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A Balanced View of the Diagnosis of Bilharziasis

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In the last two decades there have been great developments in the lowveld and other well-watered regions of Southern Africa. Agriculture has been expanded beyond all expectations. Great irrigation schemes have been constructed to nourish orchards of citrus and other tropical fruit trees and the extensive vegetable gardens. Good roads have made these regions easy of access, and recently there has been a phenomenal increase in the number of motor cars and of visitors who come to enjoy the scenery and the recreations provided by large dams, the fishing, boating and other water sports. The resident population of the areas has also correspondingly increased.

These great and important irrigation developments have favoured the breeding and proliferation of the intermediate snail hosts of the bilharziasis parasites and have greatly increased the opportunities for infection and also of acquiring heavy infections. The problem of diagnosis arises with increasing frequency in the consulting room where the physician deals with individual patients and in surveys to determine the distribution and incidence of infection.

When a patient complains of symptoms and is found to have signs suggestive of bilharziasis, the physician responsible for his care will first ask if he has been in a region where bilharziasis is endemic.

A map recently published in a *Bulletin of the World Health Organisation* illustrated the distribution of bilharziasis as presently known in the world. In all of Central Africa, except in the high mountainous regions and in the deserts, bilharziasis is prevalent in the human population. In the mountainous regions the water presumably is too cold to favour the propagation of the snails. In the deserts there is no water, but it is of interest to note several oases have been found to be infested with snails. It may be noted that the situation in Southern Africa is illustrated wrongly.

A survey was undertaken recently by the Medical Ecology Centre of the State Health Department and the South African Institute for Medical Research, in collaboration with the Malacology Research Unit of the University of Potchefstroom and of the Bilharziasis Field Research Unit of the Council for Scientific and Industrial Research at Nelspruit, to determine accurately the geographical distribution in Southern Africa.

The findings of this survey have largely confirmed the previous dogma that south of the Limpopo all rivers and streams below 4,000 feet flowing into the Indian Ocean to as far south as Humansdorp, near Port Elizabeth, are infested with the intermediate host snail *Bulinus africanus* (*Physopsis africana*). Further, that in South Africa all rivers flowing west into the Atlantic Ocean and flowing into the Indian Ocean between Cape Point and Plettenburg Bay are free of these snails.

However, there are certain important exceptions to this rule at the time of the survey. No intermediate host snails were found in either the Fish River system or the Sundays River system. These two rivers will soon be receiving water from the dams now building on the Orange River. The effect of this additional water on the whole ecology of this region will be watched with interest.

The Orange River and its tributaries are free of these snails with one important exception. Intermediate host snails were found in several of the tributaries of the Vaal, the Hartz River flowing through Schweizer Reinecke, the Schoonspruit and the Sterkspruit near Klerksdorp, the Mooi River and the Bamboo Spruit near Potchefstroom, and surprisingly in one of the tributaries of the Klip River near Henley-on-Klip and south of the Vaal in a small tributary flowing into the Vaal near Bloemhof, and on one occasion in the Vaal itself.

There is a very close correlation between the distribution of the snail intermediate hosts and

the occurrence of bilharziasis in man. Perhaps the former is slightly more extensive, but an interesting example of the correlation was noted in the Transkei. There is a focus of *Biomphalaria pfeifferi* in the St. John's district of the Transkei. Ova of *S. mansoni* were detected in the faeces of three children attending school in this district. A knowledge of the geographical distribution of the intermediate hosts is important, because nearly all patients will give a history of having swam, bathed, washed or paddled in water of the endemic region.

Many will also give a history of skin irritation following immediately after this exposure. It is relevant to recall that the cercariae—the stage shed by the snails—infect man by penetrating the skin and then migrate via the lymph vessels, lymph glands, the thoracic duct and the heart to the lungs and finally to the portal veins, where they mature. The adult worms in pairs then migrate to the radicles of the portal veins in the intestine, especially of the large intestine and of the vesical plexus, where eggs are laid and some are ultimately excreted in the urine and faeces respectively. However, the worms often stray from this predetermined course and both they and their eggs may be found in almost all conceivable situations in the body. It is evident that bilharziasis is a systemic infection and that often vital organs such as the lungs and central nervous system may be involved. In many such cases eggs are not excreted or found in rectal biopsies.

For convenience of discussion, five stages may be recognised in the development of the bilharzial parasite in its human host. These are:

(1) Infection.
(2) Migration.
(3) Egg laying.
(4) Fibrosis and contraction of fibrous tissue.
(5) Malignant change in a few.

At each stage of its life cycle the patient may present characteristic signs and symptoms whose presence should make his physician suspect that he has bilharziasis.

