition. I think if a shorter rapid course of treatment is adopted the patient should be put to bed and treated in hospital.

Astiban is antimony dimercaptosuccinate, containing 25 to 26% trivalent antimony. Promising reports are available on its use in both forms of bilharziasis, but its toxicity may be great and one should employ it only after careful assessment of the case. Alves (1958) recommends 1.6 g. given in four intravenous injections on four consecutive days, or he suggests 0.5 g. daily for three consecutive days, given either intramuscularly or intravenously. Before advocating its use in preference to SAT or Anthiomaline more evidence of its efficacy or safety should be available.

An advantage with Anthiomaline—a lithium trivalent preparation—and Fouadin is that they can be given intramuscularly. This is useful where veins are difficult to find. In small children, too, Anthiomaline can be given intravenously and with its less toxic effects is popular in certain quarters. The results, however, with intramuscular antimonial preparations are not as good as with SAT. The cure rate with *S. haematobium* is probably 10 to 15% less and with *S. mansoni* infections perhaps still less.

Lucanthone hydrochloride (Miracil D, Nilodin) has a definite place in the treatment of urinary bilharziasis. For intestinal infections it is generally agreed that the results are disappointing. Occasionally it is worth trying a course in a patient in whom other measures have failed, as it sometimes has the desired effect. It is useful, especially in light infestations of *S. haematobium*. Therefore in the European we can expect a better result than in the African, who has a heavier load. The drug has some adverse side-effects, especially cerebral ones, sometimes producing a temporary confusional state which, fortunately, resolves within a few days. It is given in some parts of Africa as 'routine treatment' in the out-patient department. I have used it with good effect in the occasional patient who had failed to respond to antimony or in whom such a preparation was contraindicated. Various regimens are employed for treatment with Lucanthone. I have had most experience with the three-day treatment of one-and-a-half tablets in the morning and one tablet (500 mg.) in the evening. The dosage is about a third to a half less for a child.

Another useful drug is emetine. Although I have not employed it as a routine measure, I have used it for the occasional patient for whom antimony had proved ineffective. It can be given in a similar course as that used for amoebiasis.

Recently I tried, with good effect, an intravenous emetine preparation, Antiamœbiaticum, which proved safe and effective for *S. haematobium*, but not for *S. mansoni*. The patients were not disturbed by its administration and were treated in bed. The preparation used was RO-1-9334, a 2,3-bisdehydroemetine hydrochloride, and it is given as an average daily dose of 100 mg. intravenously for 10 days. Dosage is based on weight at the rate of 1.5 mg./kg. (Gelfand, Reid and Simpson, 1962).

The Treatment of Complications

It is extremely doubtful whether antimony can in any way benefit an established complication of bilharziasis. It will not cure a dilated or strictured ureter. Damage already done in the form of fibrosis cannot be removed by antimony. Other measures have to be adopted. It is quite likely that a course of antimony, even at this stage, is beneficial, as it will destroy any live worms and so reduce or stop ovideposition and thus further fibrosis. Therefore it is good practice to give a course of antimony when the disease is first recognized, even if activity cannot be proven, but it is unwise to give more than one course in the absence of proof.

The treatment of ureteric complications is largely a matter for the urologist, who will determine the degree of bladder tension and so discover whether the ureter is dilated or stenosed. If stenosed, dilatation may help or excision of the lowest portion of the ureter and transplanting it into the bladder may be preferred. If the ureter is dilated and no obstruction present, little is to be gained by interference. When the lower end of the ureter is grossly affected, but not obstructed and yet there is hydronephrosis, excision of the diseased segment, if possible, should be considered, as this may assist an easier flow of urine down the ureter into the bladder. When there is a troublesome nocturnal frequency combined with a high-tension bladder and signs of hydronephrosis the bladder should be enlarged by an ileocystoplastic operation in which a loop of small bowel is attached to the bladder so as to increase its capacity. If this is

not done, the hydronephrosis will increase and sooner or later the patient will die of uræmia.

The Assessment of Cure

To assess whether a patient is cured of bilharziasis is not easy. In the majority of cases his symptoms improve greatly. His tiredness disappears, his energy returns. A child at school regains his former position in the class. All in all the person is much happier. This improvement in itself is a valuable indication that the infection has most likely been overcome. It is not absolute proof, as the treatment may have successfully eliminated the great majority of the egg-laying worms, leaving only a few alive which are not sufficient to cause any upset symptomatically. Therefore after the treatment specimens should be tested at six-weekly intervals.

There is no universal agreement as to whether the presence of non-viable ova in the excreta constitutes a cure. Some workers claim that a cure can be assumed if non-viability of the ova is proved. Others believe that cure has not been effected if dead ova are detected. If ova are found in the excreta six weeks after treatment, the disease, in my opinion, is still active. The opposing school of thought claims that dead ova continue to be discharged as foreign bodies for months or even years after the disease has been eliminated. Against this is the fact that hundreds of ova of *S. haematobium* may be found in the rectal mucosa although they are hardly ever discharged in the stool. It would seem that dead ova in this tissue fail to find their way out because they no longer secrete enzymes.

Viability of ova found at rectal biopsy is of value as a criterion of cure in cases of *S. mansoni*, but less frequently so in *S. haematobium* infections. If dead ova of *S. haematobium* are found in the rectal mucosa after treatment has been completed, there is the possibility that they were there before treatment commenced.

I wish to thank Dr. W. Sheffield, Director of Medical Services, Salisbury, for his kind permission to publish this paper.

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