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Schistosoma mansoni-related morbidity on Ukerewe Island, Tanzania: clinical, ultrasonographical and biochemical parameters

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Summary One thousand six hundred and ninety-five inhabitants of 3 rural villages on Ukerewe Island, Lake Victoria, Tanzania, were examined by clinical, parasitological, ultrasonographic and—in part—serological means to evaluate *Schistosoma (S.) mansoni*-related morbidity on a community level. Villagers frequently complained of typical colitis symptoms (abdominal pain 80.1%, bloody stools 43.1%, diarrhoea 35.1%); haematemesis, on the other hand, was rare (and reports doubtful in most cases). 16.9% of the population had been given praziquantel previously. Overall *S. mansoni* prevalence was 86.3%, with a median egg output of 176 eggs per gram (e.p.g.) and a maximum output of 17 984 e.p.g. Children and adolescents were infected more severely than adults, men more severely than women. Pretreated individuals excreted significantly fewer ova (median 124 *vs* 192e.p.g., $P<0.001$).

Hepatomegaly (determined by ultrasonography) was present in 35%, splenomegaly in 80%. Organomegaly was significantly related to egg output. Pretreated persons had lower rates of splenomegaly and left lobe hepatomegaly. Low-degree periportal fibrosis was common, while severe grades of fibrosis (MANAGIL score II and III) were present in about 6%. About 10% had other abnormalities on liver sonography (irregular parenchymal texture and/or shape); these persons passed significantly more *S. mansoni* ova than others. Clear sonographic signs of portal hypertension were seen in 2.1%. Serum procollagen-IV-peptide and γ-glutamyl-transferase levels were increased in persons with severe periportal fibrosis, irregular liver texture or portofugal collateral vessels.

Thus, *S. mansoni* infection in the western part of Ukerewe Island is frequent and often severe, leading to a high prevalence of gastrointestinal symptoms. Hepatosplenic involvement does occur, although symptomatic cases of portal hypertension were not identified beyond doubt. The overall level of schistosomal morbidity is thus considered intermediate. Serum procollagen-IV-peptide may be a promising marker of schistosomal liver disease. Our data suggest that *S. mansoni* infection may also be related to diffuse liver parenchyma alterations in this area.

keywords *Schistosomiasis mansoni*; ultrasonography, morbidity, epidemiology, children, procollagen, Tanzania

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Introduction

Schistosoma mansoni-related morbidity varies considerably between different foci; in Africa, hepatosplenic involvement with symptomatic portal hypertension has been reported from Sudan (Homeida *et al.* 1988a, b; Saad *et al.* 1991), Egypt (Abdel-Wahab *et al.* 1990), Zimbabwe (Davidson *et al.* 1991; Houston *et al.* 1993) and Cameroon (Nko'O Amvene *et al.* 1993), while studies from West Africa (Kardorff *et al.* 1994; 1996) did not reveal major liver disease despite similar endemicity of the infection. Efforts are made to map the geographical distribution of *S. mansoni*-related morbidity in Africa through population-based studies, with the aim of identifying pathophysiologically important differences between 'low morbidity' and 'high morbidity' areas (Doehring-Schwerdtfeger & Kardorff 1995). This study was the final part of a multicentre approach to this end which had then covered endemic areas in Mali, Senegal, Uganda and Madagascar with community-based surveys.

In these studies, in addition to clinical examination, ultrasonography was used to detect and quantify hepatosplenic schistosomal disease. The validity of ultrasound in the detection of late-stage schistosomal periportal fibrosis was convincingly demonstrated by Homeida *et al.* (1988a) and Abdel-Wahab *et al.* (1989). However, its accuracy in quantifying low-grade liver involvement has repeatedly been questioned (Hatz *et al.* 1992b). To test another approach to this problem, measurements of serum levels of soluble connective tissue peptides and liver enzymes were included in this study. Type III and IV collagens as well as laminin are major constituents of the extracellular matrix of the liver; they accumulate in liver fibrosis (Gressner 1991; Schuppan 1991). During fibrogenesis, procollagen peptides and the P1 fragment of laminin are increasingly secreted into serum. Procollagen III peptide (PIIINP) and laminin P1 serum levels have been shown to be increased in severe hepatosplenic schistosomiasis and to decrease after praziquantel treatment (Mincis *et al.* 1990; Zwingenberger *et al.* 1990b; Shahin *et al.* 1992). Studies of procollagen IV peptide (NC1) in schistosomiasis do not exist to the best of the authors' knowledge.

