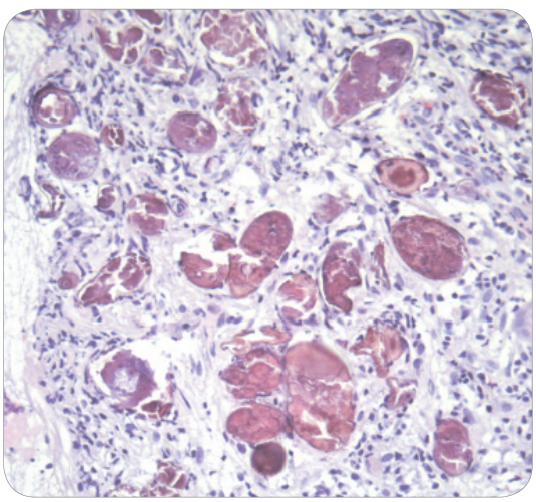
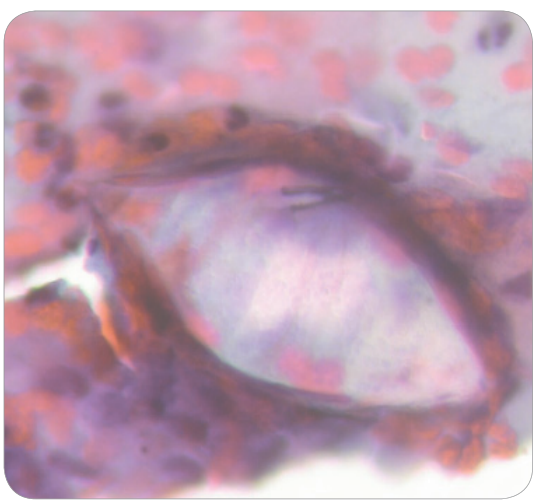
REPORT OF A MEETING TO REVIEW THE RESULTS OF STUDIES ON THE TREATMENT OF SCHISTOSOMIASIS IN PRESCHOOL-AGE CHILDREN

Geneva, Switzerland, 13–14 September 2010

World Health Organization





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EXECUTIVE SUMMARY

Children aged under 4 years (or below 94 cm in height) have been excluded from mass treatment programmes for control of schistosomiasis because of the limited documentation on the safety of praziquantel in this age group. To address this information gap, the World Health Organization (WHO) convened a meeting at its headquarters in Geneva, Switzerland, on 13–14 September 2010 to review the results of studies on the treatment of schistosomiasis in preschool-age children.

To examine the treatment of schistosomiasis (attributable to *Schistosoma mansoni* and *S. haematobium* infections) in preschool-age children, WHO supported treatment trials in Mali, Sudan and Zimbabwe. Praziquantel, in tablet formulation or as a suspension, was assessed for its safety and efficacy in treating preschool-age children. In Sudan and Zimbabwe, the praziquantel suspension did not arrive on time for inclusion in the trials. Other groups independently assessed treatment in this age group in Niger and Uganda. As part of the schistosomiasis control programme in Egypt, praziquantel suspension was developed and used to treat young schoolchildren (aged 6–7 years) who had difficulties in swallowing the tablets. Data on efficacy and safety from this study that used both praziquantel tablets and suspension to treat school-age children were also presented during the meeting.

Preschool-age children are at high risk of schistosomiasis. In areas of Mali, Niger, Sudan, Uganda and Zimbabwe, prevalence of the infection ranged from 18% to 63%. Studies on the treatment of preschool-age children conducted in these five countries (n=3198) among children aged 1 month to 7 years showed that praziquantel in a tablet or suspension formulation was safe and effective against schistosomiasis, and acceptable. In all the studies, high cure rates

were observed, and significant reductions in mean egg counts occurred for both urogenital and intestinal schistosomiasis. The two studies in Mali and Uganda that compared suspension and tablets found no difference in cure rates between the two formulations. In Uganda, there was also no difference in rates of egg reduction between the two formulations.

The effectiveness of praziquantel suspension was also compared with that of the tablet formulation among 27 406 schoolchildren in Egypt. The data showed that cure rates were lower among schoolchildren treated with suspension than those treated with tablets. However, egg reduction rates were similar regardless of the formulation of praziquantel received. In the Uganda study, which also evaluated the use of the dose pole for determining dosage of praziquantel, it was concluded that height is not appropriate for determining the standard dose of praziquantel syrup.

Adverse events were reported from all the studies. Praziquantel, in tablet or syrup formulation, was well tolerated. Reported adverse events were mild and transient, and included fatigue, dizziness, drowsiness, headache, loss of appetite and stomach ache. Assessment of adverse events was not consistent among the studies; it was only in Uganda that questionnaires were administered to mothers before and after treatment to enable differentiation between existing symptoms and treatment-related events. Less than 1% of the treated school children in Egypt experienced adverse events.

Administration of praziquantel to preschool-age children was shown to be acceptable, safe and efficacious to individual children and in group settings. Preparation of the treatment dosages varied among studies: tablets and crushed tablets mixed with various fluids were used in the different studies. In Niger, doses of the suspension were measured using syringes, whereas in Mali spoons were used.

The studies reviewed in this report had some limitations of design and methodology. Systematic review(s) involving preschool-age children, or well-designed multi-country randomized controlled trials using a standard protocol, are warranted to contribute further evidence.

The meeting participants formulated the following recommendations:

a. Preschool-age children should be regarded as a high-risk group in areas endemic for schistosomiasis; treatment should be made available to them through the regular health services;

b. Administration of praziquantel to preschool-age children should be included in ongoing public-health interventions such as the Expanded Program on Immunization (EPI) activities, Mother and Child Days, and Child Health Days;

c. In the absence of an appropriate paediatric formulation, broken or crushed tablets are recommended for administration of praziquantel. Development of a water-dispersible tablet for this age group is recommended.

1. INTRODUCTION

There is no published recommendation on the treatment of schistosomiasis in preschool-age children with praziquantel in population-based control programmes because the extent of schistosomiasis in this age group has not been fully appreciated and appropriate paediatric formulations of praziquantel are not available (*1*). Recent studies show that the prevalence of schistosome infections is high among preschool-age children whose caregivers have high levels of contact with water (*2*). Mothers and other caregivers take children to water contact sites where both groups are exposed to infection (*3*). Children as young as 4 months have been found to be infected with schistosomes (*4*). In Niger, the prevalence of schistosomiasis in children aged <5 years was 50.5% and in their mothers 55.6% in one village, and 60.5% and 72.2% respectively in another (*5*). Similar findings were noted in other countries of the African Region (2, 3, 6–8). Morbidity attributable to schistosomiasis in preschool-age children is also being investigated; preliminary findings suggest that this could be substantial (Amadou Garba, personal communication, 2010). Exposure to schistosomiasis at an early age may be a risk factor for chronic and severe morbidity in school-age years (*9*).

