Chapter 4

Schistosomiasis

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Additional information is available at the end of the chapter

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1. Introduction

Schistosomiasis is a chronic water-borne infection caused by digenetic trematodes that belong to the genus *Schistosoma*. There are two main forms of the disease namely; urinary and intestinal schistosomiasis. The major aetiologic agents of the intestinal form are *Schistosoma mansoni* and *Schistosoma japonicum*. The less common species that have also been associated with intestinal disease are *Schistosoma mekongi*, *Schistosoma guineensis* and the related species *Schistosoma intercalatum. Schistosoma haematobium* is the only known agent of urogenital schistosomiasis [1]. *S. haematobium* and *S. mansoni* infections have been widely reported in all parts of Nigeria although the former predominates [2].

Schistosomiasis is transmitted by snails. Each of the species is transmitted by a snail of a different species. The intermediate host of *S. haematobium* is a fresh water snail belonging to the genus *Bulinus*. It is a turreted snail with a left-handed opening when looked at with the spire upwards. Three main species are known to harbour the larval stages of schistosomes [3]:

- The Africanus group (sub-genus *Physopsis*) which are involved in the transmission of the disease in eastern, central and west Africa
- The truncatus group (sub-genus *Bulinus)* which transmits infection in the near East and in some parts of Africa and
- The forskalli group. This group has been associated with the transmission of urinary schistosomiasis in Nigeria among other places in Africa.

S. mansoni is transmitted by flattened planorbid snails belonging to the genus *Biomphalaria.* Four main groups have been associated with the transmission of intestinal schistosomiasis in Africa. These include:

- The Pfeifferi group which are the main vectors in Africa
- The sudanica group which occur in both east and west Africa
- The choanomphala which are found in the great lakes and act as agent in Lake Victoria and
- The Alexandrina group which occur sporadically in north, east and south Africa [3]

The intermediate host of *S. japonicum* are operculated snails that belongs to the genus *Oncomelania*. Important species such as *O. hupensis*, *O. nosophora*, *O. formosana* and *O. quadrasi* are involved in the transmission of infection in different areas of Asia where the infection predominates [3].

The role of water bodies in the transmission of infection cannot be over emphasized [4]. Such water bodies include fresh water streams, water accumulated as a consequence of construction of dams and irrigation projects and slow flowing or stagnant water. Although, the main courses of large rivers may not be associated with the transmission of schistosomiasis, but water sustained by them through seasonal flooding and impoundment may provide avenues for the sustenance of the snail intermediate host. Water also provides an opportunity for the cercariae to survive and penetrate the definitive host. Humans are also pivotal in the transmission of schistosomiasis. Through insanitary disposal of urine or faeces, water bodies are contaminated with the eggs of schistosomes. Worldwide, 900 million people do not have access to an improved water source, while an estimated 2.5 billion, half of all people in developing countries lack access to adequate sanitation [5,6]. In rural and poor agricultural communities without pipe-borne water, the locals depend on cercariae infested streams for their economic and recreational needs thereby exposing themselves to infection.

The control of schistosomiasis involves an integrated process directed at the infected subjects, snail intermediate hosts, environmental modification, health education and the provision of pipe-borne water [7]. In this review, the epidemiology, diagnosis and control of schistosomiasis is examined in details with notes on the factors impeding the control of the disease in Africa with inferences drawn from the Nigerian experience.

2. Epidemiology of schistosomiasis

Schistosomiasis is estimated to infect about 240 million people worldwide while an estimated 779 million people (more than 10% of the world population) are at risk of acquiring infection. Although, the transmission of schistosomiasis has been documented in 77 countries worldwide, only 52 of these countries are endemic for the disease, majority of which are in the Africa continent. Forty six [46] of these countries are in Africa. Unlike the situation in Africa, some countries in Latin America and Asia and most countries of the Caribbean and the Middle East have brought down the prevalence of schistosomiasis and prevented severe morbidity from the infection through a concerted public health effort. But in many of these countries, there are still endemic regions and

a potential for resurgence exists [8]. About 120 million people infected with schistosomiasis are estimated to be symptomatic while about 20 million develop severe disease. The disability adjusted life years due to schistosomiasis is about 1.7-4.5 million while between 150,000 to 280,000 people are known to die as a consequence of schistosomiasis per year. Africa accounts for 85% of the disease burden [9,10]. Urinay schistosomiasis has been reported in 38 countries in Africa. Annual mortality due to *S. haematobium* infection in east Africa has been estimated at 1 per 1000 infected adults [11]. In Malawi, Save the children's 1998 survey of schoolchildren in Mangochi found that the overall prevalence of schistosomiasis in coastal and upland schools was 36%. In some of the schools, the prevalence was as high as 87% [12]. In a related study in Cameroon, Mba and Useh [13] reported urinary schistosomiasis among 39.2% of the subjects studied. Mixed infection of *S. haematobium* and *S. mansoni* occurred in 4.5% of the subjects. The number of infected subjects treated for the disease using praziquantel rose for 12.4 million in 2006 to 33.5 million in 2010. It is estimated that 90% of those that require treatment live in Africa. This implies that over 60% of people suffering from schistosomiasis particularly in Africa are not able to procure treatment or have access to treatment due to the relatively high cost of praziquantel.

2.1. Schistosomiasis situation in Nigeria

It is estimated that 30 million Nigerians are infected with schistosomiasis. When examined against a projected population of 162 million Nigerians, it becomes clear that over 18.5% of the populace have schistosomiasis. The problem becomes more glaring when the projected population of infected people is examined in terms of those who carry the greatest burden of the disease; in this case, school age children. About 23 years ago, Ejezie *et al* [2] published a major review entitled "the schistosomiasis problem in Nigeria" where they highlighted the embarrassing and increasing endemicity of schistosomiasis without any concrete plan for control. Not much has changed almost two and half decades after. In another landmark review on the "Nigerian environment and parasitic infections", Ejezie [14] noted that "a large proportion of the people consist of men and women who are ignorant of the rules of basic hygiene. These people are entrapped by the worst manifestations of poverty, worsened by infectious tropical diseases, malnutrition, high birth and death rate". They are, as it were, caught in the so-called vicious circle-"they are sick because they are poor, they become poorer because they are sick and sicker because they are poorer" [15]. The problem seems to have grown worst. In the above publication, infection with *S. haematobium* was reported in all the regions in Nigeria with a prevalence as high as 60-75% among schoolchildren in some communities. The endemicity of *S mansoni* was also reported though not as wide spread as the former. Perhaps this report and others encouraged the government of Nigeria to constitute the 'National Schistosomiasis Control Committee". Regrettably, this Committee only existed on paper as funds were not made available to organize operational research to delineate endemic communities for treatment.