γ-Glutamyl-transferase is an enzyme of the biliary canalicular membrane. Its serum activity is known to increase in biliary diseases and other liver abnormalities mainly confined to portal tracts. ALT measurements were included to control for liver cell injury which is not a typical feature of schistosomiasis, but for hepatocellular diseases which are of differential diagnostic importance.

Study population, material and methods

Ukerewe Island is situated a few miles off the Tanzanian shore of Lake Victoria, near Mwanza. Between October 1994 and January 1995, 1695 inhabitants of the western region of the island were examined for *S. mansoni* infection and related morbidity of liver, spleen and gastrointestinal tract. To ensure representative population samples, all families from the villages Gallu, Muritilima and Muriti were registered under code numbers, and participating families were selected by means of a computer random number generator.

All selected individuals were examined ultrasonographically and parasitologically as outlined below. Due to constraints in manpower and study time, only the first 911 patients could be clinically examined. Study participants were asked for a stool sample, from which three 41.7 mg Kato slides were prepared using Helm test kits (AK Industria e Comercio Ltd, Belo Horizonte, Brazil) and analysed for *S. mansoni* ova by light microscopy (double count of each slide). In cases of major discrepancy between the readings, and in every case with negative counts, the individuals were asked to produce another sample the following day which was analysed in an identical fashion. Individual egg output was expressed as e.p.g. (arithmetic mean of all slide counts available from one person, multiplied by 24).

Villagers were asked if they had experienced diarrhoea (more than 3 loose stools per day), abdominal pain or faecal blood during the preceding 2 weeks, whether they had ever had haematemesis, and whether and how often they had ever been treated for schistosomiasis. On clinical examination, liver and spleen size below costal margin, rounded liver edge, firmness of organs and *caput medusae* were recorded. Clinical hepatomegaly was defined as a liver surpassing the costal margin by more than 5 cm

in sternal or more than 4 cm in midclavicular line; relevant splenomegaly was diagnosed when the spleen surpassed the costal margin by more than 2 cm.

Ultrasound examination was conducted by experienced observers (RK and NS) according to established protocols (Jenkins *et al.* 1992). A portable ultrasound scanner was used (Aloka SSD 500; Hellige-Aloka, Freiburg, Germany), equipped with a 3.5 MHz curved array transducer. To quantify periportal liver fibrosis, the grade according to the MANAGIL-classification (Doehring-Schwerdtfeger *et al.* 1989) was established and peripheral portal branches were measured according to the CAIRO classification (Jenkins *et al.* 1992). We measured liver and spleen sizes, portal vein diameter, classification of liver texture and echogenicity and screened for portofugal collateral veins. For age-independent analysis of organometric data, we transformed absolute values into standard deviation scores, using established height related reference data (Dittrich *et al.* 1983) and the following formula: individual SDS value=(observed value−mean value for individual height in reference population) / SD for individual height in reference population.

Ultrasonographic organomegaly was defined as liver or spleen SDS exceeding +2, which means an individual value roughly above the 97th height-related centile of the reference population.

In the first village, venous blood was taken from all examinees who had given oral consent (n=439). Five ml of blood were drawn, centrifuged on the spot and stored in a refrigerator for up to 4 days. After transport to Mwanza, the sera were frozen at −18 °C and taken to Germany. They were analysed for the following biochemical parameters: γ-glutamyl transferase (γGT) and alanine aminotransferase (ALT) in standard routine procedures; aminoterminal procollagen-III-peptide (PIII-NP) in coated tube RIA with monoclonal mouse antibody MAK 238; carboxyterminal procollagen-IV-peptide (NC1), in RIA with rabbit anti-NC1 serum; Laminin P 1 fragment (Lam P1) in commercial RIAgnost Laminin P1 assay (Behringwerke AG, Marburg, Germany). Procollagens and laminin were measured at Hoechst AG, Radiochemical Laboratory, Frankfurt; γGT and ALT were measured at the Department of Hepatology, Medizinische Hochschule Hannover. The following cut-off values were used to discriminate normal from elevated levels: ALT, 24 U/l; γGT, 30 U/l; PIII-NP, 0.6 U/mL; NC1, 11 ng/mL; LamP1, 1.7 ng/mL. As the normal range of PIII-NP, NC1 and LamP1 in rapidly growing young children is not well established, children below 5 years of age were excluded from analysis of fibrosis marker data. All individuals infected with *S. mansoni* were treated with praziquantel 40 mg/kg BW in a single oral dose.

