Foreword

by

V. DE V. CLARKE

Most investigations into bilharziasis are ultimately aimed at the control of the infection or the disease either in the individual or in the community. Whatever may be the results of the detailed research of highly sophisticated laboratories of Europe and Amercia, in the end the practicability of any control measures must be evaluated in the field in an endemic area.

Before any control measure is planned it is necessary to demonstrate that there is a need for such a control measure. It must be demonstrated that infections of bilharziasis are prevalent in the area, and also that as a result of these infections, disease patterns are evident The paper entitled "The effects of bilharziasis in Rhodesia" by Professor Michael Gelfand discusses the disease patterns resulting from schistosome infections in Rhodesia. The second paper by M. Weber outlines the rapid and reliable method of determining prevalence of viable infections in the area, thus the first two objectives are considered.

The third and fourth papers deal with attempts at a control of bilharziasis in endemic areas by the combined use of mass chemotherapy and intensive snail control. These two trials follow on the demonstration of the feasibility of mass use of Etrenol described by many workers including papers published previously in this *Journal* by Ruas and Clarke *et al,* and the successful demonstration of snail control by Clarke and Shiff, by the system of snail surveillance. These papers differ in one respect: the Mayfield experiment was conducted near the main Blair Laboratory and as a result intensive efforts could be made to eliminate the infections from the relatively small experimental area. This trial was an undoubted success. The second trial covered a much larger area where intensive work was impractical and, as expected, the control was less spectacular in its success.

The remainder of the papers deal with infections within individual patients. Too often are the results of therapy assessed on the basis of a single post-treatment examination, very often undertaken at the worst possible time after treatment. Many such cases give a false report on the efficacy of the drug concerned. The detailed and conscientious work of the authors in these latter papers demonstrates the difficulties which can be encountered in individual treatments. The majority of patients treated with the modern schistosomicidal drugs respond immediately and satisfactorily. However, where such treatment failed either partially or wholly, great care is required in the interpretation of tests undertaken.

It is hoped and believed that this collection of papers will be of assistance to individuals and authorities undertaking any form of control of the disease in an endemic area.

The Effects of Bilharziasis in Rhodesia

(With special reference to involvement of: (a) the liver; (b) the heart and lungs; (c) the urinary and genital tracts; (d) the bowel, and (e) the early allergic effects in non-immunes).

BY

MICHAEL GELFAND

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Introduction.

Surely in such an ancient and widespread disease we should know whether or not bilharziasis is serious? We know a good deal about its prevalence and we have an equally good idea as to which organs are often or seldom attacked. Our uncertainty about the disease is mainly due to the following reasons:—

1. Ova and lesions can be seen frequently in different organs, such as an ovary, appendix or lung, yet the patient is in no way upset by them.
2. Because ova are so often found in some organs, such as the liver, lung or colon, if another not uncommon disease occurs in one of them, it becomes difficult to decide whether to attribute the disorder to bilharziasis. We are apt to consider the bilharzial ova coincidental to the other disturbance. A good example of this is the occurrence of the not uncommon bladder lesion of epithelioma when bilharzial ova are present in the same organ. Since the ova are so often found in the bladder submucosa, it may be argued that, as the bladder cancer is not uncommon, the two diseases are unrelated. The same difficulty exists when we have to consider the relationship between portal fibrosis and bilharziasis.
3. The incongruity between lesions found and the number of ova present. It is not always possible to demonstrate bilharzial ova or worms in sufficient numbers in the presence of suggestive lesions in the organ. We may well encounter portal fibrosis indistinguishable from the clay pipe-stem fibrosis of Symmer's, yet very few ova may be demonstrable.

4. The reverse is also well known; well marked lesions can be demonstrated, for example in the ureter, yet no complaint at all is made by the patient.
5. Even severe lesions may resolve spontaneously.
6. A number of lesions or effects of the disease are recorded on inadequate grounds, e.g., bilharzial asthma and bilharzial pancreatitis.
7. When one practises in an endemic region the general population seems to be little disturbed by the disease.

Craib (1968) emphasises the striking divergent views one reads about the potential dangers for an infected individual. He reminds us that the incidence rates of ill-health (morbidity) in South Africa are not known. He also refers to the autopsy findings of a pathologist working in the Eastern Transvaal which is an endemic area. They were:—

1. No case of renal involvement by bilharziasis was found.
2. No instance of clay pipe-stem fibrosis.
3. No case of chronic cor pulmonale.

