

## THE PUBLIC HEALTH SIGNIFICANCE OF URINARY SCHISTOSOMIASIS AS A CAUSE OF MORBIDITY IN TWO DISTRICTS IN MALI

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**Abstract.** *Schistosoma haematobium*-related morbidity was studied in the perennial irrigation area of Office du Niger and the small reservoirs area of Plateau Dogon in Mali. Questionnaire, clinical, parasitologic, and ultrasound examination data were collected from 1,041 individuals at the baseline survey in 1991; 705 were re-examined one year after treatment. At baseline, the overall prevalence of *S. haematobium* infection was 55.2%; half of those infected had no clinical symptoms and 30% had pathologic lesions. Both infection and morbidity were more frequent in children than in adults, with a peak prevalence at 7–14 years of age. The rates of lesions were more than twice as high in those heavily infected as in lightly infected individuals. Reagent strip testing for microhematuria was more sensitive in detecting individuals with pathologic lesions than in detecting individuals with infection. One year after treatment with praziquantel, more than 80% of the urinary tract lesions had cleared. It is concluded that *S. haematobium*-related morbidity is frequent in Mali, but passive case detection for treatment would not cover a great deal of early stages of the disease; active intervention using reagent strip testing for microhematuria at the most peripheral levels would be an efficient system for morbidity control and monitoring of control operations.

Schistosomiasis *haematobium* is widely distributed in Mali. According to an unpublished report of the Schistosomiasis Control Program, one in every four of the total population of eight million people is infected. Substantial transmission occurs in five (including the capital) of the eight regions of the country. Transmission is largely confined to water development project areas and along the main rivers and streams. However, the public health significance of *Schistosoma haematobium* as a cause of morbidity is unknown. Since the primary objective of the current control strategy is the reduction or elimination of morbidity due to the schistosome infections, it is necessary to gain a clear picture of the type of morbidity to be controlled and how it is to be monitored at the most peripheral level of the primary health care system.

### MATERIALS AND METHODS

**Study areas.** The study was carried out in the two highest transmission areas in Mali: the Plateau Dogon and Office du Niger (Figure 1). The latter is a very extensive irrigation area situated at the western edge of the Delta Interieur. It is the most important agricultural development project in Mali. Inspired by the Gezira in Sudan, it was created under colonial rule in 1934. The initial very ambitious goal was to irrigate 960,000 hectares to produce sufficient cotton for the French textile industry, and enough food crops for all of French West Africa. These objectives have changed since Independence in 1960. The main crops produced today on 55,000 hectares are rice and sugar cane. The area covers the district of Niono where 165,000 people live in villages scattered in a vast flatland and surrounded by irrigation canals. The community is heterogeneous comprising several ethnic groups often with different perceptions and behaviors. The inhabitants live almost exclusively from rice cultivation (two harvests a year). Between rice seasons vegetables are grown, mostly by women. Extensive use is made of the irrigation

canals for most water-related economic, domestic and recreational activities. Both *S. haematobium* and *S. mansoni* are highly endemic.

The Plateau Dogon is located in the east central part of Mali: the spectacular location of villages either at the top or at the foot of the cliff and the richness of the social, cultural, and religious beliefs make this region one of the most fascinating places for tourists visiting Mali. This is a rocky area where it is tedious to dig wells; therefore the 170,000 inhabitants of the district of Bandiagara rely heavily on residual rain water.

Women are used to travelling very far to collect water for domestic use. The very homogeneous Dogon population live essentially from millet cultivation and vegetable growing, which is traditionally done on small plots of land on top of the rock. The soil needed to make the land suitable for agriculture is imported from various places downhill and the Dogon population have developed original methods of land conservation. In 1970, a small dam building project was started. By 1990, more than 100 dams had been built, leading to an important increase in vegetable production but also an increase in the transmission of schistosomiasis. Prevalence rates of 60–95% for *S. haematobium* infection are common in villages near dams.<sup>1</sup> Although large numbers of *Biomphalaria pfeifferi* were found in many places, very little *S. mansoni* transmission appeared to be occurring.

These two have been the main intervention areas of the National Control Program since 1982. Two villages were randomly selected among all the villages from each of the two areas that had not previously been subject to any intervention by the program (Koundougou and Kokolo in Plateau Dogon; ND11 and Nara in Office du Niger).