Statistical analysis was done with SPSS for Windows 5.0. Egg excretion, biochemical indices and sonographical and clinical measurements were not normally distributed (as tested by Kolmogorov–Smirnov test); log transformations of egg counts did not achieve a normal distribution either. Thus, median values are quoted for all these variables. Correlations were generally tested by the Spearman matched pairs/signed ranks method. Groups were compared by the Mann and Whitney U-test, χ^2-test or the Kruskall and Wallis H-test where appropriate. Statistical significance was defined as a probability of error $P<0.05$.

The study was approved by the local body for medical ethics in Tanzania and by the ethics commissions at the Medical Schools of the Universities of Bonn and Hannover.

Results

Complete parasitological and ultrasonographical results were obtained from 1659 villagers. Data on medical history were sufficient for analysis in 1639. Complete clinical examination of liver and spleen was carried out in 898 individuals. Blood samples were collected from 439 persons; due to the small amount of blood, only ALT and γGT levels could be measured in all samples, NC 1 levels in 413, PIII-NP in 372 and Lam P1 in 360.

More than half of the examinees were younger than 20 years: <10 years 25.9%, 11–20 years 28.6%, 21–40 years 27.6%,>40 years 17.9%. There were 47.1% females and 52.9% males.

Parasitology

Overall prevalence of *S. mansoni* infection was 86.3%. Among infected individuals, mean egg

Table 1 Prevalence of *S. mansoni* infection, median egg output of infected persons and proportion of individuals with >400 eggs per gram by age ($P<0.001$ by Kruskall–Wallis test)

	<10 years	11–20 years	21–40 years	>40 years
S.m. prevalence (%)	79.0	93.7	86.7	84.2
Median egg output (e.p.g.)	216	320	128	102
Individuals with >400 e.p.g. (%)	26.1	41.8	23.1	14.5
n	429	476	458	297

Table 2 Proportion of individuals with clinically detectable organomegaly related to *S. mansoni* egg output. In all columns no statistical difference between first three e.p.g. groups; significances only due to increased organomegaly prevalence in persons with >400 e.p.g. (χ^2-test)

	Liver >5 cm in sternal line (%)	Liver >4 cm in midclavicular line (%)	Spleen >2 cm in ant. axillary line (%)	*n*
Uninfected	8.6	5.0	40.3	140
1–100 e.p.g.	7.1	2.8	37.5	325
101–400 e.p.g.	5.5	3.7	43.8	218
>400 e.p.g.	18.1	13.8	51.2	217
χ^2	25	32	10	
P	<0.001	<0.001	0.02	

output was 514 e.p.g., median output 176 e.p.g., geometric mean egg output 161 e.p.g., maximum output 17984 e.p.g. Males and females did not differ in prevalence but in egg output (median in infected males 208e.p.g., in females 144e.p.g.; $P=0.001$). Prevalence and egg excretion varied with age, with a maximum in adolescence and a decline in older age groups (Table 1).

Praziquantel treatment prior to this study was reported by 277 villagers (16.9%). *S. mansoni* prevalence was 87% in untreated, 83% in pretreated individuals (*n*.s.); median ova excretions were 192 and 124 e.p.g., respectively, ($P<0.001$).

Subjective complaints

During the preceding 2 weeks, 35.1% of individuals had experienced diarrhoea, 43.1% reported bloody stools, and 80.1% had suffered from abdominal pain. Complaints were not statistically related to *S. mansoni* infection, with the exception of higher median egg output in infected persons reporting bloody stools (200 *vs* 152 e.p.g., $P=0.02$).