Powell (1967) of Durban appears to agree with Craib's views. He produces objective evidence supporting his denial that bilharziasis should be regarded in a serious light. He maintains that it is a self-limiting disease and that the natural course in the vast majority of those infected is for the disease to resolve with few or no further symptoms. His evidence is:—

1. Of 1 525 I.V.P.'s done at King George Hospital during 1964, abnormal sequelae were found in 27 cases, 12 with calcification.
2. Active changes were exceptional after the age of 30.
3. During the nine year period, 1958-1966, the records of the Department of Medicine unit were:—

Total Admissions	*Urinary Tract Bilharziasis*	*No. of deaths*
11 921	110	0

4. *Autopsy evidence. King George VI Hospital. Deaths.*

Date	*No. of Autopsies*	*No. of deaths from Bilharziasis*
1958	2 500	8 (possible)
1958/1966	14 712	22

Bilharziasis is possibly one of Africa's most common diseases. In a country like Rhodesia there are areas in which hardly a child escapes. Yet when we enter such a well populated bilharzial endemic area, we see large numbers of people moving about, living normally and obviously enjoying life as though nothing were the matter with any of them. Outwardly they are well and happy. The same can be said of malaria, for even when the parasites can be demonstrated in the blood of most of the children, they still seem to be well and reasonably active. And so the doctor comes to live with the disease and in time is apt to regard it as of little consequence. Nonetheless probably no doctor would declare that *P. falciparum* is not a most serious hazard for no one can forget the swift deaths which may occur with it. In bilharziaisis there are very few quick deaths so it is much more difficult to assess which chronic disorders, themselves leading to death, are indeed complications of bilharziasis, particularly as there is no universal agreement about them.

The Effects of Ovideposition.

In the African the severity of the lesions and their effect on the function of the organ involved is generally closely related to the degree of ovideposition in the tissues. The heavier the load, the more ova may be expected. Von Lichtenberg *et al* (1971) carried out a study on 637 unselected hospital autopsies at University College, Ibadan. Of these 135 cadavers were infected with *S. haematobium*. They found those with hydroureters had significantly higher egg burdens than those without this complication.

The severity of the disease and the prevalence of complications was directly related to infection intensity. No deaths were attributable to bilharziasis and most of the lesions in this series consisted of mild burnt out infections of no real clinical importance. The authors maintained that mild infections were self-limiting and tended to heal spontaneously. About 30 per cent. of more severe infections could be expected to develop hydroureter, mostly mild in type and not necessarily a threat to life. A small proportion of severely infected patients would progress to hydronephrotic atrophy with renal failure, acute ascending infection or other incapacitating or debilitating complications. This latter group might be proportionately larger in areas of high endemicity, such as Egypt, where high intensity infections were more frequent.

Another factor to be taken into consideration is the tissue reaction to the presence of ova, since, at times, the degree of fibrosis and granulomatous tissue formed locally may be marked, without a large number of ova. We can expect this type of reaction in Africans because of their much greater and regular exposure to the disease.

For convenience we may divide the effects of ovideposition into two broad groups. In the first the lesions tend to be diffuse and of varying severity; in the second the effect is focal, due to the development of a large granulomatous mass which may give rise to symptoms because of its size and position. I would suggest referring to this lesion as the "massive bilharzial granuloma". Secondly and more important are what I term the "diffuse lesions".

The Diffuse Lesions.

These are seen typically in the bladder and lower ureter, liver and lung. In this group the result may be serious. The lesions may lead us to a mild fibrotic bladder, to one with an increased intravesical pressure as well as a reduced capacity, incontinence, even at times to retention, overflow and not infrequently to malignant degeneration.

We know the effects of the disease on the ureters — narrowing of intramural part of the ureter, dilatation and distortion of the lower end, obstruction, reflux and at times hydronephrosis on one or both sides. The effects on the liver are those of a diffuse fibrosis in the portal tracts with subsequent portal hypertension and disturbance of liver function.

The Symmer's Liver.

From Southern Africa there have been few reports on the occurrence of the Symmer's liver. Bhagwandeen (1964) from Durban reported three cases, and added a further instance in his thesis in 1968.

Wall and Gelfand (1972) decided to analyse their cases admitted to Harare Hospital with chronic liver disease, on physical examination, into two separate groups, those with a cirrhotic picture (including bilharzial fibrosis) and those without histological evidence of cirrhosis (those classified as chronic hepatitis, siderosis alone and normal liver). In all 68 cases were examined. (Wall and Gelfand, 1972).

Table I

68 Cases with Chronic Liver Disease.

Liver histology	*No. of Cases*	*Percentage*
Cirrhosis (portal)	16	24%
Post necrotic cirrhosis	14	20%
Siderosis and cirrhosis	10	15%
Bilharzial fibrosis	10	15%
Chronic active hepatitis	2	3%
Siderosis alone	10	15%
Normal healthy liver	6	8%
	68	100

In this study we found bilharzial fibrosis of the liver was the cause of "clinical cirrhosis" in 15 per cent. of cases — all under the age of 20 years, except one male patient aged 32 years. This was a very high percentage compared with previously cited studies. These findings support those of Gelfand (1965) who showed that "cirrhosis" in Africans under the age of 20 years was often due to bilharziasis, but beyond about that age a different set of aetiological factors operated.