**Study design.** The study consisted of an initial survey of a cohort in February 1991, followed by treatment of all individuals, and a follow-up survey 15 months after treatment. During each survey an individual questionnaire was administered and clinical, parasitologic, and ultrasound examina-

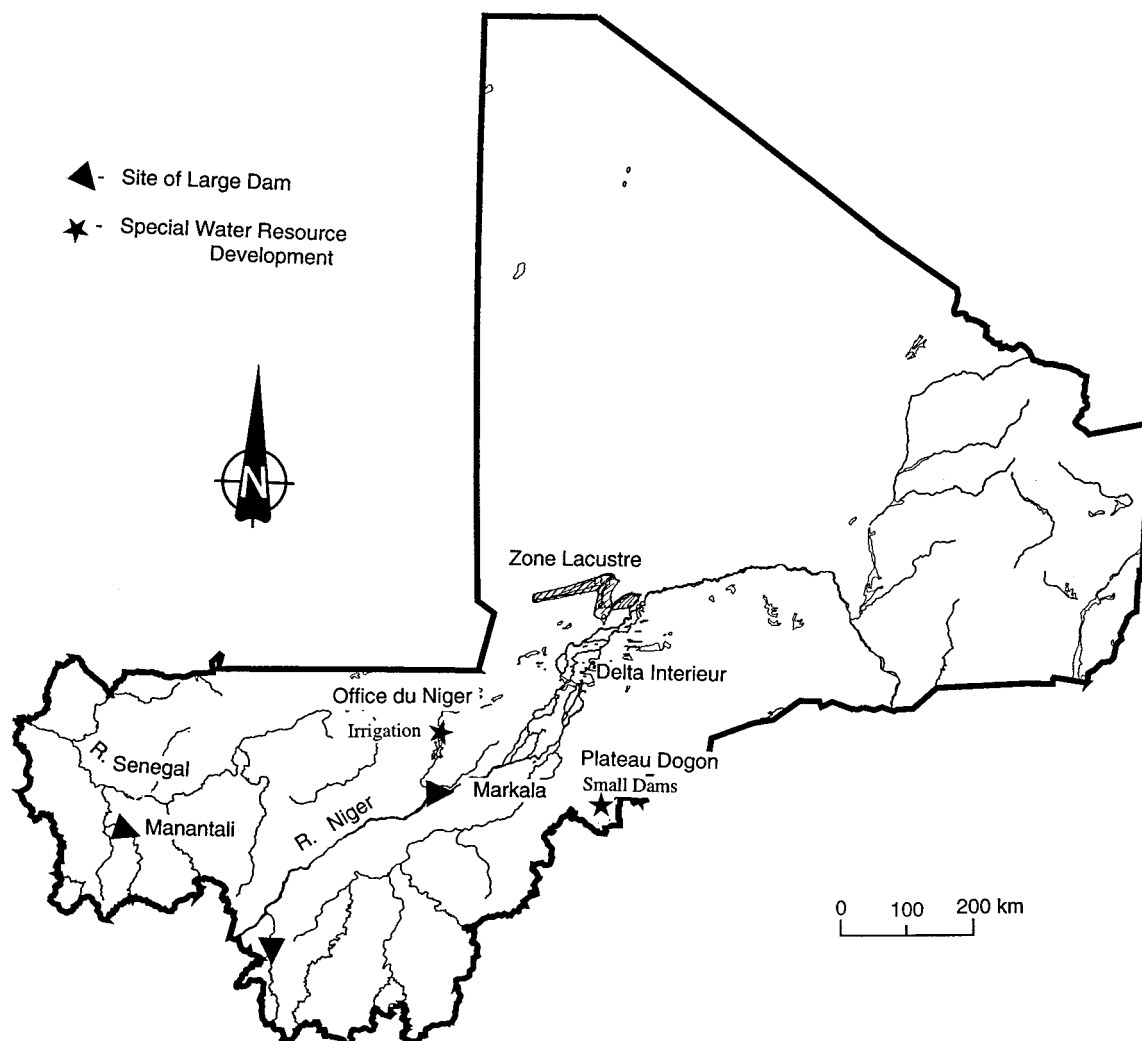


FIGURE 1. Location of study areas in relation to water sources of Mali.

tions were performed. The study population included all inhabitants in the villages greater than two years of age. However, only those who had been examined parasitologically and by ultrasound at baseline were considered eligible for follow up; one village of Plateau Dogon (Kokolo) was excluded from the follow-up survey because of its low level of infection observed at baseline.