Preschool-age children with schistosomiasis are excluded from mass treatment programmes but can be treated in health facilities. However, administration of treatment in these settings is problematic because of limited diagnostic capacity and lack of an appropriate formulation of praziquantel. Where praziquantel has been used to treat preschool-age children, the tablets have been crushed and mixed with juice or syrup to reduce the bitter taste (*9*).

To examine the treatment of schistosomiasis (attributable to *Schistosoma* and *S. haematobium* infections) in preschool-age children, the World Health Organization (WHO) supported studies in Mali, Sudan and Zimbabwe. Praziquantel – in tablet formulation or as a suspension – was assessed for its safety and efficacy in treating this age group. In Sudan and Zimbabwe, the

praziquantel suspension was not included in the evaluation because it did not arrive on time. Other groups independently assessed the results of treatment in Niger and Uganda. The results from all of these studies were reviewed during a meeting convened by WHO at its headquarters in Geneva, Switzerland, on 13–14 September 2010.

In a mass population treatment campaign in Egypt, praziquantel suspension was developed and used to treat young schoolchildren (aged 6–7 years) who had difficulties swallowing the tablets (*10, 11*). Data on efficacy and safety from this study, which used both praziquantel tablets and suspension, were also presented during the meeting.

The objectives of the meeting were:

- to review the results of studies on the treatment of schistosomiasis in preschool-age children;
- to determine whether data are sufficient to recommend including preschool-age children in preventive chemotherapy interventions for schistosomiasis.

Preschool-age children, defined as children aged under 7 years, are at high risk of schistosomiasis. In areas of Mali, Niger, Sudan, Uganda and Zimbabwe, the prevalence of the infection ranged from 18% to 63% (*Table 1*). Studies on the treatment of preschool-age children conducted in these five countries showed that praziquantel in tablet or suspension formulation was safe, effective and acceptable against schistosomiasis. The studies included 3198 children ranging in age from 1 month to 7 years. In all of the studies, high cure rates were observed, and significant reductions in mean egg counts were observed for both urogenital and intestinal schistosomiasis (*Table 2*). In the two studies in Mali and Uganda where the two formulations were compared, there was no difference in cure rates. In Uganda, there was also no difference in rates of egg reduction post-treatment between the two formulations. Where the efficacy of praziquantel treatment was assessed for both urogenital and intestinal schistosomiasis in Niger and Sudan, cure rates for urogenital schistosomiasis were significantly higher than those for intestinal schistosomiasis.

The effectiveness of praziquantel suspension was also compared with that of the tablet formulation among 27 406 schoolchildren in Egypt. Data showed that cure rates were lower among schoolchildren treated with suspension than those treated with tablets. However, egg reduction rates were similar regardless of the formulation. In the Uganda study, which also evaluated the use of the dose pole to determine dosages, it was concluded that height was not an appropriate tool for determining the standard dose of praziquantel syrup. Methodological problems may have occurred with this aspect of the study.

Adverse events after treatment were reported from all studies. Praziquantel, in tablet or syrup formulation, was well tolerated. Reported adverse events were mild and transient; they included fatigue, dizziness, drowsiness, headache, loss of appetite and stomach ache. Assessment of these events was not consistent among the studies; only in Uganda were questionnaires administered to mothers before and after treatment to enable differentiation between existing symptoms and treatment-associated events. Less than 1% of the schoolchildren treated in Egypt experienced adverse events.

Administration of praziquantel to preschool-age children was shown to be acceptable, safe and efficacious for treatment of schistosomiasis in individual and group settings. Preparation of the

treatment dosages varied among countries. Tablets and crushed tablets mixed with various fluids were used in the different studies. In Niger, doses of the suspension were measured using syringes, whereas in Mali measuring spoons were used. The current praziquantel formulations may not be the most appropriate for use in preschool-age children.

The studies reviewed in this report had some limitations of design and methodology. Systematic review(s) involving preschool-age children, or well-designed multi-country randomized controlled trials using a standard protocol, are therefore warranted to contribute further evidence.

2. COUNTRY SUMMARIES

The countries in which the studies were conducted are listed in alphabetical order; Egypt appears last because the study was conducted in primary-school children.

2.1 Mali

The revised national plan of action for schistosomiasis control is to reduce morbidity through population-based treatment campaigns with praziquantel targeted mainly to school-age children and adolescents, and adults in high-risk occupational groups such as fishermen, farmers, irrigation workers and women with intense water contact activities.

This study evaluated the efficacy, safety and acceptability of two formulations of praziquantel (syrup versus tablets) among infants and preschool-age children in an area of Mali where schistosomiasis is highly endemic. The study was also to document the extent of the burden of schistosomiasis in infants and preschool-age children by determining the prevalence and intensity of *Schistosoma haematobium* (which causes urinary schistosomiasis) and *S. mansoni* (which causes intestinal schistosomiasis); to describe the morbidity attributable to schistosomiasis from micro and macro haematuria, pathological lesions, anaemia and nutritional status (height, weight, skin fold thickness, arm circumference); and to describe the attitude of children and their parents or guardians regarding praziquantel administration. The frequency and intensity of adverse events were assessed at 1–4 hours, 24 hours and 48 hours following treatment.

Two villages in the Ségou district were included in the study: M'Pêba, located along the River Niger, and Kokry-Bozo, located in the Office of Niger irrigation area. Children in each household in these villages were registered using family cards. The eligibility criteria for inclusion in the study were: (i) child aged 1–5 years; (ii) born and living in the study area; and (iii) parents willing to consent to their child's participation. Also, a child had to be able to submit urine and stool samples for assessment before treatment of the status of the infection. Children who received praziquantel treatment within 30 days prior to the study, or who were found to be suffering from severe illness by the study physician, were excluded. Ethical approval was granted by the National Institute of Public Health (INRSP) in Mali; the participants were assured that the information obtained from them was confidential. A child could withdraw at any time during the study.

Parasitological diagnosis of the infection was made by filtration of two consecutive urine samples for *S. haematobium* and duplicate Kato-Katz thick smears for *S. mansoni* and soil-transmitted helminth infections. Clinically, urinary schistosomiasis was diagnosed by visual inspection of urine for macro-haematuria and reagent strips for micro-haematuria. The extent of pathology in these children was assessed by ultrasound according to the WHO guidelines (*12*). Anaemia was determined on the basis of haemaglobin concentration from finger-prick blood, whereas malaria parasitaemia was determined by thick blood-smear. Anthropometric measurements, including weight and height, were measured before and after treatment.

