

ULTRASONOGRAPHY IN A SENEGALESE COMMUNITY RECENTLY EXPOSED TO *SCHISTOSOMA MANSONI* INFECTION

RUEDIGER KARDORFF, FOEKJE F. STELMA, ANNA-K. VOCKE,
YAZDAN YAZDANPANAH, ANNA K. THOMAS, AMADOU MBAYE, IDRISSE TALLA,
MALICK NIANG, JOCHEN H. H. EHRICH, EKKEHARD DOEHRING, AND
BRUNO GRYSSELS

Department of Pediatrics, Medizinische Hochschule Hannover, Hannover, Germany; Laboratory of Parasitology, University of Leiden, Leiden, The Netherlands; Institut Pasteur, Lille, France; District Sanitaire de Richard Toll, Richard Toll, Senegal; Service Regional de la Sante, Saint Louis/Richard Toll, Senegal; Humboldt University, Charite, Berlin, Germany; Interdisziplinäres Therapiezentrum, Feldberg, Germany; Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium

Abstract. Inhabitants of Ndombo ($n = 614$), a village in an area recently infected with *Schistosoma mansoni* in Northern Senegal, were examined clinically, parasitologically, and ultrasonographically to investigate the presence and degree of *S. mansoni*-related hepatosplenic morbidity after a few years of exposure to schistosomal infection of regional canals. Despite previous praziquantel treatment of 56% of the inhabitants prior to our investigation, the prevalence of *S. mansoni* infection in 1993 was 90%, and 42% of the villagers excreted more than 1,000 eggs per gram of stool. Previously untreated individuals were found to have significantly higher egg counts than treated ones. Despite the high intensities of infection, ultrasonographically detected severe periportal thickening of the liver was infrequent. Grading according to body length-dependent normal values of cross-section diameter of peripheral portal vein branches of a European control group correlated with intensities of infection. Of the total group of patients, 30% ($n = 182$) had more severe thickening of portal vein branch diameters above the 97th percentile and 70% of these had a splenomegaly. The highest egg counts and the most frequent development of periportal thickening were found in 11-20 year-old individuals. Periportal thickening was less frequent in praziquantel-treated adolescents than in untreated ones. This suggests that early antischistosomal medication may be useful to limit schistosomiasis-induced hepatic morbidity especially in children, even though reinfection seems inevitable.

Ultrasonography is generally accepted as a valuable method for the study of hepatosplenic involvement in schistosomiasis¹ and for monitoring the reversibility of *Schistosoma mansoni*-related morbidity after treatment with praziquantel.^{2,3} Classical features of hepatosplenic schistosomiasis arise from periportal thickening of the liver, visualized as echogenic portal vein wall thickening on scanning.⁴ Although periportal fibrosis is known to be a chronic complication, the time-lapse for its evolution remains unclear.

The first case of *S. mansoni* infection in the area of Richard-Toll in northern Senegal was reported in 1988.⁵ Transmission was established and the infection spread rapidly^{6,7} as a consequence of ecologic changes after the construction of a dam on the Senegal river.

The rural Ndombo community is currently being investigated for the study of the immunoepidemiology in early stages of endemicity,⁶ and also constitutes a unique opportunity to monitor the onset and early development of *S. mansoni*-related hepatosplenic morbidity in an untreated population. Since parts of the community had received praziquantel prior to our study, the influence of early antischistosomal treatment on the early development of hepatosplenic morbidity could also be studied.