The study was approved by the ethical body of the National Institute for Research in Public Health in Mali and the Ethical Committees of Hannover and Bonn Universities. The populations of all villages had been informed in detail during evening assemblies about the study procedure and the teams involved, and their consent was obtained prior to the investigation. All inhabitants were treated for schistosomiasis, and any other disease that was found at clinical examination or sonography was treated according to national standards.

**Investigation.** The entire study population was registered on household forms using a door-to-door survey. The name, surname, age, and sex of all individuals were recorded, and every individual was allocated a unique code of six digits representing village, household and individual numbers.

The questionnaires followed by clinical examination were

administered by two Malian physicians. Individuals were asked if they had suffered from dysuria or macrohematuria during the last month. Height, weight, and blood pressure were measured and other physical conditions, including spleen and liver size, were also recorded.

The reagent strip testing and parasitologic examination of urine were done by the parasitologic team of the National Schistosomiasis Program. A 100-ml screw-top plastic container was labeled with the individual number using an organic solvent-based marker, and given to all individuals in the evening. They were asked to deposit specimen samples in their shower rooms, from where they were collected the following morning by the team going from house to house. The urine samples were first tested for microhematuria and proteinuria with urinary reagent strips (Combur 9; Boehringer, Mannheim, Germany), for 40 sec as recommended by the manufacturer, and then examined using the filtration technique as described by the World Health Organization (WHO).<sup>1</sup> Filtration of 10 ml of urine was done through paper filters with a pore size of one micrometer. The filters were stained with ninhydrin. All eggs on the slides were counted using microscopes with electric light illumination and the

TABLE 1  
Study population by age, sex, and area

Age (years)	Office du Niger		Plateau Dogon		Total (%)	
	Male	Female	Male	Female	Male	Female
0-6	61	40	52	42	113 (22.0)	82 (15.5)
7-14	80	71	44	38	124 (24.2)	109 (20.6)
15-24	45	74	26	33	71 (13.8)	107 (20.3)
≥25	104	124	101	106	205 (40.0)	230 (43.6)
Total	290	309	223	219	513 (100)	528 (100)

results were recorded as egg counts/10 ml of urine. Individuals found negative after a first examination were asked to provide a second specimen the following day.

Ultrasound examination was performed by two experienced Malian and German specialists who were unaware of individual parasitologic findings or results of previous ultrasound or other examinations. Two high-quality portable ultrasound machines SSD-500 (Hellige-Aloka, Freiburg, Germany) equipped with 3.5 mHz convex transducers were used. Photo documentation was done using a P-66 E thermal printer (Mitsubishi Electric Europe, Hatfield, United Kingdom). The examination was done according to the recent proposal of a WHO working group.<sup>2</sup> Care was taken to ensure adequate bladder filling for examination: the pyelon depth (renal pelvis), renal parenchyma, and bladder wall thickness were measured; the pyelon, ureters, and bladder abnormalities were recorded. When a distended renal pelvis was seen, the patient was asked to empty his or her bladder before being re-examined 20 min later to ensure that this was not due merely to stasis caused by a full bladder or vesicourethral reflux.

After the examination, the entire study population was treated with a single dose of praziquantel (40 mg/kg of body weight), regardless of whether they had positive egg counts at survey or not. The treatment was carried out going from compound to compound, using the household forms.

The data collected were entered using Epi-Info (Centers for Disease Control and Prevention, Atlanta, GA); double entry was done and inconsistencies were checked and removed.

The analysis has been restricted to individuals who complied with both parasitologic and ultrasound examinations. The analysis of the reversibility of lesions was restricted to individuals treated after the baseline survey and present at follow-up survey. The population was divided into four age groups: < 7, 7-14, 15-24, and > 25 years; for some analyses they were reaggregated into children (less than 15 years) and adults (≥ 15 years and older).

Individuals were considered positive if any *S. haematobium* eggs were found in the urine sample they had provided and uninfected only after two specimen samples remained negative at re-examination on consecutive days; infection was further classified according to intensity: light (1-49 eggs/10 ml) and heavy (≥ 50 eggs/10 ml). For individuals found to be negative at the first urine examination, those who did not provide a second specimen were excluded from the analysis; those negative at the second examination were considered negative and those found positive were considered positive.