Buchanan (1971) studied 1 000 livers in his autopsies carried out at Harare Hospital no matter what the cause of death. He did not find many examples of Symmer's liver. Whilst there were 82 cases (8,2%) with cirrhosis, only 11 (1,1%) conformed with the description of bilharzial portal fibrosis. In all 11 cases, ova of *S. mansoni* were demonstrated and in eight those of *S. haematobium* were present as well.

Table II

The Symmer's Liver at Autopsy
(*after Buchanan* 1971)

No. of livers examined at Autopsy	*Cirrhosis*	*Symmer's Liver*
1 000	82 (8,2%)	11 (1,1%)

The Bilharzial Lung and Cor Pulmonale.

When there is a widespread obliteration of the smaller division of the pulmonary artery we may expect pulmonary hypertension with the development of right heart failure. At one time I thought bilharzial cor pulmonale was either not seen or encountered so rarely that it was not of real significance. From Durban (Winship *et al.* 1969) and Ghana we have records of similar cases. Edington (1957) found evidence of pulmonary hypertension in two Ghanian subjects at autopsy. On the other hand Wolfe and Quartey (1967) in Ghana failed to find a case of bilharzial cor pulmonale and in Tanzania Forsyth and Macdonald (1965) found none in a study of 1 032 children.

In the cases seen so far the cor pulmonale seems to have been associated with the formation of large numbers of angiomatoids. Very few adult parasites were seen. In two cases (Buchanan and Gelfand, 1970) although angiomatoid formation was not encountered, severe bronchopneumonic lesions were found surrounding the dead parasites. In the past three years, I personally had under my care 25 African cases of chronic lung disease, associated with emphysema, chronic bronchitis and in some with pulmonary fibrosis. Amongst them were five cases, in which the lung disease was due to bilharziasis.

Table III

SHOWING PROVEN CASES OF BILHARZIAL LUNG DISEASE.

cor pulmonale with emphysema	14
emphysema, fibrosis, bronchitis without cor pulmonale	11
	25

Table IV

SHOWING PROVEN CASES OF BILHARZIAL LUNG DISEASE.

bilharzial cor pulmonale	4
diffuse bilharzial fibrosis of lung	1
	5

A lung biopsy was performed only in patients in whom bilharziasis was strongly suspected. The ages, sex and state of the liver in the five proven cases of bilharzial lung disease are given in Table V.

Table V

AGES, SEX AND STATE OF LIVER IN 5 PROVEN CASES OF BILHARZIAL LUNG DISEASE.

Ages: 35, 24, 12, 30, 16.
Sex: 3 male and 2 female.
Type of Bilharziasis: *S. mansoni* in 5
S. haematobium as well as *S. mansoni* in one.
Liver: Enlarged in 3 out of 4 cases with cor pulmonale.

DIFFUSE LESIONS IN URINARY TRACT.

We investigated the frequency with which organ changes occur in the urinary tract of those living in African townships round Salisbury. This was done by means of intravenous pyelography. This area is not heavily infected as the water supply to the towns is piped. Those investigated, mostly schoolboys, were referred to the outpatients department because ova of *S. haematobium* had been discovered in their urine. Although they were not drawn from an area in which the disease was very severe, it was quite possible that many of them had become infected through visiting endemic regions. The patients were X-rayed consecutively. Out of 60 cases, 28 showed abnormalities on I.V.P. Bilateral hydronephrosis was found in two, unilateral hydronephrosis in four, dilated ureters in 18 (unilateral in 10 and bilateral in eight) and calcified bladders in 10 patients. These results are somewhat similar to those of Forsyth and Macdonald (1965) in Tanzania. Of 330 primary school children infected with *S. haematobium* 27 per cent.. showed abnormal intravenous pyelograms.

Wolfe and Quartey (1967) in Ghana found lesions on I.V.P. in 18 patients (34%) out of 53 examined. Ureteral deformity or dilation was present in 11 (21%), hydronephrosis in six (11%) and calcified bladders in seven (13%).

Lesions Found at I.V.P. in 60 male patients — probably school children — passing ova of S. haematobium in their urine.

Lesion	*Number*
Nodular defects	4
Nodular defects and calcified bladder	1
Calcified bladder	5
Calcified bladder and dilated ureter	3
Calcified bladder and bilateral hydronephrosis	1
Dilated ureter	6
Dilated ureters	3
Dilated ureter and hydronephrosis	1
Dilated ureter and unilateral hydronephrosis	3
Dilated ureter with bilateral hydronephrosis	1
	28

In 10 cases there were signs of calcified bladder.
In 18 cases there was ureteric disease.
In 5 cases there was bilateral hydroureter.
In 2 cases there was bilateral hydronephrosis.
In 13 cases there were dilated ureters.