PATIENTS AND METHODS

The present study took place in Ndombo, a rural village of approximately 4,000 inhabitants located 4 km from Richard-Toll along a canal that connects the Senegal River with the nearby Lac de Guiers⁸ in September-October 1993 at the end of the hot and rainy season. It was part of an epidemiologic study designed by Gryseels and others^{6,8} in which four randomly selected population samples of approximately

400 villagers each were examined at eight-month intervals. Each cohort was a representative selection of the total village population in respects to age, sex, and occupation. We investigated the fourth cohort before treatment, and part of the first cohort, which had been treated twice before within two years. Details of epidemiologic and parasitologic methods are described elsewhere.^{6,8,9}

From each participant, two stool samples were collected between August and October 1993 and examined by a modified Kato-Katz method¹⁰ using two 25-mg slides per stool sample. The individual egg counts were calculated as the sum of the four Kato slides multiplied by 10 to give eggs per gram (epg) of stools. The clinical examination consisted of a standardized interview in the local language, a physical investigation according to Stelma and others,⁹ and a thick blood film to detect malaria infection.

Ultrasonography was performed according to international protocols¹¹ by experienced observers, using two portable machines (SSD-500; Hellige-Aloka, Freiburg, Germany, with a 3.5-MHz convex transducer, and SDR 1550 XP; Phillips, Eindhoven, The Netherlands, with a 3.0-MHz sector transducer). The ultrasonographic investigation included measurements of liver and spleen, possible signs of portal hypertension, and grading of periportal thickening.¹¹⁻¹³ The normal range of organ dimensions in growing individuals is closely related to age and body length; thus, to be able to compare organ sizes throughout all age groups, measurements were analyzed using body length-related normal values, and organomegaly was defined as organ size greater than two standard deviations in the respective body length class of a large reference population.¹⁴ The abdomen was carefully examined to rule out congestive changes and liver disorders unrelated to *S. mansoni* infection. All examinations

TABLE 1
Age distribution of the study population

Age (years)	No.	Group previously untreated	Group previously treated
0-10	238 (39%)	128 (48%)	103 (31%)
11-20	149 (24%)	57 (21%)	91 (27%)
21-40	133 (22%)	47 (18%)	82 (25%)
>40	94 (15%)	34 (13%)	58 (17%)
Total	614*	266	334

* No data on previous treatment available in 14/614.

were done without the observers being aware of individual parasitologic and clinical findings, or prior ultrasonography results.

For ultrasonographic grading of the echodense zones around the portal tree, the Cairo classification measures cross-section diameter of peripheral portal vein branches at three different locations. Jenkins and Hatz¹¹ suggested that measurements should be made "after the bifurcation, between the first and the third branching-points" (outer-to-outer measurements). We measured all cross-section diameters after the second intrahepatic branching point. To establish normal values of peripheral portal vein branches, a European control group of 160 healthy people was examined sonographically by one of the observers. Body length dependent normal values were defined and the Senegalese findings were evaluated on the basis of these data. Minor pathology was interpreted as two standard deviations above the mean body length-dependent normal value, more severe lesions as measurements above three standard deviations. To detect interobserver variations for the method, 190 villagers were re-examined by two independent sonographers (RK and YY). After the examination, all *S. mansoni*-infected participants, except pregnant women, were treated with a single dose of praziquantel (Biltricide®; Bayer, Leverkusen, Germany), 40 mg/kg of body weight. If other diseases were detected, the patients were treated according to local standards and referred to the local health service. The studies were approved by the Ministry of Health in Dakar, Senegal, the local health authorities, and the ethical committees of the Universities of Bonn and Hannover.

RESULTS

A total of 614 Senegalese villagers (336 females and 278 males) were enrolled into the study. Their ages ranged from four months to 80 years (Table 1). Although cohort 4 had not yet been examined or treated in the framework of on-going epidemiologic studies, many individuals of this group reported having received treatment in health centers. Therefore, we regrouped the study population accordingly. Of 600 individuals, 334 (56%) reported a history of previous praziquantel treatment, while 266 subjects (44%) stated not to have been treated before.

In the total study population, the prevalence of *S. mansoni* infection was 90%. Of those patients not treated before, 45% excreted more than 1,000 epg, compared with 33% in the previously treated group.