The morbidity of schistosomiasis in Nigeria reflects what has been published for endemic countries in Africa and Asia. Infection predominates in schoolchildren aged between 5-19

years and thereby decline following the typical "age verus prevalence/intensity convex curve". An earlier study conducted on urinary schistosomiasis reported a prevalence of 45.4% in Ilorin, Central Nigeria with 25.9% of infected subjects excreting 1,000eggs/10ml urine [16]. In a related study in Adim community located in south south Nigeria, this author and his colleagues reported an overall prevalence of 53.8% with males and females accounting for 53.8% and 53.9% of infection respectively. In this study, the mean haematuria, proteinuria and egg-output were 23.19 ery/ul, 49.9mg/100ml and 37.3 eggs/10ml urine [17]. Three years after, in the absence of a control programme, the prevalence of urinary schistosomiasis in this same community rose astronomically to 90.7% among children out of the school system while those who attended school had a prevalence of 86.8% [18].

The current picture of schistosomiasis endemicity in Nigeria is very worrisome. For instance in their investigation on urinary schistosomiasis around Oyan Reservoir, south west Nigeria, Akinwale *et al* [19] reported a prevalence that ranged from 20.39%-83.9% in some communities around the reservoir. In Bida, north central Nigeria, Banji *et al* [20] reported a prevalence of 28% among school children. Recently, Goselle *et al* [21] reported the endemicity of *S. mansoni* in Jos, north central Nigeria. Yet another study reported on the epidemiology of schistosomiasis in six local government areas in Plateau State, Nigeria [22]. The overall prevalence of infection was 47.8%. Many water bodies in the study communities were colonized by infected *Bulinus* snails. Snail infection rates varied significantly ($P<0.001$) between the dry and wet seasons. Most studies on schistosomiasis are based on the school system. Not much has been done on children out of the school system and on preschool children. In one of such studies among preschool children in a rural community near Abeokuta, south west Nigeria, Ekpo *et al* [23] reported a prevalence of 58.1% with the overall geometric egg count of 1.17 eggs/10ml urine. There is gross lack of work on genital schistosomiasis in Nigeria. With a high prevalence of HIV/AIDS infection in Nigeria, it is important that this be addressed. Genital schistosomiasis particularly in women may have helped to spread the transmission of HIV infection.

2.1.1. Consequences of schistosomiasis infection in Nigeria

The pathology associated with schistosomiasis in Nigeria is consistent with what have been reported in other endemic countries. The pathology of schistosomiasis is essentially a series of chronic inflammatory lesions produced in and around blood vessels by eggs which may be found lodged in practically any viscera or their products and sometimes by dead worms. There are comprehensive studies in the literature on the pathology due to urinary schistosomiasis [24,25,26,27]. In summary disorders such as cercarial dermatitis, haematuria, proteinuria, calcification of bladder, uteric stricture and dilatation, hydronephrosis and squamous cell carcinoma have been reported. Others include multi granulomatas in the bladder and vesicle calculus. Attah [28] noted that the pathology of intestinal schistosomiasis is characterized by the presence of a small superficial ulceration of colonic mucosa, with eggs and granulomas found much more frequently in the serosa than in the mucosa; and by lesions which are secondary to disintegration of eggs and aggravated by oviposition. Hepatic lesions is marked by eosinophilic infiltration of the portal tract with or without eggs. In chron-

ic cases, the major lesion in the liver is 'pipe stem fibrosis', an enlarged liver and fibrosed portal tract with a varying degree of portal vein destruction.

Schistosomal infection has been associated with other negative effects among Nigerian children. These include poor attendance at school, low cognitive ability, educational achievement and malnutrition. This is exemplified in one study in which we treated schoolchildren with urinary schistosomiasis with PZQ and monitor its effect on educational attainment in Adim community of Nigeria. The pass rate among the cohort improved following the first treatment session from 81.4% to 90.7%, latter declined to 84.2% following the second treatment session but the net improvement in performance was statistically significant [29]. On the contrary, Ejezie and Ade-Serrano [30] showed that anthropometric measurements in relation to age, to average marks scored and school attendance were not found to bear any relationship to the intensity of *S. haematobium* infection in Lagos Nigeria. Similarly, Ekanem *et al* [31] did not find any significant impact of infection on anthropometric parameters, school attendance and academic performance among infected children compared to controls in Nigeria. In Kenya, Corbet *et al* [32] showed that intensity of *S mansoni* infection correlated with hepatomegaly, which was more clearly related to nutritional status. Furthermore they noted that children with hepatomegaly were significantly more stunted and/or wasted than those without, and had less variety in their diet. Similarly, Stephenson *et al* [33,34] demonstrated that children infected with *S. haematobium* had evidence of poor nutritional status, with improved growth rates in children and weight gain in undernourished adults following treatment with metrifonate or PZQ. The consequences of infection may be a function of the morbidity of infection in the area, age, nutritional and economic status of the infected subjects.

Educational Performance	**Pre-Treatment N=210**	**Post-treatment 1 N=183**	**Post-treatment 11 N=203**	**X2**	**P**
Total attendance Pupils days	46,902	40,269	40,402		
Attendance rate (%)	86.7	81.5	81.1	2.99	0.22
Days school open	257	270	245		
No passed	171	166	171		
Pass rate	81.4	90.7	84.2	7.2	0.027

Adopted from Meremikwu et al (2000)

Table 1. Effect of treatment on attendance and pass rate in a cohort of school children over three years

3. Diagnosis of schistosomiasis

Diagnosis is pivotal in all aspects of the control of schistosomiasis. Feldmeier *et al* [35] noted that decisions on individual and community treatment, estimations on prognosis and assessment of morbidity, determination of transmission potential, evaluation of treatment and of control measures all build on the results from diagnostic testing. The diagnosis of human schistosomiasis is based on a combination of clinical symptoms, history of residence in an endemic or non-endemic area, parasitological examinations, serological findings and ultrasonography [36]. However all presently available techniques are characterized by diagnostic imperfections or inaccuracies. Consequently, Feldmeier *et al* [35] recommended that selection and application of methods should be related to information being sought while interpretation of test results should take cognizance of the drawbacks and constraints associated with the method being used.

3.1. Clinical diagnosis

The expected clinical conditions include cutaneous lesions, urticaria, eosinophilia and pulmonary disorders. Others include haematuria, cystitis, urinary calculi and vesicular disorders which should be differentiated from other disease conditions giving rise to renal calculi, nephritis, tuberculosis, haemoglobinuria, benign and malignant papillomata. This method of diagnosis is not very sensitive and specific. In endemic areas children may not be able to relay their problem to the physician. On the other hand, primary health care workers who are the first set of health workers to come in contact with infected subjects may not be knowledgeable enough to relate this clinical presentation with schistosomiasis.