Sample size was determined based on the prevalence of heavy infection, as an indicator of morbidity. On the basis of an expected prevalence of heavy infection of 60%, 369 infants and preschool-age children were due to be enrolled to enable the detection of significant effect, if this truly existed. Each child received praziquantel in syrup or tablet formulation at the standard single dose of 40 mg/kg. The praziquantel used in this study was provided by WHO; before administration, each child was offered some food. The medicine was administered by a trained member of the study team and trained local health workers involved in the ongoing mass treatment campaign. A paediatrician examined every child to establish their health status and monitor adverse events. A total of 187 children were enrolled from M'Pêba, of whom 135 (72.2%) received syrup and 52 (27.8%) received tablets. A total of 228 children were enrolled from Kokry-Bozo, of whom 136 (59.6%) received syrup and 92 (40.4%) received tablets. The children were monitored actively up to 24 hours for any adverse events that might occur after treatment.

The parents or guardians of the children receiving treatment were interviewed to establish whether any adverse events had occurred at 1–4 hours, 24 hours and 48 hours after treatment using a structured questionnaire. Thereafter, the children were followed (less actively) until 6 months to record adverse events. At each of the visits, specific signs and symptoms (abdominal pain, nausea, vomiting, diarrhoea, anorexia, fever, headache, dizziness and fever) were evaluated. Other symptoms reported by parents or guardians were also recorded. Each symptom was classified according to severity as mild, moderate, severe or life-threatening; seriousness was assessed using a grading scale. The symptoms were graded as not related, unlikely, possible, probable, most probable or insufficient data to enable adequate assessment. Therapeutic efficacy was determined at 6 months after treatment; the children were again asked to provide three consecutive urine samples and stools on three consecutive days. Children were considered withdrawn from the study if at any time after the administration of praziquantel they received treatment with any other anti-schistosomal medicine, developed any non-schistosomiasis-related illness or condition that made it impossible to continue the study, or if a parent or guardian decided to no longer participate.

The study showed that the prevalence and intensity of infection in this age group (1–5 years) were high. The results also showed that the prevalence of pathology was high. Overall, 47.9% of the children in the syrup group and 68.5% in the tablet group were found to have some form of pathology during pre-treatment assessment. The corresponding prevalence in Kokry-Bozo was 48% for the syrup and 37.5% for the tablet group. Bladder abnormality was most frequently detected: 47.9% in the syrup group and 68.5% in the tablet groups in M'Pêba. Bladder abnormalities were found in 48.8% in the syrup group and 36.5% in the tablet group in Kokry-Bozo. The prevalence of upper urinary tract abnormality was low: 3.2% (syrup group) versus 1.1% (tablet group) in M'Pêba, and 1.6% (syrup group) and 2.9% (tablet group) in Kokry-Bozo.

No serious or life-threatening adverse event was recorded following administration of the two formulations. Adverse events, predominantly abdominal pain and fever, were mostly mild-to-moderate and transient, with about 80% resolving within 24 to 48 hours after treatment. No child was referred to the health centre or hospital because of untoward events resulting from treatment with praziquantel. A focus group discussion among 10 mothers from Kokry-Bozo showed that syrup was much easier to swallow and easily accepted by their children compared with tablets (data not reported). Mothers were very satisfied with both praziquantel formulations (data not reported), with satisfaction rated as +++.

Six months after treatment, the children had no major complaints of abdominal pain, and fever had reduced significantly. The children in Kokry-Bozo had all their pathology resolved (syrup group) or with low prevalence of bladder (4.5%) and upper urinary tract (1.5%) abnormalities. In M'Pêba, the situation was different as prevalence of bladder abnormality (38.0% for syrup group versus 43.3% for tablet group) and urinary abnormalities (9.6% for syrup versus 7.8% for tablet) was still high.

The study concluded that there were no major differences between the syrup and tablet formulations of praziquantel used to treat schistosomiasis in infants and preschool children in Mali in terms of measured outcomes; the children tolerated both formulations, both formulations were accepted, and adverse events were mild and transient.

2.2 Niger

The clinical trial in Niger assessed the efficacy of praziquantel syrup for treatment of schistosomiasis in preschool-age children in endemic villages along the Niger River Valley. Three endemic villages were selected for the study: Bonfeba (endemic for *S. haematobium*), Libore (endemic for *S. mansoni*) and Zamakoira (endemic for *S. mansoni*). Overall, 246 children (mean age, 40.9 months; range, 1–75 months) were included in the study.

Mothers of the children were invited to participate in the study. Those consenting to the study protocol were asked to collect three urine samples and three stool samples on three consecutive days from their children. Urine samples were filtered and 10 ml was examined by microscopy for *S. haematobium* eggs; the stool samples were examined using the Kato-Katz thick smear method. Intensity of *S. haematobium* infection was categorized according to the WHO classification as light (1–49 eggs/10 ml of urine) or heavy (≥50 eggs/10 ml of urine). Intensity of *S. mansoni* infection was measured as the arithmetic mean of eggs per gram (epg) of stool and also categorized based on the WHO criteria as light infection (1–99 epg), moderate infection (100–399 epg) and heavy infection (>400 epg).

All the infected children were treated with praziquantel syrup (Epiquantel) at the standard single dose of 40 mg/kg body weight. Each child was given food before administration of treatment and was observed for the first 4 hours after treatment for adverse events. A structured questionnaire was administered to the mother or guardian of each child 4 hours and 24 hours after treatment to record any adverse events that might have occurred. The children were followed-up at 3 weeks and 6 weeks after treatment to assess the effect of treatment using the same diagnostic criteria as a baseline: three urine samples and three stool samples on three consecutive days.

Of the 246 children included in the study, 166 (67%) tested positive for *S. haematobium* eggs in their urine and 95 (39%) had *S. mansoni* eggs in at least one stool. Of the 166 children with *S. haematobium* infection, 144 (86.8%) had light infection and 22 (13.2%) had heavy infection. Of the 95 children with *S. mansoni* infection, 58 (61.1%) had light infection and 37 (38.9%) had moderate to heavy infection (defined as epg ≥100 in this study). The cure rate for *S. haematobium* infection was 85.8% at 3 weeks and 94.9% at 6 weeks; the arithmetic mean egg reduction rate was 99.1% at 3 weeks and 99.9% at 6 weeks post-treatment. The cure rate for *S. mansoni* was 74.7% at 3 weeks and 50% at 6 weeks post-treatment. The arithmetic mean egg reduction rate was 73.6% at 3 weeks and 12.3% at 6 weeks post-treatment. Overall, 32.5% of the children reported adverse events at 4 hours post-treatment and 6.1% at 24 hours after treatment; the most frequently reported events were abdominal pain (31%), and bloody diarrhoea and sleepiness (15.9%). No serious adverse event was recorded.