On ultrasound scanning, not a single case of severe hepatosplenic pathology was detected. Only mild and moderate

TABLE 2
Proportion of patients with periportal thickening according to *Schistosoma mansoni* egg excretion (compared with height-dependent normal values of a European control group)*

Periportal thickening SDS	Egg excretion			Total n (n = 613)
	0 epg	1-1,000 epg	>1,000 epg	
Normal, < +2 SDS	11%	55%	34%	431
+2 to +3 SDS	12%	48%	40%	121
> +3 SDS	5%	34%	61%	61

* SDS = standard deviation score; epg = eggs per gram (of feces).

periportal thickening was seen. The measurements of normal periportal vein branches in 160 Europeans showed a correlation with body height. The Cairo Score adjusted to these normal values of body length-dependent portal vein branch diameters revealed that 30% (n = 182) of the Senegalese population had cross-section diameters above two standard deviation scores of healthy Europeans. We found values above three standard deviations in 10% (n = 61). As demonstrated in Table 2, the degree of periportal thickening with this classification showed significant differences ($P = 0.0018$, by chi-square test) according to intensity of *S. mansoni* infection.

All untreated villagers without *S. mansoni* infection (n = 34) had normal findings. Previously treated people showed slightly less abnormal branch diameters than untreated villagers (19% and 25%, respectively), even in those with infections more than 1,000 epg (11% and 13%, respectively).

The interobserver variation results of measurements of periportal thickening are summarized in Table 3. The two observers produced identical results in 106 (56%) of the cases. In 74% of the cases, the deviation between the two observers was 1 mm or less, while it was more than 3 mm in 3%.

While sonographically detected splenomegaly occurred in 33% (n = 203) of the total group, 43% of the villagers with enlarged portal vein branches between two and three standard deviations had a splenomegaly, compared with 70% of those above three standard deviations ($P < 0.001$, by chi-square test). The proportion of height-related spleen enlargement correlated significantly ($P < 0.001$, by chi-square test) with *S. mansoni* egg counts (Figure 1). Mainly children four months to ten years of age were affected, with a splenomegaly rate of 54%. Of 350 malaria smears, 16 (5%) were positive for *Plasmodium falciparum* with 1-5% parasitemia. These cases were evenly distributed among *S. mansoni* egg count groups.

TABLE 3
Interobserver variance in measurements according to the Cairo classification

Observer A	Periportal thickening				Total
	B Grade 0 <3 mm	Grade 1 3-5 mm	Grade 2 5.1-7 mm	Grade 3 >7 mm	
Grade 0	0	0	0	0	0
Grade 1	8	89	16	0	113
Grade 2	0	59	17	0	76
Grade 3	0	0	1	0	1
Total	8	148	34	0	190