3.2. Direct parasitological techniques

Urine egg count is one of the three methods for estimating the intensity of infection; the other two, tissue egg burden and number of worm pairs, can only be determined at autopsy [37]. The WHO [38] noted that quantitative egg count provides reliable baseline data for studies on chemotherapy, malacology, sociology and contamination patterns in defined communities. In the same vein, it also provides information on the transmission potential of different population subgroups. Parasite counts are usually estimated by filtration with nytrel, standard filter paper (Whatman) or by centrifugation of urine. The filtration technique which gives excellent results is applicable in the field [39]. In Africa, filtration with Whatman filter paper is predominantly used in the field and has been associated with reliable and consistent results [17,40]. Smith *et al* [41] reported that in the active stage urinary excretion can be used as an indirect estimate of tissue egg burden and severity of the disease and is particularly relevant for epidemiological studies. In the inactive stage of infection, few or no eggs may be present. Urine egg counts are of limited essence in estimating the prevalence of severe disease in inactive stage of schistosomal disease or in older population. In a related study, a significant correlation was found between haematuria, proteinuria, leucocyturia

and intensity of infection as measured by egg excretion in urine [42]. The best correlation between the reagent strip findings and the intensity of infection was obtained when the three parameters were combined. After treatment with metrifonate, the reduction of egg excretion was paralleled by the normalization of the reagent strip findings. Analysis of day-to-day variation demonstrated a similar low variation of the filtration technique and the reagent strip findings. The authors concluded that polyvalent reagent strips may be a useful tool for diagnosis of heavily infected patients under field conditions, as they permit rapid and easy identification of subjects with high egg counts.

Unlike the eggs of *S. haematobium*, the eggs of *S. mansoni*, *S. japonicum* and *S. intercataltum* are passed in faeces. The formol ether concentration technique may be used to demonstrate the spined eggs of any of these parasites. The problem associated with the technique is that it is not field application. Apart from the requirements of a centrifuge and a microscope, the use of ether which is highly flammable poses a hazard. The Kato thick smear technique is more widely used in field work in Africa. The samples can be prepared in the field while examination may be done later.

For community-based studies, enormous human and financial resources are expended to establish those infected before the administration of chemotherapy. A reasonable number of skilled manpower would be required to avoid undue waste of time. In practical terms it is usually not possible to identify infected people the same day and offer them treatment in the field. In some instances during a re-visit for treatment, infected children may miss treatment either because of sickness or lending a helping hand to their parents in the farm. Thus a lot of money that ought to be used to procure treatment is expended on diagnosis. Parasitological confirmation of eggs in urine or stool have been associated with some degree of poor accuracy and sensitivity [43]. The day-to-day variations in excreted egg counts in individual patients [44] and the uneven distribution of eggs in excreta [45] and the occurrence of immature infections [46] are some of the limiting factors. Others include the immune dependence of schistosome egg excretion and the survival of worms after an immunological induced inhibition of fecundity [47]. Nonetheless, the establishment of prevalence and morbidity by the presence of ova is necessary for understanding the epidemiological profile of different endemic foci.

3.3. Detection of pathology and ultrasonography

The introduction of cytoscopy in 1879 [48] facilitated the visualization of bladder pathology as a consequence of *S. haematobium* infection *in vivo*. Pyelographic and histopathological studies have been used to assess urinary tract pathology due to *S. haematobium* infection in Nigeria [24,27,49]. Modern radiological techniques have finally provided a variety of methods for the detection and follow-up of schistosome related morbidity. Such procedures include various radiographic techiques, isotype investigations of the kidney and liver, computed tomography and more recently, ultrasonography [50]. Table 2 is a summary comparing *S. haematobium*-related morbidity with currently available methods of detecting morbidity.

	CYSTOSCOPY	RENAL FUNCTION TEST	X-RAY	COMPUTED TOMOGRAPHY	SONOGRAPHY
A. BLADDER					
Granuloma	+	-	+	+	+
Sandy Patches	+	-	-/+	+	+
Ulcers	+	-	-/+	+	-/+
Cystitis	+	-	-	-/+	-
Stones	+	-	+	+	+
Calcification	-/+	-	+	+	-/+
Polyps	+	-	+	+	+
Carcinoma	+	-	+	+	+
B. URETER					
Hydroureter	-/+	-/+	+	+	-/+
Stricture	-/+	-/+	+	+	-
Dilatation/ Distortion	-	-	+	+	-
Calcification	-/+	-	+	+	-/+
Polyps	-/+	-	+	+	-/+
C. KIDNEY					
Congestion	-	-/+	+	+	+
Hydronephrosis	-	-/+	+	+	+
Performance	-	+	+	+	-

Adopted from Hatz *et al* [50].

Table 2. Comparison reflects possibility of detecting without rating efficiency and applicability.

3.4. Indirect parasitological techniques

3.4.1. Haematuria and proteinuria

The detection of haematuria and proteinuria is widely used in Nigeria and the rest of endemic communities in Africa to diagnose urinary schistosomiasis. Haematuria arises when migrating eggs puncture small capillaries of the viscal plexus to get into the bladder [51]. Haematuria was the first sign to be associated with schistosomiasis [52] while proteinuria was described later. Haematuria is usually seen at the end of urination (terminal haematuria), although haematuria throughout micturition may be seen in some severely infected cases. High levels of urinary protein in *S. haematobium* infection has been linked with nephritis [53], nephritic syndrome [54] and bladder pathology [55]. Some authors have cited the reversibility of proteinuria after treatment to support the renal origin of proteinuria [56,57]. It is now generally accepted that bilharzial proteinuria is of post–renal origin and not a sign of impaired renal function [58].

Several studies have confirmed that the detection of proteinuria and haematuria when used together is a better means to measure morbidity than when used separately [25,40,59]. In Lagos, Nigeria, Ejezie and Ade-Seranno, [40] reported haematuria in 655 of infected children with the

greatest intensity in patients with the highest egg output. Relatedly, Mottt *et al* [59] and Tanner *et al* [60] noted that all children between 5-14 years with more than 50 eggs per 10ml of urine had blood in the urine detected by chemical reagent strips. This author and his colleagues tested the usage of the presence/absence of haematuria and proteinuria in monitoring the outcome of treatment of urinary schistosomiasis with artesunate. The mean ova count, haematuria and proteinuria of 87 infected subjects who were treated significantly reduced from 55.5± 1.3ova/10ml urine, 168.6±1.23 ery/μL and 458.6± 1.4 mg/dl to 1.8±0 ova/10ml urine, 9.1±0.4 ery/μL and 65.4 mg/dl respectively ($P<0.05$ in all cases). We therefore concluded that reagent strips are reliable in monitoring the efficacy of treatment with artesunate [61].