Only 1.3% ($n=22$) reported ever having vomited blood, all of them only once. In several cases it could not be clarified whether this might have been severe epistaxis. This group did not differ from the rest of the population in the degree of *S. mansoni* infection.

Physical examination

Prevalence of hepatomegaly was 9.6% in sternal and 6% in midclavicular line by abdominal palpation, while splenomegaly was more frequent (42.8%). Organomegaly was significantly more common in persons passing more than 400 e.p.g. than in the rest of the population (Table 2).

Ultrasonography

Organomegaly

Ultrasonography detected substantially more cases of organomegaly (defined as individual SDS of respective measurement >+2) than clinical palpation. There was a clear and consistent increase in the proportion of hepatomegaly (both lobes) and splenomegaly with increasing egg output (Table 3). Pretreated persons had a lower proportion of sonographically proven splenomegaly (75.2 *vs* 83%, $\chi^2=10$, $P<0.01$) and left lobe hepatomegaly (27.2% *vs* 36.1%, $\chi^2=8$, $P<0.01$) compared to untreated patients.

Table 3 Proportion of individuals with sonographically detected organomegaly related to *S. mansoni* egg output (*P* by χ^2-test)

	Liver sternal line SDS >2 (%)	Liver ant. axillary line SDS >2 (%)	Spleen SDS >2 (%)	*n*
Uninfected	28.8	24.8	76.0	225
1–100 e.p.g.	32.4	33.0	77.9	551
101–400 e.p.g.	31.7	42.9	81.5	417
>400 e.p.g.	42.5	50.0	90.2	458
χ^2	19	53	33	
P	<0.001	<0.001	<0.001	

Table 4 Prevalence of MANAGIL periportal fibrosis score grades 0–III in different age groups; χ^2=266, *P*<0.001, Spearman's *r*=0.39

	Grade 0	Grade I	Grade II	Grade III	*n*
Up to 10 years	86.4	13.3	0.2	0	435
11–20 years	70.8	25.6	3.3	0.2	480
21–40 years	54.9	37.5	6.3	1.3	461
Over 40 years	34.0	49.0	13.0	4.0	300

Periportal fibrosis

Two methods were used to quantify periportal fibrosis. Using the MANAGIL-Score, 64% of the population were considered to have no fibrosis (grade 0), 29.8% had grade I, 5.1% had grade II and 1.1% had grade III. Fibrosis grades clearly increased with age (Table 4). In grade II or III patients, spleen length, portal vein diameter and length of left liver lobe were significantly increased and the right liver lobe was diminished in length when compared to persons with grade 0 or I (Table 5). There was a trend for higher egg output in persons with higher Managil scores, but this was not quite significant.

Measurements of peripheral portal branches initially were graded according to the CAIRO-score (Jenkins *et al.* 1992): <=3 mm grade 0, 3.1–5 mm=grade 1, 5.1–7 mm=grade 2,>7 mm=grade 3. These scores depended mainly on age. Therefore, values were corrected for body height by calculation of height-related standard deviation scores of portal branch diameters. Portal branch SDS was >+2 in 52.9% and >+3 in 39.5%, median SDS in the total population sample was +2.5. Persons with portal branch SDS >+2 had significantly (all p's<0.001) larger spleens, left liver lobes and portal veins, but smaller right liver lobes than those with portal branch SDS<+2. They also excreted significantly more eggs (χ^2=121, *P*<0.001).