At the ultrasonometric assessment, the following organo-

TABLE 2  
Age-specific prevalence rate of *Schistosoma haematobium* infection by village\*

Village	Age (years)				Total	
	0-6	7-14	15-24	≥25	Examined	Prevalence rate (%)
ND11	52.5	76.3	58.5	37.6	305	53.8
Nara	61.9	93.3	77.3	61.3	294	73.1
Kokolo	17.9	20.5	18.2	7.9	212	13.7
Koundougou	70.9	86.0	88.5	64.2	230	72.6
Overall prevalence	52.8	74.2	62.4	43.2	1,041	55.2

\* Of the four villages studied, ND11 and Nara were in the Office du Niger and the other two in Plateau Dogon.

metric values were considered to be pathologic: a pyelon depth of 10 mm or more (a pyelon depth of 8 mm or more in individuals with a body height less than 121 cm), a renal parenchyma less than 11 mm, and a bladder wall thickness greater than 5 mm.

Any pathologic change was considered as a morbid condition, whether it was perceived by individuals or observed by investigators. Morbidity as used in this paper is the presence of one or more morbid conditions.

## RESULTS

**Study population and infection pattern.** A total of 1,098 individuals were recorded; two urine samples were obtained from 1,091 (99.4%) and 1,041 (94.8%) were examined by ultrasonography. The analysis of infection and morbidity has been restricted to those individuals examined parasitologically and by sonography. The distribution of the population by age and sex and by village is shown in Table 1.

The age distribution was similar in the two areas, although there was a slight under-representation of males in Office du Niger and of those 15-24 years of age in Plateau Dogon. Overall, the proportion of children less than 15 years of age (41.1%) and the male:female ratio (0.97) were slightly below the national figures, which were 43% and 1.03, respectively.<sup>3</sup>

Table 2 shows the age specific prevalence rates of infection by village. The overall prevalence rate of infection was high in all but one village of Plateau Dogon (Kokolo), in which the prevalence was 13.7%. The age-specific prevalence shows the classic pattern with a peak in those 7-14 years of age and a significant decrease afterwards. After adjusting for the confounding effect of village and age the logistic regression analysis showed that males were more frequently found infected than females; (likelihood ratio statistic with one degree of freedom = 5.703,  $P = 0.017$ ).

**Morbidity indicators.** The intensity of infection was in general low: only 10.5% of the population was excreting 50 or more eggs/10 ml; the highest rate of heavy infection was observed in Nara (16.9%). The prevalence rates of the different *S. haematobium*-related morbidity indicators were closely related to the prevalence and the intensity of infection as shown in Table 3. The proportion of individuals with all morbid conditions other than ureter dilatation was the lowest in the village with the lowest prevalence of infection.

Figure 2 shows the pattern of increasing morbidity with increasing intensity of infection. The rates of all morbid conditions were more than twice as high in heavily infected as

TABLE 3

Prevalence rates of *Schistosoma haematobium* infection and the proportion of individuals presenting clinical symptoms and urinary tract abnormalities by village

	ND11	Nara	Kokolo	Koundou-gou	All villages
Infection rate	53.8	73.1	13.7	72.6	55.2
Heavy infection rate*	9.4	16.9	0.4	13.5	10.45
Macrohematuria	32.4	42.8	8.4	25.7	28.5
Dysuria	32.1	45.1	19.7	32.2	32.7
Microhematuria	44.3	57.4	22.1	65.8	47.6
Proteinuria	35.8	51.7	21.6	53.4	40.8
Bladder abnormalities	28.0	30.6	14.7	33.1	27.0
Ureter dilatation	11.0	22.9	12.6	26.1	18.0
Pyelon dilatation	15.7	29.6	5.0	11.4	16.3

\*  $\geq 50$  eggs/10 ml of urine.

in lightly infected individuals (Mantel-Haenszel weighted odds ratio = 2.47, 95% confidence limits = 2.09–2.88;  $P < 0.0001$ ).

A high proportion of individuals had microhematuria and proteinuria as detected by urinary reagent strips, but significantly less had any clinical symptoms: 28.5% reported gross hematuria and 32.7% reported dysuria during the last month following the survey.