The study concluded that praziquantel syrup was well tolerated by preschool-age children; the cure rate was high for *S. haematobium*, but very low for *S. mansoni*. The authors consider that further studies with larger sample sizes are warranted.

2.3 Sudan

The study in Sudan (a non-controlled trial) was conducted in Hassahesa and Kamlin along the Gezira Irrigation Scheme to determine the prevalence and intensity of urogenital schistosomiasis (attributable to *S. haematobium*) and intestinal schistosomiasis (attributable to *S. mansoni*) in preschool-age children (aged 1–6 years), and to assess the acceptability, safety and therapeutic effect of praziquantel. Three villages (Hilat, Daoud and Branco) endemic mainly for *S. haematobium* and one village (Hamad Alla) predominantly endemic for *S. mansoni* were selected for the study. These villages were chosen for the study because earlier surveys in schools had shown that prevalence exceeded 40% in schoolchildren. A total of 188 preschool-age children were included in the study.

The Kato-Katz thick smear was used for parasitological diagnosis of the infection; the egg count was expressed as eggs per gram (epg) of stool. Three slides were examined from a single stool sample. *S. haematobium* was diagnosed by the urine filtration technique; the egg count was expressed as eggs per 10 ml of urine. The intensity of infection was categorized according to the WHO classification as light (1–99 epg) moderate (100–399 epg) and heavy (≥400 epg) for *S. mansoni* and for *S. haematobium* as light (≤50 eggs/10ml urine) and heavy (≥50 eggs/10 ml). Blood in urine (haematuria) was used for clinical diagnosis of urinary schistosomiasis. All the children were examined by the study physician before treatment.

Praziquantel (Distocide) produced in the Republic of Korea and provided by WHO was used in this study at the recommended dose of 40 mg/kg body weight. For the children who could not swallow, the tablets were crushed and administered with honey to reduce their bitter taste. Administration of the medicine was supervised using a modified directly observed therapy (DOT). All the children included in the study received a snack before the medicine was administered. The mothers or guardians of the treated children were interviewed 24 hours after treatment for 7 days by the clinicians for episodes of treatment-related adverse events. The efficacy of praziquantel was assessed at 1, 3 and 6 months. A child was considered cured if three slides of

the stool sample presented at follow-up were free of eggs (for *S. mansoni*) or no egg was found in the urine sample (10 ml) for *S. haematobium*. Acceptability was determined by the provision of stool or urine samples by respondents, and acceptance of the treatment. The height of each child was also measured.

Overall, examination of urine revealed a prevalence of *S. haematobium* in preschool-age children of 22% in Hilat Daoud and 43% in Branco; the prevalence of *S. mansoni* was 44% in Hamad Alla. The age-specific prevalences were 1–3 years (22.3%), 3–5 years (18.2%) and 5–6 years (22%) in Hilat Daoud; 1–3 years (32.6%), 3–5 years (43.9%), and 5–6 years (60.9%) for *S. haematobium* in Branco and 1–3 years (18.2%), 3–5 years (63.2%), and 5–6 years (44.3%) for *S. mansoni* in Hamad Alla. For children aged 1–3 years, their weight ranged from 6 kg to 20 kg (mean, 13 kg), and the corresponding mean dose administered was 518 mg; the number of tablets a child received ranged from ⅓ to1⅓ (mean, 1 tablet). The weight of children aged 3–5 years ranged from 12 kg to 28 kg (mean, 18.6 kg) and the mean dose was 740 mg; the number of tablets ranged from 1 to 2 (mean, 1¼ tablets). The weight of children aged 5–6 years ranged from 17.5 kg to 33 kg (mean, 24.5kg) and the mean dose was 977 mg; the number of tablets ranged from ¼ to 2¼ (mean, 1⅔ tablets).

In Hilat Daoud, 59 of 77 (76.6%) children assessed at baseline were available for treatment, of whom 48 (81%) were available at 1 month's follow-up (36 (61%) at 3 months and 29 (49%) at 6 months). The overall cure rate was 89.6% at 1 month, 91.6% at 3 months and 100% at 6 months.

In Branco, 50 of 64 (70.1%) of children were available for treatment, of whom 38/50 (76%) were available at 1 month's follow-up, 35 (70%) at 3 months and 36 (72%) at 6 months. Cure rates were 92.1% at 1 month, 91.4% at 3 months and 91.7% at 6 months.

In Hamad Alla, 29 of 47 (61.8%) children were available for treatment. The cure rate was 90.5% at 1 month, 58.8% at 3 months and 69.2% at 6 months. For the two villages where *S. haematobium* infections were investigated, the geometric mean egg count was higher for the children in Hilat Dauod (166.1 eggs/10ml) than for those in Branco (28.2 eggs/10ml). One month after treatment, egg count in the children from Hilat Dauod reduced to 1.5 eggs/10ml (a reduction rate of 99.4%) and that of Branco to 1.3 eggs/10ml (a reduction rate of 96.4%). In Hamad Alla where *S. mansoni* was investigated, the initial egg count of 97.8 epg was reduced to 1.5 epg 1 month after treatment (a reduction rate of 99.0 %).

All the children accepted the treatment except one child (aged 1½ years) whose dose had to be repeated because of spitting the first dose. No drug-related adverse events were reported in all the treated patients during follow-up visits at 24 hours and 1, 3 and 6 months. There was a slight increase in weight one month after treatment.

The results of this study show that praziquantel treatment for children aged <6 years is safe, effective and acceptable.

2.4 Uganda

Two comparative non-randomized studies were conducted in an area endemic for *S. mansoni* in northwest Uganda along Lake Albert to assess the safety, therapeutic effect, tolerability and treatment compliance of praziquantel tablets and syrup in preschool children aged 1–5 years. The first study (n=1114 preschool children) compared praziquantel syrup with crushed tablets in six villages: Nyamukuta, Sonsio, Piida A, Kawenbanda, Booma and Tugombiri. The second study (n=1095) was a mass treatment campaign in which praziquantel syrup was assessed in seven villages: Kigungu, Piida A, Piida B, Serule A, Serule B and Walukuba for compliance and adverse events in preschool children infected with *S. mansoni* and those not infected. Children whose parents did not provide written consent or those who were found to be unwell during the baseline assessment were excluded from the study. Ethical approval for the studies was granted by the Ugandan National Council of Science and Technology and the London School of Hygiene and Tropical Medicine (UK).