Reagent strips are cheap, fast, simple and can be readily integrated into the primary health care programme. But there may be gender bias in females that may lead to under-reporting or over-reporting (false positives). The contamination of urine with menstrual blood would yield false positive results for haematuria. A similar finding may be noted for leucocyturia and proteinuria [62]. The usefulness of a semi-quantitative grading of haematuria as a correlate to intensity of infection has to be questioned in women with schistosomiasis, since the ectopic localization of eggs in the vagina, cervix or the endometrium may lead to contact bleeding, intermenstrual bleeding or to bloody discharge [63]. Evidence for false positive reagent strip readings in women has been shown in a population based study on Pemba Island, Tanzania. A higher prevalence of haematuria readings were observed in women of child-bearing age than in males of similar age, although intensity of infection and morbidity as measured by the number of eggs per unit of urine, and as indicated by pathological ultrsonography was significantly less in women than in men [64]. Vester *et al* [65] reported culture-related biases for mass screening with urine analysis strips. About 15% of schistosomiasis-free Sudanese girls and women circumcised either by the "pharaonic" or the "sunna" method constantly or intermittently show mild haematuria and/or leucocyturia. Since female circumcision is practiced not only in Muslim and Coptic societies in the Sudan, but also in more than 40 ethnic groups in Africa and Arabia [66], false positive reagent strip readings are expected to occur where this tradition and schistosomiasis overlap.

3.4.2. Rapid Assessment Procedure (RAP) using questionnaires

A greater proportion of money slated for the control of schistosomiasis is usually spent on diagnosis particularly when eggs are to be counted. The fact that schistosomiasis is focal in distribution with millions of infected subjects in endemic communities showing different prevalence and morbidity rates compound the problem. The problem is more felt in Africa with her lean financial resources but with the largest burden of the disease. The rapid assessment procedure was conceived to maximize resources in diagnosis which could be directed to possible chemotherapeutic control of infection

The RAP involves the use of a rapid and inexpensive method to identify communities with a high prevalence of and morbidity due to urinary schistosomiasis. It is based on using simple questionnaires to find out how frequent schistosomiasis is in a community [67]. Kroeger [68] and Ross and Vaughan [69] showed that health interview surveys can be used in both developed and developing countries to assess morbidity as it is perceived by community members, and to in-

vestigate the utilization patterns of health services. Tanner [70] demonstrated that asking the beneficiaries of the health system about their perceptions of disease and health problems, and especially about their priorities with regard to health related actions, can add an important element in the health planning cycle. Lengeler *et al* [71] observed that indirect health interview represents a methodical evolution of the traditional interview approach by the fact that questionnaires are not administered directly by the investigators or their field staff to the key informants. Rather, they are distributed through an existing administrative channel and self-administered by the recipients. The school system is therefore the appropriate structure to base a study on the prevalence of schistosomiasis. This is anchored on the fact that those who bear the greatest burden of the disease can be easily reached through this channel. Additionally, schools are widely cited and are very likely to be located in remote endemic areas. Thirdly, teachers are competent enough with minimal training to carry out an exercise of this nature.

Several epidemiological studies are available in the literature that tested the usefulness of this mode of diagnosis. Useh and Ejezie [72] worked on the "evaluation and validation of the questionnaire approach for the diagnosis of urinary schistosomiasis in Biase Local Government Area of Nigeria among school pupils". The questionnaire which enquired whether pupils had urinary schistosomiasis or blood in urine in the preceding month, was administered by class teachers to the pupils. Urines samples collected for the validation of the questionnaire diagnosis was also examined using dipsticks (by teachers and the research team). There was a strong positive correlation between the pupils's knowledge of schistosomiasis as a disease and the reported presence of blood in urine (r=0.96) although the later was a better indicator of the disease. The questionnaire technique (blood in urine) gave a comparable sensitivity (85.8%), specificity (81.4%), positive and negative predictive values (96.6% and 47.9%) to the dipstick test with values of 96.6%, 88.4%, 98% and 69.1% respectively. Teachers were able to detect haematuria with a high degree of accuracy. We found this approach to be simple, cost-effective and reliable and recommended its usage in other endemic settings with large land mass and dense population like Nigeria (See Table 3).

Survey Method	**TP a**	**FP B**	**FN C**	**TN d**	**SENS (%)**	**SPEC (%)**	**PPV (%)**	**NPV (%)**	**VAL (%)**	**BIAS (%)**	**P Value**
Blood in Urine	229	9	38	35	85.8	81.4	96.6	47.9	83.3	88.8	P<0.001
Schistosomiasis	207	15	60	28	77.5	65.1	93.2	31.8	73.4	83.1	P<0.001
TDST	231	7	36	36	86.5	83.7	97.1	50.0	84.3	89.1	P<0.001
RDST	250	5	17	38	93.6	88.4	98.0	69.1	91.9	95.5	P<0.001

True Positives, TP were defined as those with ova in urine (n=267). Altogether 310 pupils were examined.

TN- True Negative, FP- False Positive, FN- False Negative

SENS- Sensitivity, SPEC – Specificity, PPV- Positive Predictive Value, NPV- Negative Predictive Value, TDST- Teachers Dipstick Testing, RDST- Researchers Dipstick Testing.

Adopted from Useh and Ejezie, [72].

Table 3. Comparison of the performance of different survey methods in relation to parasitologically confirmed diagnosis

Elsewhere, self-administered questionnaires, distributed by existing administrative channels to village party chairmen, head teachers and school children, showed good diagnostic performance for the qualitative assessment of urinary schistosomisasis endemicity. At a cost 34 times below that of the WHO-recommended parasitological screening strategy, the school children's questionnaire allowed the screening of 75 out of 77 schools of a rural Tanzanian district in 6 weeks, and the exclusion of schools not at high risk for urinary schistosomiasis with over 90% confidence. The head teacher and party chairmen questionnaires made it possible to assess the perceived importance of a spectrum of diseases and symptoms, among which was schistosomiasis. The priority rank of schistosomiasis control was strongly correlated with the prevalence rate of the disease in the community. The questionnaires also looked at the prioritization of health among other community issues and thus contributed important information for planning at the district level [73].

Using questionnaires facilitate immense savings in cost as well as reaching a vast land mass. However, in areas of low school attendance, reliable information may not be collected. Infected but unidentified school-age children that are out of school would invalidate control efforts, as they would continuously contaminate water bodies. Other limitations as outlined by Chitsulo *et al* [67] are-

- results obtained with school children may not always be typical for the whole community especially if a lot of the children of this age are not in school or where one sex is badly under-represented
- the methodology does not identify which child is infected. To obtain this information, a second step using conventional diagnostic method would be necessary
- true prevalence is usually underestimated since the method relies on re-call as those who are mildly infected may not recall having had haematuria
- in some countries, girls and boys may perceive the disease differently or give different answers to questions asked about it.