In an earlier study bladder calcification was found in 15 out of 103 boys (4,8%) between the ages of 14 and 18 years in a secondary school near Salisbury. These boys either gave a past history of urinary bilharziasis or were passing ova of *S. haematobium* in their urine (Gelfand 1965).

CHRONIC BILHARZIASIS.

In a prospective study I personally examined 57 Africans, admitted with chronic bilharziasis. It was possible to do a cystoscopy in every case and a retrograde pyelogram on most of them. Twenty-four of them mentioned dysuria, fourteen suprapubic pain and eight haematuria as the presenting symptom. Some also had pain in the perineal or lumbar region or in the thighs and lumbar region. More striking, however, were the four patients admitted with acute retention of urine. In none of these was there any signs of obstruction or any neurological lesion in the limbs. After several days the bladder regained its tone and the patients made apparently good recoveries. Their ages were 13, 32, 34 and 59. Attention was drawn to this strange bladder effect in 1948, but, although bilharzial disease of the bladder was noticed, it was only subsequently that I began to associate the condition with the disease. As well as these four cases, seven were admitted with a dribbling incontinence. One was a woman aged 37 years and the men were 35, 70, 70, 36, 27 and 48 years old. In these cases too, like those

with acute retention, diffuse bilharzial disease was found in the bladder on cystoscopy. Thirdly four men out of the 57 patients studied prospectively complained of a poor stream. Their ages were 35, 36, 57 and 38 years.

Table VII

MANIFESTATIONS IN 57 AFRICANS ADMITTED WITH CHRONIC BILHARZIASIS.

Dysuria	24	
Suprapubic pain	14	
Haematuria	8	
Acute retention	4	
Dribbling incontinence	7	
Poor stream	4	
Hydronephrosis	11	(six bilateral)

I consider these effects of bilharziasis serious but little is written of them and they are often forgotten, because, I believe, little attention is paid to the taking of the history.

Some hydronephrosis was discovered in 11 out of the 52 cases investigated. In six it was bilateral. The blood pressure was within normal limits in all except one with unilateral hydronephrosis in whom it was 160/100.

The relationship between urinary bilharziasis and hypertension has interested me for a long time. In two previous publications I attempted to show that there might well be an association between the two in the presence of ureteric disease and hydronephrosis with a possible secondary pyelonephritis. Renal biopsies were done on a number of patients with chronic bilharziasis in whom histological evidence of chronic pyelonephritis was demonstrated. I believe that such a relationship exists, but there has been very little support of this finding from other workers in Africa. I also believe that chronic urinary bilharziasis might be a factor leading to the nephrotic syndrome through an ascending pyelonephritis and again my evidence is not conclusive.

In 49 of the present series of patients with chronic bilharziasis the blood pressure was recorded as being abnormal in 11. In three the diastolic pressure was 105-112/105, 170/105, 180/105. In one the diastolic pressure was 110-170/110; in five it was 100-150/100, 150/100, 160/100, 160/100, 180/100 and in two it was 90-150/90.

Wolfe and Quartey (1967) recorded the blood pressure in 53 subjects who showed an abnormal intravenous pyelogram or a calcified bladder. They took a diastolic pressure of 90 mm Hg. and over as being abnormal. This was found in five cases the highest level being 100 mm Hg. in two cases.

In six of the 23 urine cultures done in our series of patients, a positive result was obtained (3 Klebsiella, one E. coli, 1 coagulase negative strepococcus and 1 mixed growth). Two of these patients had bilateral hydronephritis, three had severe lesions of the bladder, one of them with a bladder capacity reduced to 200 ml.

The frequency with which bilharziasis may be responsible for renal failure was assessed in a recent study of the cases with renal failure admitted to the medical wards of the University Unit of Harare Hospital (patients showing a blood urea of 100 mg% and over were included). Out of the 111 cases in this series, bilharziasis was considered responsible for 11 (this included one with carcinoma of the bladder).

Table VIII

CONDITIONS RESPONSIBLE FOR AN ELEVATED BLOOD UREA OF 100 MG AND OVER.

Condition	*No. of Patients*
Cardiac failure	7
Extrarenal uraemia	30
Chronic renal failure (normotensive)	10
Eclampsia	1
Chronic renal failure (bilharzial)	10
Chronic renal failure (hypertensive)	22
Chronic proliferative renal failure	2
Acute nephritis	4
Acute renal failure	14
Nephrotic syndrome	5
? cause	6
	111

Another study carried out at Harare Hospital by Dukes, D. C. *et al* (1970) showed that of 23 cases of chronic renal failure, seven with obstructive renal disease, were bilharzial in origin.