The most common bladder abnormalities as detected by sonography were bladder wall irregularities (20.2%) and bladder wall thickening (10.3%). Bladder masses and polyps were observed less frequently in 7.6% and 2.7% of the individuals, respectively. Ureter and pyelon dilatation were not uncommon; even in the low prevalence village of Kokolo, they were observed in 12.6 and 5% of the population, respectively. Bladder calcification and calculi were observed in only three individuals.

**Age-related pattern of infection and morbidity.** Table 4 shows the age specific prevalence rates of infection and of urinary tract lesions. Infection and morbidity follow the

TABLE 4

Age-specific prevalence rates of infection and of morbid conditions by age, all villages combined

	Age (years)				All ages
	2–6	7–14	15–24	$\geq 25$	
Infection rate	52.8	74.2	62.4	43.2	55.2
Heavy infection rate*	10.7	23.8	7.1	4.8	10.4
Macrohematuria	33.3	50.2	34.1	12.9	28.5
Dysuria	26.6	32.0	33.5	36.1	33.0
Microhematuria	43.1	71.5	49.5	36.1	47.6
Proteinuria	44.7	62.1	41.3	27.6	40.8
Bladder abnormalities	32.9	44.8	21.6	17.2	27.0
Ureter dilatation	18.8	29.9	14.6	12.7	17.9
Pyelon dilatation	12.1	16.6	22.7	15.3	16.2

\*  $\geq 50$  eggs/10 ml of urine.

same age-related pattern: higher in children than in adults, with a peak prevalence occurring at 7–14 years of age.

Adjusting for the confounding effect of village and sex, the logistic regression analysis showed that children less than 15 years of age were at least twice as likely to have an infection and urinary tract lesions than individuals 15 years of age or older. Only dysuria was significantly more frequent in adults than in children and pyelon dilatation was observed in all age groups with similar frequencies. Similarly, when adjusted for the confounding effect of village and age, all the morbid conditions but microhematuria, proteinuria, and pyelon dilatation were more frequently observed in males than in females.

**Sensitivity of urinary reagent strip testing.** The sensitivity and specificity of reagent strip testing for hematuria and proteinuria were evaluated using two urine samples examined by the filtration technique as the standard. Microhematuria was more sensitive than proteinuria: 73.3% compared with 59.1%, but the specificities of the two tests were similar: 84.2% and 81.9%.

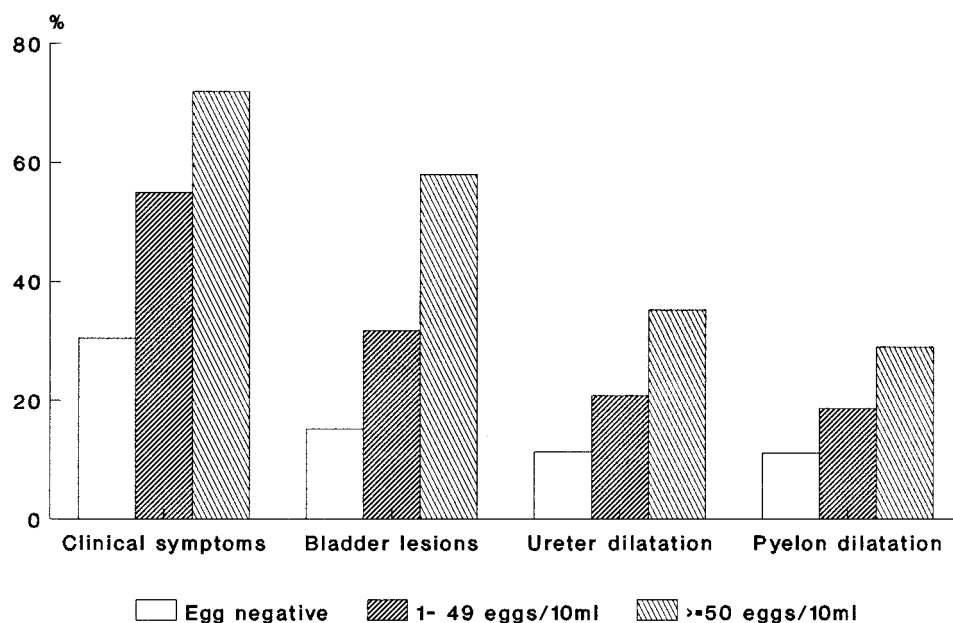


FIGURE 2. Age-specific prevalence rates of mixed infections with both *Schistosoma haematobium* and *S. mansoni* at baseline and one and two years following treatment in Office du Niger, Mali.