Parasitological diagnosis of *S. mansoni* infection was based on duplicate Kato-Katz thick smears from a single stool. Intensity of infection was measured as the arithmetic mean of eggs per gram of stool and categorized based on the WHO criteria as light (1–99 epg), moderate (100–399 epg) and heavy (>400 epg). The circulating cathodic antigen (CCA) was also performed before and after treatment to enable comparison with the Kato-Katz technique. However, given the lack of sufficient CCA dipsticks during the period of the study, only 473 children could be tested. To assess the impact of malaria, which was highly endemic in this area, finger-prick blood samples were collected from 928 children to measure levels of haemoglobin.

All the children included in the first study were treated with the standard single dose of praziquantel (40 mg/kg body weight) tablets or syrup regardless of their infection status. For younger children, the tablets were crushed and mixed with a sweetener (orange juice in this study) before administration. All the treatments were supervised by experienced local nurses and the investigators. In the second study, the accuracy of height poles to determine the dose of praziquantel for these children was also evaluated. Although both height and weight of every child were measured, body weight was used to determine the dose that was administered to them. Height was used to calculate the equivalent dose that would have been administered if the dose pole were to be used. Compliance (defined in this study as the number of children spitting or vomiting during administration of the medicine) was assessed by direct observation. Adverse events were assessed before and 24 hours after treatment in both studies, and each mother or guardian had to be interviewed by questionnaire about the type of adverse events their children may have experienced after the treatment. An adverse event was defined as a symptom not present before treatment that occurred after treatment. Parents were asked to report immediately to the dispensary if their child experienced any serious adverse events. Cure rate and egg reduction rate were assessed 3 weeks after treatment, also from duplicate slides of Kato-Katz thick smear from a single stool.

Of the 1144 preschool-age children examined in the first study from the six villages, 308 were found positive for *S. mansoni* eggs in stool, giving an overall prevalence of 26.7%. The prevalence of infection in the individual villages differed: Tugombiti (52.3%), Nyamukuta (42.6%), Sonsio (35.5%), Piida A (23.9%) and Kawenbanda (19.0%) and Booma (2.3%). Overall, mean egg count (arithmetic mean) among the children who were stool-positive for *S. mansoni* eggs was 82 egg per gram (epg) of stool: 178 (57.8%) had light infection, 71 (23.1%) had moderate infection and

59 (19.1%) had heavy infection. Some 25 (8.1%) children recorded an egg count greater than 1000 epg, most of whom were aged 4–5 years; the heaviest egg load (2400 epg) was found in a 1-year-old girl from Sonsio. The tests comparing Kato-Katz and CCA showed the prevalence of infection determined by the Kato Katz method (25.3%) to be much lower than CCA dipstick (48.4%).

Both the tablets and syrup showed high effectiveness against *S. mansoni* infection. The cure rate 3 weeks after treatment was 80.1% for crushed tablets and 81.9% with syrup using the Kato-Katz method. However, the cure rate dropped to 57.5% for crushed tablets and 57.1% for syrup when CCA dipstick was performed, suggesting that CCA dipstick was probably more sensitive in picking up light infections not detected by the Kato-Katz method. The cure rate was related to the intensity of infection, with the highest rate observed in the light infection group (88.6%), followed by moderate infections (74.5%), whereas in heavily infected children, the rate was only 67.4% based on Kato-Katz method. The egg reduction rate achieved with crushed tablets was 88.5% and with syrup was 87.9%, showing no difference between the two formulations of praziquantel. It should be noted that cure rate could have been influenced by the co-administration of Coartem, an antimalarial medicine with anti-schistosomal activity. Overall, compliance was high and similar for both formulations: crushed tablets (85.3%) and syrup (88.9%). Very young infants (aged 1–2 years) were more likely to resist or refuse treatment compared with those aged 3–5 years; around 80% of the children who resisted treatment were aged 1–2 years.

Adverse events reported 24 hours after treatment showed no statistically significant difference between children who received praziquantel tablets and those treated with syrup. The most commonly reported events were fatigue, dizziness, drowsiness and swelling of a body part; rates of adverse events were significantly higher among uninfected than infected children. The symptoms were generally mild, short lived and did not require further medical attention. Malaria and soil-transmitted helminthiases are common in this area and, given the co-administration of an antimalarial with praziquantel in some villages, it was not possible to determine which symptoms and/or adverse events were caused by *P. falciparum* infection.

Height was found not to be an appropriate tool for determining the standard dose of praziquantel syrup because significant differences occurred in each of the dosing categories when height was used as the dosing tool. In total, 344 (37.6%) of the children investigated would have received a lower dose and 172 (18.8%) would have been over-dosed based on dosing poles. The number of children given 2.5 ml of praziquantel syrup (¼ tablet) based on height was significantly higher (odds ratio [OR], 1.57; $p<0.0001$) than the number who would have been given the same dose by weight. The number of children given 3.75 ml of praziquantel syrup (¾ tablet) based on height was significantly higher (OR, 1.47; $p<0.0001$) than the number who would have been given the same dose by weight. However, the number of children given 5 ml of syrup (½ tablet) based on height was significantly lower (OR, 0.58; $p<0.0001$) than the number who would have been given the same dose by weight. The number of children given 7.5ml of syrup (1½ tablets) based on height was significantly higher (OR, 0.37; $p<0.0001$) than the number who would have been given the same dose by weight.

The finding from these studies showed that *S. mansoni* infection is common in preschool-age children (aged 1–5 years). At the recommended dose of 40 mg/kg body weight, no differences in terms of safety, tolerability, therapeutic effect or compliance were observed between praziquantel tablets and syrup.

2.5 Zimbabwe

This study (a non-controlled trial) was carried out to assess the accessibility, efficacy and safety of praziquantel treatment for schistosomiasis and to assess the effect of treatment on immune responses in children aged 6 months to 5 years living in an area of Zimbabwe where *S. haematobium* is endemic. The efficacy outcomes were parasitological cure rate, egg reduction rate and anthropometry (height and weight). The safety outcomes were the reported side-effects following treatment.

Children were selected for the study from two communities with moderate and high levels of schistosomiasis transmission (as defined by WHO) in the Murehwa district of Mashonaland East Province. The overall prevalence of infection of urogenital schistosomiasis, in populations ranging in age from 6 months to 80 years, was 14% in Chitate village and 69% in Magaya village. These communities had no prior treatment or control programmes for helminthiases. The prevalence of *S. mansoni* and other intestinal helminthiases was very low in this region. Permission to use schools as treatment centres was granted by the ministries of education and of health. Ethical approval for the study was granted by the Medical Research Council of Zimbabwe and the University of Zimbabwe's Institute Review Board.