Dukes, H. M. and Mynors (1970) were quite definite in their conclusion that death from bilharziasis was most often due to obstructive renal disease. In their experience bilharziasis was the most common cause of death from renal disease, accounting for about four deaths per 1000 medical admissions, excluding carcinoma of the bladder, in which bilharziasis might have also an aetiological significance. They described 10 patients seen in advanced uraemia due to ureteric stricture consequent upon bilharzial infestation. Six of these patients died.

Many of us interested in this disease, especially workers in Egypt and myself, attributed a good deal of the severe results of obstructive uropathy to a secondary infection, thus leading more readily to renal failure. However, there

has been a move against the theory of secondary infection as an added risk of the disease. Wolfe and Quartey (1967) remarked on the relative absence of secondary bacterial infection, even though most patients were passing large numbers of white and pus cells in their urine. It was found in only three of the 38 urine cultures performed. This may be explained by recent work done by Powell *et al* (1965) who showed that the differential analysis of stained urinary leucocytes revealed that the so-called pus cells were predominantly eosinophils and cultures for bacteria were uniformly negative. Similar findings were noted by Forsyth and Bradley (1964) in Tanzania.

Although Dukes (1969) considered bilharziasis the most important cause of chronic renal failure in endemic regions, he did not believe secondary infection in bilharzial uropathy and hydronephrosis was of any consequence. As a result of his investigation in Salisbury, he pointed out that bacteriuria was not more prevalent in patients with obstruction due to biharziasis than in other states. Indeed he claimed that bacteriuria was not found in any form of obstructive biharzial disease, but was due to the presence of predisposing factors, the most prominent of which was catheterisation. He stated that 18 out of 23 cases of obstructive disease, due to unrinary bilharziasis, were the result of simple back pressure effects caused by sterile urine on the kidney and showing no evidence of pyelonephritis. Five of the patients died in hospital. This Dukes attributes to secondary infection introduced by catheterisation.

This has not been my experience, which is that, although secondary infection is rarely encountered in uncomplicated acute bilharziasis, it may develop in a damaged ureter and hydronephrotic kidney. Stauffer Lehman *et al* (1971) has closely studied the effects of hydronephrosis, bacteriuria and maximal urine concentration in urinary bilharziasis. They concluded that obstructive bilharzial lesions were associated with reduced maximal urine concentration, but that this was sometimes reversible with anti-bilharzial therapy. They showed that impaired urine concentration was related to urinary tract obstruction rather than to bilharzial infection *per se;* that bacteriuria further hindered function in the setting of bilharzial uropathy, that the effects of hydronephrosis and bacteriuria or urine concentration were both additional and reversible.

Whilst bilharziasis may be grave in the early hypersensitivity state in Europeans it is not frequently serious in them nor does it often lead to complications causing death. One rarely meets a Symmer's liver, cor pulmonale or bilateral hydronephrosis sufficient to produce uraemia. Such complications are hardly ever seen in the European but in the African the reverse occurs. Honey and Gelfand (1960) compared the cystoscopical lesions found in 300 European and 100 African subjects.

Table IX

LESIONS FOUND ON CYSTOSCOPIC EXAMINATION OF AFRICAN AND EUROPEAN PATIENTS. 1960.

Lesion	*Percentage*	
	European	*African*
Bilharzial lesions	77	24
Sandy patches	26,5	80
Papilloma	7	32
Carcinoma	0	4

In the same series hydronephrosis was seen in 42 European patients, involving 53 kidneys. It was always relatively mild in degree. In the African hydronephrosis was associated with a reduced bladder capacity and a high intra vesical pressure in 20 patients (20%) involving 40 kidneys. The average capacity of the bladder was 200 ml. the lowest 60 ml. and the highest 350 ml. The hydronephrosis varied from slight clubbing of the calyces to gross dilatation of both calyces and pelvis.

Table X

INCIDENCE OF HYDRONEPHROSIS IN EUROPEAN AND AFRICAN CASES.

(*after Honey and Gelfand* 1960)

	Percentage
European (42 cases out of 300)	14
African (58 cases out of 100)	58

VESICAL CARCINOMA AND BILHARZIASIS.

Ever since Ferguson noticed the relationship between urinary bilharziasis and vesical carcinoma in 1911, opinion has been divided on the existence of a true aetiological association of the two conditions. Those who do not believe this argue that, since bilharziasis is so universal in tropical regions its association with bladder cancer is merely fortuitous. On the other hand, bladder cancer in Africans is seen in a much younger age group than in Europeans and the squamous cell variety is more common in bilharzial endemic regions. Europeans with bilharzial disease of the bladder very rarely have carcinoma of this organ even though bilharziasis is by no means infrequent among them in endemic regions. This difference between the two races in Rhodesia is so striking that Honey and Gelfand (1960) were led to believe that as vesical bilharziasis is far more common amongst the

African population, more of these people are liable to have such severe infestations leading to malignant changes in the bladder mucosa, than in the Europeans.