Table 5 Median organometric values in minimal or absent *vs* severe periportal fibrosis (MANAGIL score; *P* by Mann–Whitney test)

	Fibrosis grade 0 or I	Fibrosis grade II or III	*P*
Spleen length SDS	+4.3	+7.2	<0.001
Portal vein diameter (mm)	9	13	<0.001
Left liver lobe SDS	+1.43	+1.86	0.01
Right liver lobe SDS	+1.56	+0.11	<0.001
n	1560	103	

Portal hypertension

Portofugal collateral veins were found in 34 individuals (2.1%), 27 of whom were adults over 20 years, who did not significantly differ from the other examinees in intensity of *S. mansoni* infection. Only one person in this group claimed to have experienced an attack of haematemesis. All individuals with collaterals had splenomegaly (SDS >+2 by

Table 6 Overview of biochemical test results

Test	Normal range	Mean	Range	Median	SD	Percentage above normal	*n*
ALT (U/l)	<25	12	2–107	10	8.4	5.5	439
γGT (U/l)	<30	25	1–297	16	29.5	18.7	439
NC1 (ng/ml)	<11	9.5	5.7–20.9	9.2	1.8	14.5[1]	415
Lam P1 (ng/ml)	<1.7	1.79	0.94–3.59	1.74	0.41	54.7[1]	362
PIII-NP (U/ml)	<0.6	0.40	0.04–1.01	0.38	0.17	12.8[1]	374

[1] Excluding children below 5 years of age, see Methods in text.

ultrasound), and 22 (63%) had MANAGIL scores II or III, as opposed to 5.0% of those without collaterals ($P<0.001$, χ^2-test). Portal branch SDS was >+2 in 82.9% of those with collaterals, as opposed to 52.3% of others ($P<0.001$, χ^2-test).

Unspecific liver alterations

Irregular or nodular liver surface was present in 81 individuals (5%), the dorsal surface of the liver was pathologically convex in 64 (3.9%) and the liver edge was abnormally rounded in 95 (5.7%) patients. None of these pathological ultrasound features was significantly related to *S. mansoni* infection or to previous schistosomicidal treatment. Irregular rough parenchyma texture of the liver was present in 10.7% of individuals ($n=178$), with a higher prevalence in adolescents (14.6%) than in younger children (7.4%) or adults (9.9%; $\chi^2=13$, $P<0.01$). In this group, ova output was significantly higher than in those with normal texture (median 240 *vs* 112 e.p.g.; $P<0.001$). Median SDS of spleen length in this group was +6.6 (*vs* +4.1 in others, $P<0.001$), median portal vein diameter was increased to 11 *vs* 9 mm ($P<0.001$).

Serum parameters

Pathologically increased serum levels of LamP1 were encountered in 54.7%. NC1, PIII-NP and γGT were above normal in about 15% of persons, respectively, while ALT was increased in only 5.5%. Further results of liver enzyme and connective tissue peptide (CTP) measurements are summarized in Table 6. Relations of biochemical data with parasitological and sonographical results can be summarized as follows:

S. mansoni infection

Persons with high egg output did not show a higher prevalence of abnormal levels of any biochemical parameter tested than others with low or absent egg output.

Periportal fibrosis

The proportion of pathologically increased levels of NC1 and γGT was significantly related to periportal fibrosis, irrespective of the scoring system used (Table 7). A parallel increase in pathological ALT results did not quite reach statistical significance; PIII-NP and LamP1 levels were unrelated to fibrosis scores.

Liver texture

In cases with irregular liver texture, the proportion of serum values above normal was increased to 56.1% for γGT (*vs* 13.2%, $\chi^2=60$, $P<0.001$), 28.6% for NC1 (*vs* 12.3%, $\chi^2=10$, $P<0.01$) and 17.5% for ALT (*vs* 3.7%, $\chi^2=18$, $P<0.001$).

Collaterals

In persons with sonographically visible portofugal collateral vessels, the prevalence of pathological levels was increased to 45.5% for NC1 (*vs* 12.8%, $\chi^2=18$, $P<0.001$) and 62.5% for γGT (*vs* 16.3%, $\chi^2=32$, $P<0.001$), while levels of the other biochemical parameters were not significantly related to the presence of collaterals.