The populations of Chitate and Magaya villages were screened for urogenital schistosomiasis through the urine filtration technique and for intestinal helminthiases, including schistosomiasis, through the Kato-Katz technique. Urine samples from children were assessed for haematuria using Hemastix® and visually. Blood samples were also collected from all those screened for schistosomiasis infection at baseline and at 6 weeks after treatment. Levels of parasite-specific antibodies against cercariae, egg and adult worms were used as an indicator of exposure to infection. Responses to allergens were also assessed before and after treatment. The praziquantel used in this study was obtained from the IDA Foundation.

The study started in February 2009 and was completed in June 2010. A total of 170 children were recruited to the study having met the inclusion criteria of (i) aged below 6 years, (ii) providing two urine and two stool samples on consecutive days (iii) had urogenital schistosomiasis, and (iv) successfully taken the praziquantel treatment. The children were free to drop out at any point during the study. Parents or guardians of 104 children were interviewed 24 hours after treatment to elicit any side-effects that may have been observed following treatment. A total of 134 children aged <6 years were followed up 6 weeks after treatment and screened for urogenital schistosomiasis, with sera collected for serological diagnosis.

The baseline prevalence of urogenital schistosomiasis among recruited children was 30.8% in Magaya and 2.6% in Chitate. Pre-treatment haematuria (macro- and micro- haematuria) was low (3%) in this group. The arithmetic mean intensity of urogenital infection in the general population screened for infection was 58 eggs/10 ml urine (Magaya) and 15 eggs/10 ml urine (Chitate). No intestinal helminths were detected in those screened for infection. For the serological results, the prevalence of anti-schistosome antibodies was 57.7% in Magaya and 10.3% in Chitate; this is much higher than the respective parasitological prevalence for the two villages.

All children screened for schistosomiasis at baseline were treated with the standard dose of praziquantel (40 mg/kg body weight). Each child included in the study also received praziquantel at 40 mg/kg of body weight in tablet form and was followed up at 6 weeks for parasitological

and growth assessment. The administration of praziquantel using a dose pole, based on height, was also assessed, but all treatment was based on weight.

For small infants, the tablets were crushed, and bread and juice was provided before and after oral administration of praziquantel tablets to decrease their bitter taste. Children were assessed for current health conditions before administration of praziquantel. The parents or guardians were asked to report back 24 hours after treatment with their children to answer a questionnaire on adverse events following treatment with praziquantel. Treatment uptake was significantly higher in Magaya (81%) than in Chitate (51%) for all age groups (aged 6 months to 80 years). The low uptake in Chitate was due to disruption of treatment by social unrest at the time. A total of 134 preschool-age children (aged 3 months to 5 years) were followed up 6 weeks after treatment to assess the efficacy of praziquantel in terms of parasitological cure and anthropometry (height and weight).

Adverse events were only reported for 4 (3.8%) of 104 children whose parents were interviewed within 24 hours after administration of praziquantel treatment. The reported adverse events were minor (headache, loss of appetite, stomach ache, inflammation of the face and body and general weakness) and transient (resolved by the time the parents or guardians reported for the 24-hour post-treatment questionnaire). For the 134 children followed-up at 6 weeks post treatment, treatment with praziquantel significantly reduced both the overall prevalence of the infection (from 29.5% to 5.68%) and its intensity (from 19.7 to 1.39 eggs/10ml urine). This was a 91% reduction in prevalence of infection between baseline and the follow up 6 weeks post-treatment. For the 8 children infected with schistosomes who did not receive treatment but were followed up, the prevalence of infection at follow up was only 19% below the baseline level. The efficacy of praziquantel treatment in preschool-age children was comparable to levels observed in children aged 6–10 years.

A feeding programme that was started in the participating schools and centres catering to preschool-age children a week after the initiation of treatment compromised the assessment of the impact of praziquantel treatment on the growth of children.

Treatment with praziquantel resulted in altered schistosome-specific responses in these children but not in detectable levels of effect on atopic reactivity. Pre-treatment analyses of the IgM levels directed against schistosomes (cercariae, adult worm and soluble egg antigens) showed that levels were present in preschool-age children. Antibody levels were associated with age for all three antigens tested. Post-treatment analysis showed a significant change in IgM levels (increases in anti-cercariae and anti-adult responses, but not in anti-egg IgM responses), reflecting a change in exposure to parasite antigens. This change in IgM levels suggests that levels of anti-cercariae and anti-worm antibody may not be a reliable indicator of the presence of schistosome infection in people who have received previous anthelminthic treatment. There was also a significant increase in IgE responses, which have been associated with protection to reinfection. Specific analysis was made using data for the whole population (aged 6 months to 80 years) from the village (Chitate) where schistosome infection is low to assess the impact of the infection's intensity on atopy (skin-prick tests). Atopic reactivity was also determined serologically by measuring levels of IgE directed against the house-dust mite, and this confirmed the skin-prick test results of a significant negative association between intensity of schistosome infection and atopic responses. The prevalence and intensity of atopic responses in children aged <5 years remained unchanged 6 weeks post-treatment with praziquantel.

The study concluded that praziquantel is effective and well-tolerated by preschool-age children and that treatment did not alter immune responses in children. Furthermore, the effects of praziquantel on the immune responses to schistosome antigens and allergens in children aged 5 years and under were similar to those observed in older children aged >6 years.

2.6 Egypt

The primary objective for control of schistosomiasis in Egypt is to reduce or eliminate morbidity or severe disease with praziquantel. The National Schistosomiasis Control Programme (NSCP) in the Nile delta was initiated in 1996 by the Ministry of Health with the mandate to implement the national schistosomiasis control schemes, including systematic mass treatment campaigns targeted to school children aged 6–18 years in the endemic rural settings. Mass treatment of the whole village was recommended if prevalence of *S. mansoni*, as determined among outpatients by the rural health units, was ≥20%; only those found positive received treatment if prevalence of the infection was <20% (selective treatment). The selective treatment campaigns were complemented by focal molluscicding, mass media health education and environmental management aimed at reducing the transmission potential in these settings. For the purposes of this report, evidence on two main objectives was sought retrospectively: (i) safety and practicability of mass administration of praziquantel syrup or suspension; and (ii) therapeutic effect of praziquantel syrup or suspension in the treatment of schistosomiasis infection among primary-school children.