It is worthy of note that bladder cancer is high up on the list of cancer in Harare Hospital. It is the third in the order of frequency and I suggest this is related to the high incidence of vesical bilharziasis in this part of the country.

Table XI

FREQUENCY OF CARCINOMA AT HARARE HOSPITAL, 1969-1971.

Cervix	418
Oesophagus	361
Bladder	355
Lung	271
Liver	248

Gelfand, Weinberg and Castle (1967) were able to show in patients with positive rectal biopsies for *S. haematobium*, calcification of the bladder was more frequent in vesical cancer cases than in the control group.

For the purposes of the present study, I X-rayed the bladder in 14 patients with proven vesical cancer and compared the extent of calcification seen in them with that in 14 control subjects. The table below confirms our findings of 1967.

Table XII

CARCINOMA OF THE BLADDER.

	13 cases
Bladder calcified	5(38%)
Squamous cell carcinoma in	10
Bladder calcification in control series	2(15%)

MASSIVE BILHARZIAL GRANULOMA.

This is indeed a very extensive focal lesion we encounter in the established form of the disease from time to time in the African woman in the cervix, clitoris, vulva, fallopian tube or ovary and in the seminal vesicles, prostate and testis in the African man. In both sexes these tumours may occasionally be found in the spinal cord, lower end of the common bile duct and the skin. Abbott and Spencer (1953) in the Sudan recorded the example of a patient who developed pains in his back followed by weakness of both legs. Bilharzial ova were found in the lumbar enlargement of the cord. In 1965 Gelfand described a case of paraplegia caused by *S. mansoni* in a coloured man from Tete in Portuguese East Africa.

We are meeting these tumour masses in the bowel and two papers from Rhodesia dealing with them have been published. Stephens (1966) described a case in an old African man from the Zambesi Valley, whom he saw because of a bloody diarrhoea.

A mass was noted in the left lower quadrant of the abdomen but a barium enema was normal. Nevertheless a provisional diagnosis of carcinoma of the sigmoid colon was made and at laparotomy the left colon from the middle of the transverse to the middle of the sigmoid region was greatly thickened giving the gross appearance of a malignant growth. In the liver were multiple white nodules. The affected colon was resected and on section bilharzial granulomatous tissue with fibrosis was found. Gelfand and Hammar (1966) reported the occurrence of chronic inflammatory masses in two patients (one in the appendix — and the other in the caecum) causing obstructive symptoms, entirely due to *S. haematobium* ova, despite the fact that ova of *S. mansoni* were present in the stool.

Most authorities agree that if the local tubal damage is severe enough an ectopic pregnancy may result. The reaction of the fallopian tubes to *S. haematobium* is very variable, mostly mild or negligible and ova are found in the tube without demonstrable reactions. However, sometimes there is a more granulomatous reaction and occasionally the mass assumes large proportions. The disease appears to have no significant effect on fertility.

When ulcerative lesions are in the cervix uteri, marked distressing symptoms such as intermenstrual or postcoital bleeding may occur. There is little doubt that in advanced cases of cervical bilharziasis an erroneous diagnosis of carcinoma may be made. Occasionally large warty growths are seen on the vulva or clitoris. But, on the whole, except for ectopic pregnancy, which may develop at times, the effect of the disease on the female genital tract is insignificant.

Although these complications appear from time to time in the non-indigenous population, for practical purposes they are seen only in the African people. The only exception is involvement of the ureter, appendix and fallopian tube, which is similar in both populations.

Narrowing and dilatation of the ureter and occasionally even a mild hydronephrosis are found in the European although not as severely as in the African. Calcification of the bladder seen regularly in the African, occurs only rarely in the European.

We also attempted to determine what lesions, if any, occur in the genital tract and carried out an autopsy study in which we showed that ova were frequently deposited in this part of the body, especially in the seminal vesicles and less often in the prostate. It is relatively less common for ova to be deposited in the testis, epididymis and cord.

In a recent investigation I carried out with Prof. Mynors we were unable to find a case of bilharzial hydrocele at operation when portions of the tunica vaginalis were submitted for histological examination. However, in 50 cases of the series referred with chronic urinary bilharziasis to hospital, one showed definite right epididymo-orchitis and hydrocele with slight enlargement of the left testis. The section revealed bilharzial granulomatous tissue. The patient was a boy of 13 years. In the series were three other cases of orchitis, which I would accept as bilharzial in causation, although actual proof was not obtained by biopsy.

These were:—

1. A left epididymo-orchitis with hydrocele and hard mass in prostate (patient aged 29).
2. Hard head of left testis in a man aged 66 years.
3. Thickening of right cord with hydrocele and swelling of left epididymo in a patient 42 years old. The left testis was also hard and irregular.