3.5. Immunodiagnosis

Immunodiagnositic methods are so far the only alternative to parasitological test. They allow the demonstration of specific anti-schistosomal antibodies and to a certain extent, the tracing of circulating antigens and/or immune complexes in sera of parasite carriers [36]. Wilkins *et al* [55] noted that they offer the most practical assays for epidemiological studies and patient management. They are particularly valuable if the density of the parasites (or their developmental stages) in a specimen is very low or if the biology of the parasite does not allow its direct demonstration e.g localization of certain stages in internal organs.

Serological procedures such as immunodiffusion, complement fixation test, indirect haemagglutination assay, immunoflourescent antibody assay have been used for the diagnosis of schistosomiasis. Others include enzyme linked immunosorbent (ELISA), radioimmunoassy and radio-allegrosorbent assay among others. The relevance of antibody detection in the diagnosis of schistosomiasis has been reviewed in great details by Hamilton *et al* [74]. They

concluded that due to the relative insensitivity of both parasitology and antigen detection, antibody detection methods could find increasing use in situations of low infection intensity. The performance of antibody detection for the diagnosis of schistosomiasis has been tested in Kenya. Approximately 1500 blood samples from 3 areas with endemic schistosomiasis and from a non-endemic control area, were tested for their antibody reactivity in ELISA. The results were compared with infection status determined by parasitological examination. Two test antigens were used ;unfractionated *S. mansoni* egg homogenate (SEA) and CEF6, a partially purified fraction of SEA containing 2 cationic antigens. Blood from patients with *S. haematobium* infection cross-reacted significantly with the two *S. mansoni* antigen preparations, but reactivity against CEF6 appeared more specifically indicative of *S. mansoni* infection. There was a significant positive correlation between blood ELISA results and the number of eggs excreted by infected subjects in the area endemic for *S. mansoni* only. Highest correlation coefficients were obtained in children aged 10 years and CEF6 gave marginally higher correlation coefficient than SEA. The graphs of prevalence and intensity of schistosome infection drawn from the serological results were similar in shape to the graph of these 2 quantities based on parasitological results, and the results indicate that serology merits wider use as an epidemiological tool for determining infection status in schistosomiasis [75]. In a different but related study, the relative concentration of IgM and IgG antibodies to *S. mansoni* soluble egg antigen were evaluated in paired samples of venous blood, sera and buffer elutes of capillary blood drops dried on filter papers [76]. The samples were obtained from school children at early and chronic stages of schistosomiasis diagnosed on the basis of history, clinical symptomatology and parasitological criteria. ELISA simultaneously performed, revealed paired samples to display comparable antibody levels in all cases. Samples from children with early schistosomiasis had specific IgM : IgG ratios greater than 1 in sera and blood elutes. This ratio, however was less than 1 in samples from chronically infected children. The specific advantages of this simplified technique are the use of anti-SEA antibodies in finger-stick blood elutes, rather than sera or venous blood to serologically diagnose schistosomiasis and to differentiate early from chronic infections particularly when used for mass screening such as epidemiological surveys. Elsewhere, Mclaren *et al* [77] showed that *S. mansoni* SEA gave a sensitivity of 92.3% in diagnosing *S. haematobium* infection and 96.2% for *S. mansoni* and a specificity of 97.4% in ELISA. Recently, Chand *et al* [78] reported on the development of a new assay for the diagnosis of schistosomiasis, using cercarial antigens. They showed that the cercarial antigen assay was equivalent to the SEA assay for serodiagnosis of schistosomiasis in a non-endemic setting. Since the cercarial antigens is more easily obtained and prepared than SEA, the authors inferred this assay may be preferred for routine clinical use and may be amenable for scaling up.

Although the application of serological tests has, without doubt, contributed to epidemiological surveys, such studies are of limited use because some of the tests lack reasonable levels of acceptable sensitivity and specificity or are technically difficult to be carried out in field surveys. Other drawbacks as outlined by Weiland [36] are;

- inability to indicate the intensity of infection or differentiate active from chronic infection
- no correlation between morbidity and sero-reactivity

- cross-reaction with antibodies to other helminthes including animal schistosomes
- unresolved seropositivity remain for years after treatment or after an infection has died out.

The greatest impediment hindering the utilization of immunodiagnosis in third world countries particularly in Africa is lack of financial resources to procure the sophisticated equipment required to carry out some of these procedures and the training of skilled manpower to handle them.

3.6. Rapid diagnostic test

The advent of rapid diagnostic tests has facilitated the immediate treatment of subjects with infectious diseases in the field after diagnosis. Results are usually available within 30 minutes compared to the conventional tests. Apart from its simplicity and ease of carrying out devoid of technicality, the availability of electricity is not required. Rapid diagnostic tests are being deployed in endemic countries for the identification of subjects with malaria, HIV and hepatitis for prompt treatment. Encouraging reports are available in the literature on the development of rapid diagnostic test for schistosomiasis. De jonge *et al* [79] developed a reagent strip test for detection of circulating cathodic antigen in urine. In a related study, Bosompem *et al* [80] showed that *S. haematobium* antigen complexed with complement C3 can be isolated from the urine of infected persons by using a mouse monoclonal antibody. These investigators demonstrated that goat anti-human C3 would also detect schistosome antigen/complement complex in urine of infected persons used as case-controls and subsequently developed a monoclonal antibody dipstick test on the basis of these findings. However, a lot of standardization would be required before these strips are approved by the WHO and other regulatory organizations for deployment in endemic countries.

4. Control of schistosomiasis

The cardinal objective in the control of schistosomiasis is the reduction of morbidity and mortality to levels below public health significance. Over the years, emphasis has shifted from the non-realizable goal of eradication to the more realistic goal of morbidity control. In this context, Gemmel *et al* [81], defined "a control programme" as the "implementation of specific measures by a disease control authority to limit the incidence of the disease". Such implementation may involve specific technical interventions and perhaps legislation to enforce compliance. The success of this type of approach is predicated on an accurate ecological diagnosis, that is, a diagnosis of the human community, its parasitological characteristics, its physico-geographical environmental attributes and man's behavioural attitudes and customs [82].