The penetration of the skin at the time of infection is associated with a sharp nettling pain similar to minute pin pricks. This irritation continues for some hours after the individual has left the infected water. After the first exposure the reaction is evanescent. After repeated exposures the patient may become sensitised and suffer marked irritation associated with dermatitis which may last several days. This is one form of cercarial dermatitis. A similar picture may follow the penetration of non-human schistosomules usually of avian origin. Such cases are common in Southern Africa. From the patient's point of view the differentiation of the species is important, for unlike the non-human cercaria which undergo little further development, the human forms develop to maturity.

During the stage of migration the patient may develop signs and symptoms referable to the involvement of the lung, such as a slight irritative cough, and to the liver, which may be slightly enlarged and tender and often associated with vague abdominal pain and anorexia.

Towards the end of this stage two to three weeks after infection the patient may begin to suffer from signs and symptoms resulting from the general and allergic reactions to the infection, remittent fever lasting one to six weeks and skin rashes, usually urticarial in type. He also develops an eosinophilia which may persist for many years.

The stage of egg laying in *S. haematobium* infections is characterised by vague lower abdominal pain associated with frequency and irritation on micturition, followed by haematuria which is characteristically terminal and sometimes aggravated by exercise. The blood is bright red and the haematuria may continue for years.

In *S. mansoni* infections the commonest manifest symptom is diarrhoea sometimes associated with the passage of blood and mucus. It may be so slight as not to worry the patient or it may be so severe as to simulate acute dysentery and, when chronic, ulcerative colitis.

It is during this stage that involvement of other organs, such as the lung or central nervous system, may become manifest.

The contraction and cicatrisation of fibrous tissue may cause stenosis of tubular organs such as the ureters, which may result in hydronephrosis and ultimately kidney failure.

The involvement of the liver and spleen may result in a condition simulating Banti's disease with the development of anaemia, leukopenia and thrombocytopenia, with a tendency to haemorrhage from oesophageal varices.

In Southern Africa bilharziasis is the commonest condition preceding cancer of the bladder and appears to be directly associated with its development. Its association with primary cancer of the liver remains an unresolved question, but the evidence suggests the conditions are not related.

Laboratory Diagnosis

In each of these stages laboratory tests are of value in assessing the patient's condition and in arriving at a diagnosis. The tests currently available for routine application include the detection of the ova in the excreta or in biopsy material and serological tests to detect specific reactions to the presence of the worms and their ova. Those in routine use are the complement fixation and fluorescent antibody tests and skin tests with antigens prepared from extracts of the worms.

There are a number of changes which may suggest but not specifically confirm a diagnosis of bilharziasis. These include changes in the blood count.

The haemoglobin and total red count rarely show any significant change—perhaps a somewhat surprising result when one thinks of the haematuria and the apparent great loss of blood each day. However, as Walker and Gerritsen have shown, the loss of blood rarely exceeds 5 c.c. per day, a loss which can readily be made good, especially in people living in a region like Southern Africa, where the iron intake is adequate, often more than adequate.

The white cell count often shows an eosinophilia. Indeed, most patients in the early stages of bilharziasis show an eosinophilia, and in South Africa the possibility of bilharziasis should be considered in all patients with eosinophilia.

Eosinophilia appears most commonly about five weeks after contracting the infection and then persists for a variable time thereafter, usually for many years; but from the very high counts reached in the acute feverish stage, often as high as 30 per cent., occasionally 50 per cent. and rarely over 70 per cent., it gradually decreases and in long-standing chronic infections often falls below the upper limits of normal.

However, in the course of other acute infections such as influenza, and especially in typhoid fever, the count drops to relatively low figures and in many cases of typhoid fever may be nil. Of course, too, eosinophilia is a feature of most helminthic infections and in other allergic and hypersensitivity states. It is therefore not of specific value.

Liver function tests also characteristically show significant changes in bilharziasis. These include the changes indicative of parenchymal damage and in the response of the reticulo-endothelial system to the presence of worms and their products.

Bilharziasis Survey of South Africa

We recently had ample opportunity of assessing the relative value of these tests in the large surveys undertaken to define the incidence of the infections in South Africa.

In this survey one team from the Medical Ecology Centre collected and identified snails in the area. These were tested for the shedding of cercariae and then sent to Professor J. A. van Eeden, of the C.S.I.R. Malacology Research Unit of the University of Potchefstroom for final identification.

The other team collected specimens of urine and, where indicated, specimens of faeces for ova and blood for differential white cell counts and for the serological tests, including the complement fixation test and the fluorescent antibody test. In the complement fixation test antigens were prepared separately from cercariae, adult

Table I

Bilharziasis—S. haematobium

Bantu Children 8-15 Years—Transkei

\+ Ova S. haematobium

Ova		Complement Fixation Test + ±	
Urine	Faeces		
No +	No +	No +	% +
44	10/44	39	88.6

Table II

Bilharziasis—Bantu Children and Adults

Age Group	Ova + %		+ %
	Urine	Faeces	Skin Test
1-5 years, Komatipoort	70.6	91	66
6-14 years, Harteebeest-poort	100		95.2
Adults, Simmer & Jack	42	12.2	90

worms and ova and from a mixture of these three components.