A significant number of the patients in this series of 50 cases with chronic urinary bilharziasis had lesions in the prostate or seminal vesicles. I could not prove them to be bilharzial since this is not an easy region from which to obtain biopsy material. In six cases the lesions consisted of an irregular or localised hardness in the seminal vesicles. The changes in the prostate included localised nodular formations or atrophy of the gland itself. Ten patients had this type of abnormality. I was not able to follow up the effects of specific treatment on them as the patients were all discharged from hospital, but I have treated children with similar disorders and the masses became greatly reduced with bilharzial therapy.

Table XIII

CHANGES IN PROSTATE AND SEMINAL VESICLES IN PATIENTS WITH CHRONIC BILHARZIASIS.

Total number of cases with chronic bilharziasis	50
Number with changes in prostate	10
Number with changes in seminal vesicles	6

BILHARZIASIS IN THE "ALLERGIC".

When they think of bilharziasis, most people regard it as it is seen in the African. It is true, that since the indigenous people of tropical Africa constitute the great bulk of the population, the features of the disease should be stressed from this angle. We might expect this picture to that of "immune bilharziasis" since the African has lived in these parts for many centuries and has built up some degree of tolerance albeit an imperfect form of protection. On the other hand the European is more allergic or hypersensitive, being a recent arrival in these parts and having little or no previous contact with the disease. Therefore his reaction to the infection tends to be different from that of the African; he often reacts more violently, even though the initial dose of infection may be much less. Indeed at times an individual shows a hypersensitivity reaction, developing the Katayama syndrome with urticarial and joint swellings, with a high blood eosinophilia. (Gelfand). Clarke, Warburton and Blair (1970) reported an epidemic out-break in Rhodesia, following single exposures. In all they saw 24 patients with this syndrome, two of whom were Africans. Only *S. mansoni* appeared to be responsible.

Recent experience, especially in Rhodesia, has revealed that at times this early phase of the disease, usually occurring six weeks after exposure to the infection, may be extremely serious. The patient may pass rapidly into a state of encephalopathy with hemiplegia; in other patients a paraplegia ensues. Such cases were overlooked in the past and in the absence of a better diagnosis were attributed to encephalitis, brain fever or even sunstroke. Zilberg and his colleagues in Salisbury were the first to report these serious potentialities in this early hypersensitivity state. In 1967 he, Sanders and Lewis described two such cases. The first was a European girl of nine, who was very ill with encephalitis; she also developed right heart failure and lung biopsy showed bilharzial tubercles. She was infected only with *S. haematobium*. The second group of cases described by Zilberg suffered from the features of the Henoch-Schonlein syndrome in the early phase of Katayama disease (Zilberg 1970).

In addition to these serious effects on the brain we are now encountering cases with an acute paraplegia and retention of urine. Levy and Taube (1969) describe two very classical cases in Europeans — one in a lad of 14 years, who developed sudden weakness in his legs. He had an eosinphilia 43 per cent. Ova of *S. haematobium* were found in his urine. The second case was that of a young man, aged 23 years,

who, after swimming in Lake Kariba a few weeks previously, became ill with backache, weakness in his legs and urinary retention. *S. mansoni* were found in his rectum.

Only a minority of Europeans who contract bilharziasis develop the Katayama syndrome, but a fairly significant number of European children and even adults complain of constitutional upset, especially tiredness. This subjective feeling of debility varies greatly but it is significant at times. I have met children and adults too so affected with this symptom as to resemble a case of myasthenia gravis. But the African child seldom presents with this complaint. A few mention it but the usual complaint in the African is one of dysuria or the loss of blood in the urine. In the European the effect is mainly on his physical capacity. If one compares the African who presents himself for examination because of *S. mansoni* infestation, with the European, one will find that whereas *tiredness* is often a presenting complaint with the European, the African rarely mentions it, unless directly questioned, but complains rather of local bowel symptoms (see Table).

The situation arises in which the child falls behind in his studies at school or withdraws from games. In order to test the accuracy of these observations, surveys have been made on the attainments of school children. The first of these studies was carried out by Loveridge, Ross and Blair (1948), who showed that bilharziasis affected the standard of educational attainment in European teenage school children, but for some reason not fully appreciated, this was not apparent in African children infected with the disease.

In another well-planned survey, Clarke and Blair (1966) studied the effect bilharziasis had on the educational attainment of European boys. They demonstrated a definite association between the prevalence of bilharziasis, particularly *S. mansoni* infestation, and intellectual ability of the boys, as evidenced by class and "stream" positioning. There are two possible explanations for this association. First the infestation, especially if long-standing, may prevent the children from attaining their full educational potential. Secondly, boys whose limited intellectual capacity makes them less interested in academic activities out of school, set more emphasis on outdoor pursuits and therefore may be exposed to the infection more often.