Discussion

Morbidity in schistosomiasis mansoni has a broad spectrum of presentations which have to be

Table 7 Prevalence rates (%) of pathologically increased γGT, NC1 and ALT levels in different grades of periportal thickening (*P* by χ^2-test)

	MANAGIL score					CAIRO score			
	0	I	II	III	*P*	I	II	III	*P*
γGT	10.3	30.3	51.7	66.7	<0.001	6.5	23.8	59.4	<0.001
NC1	11.6	15.4	28.0	50.0	<0.01	10.0	15.0	34.5	<0.01
ALT	4.1	8.3	10.3	0	ns	4.0	6.3	9.4	ns
n	267	104	25	6		180	193	29	

addressed by epidemiological studies (Gryseels 1992). While organomegaly can be detected by abdominal palpation and symptoms of colitis can be asked for, presymptomatic periportal liver fibrosis and portal hypertension can be diagnosed only by more advanced methods. For this purpose, ultrasonography remains the most valuable method for field application although its reliability to quantify low grade liver involvement has recently been questioned (Doehring 1988; Doehring-Schwerdtfeger *et al.* 1990; 1992a;b; Hatz *et al.* 1992a;b; Doehring-Schwerdtfeger & Kardorff 1995). In our study, designed to evaluate schistosomal morbidity in the endemic area of western Ukerewe Island in Lake Victoria, measurements of liver enzymes and serum levels of connective tissue peptides were therefore used as additional and independent markers of hepatic involvement.

We found a high prevalence and intensity of infection in all 3 villages; age and sex distribution of infection was typical for a long-standing focus, with children and adolescents more severely infected than adults, and males excreting more eggs than females. Comparable results have been obtained and discussed by many authors, explaining sex and age differences mainly with varying patterns of water contact and acquired partial immunity (Gryseels 1992).

Enterocolitis symptoms such as abdominal pain, diarrhoea and bloody stools were very common. Haematemesis was rarely reported, with not a single person complaining of repeated and severe attacks. Ultrasonography still revealed typical signs of portal hypertension in a small subgroup of villagers (2%): patent portofugal collaterals, severe splenomegaly, often associated with rounded and heterogenous liver and high periportal fibrosis scores. Normal ALT but significantly raised γGT and NC1 levels in these suggest a portally located fibrosing disease without hepatocyte injury, which is well compatible with schistosomal liver fibrosis. We thus conclude that in this population, hepatosplenic schistosomiasis does progress to the stage of established portal hypertension—less frequently than in Sudan or Zimbabwe but more often than in West Africa (Homeida *et al.* 1988b; Saad *et al.* 1991; Gryseels 1992; Houston *et al.* 1993; Kardorff *et al.* 1994; 1996).

Overall hepatomegaly prevalence, as determined by ultrasonography, was about 35%, splenomegaly prevalence about 80%, with a clear correlation of both liver and spleen size with egg excretion; thus *S. mansoni* infection seems to be a causal factor for hepatosplenomegaly in this region. The reason for the rather high rate of 'background organomegaly' even in individuals without egg excretion, remains speculative: certainly a proportion of these might in reality have been lightly infected; using European reference data for organ sizes might lead to some bias when investigating African populations; splenomegaly rates may be explained by malaria endemicity.

Clinical palpation detected fewer cases of organomegaly than sonography. While the higher prevalence of organomegaly in severe infection was also detected by palpation, the moderate increase of organomegaly prevalence in infected persons excreting fewer than 400 e.p.g. would have been missed with palpation alone. Lower sensitivity of palpation compared to sonography was also found by others (Homeida *et al.* 1988b; Doehring-Schwerdtfeger *et al.* 1992c; Richter *et al.* 1992) and has to be considered when comparing different morbidity studies.

Like other studies, this investigation lacked a satisfactory sonographical method to quantify periportal fibrosis in all age groups (Hatz *et al.* 1992b). We used two scoring systems: the MANAGIL score, according to Doehring-Schwerdtfeger *et al.* (1989) and the CAIRO score, according to Jenkins *et al.* (1992). The CAIRO score was modified, adding height-related SDS values to the absolute cut-off values suggested by Jenkins *et al.* ; only with this modification does the application of this score to children seem justified at all. Summarizing results from both scoring systems, low-grade periportal fibrosis in this population seems to be frequent. The steady increase in low-grade fibrosis prevalence with age we found agrees with other studies (Kardorff *et al.* 1994), where this was seen even in *S. mansoni*-free areas. It is suggested that a supposedly physiological ageing effect may imitate the aspect of low-grade periportal fibrosis. More severe MANAGIL grades (II and III) of fibrosis and portal branch SDS above +2, respectively, were clearly correlated with independent features of schistosomal liver disease such as splenomegaly, portal vein dilatation and alteration of liver shape with increasing left and shrinking right lobe—a sign well known from classic post-mortem studies (Cheever & Andrade 1967).