The enormous morbidity associated with schistosomiasis which ranks it next to malaria in terms of public health significance re-emphasizes the need for a coordinated and sustainable means for the control of the disease. There is a consensus of opinion that the control of the disease should be integrated. In this model of control, King [83] identified the applicable approaches as:

- Population based chemotherapy
- Snail control which involves habitat modification and use of plant and chemical molluscicides,
- Proper treatment of sewage,
- Good environmental engineering designs for the development of irrigation and hydroelectric schemes to limit the availability of breeding grounds for the snail vectors
- Provision of clean and safe piped water and
- Massive health education and mobilization of the population to claim ownership of the programme

The WHO Expert Committee on Epidemiology and Control of Schistosomiasis took a holistic approach at the control of the disease and noted that "comprehensive understanding of the environment, demographic, social, human behavioural and economic factors" in schistosomiasis is essential for the design of control programmes that are successful in the long run [84]. With the advent of praziquantel (PZQ) as a safe and efficacious drug for the treatment of schistosomiasis, the WHO in 1991 reinforced its 1984 recommendation to shift from transmission control (focusing on the prevalence of infection) to morbidity control (laying emphasis on intensity of infection) [8]. Morbidity control will not only reduce the number of people infected but it will also drastically reduce environmental contamination with the eggs even when cure is not attained. A drastic reduction of the pollution of the environment with the eggs would also reduce the chances of transmission. Should this occur at a level below public health importance, the probability of eventual elimination of disease is certain with a sustained integrated approach

4.1. Chemotherapeutic control of schistosomiasis

Of all the methods of control listed above, chemotherapy is the only one that is widely used presently in endemic areas for the control of morbidity due to schistosomiasis. Among the first group of drugs used for the treatment of schistosomiasis included; antimonials, niridazole, hycanthone, lucanthone, oxamniquine and albendazole. PZQ is currently used for the treatment of all the species while metrifonate is active against *S. haematobium* only. Recently, artemisinins earlier synthesized for the treatment of malaria infection is being used in some endemic communities to treat schistosomiasis. The WHO [11] identified four approaches in the administration of chemotherapy programme namely;

i. Mass treatment: treatment of the entire population. This is often limited by availability of finance.

ii. Selective population treatment: treatment of infected persons identified by a diagnostic survey of the whole population

iii. Selective group treatment: treatment of all or infected members of a high risk age or occupational group

iv. Phased treatment: use of the above strategies in a sequence of progressively greater selectivity.

Only the chemotherapeutic form of control of schistosomiasis is covered in the present review. This does not in any way reduce the importance of the other methods. It has already been emphasized above that the sustainable control of schistosomiasis involves the integration of several methods listed above. A comprehensive review on the control of schistosomiasis by this author can be found elsewhere [85]. In the next few paragraphs, the modes of action of several drugs use for the treatment of schistosomiasis are examined.

4.1.1. Praziquantel (PZQ)

4.1.1.1. Biochemical properties and pharmacokinetics

Praziquantel (PZO) is the drug of choice for the treatment of schistosomiasis. It is a broad spectrum anti-schistosomal which is principally active against the adult stage of all the schistosome species infective to man. It is a 2-cyclohexycarbonyl 1,2,3,6,7,11b-hexahydro-4H-pyrazino(2,1-a Isoquinolin-4one) compound with a melting point at 136-140C. It was developed in the laboratories for Parasitological Research of Bayer AG and Merck KGaA in Germany (Elbert and Darmstadt) in the mid 1970s. It has a molecular mass of 312.411 with a serum half life of 0.8 to 1.5 hours in adults with normal liver and kidney function and is mainly excreted in urine. PZQ is a white crystalline powder with bitter taste. It is stable under normal storage conditions. Although, it is insoluble in water, it is soluble in chloroform, dimethylsulfoxide and ethanol. It is sold as a racemate mixture consisting of equal parts of 'laevo' and 'dextro' isomers, of which only the laevo component displays anti-schistosomal properties.

The recommended dose of PZO is 40 mg/kg body weight. The drug is available as a 600mg tablet. The quality of PZQ (proprietary and generic) currently available in the market is quite high and acceptable. Thirty four [34] PZQ samples from different manufacturers were collected at the user level in various countries and subjected to quantitative analysis of active ingredient, purity, disintegration and dissolution in accordance with established pharmacopoeial standards. The results showed that most of the samples were of high quality except two samples from the same manufacturer that had no PZQ [86]. About 90% of the damage done to organ function is known to reverse six months following the administration of PZQ. Although it is exceptionally well tolerated, reported side –effects include abdominal discomfort, nausea, headache, dizziness, drowsiness and pyrexia especially in subjects with high egg counts [87].

4.1.1.2. Mode of action of PZO

The mode of action of PZQ has been extensively reviewed elsewhere [88,89]. The exact mechanisms of action of PZQ is still poorly understood. PZQ is known to induce rapid calcium influx that distort the morhoplogy and physiology of schistosome. Jeziorski and Greenberg [90] showed that the B subunits of voltage-gated Ca^{2+} channels is the prime molecular target of PZQ. It has recently been reported that cytochalasin D abolished the schistosomicidal activity of PZQ but calcium influx into PZQ exposed schistosomes was not halted. This therefore raises doubts whether calcium influx is essential in the antischistosomal activity of

PZQ [91]. PZQ induces contraction of schistosomes which manifest in paralysis in the contracted state. Additionally, vacuolation and blebbing near and on the surface of the worm have equally been reported [92].

PZQ is known to increase exposure of antigens on the worm surface. It is believed that this in turn renders the worm more susceptible to antibody attack. Doenhoff *et al* [93] inferred that this drug induced antigen exposure is assumed to account for the synergistic effect between PZQ and the host antibodies in killing worms invivo. Recently, it has been shown that PZQ seems to interfere with adenosine uptake in cultured worms. This may have therapeutical relevance given that the schistosome is unable to synthesize purines such as adenosine *de novo.* It may be assumed that the drug interferes with schistosome's obligate need to acquire adenosine from its host. This is confounding as a relationship between Ca^{2+} channels and adenosine receptors has been demonstrated in cells of some other animals and adenosine can antagonize Ca^{2+} release. This informs the inference drawn by Angelucci *et al* [94] that PZQ-induced Ca^{2+} influx and adenosine receptor blockade may be connected.

4.1.1.3. Oxamniquine – Molecular structure and pharmacokinetics

Oxamniquine was first described in the late 1960s. The compound is 6-hydromethyl-2-isopropyl-aminomethyl-7-nitro 1,2,4-tetrahydroquinoline. It is produced by biological processes. The drug is administered as 15mg/kg body weight for adults while children are treated with 20mg/kg given in two doses of 10mg/kg each in an interval of 3-8 hours. It is extensively metabolised through oxidation process. The metabolites are active and excreted in urine. The side effects are mild, transient and well tolerated especially when given after a meal [95].