Clarke, Castle and Hendrikz (1972) using a control matched group for social class carried out an extensive study, in Marandellas, among European school children, infected with bilharziasis, came to the conclusion that fatigue alone was more responsible for the lowering of accuracy and productivity. Bilharzial sufferers performed significantly worse than the control group.

As mentioned previously Loveridge *et al* were not able to detect any effect by the disease on the scholastic ability of African school children. More recently other workers have studied the African school child. Jones and Bell have just completed a survey on the intellectual ability of 107 of the 320 children with active bilharziasis (aged eight to 11) at Epworth Mission. Fifty-seven of the 107 children with urinary bilharziasis were given hycanthone.

They claim to have shown that the disease can have an adverse effect on the child's intellectual ability and that one-dose treatment with hycanthone can produce a significant improvement in children infected with the parasite. Infected children obtained a lower score than their uninfected and successfully treated class mates.

Undersized children and those with small heads performed poorly in class examinations, suggesting that malnutrition is related to brain size and development.

In a country town in the Eastern Transvaal, Walker, Faith Walker and Richardson (1970) studied African school children between the ages of 7 and 17 years. A control series was carried out as well. Both *S. mansoni* and *S. haematobium* infections were present. The study paid special regard to nutrition, egg load, haematuria, albuminuria, physical fitness and intelligence. As a result these workers considered that bilharziasis of the prevalence and continuity found in the African children studied was not associated with detectable disabilities. No case of anaemia less than 10 haemaglobin per 100 ml was found in the Bantu children of all three areas.

Thus in the European (allergic) the disease has a retarding effect on the child and even adult until treatment is instituted. In the early Katayama phase the disease can be extremely serious if the main brunt of the hypersensitivity reaction is on the brain (encephalopathy or a paraplegia). Besides this the disease may cause pain and discomfort when it becomes localised to the lower ureter. Occasionally a hydronephrosis may develop but, on the whole, these effects are much less striking than in the African.

When the African child or young adult comes to Salisbury with the disease, he generally complains of localising symptoms. Out of 179

patients seen with active urinary bilharziasis (ova of *S. haematobium* in the urine), 161 (89%) complained of haematuria and 120 (67%) of dysuria. Hardly any mentioned tiredness as a presenting symptom. In European children localising symptoms are much less in the foreground, but in this series of young Africans constitutional symptoms, such as debility, were very much in the background. The same applies to *S. mansoni.* I collected stool specimens of Europeans who were found to harbour viable ova of *S. mansoni* (on rectal biopsy) and compared the egg counts of *S. mansoni* in the stool with similar egg counts in the African. This clearly revealed a great difference.

When I studied a separate series of 33 Europeans (mostly young adults), passing viable ova of *S. mansoni,* the great majority mentioned tiredness as the most important presenting symptoms (Gelfand 1967).

Table XIV

MAIN COMPLAINT BY 33 EUROPEANS (MOSTLY ADULTS) WITH *S. mansoni* DISEASE.

(*Gelfand* 1967)

Main Complaint	*No. of Patients*
Tiredness	19
Abdominal pain or discomfort	7
Diarrhoea	3
Haematuria	1
No complaints	3
	33

Table XV

PRESENTING SYMPTOMS IN 24 AFRICAN ADULT PATIENTS PASSING OVA OF *S. Mansoni* IN STOOLS.

(*Gelfand* 1967)

Main Complaint	*No. of Patients*
Tiredness	1
Abdominal pains	19
Bowel upset (diarrhoea, blood and mucus)	2
	22

These findings are of interest as they would probably explain the differences in attainment, such as scholastic achievement at school. I have already mentioned the studies by Loveridge *et al* and the very recent one by Professor Jones and his colleagues, which showed that there was no difference in attainment between infected and uninfected African school children, whereas other publications revealed a definite falling behind a scholastic attainment in European children. This effect on the latter probably arises from the general or constitutional effects of the disease.

SUMMARY.

In Rhodesia, bilharziasis is a serious disorder.

In the African we encounter a diffuse fibrosis of the lower ureter and bladder, liver and lung and every now and then we encounter the massive bilharzial granuloma in sites like the colon, clitoris and vulva. In the European, Coloured and Indian populations, however, the disease tends to be more serious in its early stages, presumably with the hypersensitivity state (Katayama) which may be associated with a paraplegia, hemiplegia and an encephalopathy. Although these effects are relatively uncommon more often the child or young person is affected by a fatigue which may interrupt his studies causing him to fall behind in his scholastic attainments.

The study also records the frequency which certain complications such as hydronephrosis and uraemia, cor pulmonale and bilharzial fibrosis of the liver is seen in my wards. All these effects are significant and serious.

Reference is also made to the occurrence of the so-called massive bilharzial granuloma especially of the bowel, vulva, clitoris, epididymis and prostate.

In Rhodesia bilharziasis, both the urinary and intestinal is to be regarded as having serious consequences.

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