In about 10% of the villagers the sonographic aspect of the liver was pathological, with grossly inhomogeneous texture, rounded shape and/or irregular surface, but with no periportally localized increase of echogenicity. These persons had significantly bigger spleens and larger portal veins. All in all, this image much resembled that of chronic parenchymal liver disease. However, it was associated with increased ALT levels in only a few cases. On the other hand, persons with these findings had significantly increased *S. mansoni* ova excretion which suggests that this might be another pattern of schistosomal liver disease—possibly a more 'acute' one because of the relation with egg output and the prevalence peak in adolescence.

The effect of praziquantel treatment cannot be sufficiently judged from this cross-sectional study, as no follow-up data after our systematic treatment have yet been collected, and only unsystematic treatment had been given to a small subgroup of villagers prior to this study. Still, pretreated individuals not only presented with lower egg output, but also with lower prevalences of splenomegaly and left-lobe hepatomegaly, although prevalence of infection was not significantly lower in this subgroup. This is in accord with earlier reports that schistosomicidal therapy results in improvement of hepatosplenic disease even if complete parasitological cure is not achieved (Polderman & De Caluwe 1989; Zwingenberger *et al.* 1990a; Homeida *et al.* 1991; Doehring-Schwerdtfeger *et al.* 1992a).

Procollagen-IV-peptide (NC1) levels were frequently increased in cases with severe periportal fibrosis, irregular liver texture or patent portosystemic collaterals. On the contrary, no such associations with sonographic features were found for procollagen-III-peptide (PIII-NP) and laminin P1. PIII-NP has been used as a marker of hepatic schistosomiasis in Brazil (Zwingenberger *et al.* 1988; 1990b) and the Philippines (Ohmae *et al.* 1992). The discrepancy may be due to the fact that late cases with symptomatic portal hypertension were absent from our study population, and probably only severe and rapidly progressing liver involvement leads to substantially increased PIII-NP levels—it has to be kept in mind that serum levels of connective tissue peptides represent connective tissue turnover, not actual collagen content of tissues. Slowly progressing fibrotic disorders may therefore go undetected. Moreover, we cannot exclude technical failure due to suboptimal storing and transport conditions of serum samples. The reason for the surprisingly high general prevalence of increased laminin levels (above 50% !) remained unclear. One could speculate that laminin may be influenced by gastrointestinal involvement in schistosomiasis which was certainly present in the majority of the population, but with the available data this hypothesis cannot be tested.

In summary, the following picture of schistosomal morbidity in the Ukerewe Island area emerges: prevalence and intensity of *S. mansoni* infection are high, and typical clinical complaints of colitis are common. So are hepatomegaly and splenomegaly, which are clearly related to excretion of ova. Minimal periportal fibrosis seems to be common but remains difficult to quantify exactly by ultrasonography. A more severe type of liver alteration with rough parenchyma structure, changes in liver shape, further increase in spleen size, higher prevalence of portal hypertension and increased γGT and NC1

levels was seen in about 10% of the population, and was associated with high egg output. 'Classic' late stage disease with a high degree of periportal fibrosis, shrinking of the right lobe of the liver and features of portal hypertension was seen in about 2%. This pattern is not related to egg excretion.

We conclude that the prevalence of intestinal and low-grade hepatic disease was high in the villages screened, while the typical late stage of periportal fibrosis, as detected by ultrasonography, was present but rare. Cases with symptomatic and decompensated portal hypertension were not unequivocally identified. Thus the overall level of schistosomal morbidity in this Lake Victoria region has to be classified as intermediate compared to Sudan (Homeida *et al.* 1988b; Saad *et al.* 1991), Egypt (Abdel-Wahab *et al.* 1990) or Zimbabwe (Davidson *et al.* 1991; Houston *et al.* 1993) on one hand and West Africa (Kardorff *et al.* 1994; 1996) on the other.

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