4.1.1.4. Mode of action

Unlike PZQ, the mechanism of action of oxamniquine is fairly well understood. Oxamniquine is only active against *S. mansoni* but not effective against *S. haematobium* and *S. japonicum*. The active ingredient is tetrahydroquinoline which acts on the adult *S. mansoni* and immature invasive stages, with males more susceptible than the females. Its anticholinergic effect, which increases parasite motility and inhibits nucleic acid synthesis, has no notable effect on the other *Schistosome* species [96]. The mechanism of action of oxamniquine is related to irreversible inhibition of nucleic acid metabolism of the parasite. The drug is activated in a single step, in which the *Schistosoma* enzyme converts the oxamniquine to an ester, and spontaneously dissociates resulting in an electrophilic reactant and alkylation of the Schistosoma DNA. Worm death is associated with the formation of sub-tegumental vesicules in adult parasites. Different responses are observed after therapy, with less specific morphological alteration and hepatic shifts, occurring over a period of six days post treatment [95].

4.1.1.5. Metrifonate

Metrifonate was initially introduced as an insecticide in 1952, but later in 1960, it was used to treat helminth infection. The drug also refer to as trichlorophone is a organo-

phosphorus ester which is only active against *S.haematobium*. It is rapidly absorbed, metabolized and excreted. The metabolic pathway yields DDVP (2,2-dichlorovinyl dimethylphosphate), a cholin esterase inhibitor which is the active compound. The mechanism of action is not known. It is relatively cheap and is not toxic. Metrifonate is administered as 7.5-10 mg/kg body weight, given in three divided doses in two weeks interval. Among the side effects reported following the administration of the drug include abdominal pains, diarrhoea, fatigue and muscular weakness which dissipates within 12 -24 hours [97]. The reasoning behind the widely spread dosage has to do with its inhibitory effects on red cells and plasma cholinesterase.

Metrifonate is not currently used for the treatment of urinary schistosomiasis. Several reasons account for this. One of which is poor compliance by patients as a result of the spacing and multiple dosing. The second reason is reduced level of efficacy. For instance, Mgeni *et a*l [98] reported a cure rate of 40% and egg reduction rate of 90% in Zanzibar. Lastly, the advent of PZQ with its superior efficacy rate and broad spectrum activity meant that it was no longer cost effective and sustainable to rely on metrifonate.

4.1.1.6. Artemisinin and its derivatives – Biochemical characteristics and pharmacokinetics

The artemisinins though syntheised for the treatment of malaria is the newest drug used for the treatment of schistosomiasis. Unlike PZQ, which is active against the adult stages of the parasite, artemisinin is active against the immature stage of parasite. It is a sequitterpene lactone with a peroxide group, obtained from the leaves of the plant, *Artemisia annua* which are grown in Central Europe, China, USA and Argentina among others. The major derivatives of artemisinin are artesunate, artemether, arteether with dihydroartemisinin as the principal active metabolite. Primarily they are antimalarials, but the anti-schistosomal properties were discovered by Chinese scientists in the 1980s especially for the treatment of *S japonicum* infection [99]. They are well tolerated with only minor side effects.

4.1.1.7. Mode of action of artemisinin

The precise mode of action of this drug is not known. Artemether is the most potent. It exhibits the highest level of activity on one to three weeks old liver stages of the parasite. When a dosage of 6mg/kg weight is administered, it kills the schistosomulas during the first 21 days. The invasive and adult stages are less affected and the adult females are more susceptible than the males [100]. Following treatment, artemether induces severe and extensive tegumental damage and significant reduction in glycogen contents through the inhibition of glycolsis, but the onset of this alteration is slow. It also hinders the development of egg laying adult worm pairs [101].

PZQ is currently the drug of choice for the treatment of all forms of the disease. It is safe and well tolerated. Readers are referred to a very detailed review on "praziquantel: its use in control of control of schistosomiasis in sub-Saharan Africa and current research needs [89] and "praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis" [88]. Elsewhere, we reported on the high efficacy and tolerability of PZQ [102] and arte-

sunate [103] for the treatment of urinary schistosomiasis in Nigeria.These authors noted that despite the fact that PZQ is being widely used, there is no clinically relevant evidence for resistance to date, but worrying low-cure rates have been recorded in some studies. They also observed that there is also no assurance that PZQ and/or Schistosomes are in any way unique and that resistant organisms will not be selected as a result of widespread usage. Artesiminis and the related 1,2,4-trioxolanes are now promising antischistosomal compounds, as are inhibitors of a schistosome-specific bifunctional enzyme, thioredoxin-glutathione reductase. In some endemic communities, artesunate is also used for the treatment of malaria singly or in combination. Therefore, where artesunate is used for the treatment of urinary schistosomiasis, resistance may likely develop to malaria. It is pertinent to do an analysis on why schistosomiasis is still highly endemic in some parts of Africa including Nigeria when a potent drug is available for the management of the disorder.

4.1.1.8. Impediments of control of schistosomiais

Several factors are responsible for the continuing endemicity of schistosomiasis in Africa. Some of the factors are examined below;

4.1.1.8.1. High cost of PZQ

Richards [104] identified community-based annual mass drug administration with safe and effective oral drugs as the principal strategy for the control of onchocerciasis, lymphatic filariasis and schistosomiasis. It has been demonstrated that annual treatments with the microfilaricide ivermectin (Mectizan, donated by Merck &Co., Inc.) prevents severe eye disease and skin manifestations of onchocerciasis while the transmission of LF by mosquitoes can be interrupted in Africa by annual single-dose combination therapy with ivermectin and albendazole (donated by GlaxoSmithKline) [105]. Mass distribution of PZQ can significantly reduce schistosomiasis morbidity [106]. However, unlike ivermectin and albendazole, PZQ is not donated and costs approximately US $0.20. Schistosomiasis is a disease that affects poor rural agricultural workers who in most cases cannot afford the cost of PZQ. This is one of the greatest impediments in the control of the disease.

4.1.1.8.2. Lack of political commitment and provision of finance

Until recently, there was no sustained political and financial commitment by the WHO and her health-related agencies and governments of schistosomiasis endemic countries towards the control of schistosomiasis. The success story reported in the control of schistosomiasis in Brazil, China, Egypt, Laos and the Philippines [10,107,108] is an encouragement that the disease can be controlled when the right programmes and processes are in place. Over the years, emphasis on funding of infectious disease control was placed on HIV/AIDS, malaria and tuberculosis/leprosy. That informed the categorization of schistosomiasis as one of the neglected tropical diseases. However, the situation changed during the 54th World Health Assembly held in May, 2001 where resolution WHA 54.19 namely that at least 75% of school-age children in the high-burden regions should be treated regularly with PZQ. This was further enhanced by the launch of the Schistoso-

miasis Control Initiative [SCI] supported by a US$ 30 million grant from the Bill and Melina Gates Foundation. The SCI is a partnership between Imperial College, London, UK; the Seattle-based Gates Foundation, WHO, Geneva; Harvard School of Public Health, Boston and high-burden country representatives. This renewed interest has encouraged the Carter Centre to be involved in the control of schistosomiasis in Nigeria. The Centre is assisting in the control of schistosomiasis in three states namely; Plateau, Nasarawa and Delta. The Centre is doing this by using the grassroots distribution system of health workers and village volunteers for onchocerciasis to also deliver health education and conduct mass drug administration with PZQ annually in areas affected by both parasites. Since 1999, this programme has delivered a cumulative total of 1,079,335 treatments with PZQ. Studies in a sample of villages in two areas showed a reduction in prevalence of bloody urine assessed by dipsticks from 47% in 1999 to 8% in 2002, after just two years of annual treatments [109]. This success means that LF, onchoceriasis and schistosomiasis can be treated by community health workers at the same time thereby saving enormous cost as a recent clinical trial in Thailand found no clinically relevant pharmacokinetic changes or adverse reactions when ivermectin, PZQ and albendazole were given concurrently [110]