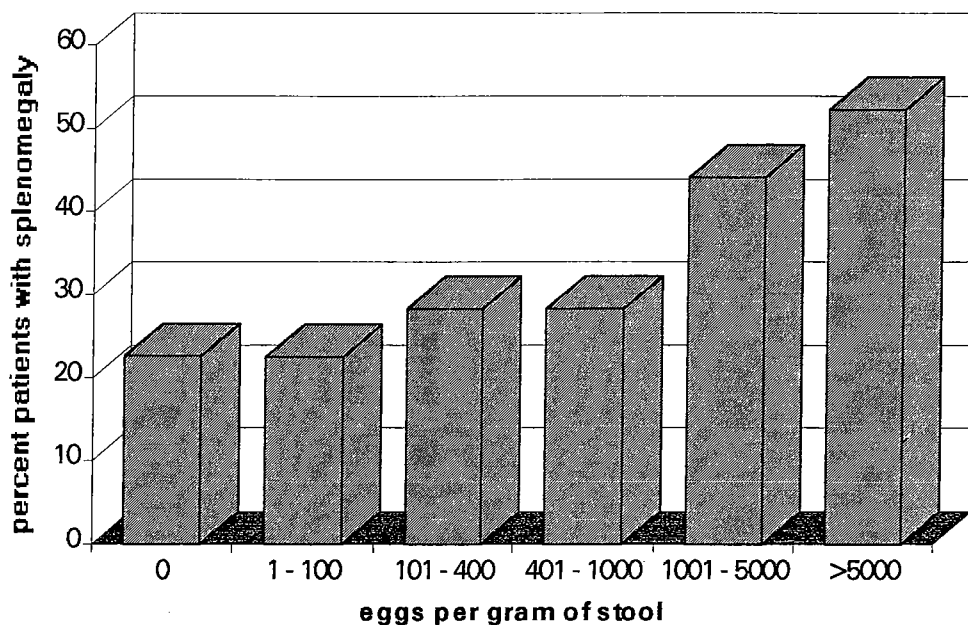


FIGURE 1. Proportion of patients with splenomegaly according to intensity of *Schistosoma mansoni* infection.

No ascites or other signs of congestion were found in any of the individuals. Hepatomegaly occurred mainly in children. Enlargement of the left lobe was detected in 38 individuals (6%), 34 of them being *S. mansoni*-positive. The right liver lobe was enlarged in 76 cases (12%), 69 of them being infected.

Enlargement of the gallbladder wall of more than 6 mm was found in six patients, all of them being infected with 1–1,000 epg. No hepatic alterations were found in two of them, whereas three had moderate periportal thickening. The sixth individual, a young woman, was the only patient with more severe *S. mansoni*-related morbidity, portal vein branch diameters above three standard deviation values, splenomegaly, gallbladder wall thickening, and portofugal collaterals.

DISCUSSION

The outbreak of *S. mansoni* infection in the study area, leading to a 90% infection prevalence within a few years,^{5,7} presents a unique opportunity to study onset and development of *S. mansoni*-related morbidity in a presumed non-immune community. The parasitologic results confirm that the Ndombo population ranks among the most heavily infected in the world.¹⁵ Nevertheless, our ultrasound results demonstrated very little severe hepatosplenic pathology, as suggested by a previous clinical study⁹ and an earlier preliminary ultrasound investigation.¹⁶

Ultrasonographic grading of *S. mansoni*-induced periportal thickening of the liver is based upon the diameters of peripheral portal vein branches.¹¹ Our investigation of peripheral portal vein branch diameters in healthy Europeans showed that values are age- and body height-dependent. In the Senegalese population examined, a positive correlation was found between branch enlargement and egg output. Furthermore, there was a close correlation between branch enlargement and prevalence of splenomegaly. Thus, using the Cairo classification modified for a pediatric population, we

detected a mild prevalence of early *S. mansoni*-related hepatosplenic alterations. However, the value of our body length-dependent normal diameters is limited because norms of African populations may show a different range.

The lack of ultrasonographically detectable severe hepatosplenic morbidity in this focus mirrors the findings of our group in endemic regions in Mali.¹⁷ For yet unknown reasons, severe morbidity as seen in Sudan, Egypt, Zimbabwe, and east African foci^{15, 18–20} seems to be rare in western Africa. Possible explanations for these geographic variations may include immunogenetic factors, parasite strain differences,^{21, 22} concomitant infections, or toxins. However, in the Senegalese focus, the recent exposure to *S. mansoni* would be an obvious alternative explanation.

While hepatomegaly occurred only in a small number of children, splenomegaly was present in one-third of the individuals. The prevalence of splenomegaly correlated with egg counts. Malaria was infrequent and evenly distributed among the egg count groups. Thus, schistosomiasis appears to be the main cause of splenomegaly in this focus. In view of the minor hepatic alterations, it seems as if splenomegaly was not caused by portal hypertension, but probably directly by egg-induced reactions.⁴

Although many individuals had received praziquantel treatment prior to the study, a large proportion of these were heavily infected. However, treated patients had a slightly lower prevalence of periportal thickening than persons without prior treatment. This may be due to reversibility of pre-existing lesions after treatment, as demonstrated earlier in Sudanese children,² or to a protective effect of early treatment against the early development of lesions, possibly by shortening the duration of infection.