As part of an effort to evaluate the impact of the national schistosomiasis control programme in Kafr El Sheikh governorate, a study was conducted in 14 primary schools during 1997–2000. Every child attending these schools was treated annually with praziquantel at the standard single oral dose of 40 mg/kg irrespective of their infection status. In 1996, all the children received praziquantel tablets, but from 1997 to 2000 children aged <7 years (who had difficulties in swallowing tablets) received praziquantel syrup or suspension, while older children (aged 7–12 years) received tablets. Overall, 5728 doses of praziquantel syrup were administered during the period 1997–2000. Children aged 8–12 years were treated with praziquantel tablets, with a total of 21 678 doses of praziquantel tablets administered from 1997 to 2000 (*Table 3*).

For the assessment of therapeutic effect of praziquantel suspension, children attending El Rouse primary school in 1998 were included in the study. Each child received the standard dose of 40 mg/kg of praziquantel. A total of 886 children received treatment in 1998, 1127 children in 1999 and 1504 children in 2000, with an overall 3517 doses of praziquantel administered during 1998–2000. Parasitological diagnosis of *S. mansoni* infection was based on duplicate slides of a single stool sample using the Kato-Katz method; egg count was reported as geometric mean of egg per gram of stool. Therapeutic effect was assessed 4 weeks after treatment.

In terms of safety and practicability, the results showed that it was easier to administer praziquantel syrup or suspension to these children compared with tablets. The children accepted and tolerated the syrup or suspension, with no recorded serious adverse events. Overall, around 1% of the children experienced adverse events, mainly minor and transient (colic and headache), and required only minimal medical attention. The recorded adverse events did not differ in terms of frequency or severity between syrup or suspension and tablets.

The therapeutic effect of syrup or suspension against *S. mansoni* infection was assessed in terms of cure rate 4 weeks after treatment in each year, which showed that although cure rate for tablets was lower than reported in previous studies, the cure rate achieved with syrup or suspension was consistently lower than that of tablets. Cure rates recorded in 1998 were: 69/207 (33.3%) versus 311/608 (51.2%) and in 1999 (29.3% versus 66%) for syrup and tablets, respectively (*Table 4*). In 2000, praziquantel was administered in two successive doses at 4-weeks intervals. Although cure rates improved with both formulations, the 67.3% achieved with syrup was still lower compared with the 81.9% for the tablets. The trend of lower cure rate with syrup remained when the data were analysed based on pre-treatment intensity of infection (*Table 5*). However, no significant difference was observed between syrup and tablets in terms of egg reduction rates (around 70% for both) among the children not cured (*Table 6*).

The study concluded that praziquantel syrup or suspension did not lead to any recorded serious adverse event, and was well tolerated and acceptable to the children, but there was a trend with lower cure rate than tablets.

3. CONCLUSIONS

1. Participants reviewed data from studies of the treatment of schistosomiasis in preschool-age children (in Mali, Niger, Sudan, Uganda and Zimbabwe) and of school-age children (in Egypt). The evidence generated by field studies conducted in five countries where schistosomiasis is endemic (Mali, Niger, Sudan, Uganda, Zimbabwe) shows that:

    a. Schistosomiasis can represent a significant public-health problem in children aged under 5 years;

    b. Preschool-age children living in areas where endemicity for schistosomiasis is high have levels of infection comparable with those of school-age children; prevalence of the infection may exceed 50%, and pathological lesions may be detectable by ultrasonography and other signs of morbidity;

    c. Administration of praziquantel to preschool-age children is acceptable, safe and efficacious in the context of individual case management and in group settings, such as in the studies reported.

2. Based on the above considerations, the following recommendations were formulated:

    a. Preschool-age children should be regarded as a high-risk group in areas endemic for schistosomiasis; treatment should be made available to them through the regular health services;

    b. Administration of praziquantel to preschool-age children should be included in ongoing public-health interventions such as the Expanded Programme on Immunization (EPI) activities, Mother and Child Days, and Child Health Days;

c. In the absence of an appropriate paediatric formulation, broken or crushed tablets are recommended for administration of praziquantel; development of a water dispersible tablet for this age group is recommended.

3. Recognizing the existence of knowledge, operational and regulatory gaps, it was further recommended that:

a. WHO should consider formally recommending the use of praziquantel in preschool-age children in areas where schistosomiasis is endemic, and that measures should be taken to include preschool-age children among the target population for administration of praziquantel within an appropriate health-care setting;

b. In situations where weight scales are not available, an appropriate tool for calculating the correct dose of praziquantel to be administered to preschool-age children should be developed; the possible adaptation of the WHO dose-pole to children measuring less that 94 cm in height should be explored and further validated;

c. An efficient monitoring and evaluation system should be established in conjunction with administration of praziquantel to preschool-age children, in order to further document its efficacy and safety and contribute to the refinement of existing WHO recommendations;

d. The appropriate frequency of retreatment to be applied in each target area should be based on the assessment of school-age children (aged 5–14 years) living in that area, in accordance with existing guidelines; the frequency of retreatment for preschool children should be locally defined;

e. The feasibility of administration, efficacy and safety of child-appropriate formulations of praziquantel should be further investigated and assessed; to determine the optimal dose of praziquantel for the treatment of schistosomiasis in children, a pharmacokinetic study is warranted.

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ANNEXES – Tables

Table 1. Characteristics of studies assessing the treatment of schistosomiasis in preschool-age children with praziquantel

Country	Sample size	Study design	Age range	Schistosome type	Diagnostic criteria	Prevalence (%) by age (years					Prevalence by age (years)		Follow-up	Praziquantel formulation (Yes/No)		Morbidity outcomes
						1	2	3	4	5	<6	>6		Tablets	Syrup	Yes/No
Egypt	27406	Survey	6–11 years	S. m	Kato-Katz, 2 slides, 1 stool	–	–	–	–	–	–	–	4 weeks	Yes	Yes	No
Mali	415	RCT	1–5 years	S. h	2 urines, 10 ml	–	–	–	–	–	NA	NA	6 months	Yes	Yes	Yes
				S. m	Kato-Katz; 2 stools	–	–	–	–	–	NA	NA				
Niger	246	Selective	1–75 months	S. h	3 urines, 10 ml	–	–	–	–	–	–	–	3 and 6 weeks	No	Yes	Yes
				S. m	Kato-Katz, 3 slides, 1 stool	–	–	–	–	–	–	–				
Sudan	188	Selective	1–6 years	S. h	1 urine, 10 ml	22; 32.6		18.2; 43.9		22; 60.9		–	1, 3 and 6 months	Yes	No	Yes
				S. m	Kato-Katz, 3 slides, 1 stool	18.2		63.2		44.3		32% in school children				
Uganda	2209	Selective and mass	1–5 years	S. m	Kato-Katz, 2 slides, 1 stool	26.7					NA	NA	3 weeks	Yes	Yes	Yes
Zimbabwe	140	Selective	3–59 months	S. h	At least 2 urines, 10 ml	29.5					NA	NA	6 weeks	Yes	No	No