TABLE 5

Specificity and sensitivity of urine filtration, reagent strip testing for microhematuria, and history of gross hematuria in detecting individuals with morbid conditions\*

	Total cases	Filtration		Microhem		Macrohemat	
		Sens	Spec	Sens	Spec	Sens	Spec
Macrohematuria†	311	81.0	55.7	77.0	64.3	—	—
Dysuria†	357	62.5	48.6	55.4	56.1	46.9	80.4
Bladder shape abnormal	30	60.0	44.9	43.3	52.0	36.7	71.2
Bladder wall thick	107	86.0	48.3	82.5	56.1	70.9	74.8
Bladder wall irregular	220	75.5	50.5	73.5	59.0	65.1	76.7
Bladder masses	79	92.4	47.8	84.8	55.3	75.9	74.4
Bladder polyps	28	96.4	45.8	92.9	53.4	75.0	72.4
Ureter dilatation	196	71.4	49.0	69.5	57.3	61.6	75.5
Pyelon dilatation	178	69.1	47.7	59.5	54.6	48.0	72.8

\* Sens = sensitivity; Spec = specificity; Microhem = reagent strip testing for microhematuria; Macrohemat = history of gross hematuria.

† These refer to current history.

Table 5 shows a summary result of the sensitivity of reagent strips compared with that of the urine filtration technique in detecting individuals with morbid conditions. More than 80% of the bladder lesions could be detected by reagent strip testing for microhematuria. This test was more sensitive in detecting bladder pathology than in detecting egg positive urine (80% compared with 73%). Its sensitivity was relatively poor only with bladder shape abnormality and pyelon dilatation. However, overall it was as sensitive as parasitologic examination in detecting individuals with any urinary tract morbidity; the sensitivity of proteinuria was in general significantly lower.

#### Reversibility of morbid conditions following treatment.

One village of Plateau Dogon (Kokolo) was excluded from the follow-up investigation for the assessment of reversibility of lesions because of its low prevalence rates of infection and morbidity at baseline. In the three remaining villages, 705 individuals had their urine examined at baseline and one year after treatment; 682 (96.7%) complied with the clinical examination and 648 (91.9%) with the sonographic examination.

Table 6 shows the prevalence rates of infection and of morbidity indicators at the two surveys and the rates of reversion and conversion. The rate of reversion is the proportion of individuals found noninfected (or free of a morbid condition) at the follow-up survey of those who were infected or had the condition at baseline; the conversion rate is the proportion of individuals found infected or with a morbid condition at follow-up of those who were not infected or were within normal limits at baseline.

More than 80% of all urinary tract lesions had cleared one

year after treatment. Adults and children had similar reversion rates (Mantel-Haenzel weighted odds ratio = 0.8, 95% confidence limits = 0.48–1.34). The reversion rates of bladder shape abnormalities and pyelon dilatation were significantly lower than those of bladder polyps and ureter dilatation.

#### DISCUSSION

Since 1982, the overall objective of schistosomiasis control in Mali has been defined as “to reduce the prevalence of infection to a level below which it is no longer of public health importance, in all areas”.<sup>1</sup> This level of public health importance was arbitrarily set to a prevalence of 20% for all infections and of 5% for heavy infection (50 or more eggs/10 ml in urine, more than 100 eggs/gram in stools). It was assumed that this corresponded to the minimum level of morbidity in the community that would require active intervention. Recently, when the emphasis of the global policy of schistosomiasis control has shifted from transmission control to morbidity control,<sup>4</sup> the Malian health authorities, as those of most endemic countries, were confronted with the problem of defining the type and level of morbidity that would need to be controlled. The introduction of ultrasonography in community based studies has substantially contributed to filling the gap, making it possible to assess schistosomiasis-related morbidity in field conditions in a non-invasive and relatively inexpensive way.<sup>5,6</sup>

The objective of the Malian study was to assess morbidity due to schistosomiasis, but above all to define the relationship between infection and morbidity. It was one of the first investigations covering entire communities; most of earlier studies were limited to children or infected individuals. Our study covered villages from those with a low prevalence of infection (less than 20%), to very high prevalence of infection (more than 70%); therefore, it provides information on the influence of different endemicity levels.