Untreated adolescents were the most heavily infected and presented with the highest percentage of periportal thickening. These findings are in accordance with previous studies in Sudan^{12, 23} and show the need to focus further treatment efforts on this age group because even in this recently in-

ected, presumably nonimmune community, children and adolescents seem to be at the highest risk for intense infection and periportal thickening of the liver.

Comparing different ultrasound methods for grading of periportal thickening in schistosomiasis^{11,13} resulted in problems exceeding those reported previously by Jenkins and Hatz.¹¹ It is mainly the distinction between normal and mildly abnormal findings that remain a point of discussion. The Cairo classification, recently established to minimize inter-observer variation, is based upon single millimeter differences of portal vein branches.¹¹ In our study, examinations by two independent observers gave the same grading in only 56% of the cases, 74% of results differed only up to 1 mm, and 3% deviated more than 3 mm. Thus, even after establishing of the body length–modified Cairo classification, these data show that ultrasonographic quantification of early and mild *S. mansoni* morbidity still remains difficult, irrespectively of the method used. In conclusion, a second consensus conference seems to be necessary to establish a grading system of *S. mansoni*-related morbidity.

In summary, the assumed five-year exposure of the Senegalese community to *S. mansoni* resulted in high intensities of infection. However, this was not paralleled by severe hepatosplenic morbidity detectable by ultrasound. For detection of mild periportal thickening, the newly established body length–dependent modified Cairo classification showed the best correlation with the number of excreted eggs. Untreated adolescents had the highest intensities of infection and consequently a slightly higher percentage of periportal thickening. Previously treated individuals had lower morbidity despite being heavily reinfected. Thus, early antischistosomal treatment appears to reduce early and mild hepatic morbidity although it does not prevent reinfection. The population in our study area as well as those in other new endemic areas have to be closely monitored, since severe periportal thickening may develop as a result of more chronic infections over the following years.

Acknowledgments: We thank all villagers and leaders of Ndombo, especially A. Taye, for participation, and the field team and their supervisor S. Sow for dedication and excellent technical assistance. We are also grateful to Mrs. A. Iwanowski, Dr. G. Schuler, and all teachers and pupils of the Sankt Ursula-Schule in Hannover for acting as a control population, to H. Geerlings for professional assistance in statistical analysis, and to Martin Mills and Jennifer Hails for reviewing the manuscript. This study is part of a project of the European Special Programme for Operational and Integrated Research (ESPOIR) on schistosomiasis in northern Senegal. The praziquantel used in this study was donated by Bayer AG (Leverkusen, Germany).

Financial support: This investigation received financial support from the European Community (Science and Technology for Development III; grant number TS3-CT-910 041) and the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (grant number ID 900 286).

Authors' addresses: Ruediger Kardorff and Anna-K. Vocke, Department of Pediatrics, Medizinische Hochschule Hannover, 30623 Hannover, Germany. Foekje F. Stelma, Laboratory of Parasitology, University of Leiden, PO Box 9605, 2300 RC, Leiden, The Netherlands. Yazdan Yazdanpanah, Department of Gastroenterology, Hopital Claude Huriez, 2 Avenue Oscar Lambert, 59327 Lille Cedex, France. Anna K. Thomas, Institute of Medical Parasitology, University of Bonn, Sigmund-Freud-Strasse 25, 53127 Bonn, Germany. Amadou Mbaye, District Sanitaire de Richard Toll, Senegal. Idrissa Talla, Service Regional de la Sante Saint Louis/Richard Toll, PO

Box 394, Saint Louis, Senegal. Malick Niang, Ministry of Health, PO Box, Dakar, Senegal. Jochen H. H. Ehrich, Pediatric Nephrology, Humboldt University, Charite, Schumannstr. 20/21, 10117 Berlin, Germany. Ekkehard Doehring, Interdisziplinäres Therapiezentrum, Paßhoehle 5, 79868 Feldberg, Germany. Bruno Gryseels, Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium.

Reprint requests: Ruediger Kardorff, Department of Pediatrics, Medizinische Hochschule Hannover, 30623 Hannover, Germany.

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