NA = not applicable; RCT = randomized controlled trial; S. h = Schistosoma haematobium; S. m = Schistosoma mansoni; selective study = screening whole population and treating only the positives

Table 2. Results of studies assessing the treatment of schistosomiasis in preschool-age children with praziquantel

Country type	Schistosome	Treated compliance		Acceptability/ 4 hours		Adverse events 24 hours		Adverse events 48 hours		Adverse events		Cure rate (%)		ERR (%)		Reinfection (%)	
		Tablets (n)	Syrup (n)	Tablets (%)	Syrup (%)	Tablets	Syrup	Tablets	Syrup	Tablets	Syrup	Tablets	Syrup	Tablets	Syrup	Tablets	Syrup
Egypt	S. m	21678	5728	95	100	1% of children experienced minor events; frequencies were similar between syrup and tablets						51–82	33–67	67–74	71–76	–	–
Mali	S. h	144	271	100	98	–	–	–	–	–	–					–	–
	S. m	–	–	–	–												
Niger	S. h	0	246		95	–	32.5% combined	–	6.1% combined	–	–	–	85.8 at 3 weeks; 94.9 at 6 weeks		99.1% at 3 weeks; 99.9 at 6 weeks	–	–
	S. m	–	–	–	–	–				–	–	–	74.7 at 3 weeks; 50 at 6 weeks		73.6% at 3 weeks; 12.3% at 6 weeks	–	–
Sudan	S. h	138	0	100	NA	None	–	None	–	None	–	None	Cure rate[a]	ERR[b]	–	–	–
	S. m	–	–	–	–	None	–	None	–	None	–	None	Cure rate[a]	Not reported	–	–	–
Uganda	S. m	572	1847	85.3	88.9	Mild and short-lived						80.1	81.9	88.5	87.9	–	–
Zimbabwe	S. h	178	0	100	NA	3.8%		–	–	–	–	Overall prevalence reduced from 29.5% to 5.68%		Overall, geometric mean egg count reduced from 1 9.7 to 1.39 eggs/ 10 ml urine		–	–

ERR = egg reduction rate; S. h = Schistosoma haematobium; S. m = Schistosoma mansoni; NA = not applicable

[a] The cure rates for the three villages are presented separately: in Hilat Daoud the cure rate was 89.6% at 1 month, 91.6% at 3 months and 100% at 6 months; in Branco was 92.1% at 1 month, 91.4% at 3 months and 91.7% at 6 months; and in Hamad Alla was 90.5% at 1 month, 58.8% at 3 months and 69.2% at 6 months.

[b] The ERR was 26% in Hillat Daoud and 49% in Branco. No study reported reinfection rate.

Table 3. Number of primary-school children offered praziquantel (PZQ) in 14 schools, Kafr el Sheikh governorate, Egypt, 1997–2000

Year	PZQ suspension	PZQ tablets	Total
1997	1496	5000	6496
1998	1587	4845	6432
1999	1605	5406	7011
2000	1040	6427	7467
Total	5728	21 678	27406

Table 4. Cure rate after treatment with praziquantel (PZQ), El Rouse primary school, Kafr el Sheikh governerate, Egypt, 1998–2000

Year	PZQ formulation	No. treated	Cured	
			No.	%
1998	Suspension	207	69	33.3
	Tablets	608	311	51.2
1999	Suspension	184	54	29.3
	Tablets	470	310	66.0
2000	Suspension	171	115	67.3
	Tablets	459	376	81.9

Table 5. Cure rate after two consecutive treatments with praziquantel (PZQ) suspension and tablets according to intensity of infection before treatment, El Rouse primary school, Kafr el Sheikh governerate, Egypt, 2000

PZQ formulation	Intensity of infection before treatment	No. treated	Cured	
			No.	%
Suspension	Low	94	81	86.2
	Moderate	36	26	72.2
	Heavy	36	26	72.2
Tablets	Low	322	304	94.4
	Moderate	99	92	92.9
	Heavy	32	27	84.4

Table: 6. Percentage of reduction in geometric mean egg count (GMEC) of uncured children after treatment with praziquantel (PZQ), El Rouse primary school, Kafr el Sheikh, Egypt governerate, 1998–2000

Year	PZQ formulation	No. uncured	GMEC		
			Before treatment	After treatment	% reduction
1998	Suspension	138	158.2	46.5	70.6
	Tablets	297	113.4	29.6	73.9
1999	Suspension	130	119.3	34.7	70.9
	Tablets	160	97.9	22.9	73.9
2000	Suspension	56	162.5	38.15	76.5
	Tablets	83	100.1	33.1	66.9

ANNEXES – Agenda

Day 1: Monday, 13 September 2010

	Item	Name
09:00–09:30	Welcome address, meeting objectives and introduction of participants Chairperson: Dr Russell Stothard Rapporteur: Dr Anthony Danso-Appiah	Lorenzo Savioli/ Dirk Engels
	Schistosomiasis in young children	
09:30–10:00	Schistosomiasis in young children: an overview	Russell Stothard/ Albis Gabrielli
10:00–10:30	The use of NTD drugs in young children.	Anna Ridge
10:30–10:50	Coffee break	
	Treatment of schistosomiasis in young children	
10:50–11:10	Use of praziquantel suspension in children of school age	Rashida Barakat
11:10–11:30	Protocol for treatment preschool children for schistosomiasis	Moussa Sacko
11:50–12:10	Treatment of young children in Mali	Moussa Sacko
12:10–12:30	Treatment of young children in Sudan	Mutamad Amin
12:30–14:00	Lunch	
14:00–14:20	Treatment of young children in Zimbabwe	Francisca Mutapi
14:20–14:40	Treatment of young children in Uganda	Narcis Kabatereine

14:40–15:00	Treatment of young children in Niger	Amadou Garba
15:00–15:30	Discussion	
15:30–16:00	Coffee break	
16:00–17:30	Discussion	
18:00	Reception	

Day 2: Tuesday, 14 September 2010

	Item	**Name**
	Chairperson: Dr Russell Stothard	
	Rapporteur: Dr Anthony Danso-Appiah	
	Interpretations of results and policy implications	
09:00–10:30	Discussions on interpretation of results	
10:30–11:00	Coffee break	
10:30–12:30	Policy implications	
12:30–14:00	Lunch	
	Treatment of young children for schistosomiasis	
14:00–15:30	Way forward	All
	And research required	Piero Olliaro
15:30–16:00	Coffee break	
16:00–16:30	Closure of meeting	

ANNEXES – List of participants

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