The area covered by this survey has embraced a large part of the region where bilharziasis is endemic and also the districts bordering on this region.

Of special interest to us at present are the findings of this survey in the Crocodile River Valley, where bilharziasis is hyperendemic and most children are infected with both *S. haematobium* and *S. mansoni* and a large proportion ± 40 per cent. with *S. mattheei* and in the vicinity of Hartebeestpoort Dam, where only *S. haematobium* occurs, and in adult workers of the Simmer and Jack Mine from hyperendemic regions who have infections of many years' duration, and in school children of a Bantu township of Johannesburg free of infection, and in the Orange River Valleys also completely free of the bilharzial snails, and finally of school children of the Vaal Valley and the Transkei, where bilharziasis is found in some but not all districts.

In this survey over 2,000 children were examined for the presence of ova in the excreta, usually the urine, and for their reactions to the bilharziasis skin tests, and about 1,000 bloods were tested in the complement fixation tests and other serological tests.

In addition to enabling us to determine the geographical distribution of the intermediate hosts and the distribution and incidence of the human bilharzial parasites, this survey gave us an opportunity of comparing and assessing the value of the diagnostic tests commonly used to confirm or establish the diagnosis of bilharziasis.

We are at present mainly concerned with the latter aspect of this investigation. It may be relevant to note briefly some of the findings of

Table III

BILHARZIASIS—BANTU ADULTS—S & J

Urine or Faeces Ova	Complement Fixation Test +	Eosinophilia 5% +	Skin Test +
+ 16	13	10/13	15
— 17	9	6	10

Table IV

BILHARZIASIS—BANTU ADULTS—S & J

Skin Test	Ova Urine Faeces +	Complement Fixation Test +	Eosinophilia 5% + +
+ 29	14	21	16
— 7	1	5	3

Table V

BILHARZIASIS—BANTU ADULTS—S & J

Complement Fixation Test	Ova Urine +	Ova Faeces +	Eosinophilia 5% +	Skin Test +
+ 16	6	2	13	14
± 9	6	1	3	9
— 6		0	1	5
AC 3	1	2	2	3

which representative samples are set out in the accompanying tables.

Of those giving positive reactions in the serological tests, the majority of children were excreting eggs. However, in a significant proportion of adults giving positive results in the serological tests and in the skin tests ova were not found in the single specimens of urine and faeces collected at the time of the survey.

Of several hundred children who were tested in the schools in non-endemic areas, very few gave positive results in either the serological or skin tests. Of those few there was good reason to suspect that most of them had been exposed to bilharzial infection whilst on holiday in the endemic zone away from home.

From these findings the following conclusions have been drawn regarding the interpretation of the results.

In a patient with signs and symptoms suggestive of bilharziasis, a + + positive reaction or a + positive reaction in the complement fixation test or in the fluorescent antibody test is indicative of this infection.

A trace ± reaction in either test is suggestive of infection, but further confirmation should be sought before accepting the diagnosis.

A negative reaction in either or both tests usually means freedom from infection, but does not exclude it, especially in chronic cases of several years' duration or of course in recently acquired infections.

Except in the youngest age group of one to five-year-old children, a positive skin test is indicative of present or past infection. A large proportion of young children excreting bilharzial ova give negative reactions in the skin test.

The effect of treatment cannot be assessed on the results of the serological tests. They may continue to give positive reactions for many months after successful treatment. The success of treatment is best judged on the continuing absence of ova from the excreta and/or an amelioration of the clinical signs of illness.

Finally, it should be emphasised that the best laboratory method for establishing the diagnosis of bilharziasis is the finding of the characteristic ova in the excreta or in biopsy specimens. This direct method also reveals the species of parasite responsible for the infection. In all cases suspected of having bilharziasis, specimens of urine and faeces and, if indicated, rectal snips should be examined for the presence of ova. The serological tests should be regarded as complementary to this examination.

Table VI

BILHARZIASIS—BANTU CHILDREN (6-15 YEARS)

NON-ENDEMIC AREAS—ORANGE RIVER VALLEY

	No.	OVA +		SKIN TEST			
		Urine	Faeces	No.	+	±	% + or ±
Johannesburg	97	1	1	60	3		5
Aliwal North	50	0	*	50	0	2	4
Bethuli	50	0	*	50	0	4	8
Norvalspont	50	0	*	50	0	3	6
Preiska	50	0	*	50	1	3	8
Kakamas	50	0	*	50	1	3	8