The prevalence rates of clinical symptoms related to *S. haematobium* infection (gross hematuria and dysuria) were surprisingly low if compared with the rates of infection and of microhematuria. Assuming that a proportion of the population surveyed might have falsely reported symptoms (as is often the case) to get free treatment, the true rate of clinical symptoms may be even lower. As a result, the number

TABLE 6

Prevalence rates of infection and of morbidity in 1991 and 1992: reversibility of lesions

	Number examined	Prevalence 1991	Prevalence 1992	Conversion rates	Reversion rates
Infection	705	66.7	17.7	9.8	78.3
Macrohematuria	682	33.0	11.6	5.9	76.9
Dysuria	682	36.0	22.3	10.8	57.1
Bladder shape abnormal	648	25.5	15.0	10.1	70.9
Bladder polyps	648	11.8	4.6	3.7	88.2
Ureter dilatation	648	17.0	4.9	2.5	83.3
Pyelon dilatation	648	16.4	11.1	7.7	71.4

of individuals not becoming ill at the early stage of *S. haematobium* infection in Mali is probably very high; a control strategy based on passive case detection for morbidity is therefore likely to cover only very late stage complications of the disease, especially if the drugs are not free. Although macrohematuria has always been considered as associated with urinary schistosomiasis, this confirms its transitory or intermittent and painless nature.<sup>7</sup>

This study showed that urinary tract lesions were frequent, especially in study villages with high prevalence rates of infection. As reported by many investigators, children had higher rates of infection, heavy infection, and pathologic lesions than adults.<sup>5, 8, 9</sup> One third of the 7–14-year-old children had ureteric dilatation and about half of them had bladder lesions; similar figures were reported from Tanzania.<sup>10</sup> Bladder lesions included mostly bladder polyps, bladder wall thickening, and irregularities. Bladder calcification, suggested to be the most characteristic lesion of *S. haematobium* infection and an important risk factor for bladder cancer, was rarely seen.<sup>11</sup> This is in accordance with reports from Tanzania.<sup>5</sup> One study<sup>12</sup> did not find a correlation between ultrasonography and radiographic examinations for the detection of bladder calcification; the location of bladder calcifications mostly in the anterior part of the bladder was considered to be the main reason.<sup>13</sup> More than 15% of the population studied had pyelon dilatation, and they were therefore at risk of developing renal function impairment. This late-stage complication of urinary tract lesions was most frequent in adolescents but was also observed in children less than seven years of age; even in the very low prevalence village of Kokolo, 5% of the population had pyelon dilatation. This demonstrates either a high baseline of nonschistosomal pyelon dilatation or high noise level in the assessment or it confirms the view that even in very low endemic areas a few infected individuals may still be subject to severe morbidity.<sup>7</sup> A third possibility is that pyelon dilation remains when bladder lesions clear.

Microhematuria was shown to be closely related to the presence of infection as has been observed in various places.<sup>14–16</sup> Our study showed that reagent strip testing was as sensitive as and more specific than urine filtration in detecting individuals with urinary tract pathology. Similar results were reported in another study.<sup>5</sup> Compared with microhematuria, a history of gross hematuria was more specific and had a reasonably good sensitivity in detecting morbid conditions. This makes reagent strip testing for microhematuria and history of gross hematuria appropriate methods for the monitoring of morbidity control.

Earlier studies gave conflicting views on the regression of urinary tract pathology: observing gross lesions by intravenous pyelography, several studies reported that the resolution of uropathy after treatment was very limited.<sup>17–19</sup> Others found that many lesions were reversible especially in children.<sup>20–22</sup> The limited resolution observed in the 1960s could possibly be due to the lower efficacy of the drug available at that time. Our result is in agreement with those of most recent studies.<sup>23–27</sup> More than 80% of the urinary tract lesions were cleared one year after treatment with praziquantel; pyelon dilatation had the lowest clearance rate in our study, this may be due to irreversible damage caused to the renal parenchyma. This high clearance rate following treatment

leaves no doubt that chemotherapy will continue to play a major role in the control of morbidity due to schistosomiasis.

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