4.1.1.8.3. Lack of strong health system

The health system of many countries in the developing world are not synchronized and integrated. This renders the delivery of health packages difficult and cumbersome. However, there is a conseneus that strong, well integrated and effective health systems are essentials to reduce disease burden and to achieving the health related MDGs. A Strong health systems typically consist of seven building blocks [111,112]. These include: service delivery, governance structures, financial mechanisms, human resources, medicines and technology supply system, health information system and participatory community mechanisms (people). In an ideal situation, these seven components must exist and work together to generate quality (accessible, equitable, responsive health care)

4.1.1.8.4. Health failures

Failures associated with the planning and delivery of healthcare are critical issues that should be targeted to ensure success in the control of infectious diseases including schistosoimasis. In this context, Mahoney and Morel [113] argued that innovation disparity has created 3 kinds of "health failures" namely "science failure, market failure and public health failure". Science failure refers "to a lack of knowledge and tools to address health problems e.g there are still no effective vaccines or drugs for schistosomiasis". Market failures happen "when stock-outs occur due to high demand or when the purchase costs of drugs, vaccines and health interventions prevent the poor from accessing them". Often the new drugs and diagnostics are very expensive to develop and /or require sophisticated technical and health infrastructure for optimal use. Public health failure arises "due to lack of good governance, transparency and effective delivery systems and a clear articulation of priorities and values". Political and economic instability, cultural and religious barriers and shift in govern-

ment priorities can block the uptake and implementation of health innovations. This is particularly true in Africa where frequent changes of government and dislocation of communities as a result of natural disasters and inter and intra-tribal wars have contributed to hinder outcome of disease control programmes.

5. Development of a schistosome vaccine

Despite the existence of effective chemotherapeutic agents, progress towards controlling schistosomiasis has been slow. Additionally, the possible development of resistance to PZQ and other compounds, rapid re-infection and the overall economic cost, demand that other approaches be pursued [114]. Butterworth *et al* [115] argued that the aim of vaccination is to reduce morbidity. As in the various animal models, immunity in humans appears to be frequently incomplete. "Immune" adults often do become infected, but at lower intensities than "susceptible" children. Several investigations have confirmed that the severity of clinical disease is dependent on intensity of infection rather than simply the presence or absence of infection [116,117] implying that even an incomplete immunity may be of considerable value.

An excellent review on the search for a schistosome vaccine was published not too long ago [118]. These authors rightly chronicled the search for the discovery of candidate vaccine molecules to have transited through mining crude extracts, monoclonal antibody targets, anti-idiotypes, expression library screening and immunogenicity. The early disappointment that was recorded with the vaccination of mice with crude worm extracts or purified components, followed by cercarial challenge [119,120] and utilizing the idea of concomitant immunity [121] were equally reviewed. Wilson and Coulson [118] concluded that the sequencing of *S. mansoni* transriptome and genome and the development of proteomic and microarray technologies has drastically improved the possibilities for identiflying novel vaccine candidates, particularly proteins secreted from or exposed at the surface of schistosomula and adult worms. The parameters of an attenuated schistosome vaccine has been evaluated in the Olive Baboon [122]. Five exposures of baboons to the attenuated schistosome vaccine gave greater protection than three exposures, but this attenuation was not sustained when challenge was delayed. Within the scope of the data collected, faecal and circulating antigen levels did not accurately predict the observed worm burdens. Levels of immunoglobulin G at challenge correlated best with protection, but there was little evidence of a recall response. In a related study in baboons, Coulson and Kariuki [123] showed that neither a preceding infection, terminated by chemotherapy, nor an ongoing chronic infection affected the level of protection. Whilst IgM responses to vaccination or infection were short-lived, IgG responses rose with each successive exposure to vaccine.

The greatest hope for the discovery of a schistosome vaccine lies in Sh28GST which has already undergone Phases 1 and 2 human trials [124]. No adverse side effects were recorded in human recipients and high titres of antibodies were elicited in Phase 1 and phase 2 trials [125]. The results of phase 3 human trials is being awaited. As noted by Curwen *et al* [126]

and Dillion *et al* [127], current advances in post-genomic techniques are providing new avenues and hope to identify the secreted and surface-exposed antigens that mediate protection. The search must be sustained as vaccination is the most cost-effective and sustainable means of controlling endemic infectious diseases.

6. Conclusion

Schistosomiasis is still endemic in many parts of Africa particularly Nigeria. Activities related to electric power development/generation and agriculture have extended areas of endemicity just as new foci of infection are being described. The control of schistosomiasis requires an integrated process. However, chemotherapy with PZQ is the mainstay for the control of the disease in the short-term. Poverty on the part of infected subjects, lack of deployment of political and financial resources by disease endemic countries are the major factors limiting the control of the disease. The global economic recession has contributed in reducing financial resources available through bilateral and multilateral avenues for the control of the infectious diseases just as increase in international travels and tourism have led to the reporting of "imported schistosomiasis" in non-endemic countries.

Recommendation

The following recommendations are suggested for the control of schistosomiasis;

- Governments of disease endemic countries should show serious political and financial commitment towards the control of schistosomiasis. Overall, the health sector should be funded in line with the recommendation of the WHO.
- Pharmaceutical companies should be encourage to donate PZQ free as is obtainable with albendazole and ivermectin or in the alternative reduce the cost of the drug.
- The delivery of PZQ should be integrated into ongoing programme of distribution of ivermectin and albendazole by community health workers as it has been shown that taking the three drugs concurrently is safe and effective
- There should be a deliberate policy of providing piped water in endemic communities to reduce the chances of coming in contact with cercariae infested water bodies
- Researchers should be encouraged to develop rapid diagnostic and cost-effective test based on antibody detection which can provide results within 15-20 minutes in the field for the diagnosis of schistomiasis and instant treatment.
- More researches are required to hasten the development of a vaccine for schistosomiasis. This is the only means of long term control of this disease.

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