An evaluation of urine-CCA strip test and fingerprick blood SEA-ELISA for detection of urinary schistosomiasis in schoolchildren in Zanzibar

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1. Introduction

Urinary schistosomiasis, caused by infection with Schistosoma haematobium, is endemic on each of the two major islands of Zanzibar, Unguja and Pemba (Stothard et al., 2002a). The active disease transmission zone is broadly determined by the geographical distribution of aquatic habitats that harbour Bulinus globosus, the parasite’s local permissive intermediate host snail (Stothard et al., 2000, 2002a). On Unguja this zone is restricted to central/northern areas (Rudge et al., 2008) but it is sometimes possible to encounter infected individuals elsewhere which are typically explained by peripatetic travel histories to either the endemic zone or to others on the nearby mainland or Pemba (Stothard et al., 2002a,b; Clements et al., 2008). The realisation that the spatial distribution of urinary schistosomiasis was confined led to selective geographical targeting of control as implemented by the Piga Vita Kichocho campaign (translates to “Kick Out Schistosomiasis” in English) (Southgate et al., 2005). Initiated in 2003, Piga Vita Kichocho has co-ordinated and overseen the annual delivery and large-scale administration of praziquantel for urinary schistosomiasis to children attending primary schools within the endemic zone as well as albendazole for control of soil-transmitted helminthiasis (STH) across all Ungujan primary schools (Stothard et al., 2009). Piga Vita Kichocho is managed by the Helminth Control Laboratory Unguja (HCLU) which is also in charge of sentinel parasitological monitoring of selected schools. Through capacity strengthening of HCLU, there has also been an expanding programme of thematic research for disease surveillance.

Recognising the difficulties in detecting schistosome infections (Wilson et al., 2006) has been a central challenge of this monitoring and surveillance programme, and for this reason, development and validation of alternative diagnostic approaches within school-aged children has become a long-term commitment (Rollinson et al., 2005). This has taken the form of both developing and
assessing more logistically demanding methods as infrastructure of HCLU improved and the skills-base increased, e.g. measuring excreted urine-albumin levels (Rollinson et al., 2005), as well as, implementing and evaluating less demanding methods on a much larger scale, e.g. assessing the dynamics of micro-haematuria with urine reagent strips (French et al., 2007). As new diagnostic products have become obtainable through commercial production, *Piga Vita Kichocho* has been able to investigate their immediate and future value set within the programme’s own evolution. For example, we have found – unexpectedly – that a commercially available urine-circulating cathodic antigen (CCA) dipstick, used for detection of both intestinal and urinary schistosomiasis and produced by the European Veterinary Laboratory (EVL), failed to detect *S. haematobium* infections (Stothard et al., 2006). This observation, and its limited sensitivity (52%) for urinary schistosomiasis reported from Ethiopia (Ayele et al., 2008), prompted a subsequent reformulation of this test by the Department of Parasitology, LUMC, Leiden and eventual production with a different commercial supplier, namely Rapid Medical Diagnostics, South Africa.

Despite the widespread use of other immuno-diagnostic methods, e.g. the enzyme-linked immunosorbent assay (ELISA) (Hamilton et al., 1998; Al-Sherbini et al., 1999; Doenhoff et al., 2004) in schistosomiasis research and sometimes during control (Zhu, 2005), it has only recently been possible for non-specialist laboratories to measure antibody responses against schistosome soluble egg antigen (SEA). Indeed, a commercially produced SEA-ELISA kit (IVD Research Inc.; Carlsbad, USA), using SEA sourced from eggs of *S. mansoni*, has only just become available. There are two particularly attractive features of this kit. First, only a small amount of fingerprick blood is needed for measuring anti-*Schistosoma* antibodies (primarily IgG) which are thought sufficiently cross-reactive against heterologous schistosome species. Second, the protein A-horse radish peroxidase conjugate utilises a chromogen (TMB-tetramethylbenzidine), which, upon completion of the test, elicits a visible colour change (colourless to yellow), thus negating an essential need for an ELISA plate reader. While serology remains the method of choice for travellers returning home from disease-endemic areas (Turner et al., 2004) where demonstration of excreted eggs can be problematic (Whitty et al., 2000; Lawn et al., 2003), known drawbacks of the SEA-ELISA in endemic settings are its postulated lack of specificity owing to cross-specific reactions with other parasitic helminths or insensitivity in those with chronic schistosomiasis or compromised immune responses (Doenhoff et al., 2003, 2004; Sarner et al., 2007).

In this study we sought to compare and evaluate the diagnostic potential and application of these two new commercially available tests; namely, (i) the urine-CCA strip in the new LUMC reformulation, and (ii) a SEA-ELISA. To provide a deeper insight into the performance of each test across a range of *S. haematobium* prevalence settings, school-aged children originating from high, medium and low/null transmission environments were examined.

2. Materials and methods

2.1. Study area, selected schools and participants

The *Piga Vita Kichocho* programme is operating across all primary schools in Unguja. For this study, five schools (Kiboje, Kilombero, Kinyasini, Mweru and Muyuni) were selected based on previous *S. haematobium* prevalence data and their geographical locations to the known disease-endemic zone. Kinyasini and Mweru represented high transmission locations, Kiboje and Kilombero represented medium transmission locations while Muyuni represented a low/null transmission location. Further details of the selected schools have been presented elsewhere (Knopp et al., 2008; Stothard et al., 2009). The study was carried out in early June 2008, approximately 11 months after the last round of annual mass drug administration with anthelmintics in Unguajan schools.

After explaining the objectives of this study, written informed consent was obtained from the headteacher of each of the five schools. Informed oral consent was requested from the children attending grade 3 (typically aged between 8 and 14 years) before randomly drawing 30 children (15 boys and 15 girls) for study enrolment following guidelines put forth by the World Health Organization (WHO) (Montresor et al., 1998). Each child then provided a mid-morning urine specimen in a 250 ml plastic container and a fingerprick blood sample was taken using a disposable safety lancet and Gilson pipette. Finally, each child was asked four questions; namely (i) age, (ii) location of birth, (iii) duration of attendance at this school within the last 3 years, and (iv) history of anthelmintic treatment(s).

2.2. Parasitological and urological assessment

Parasitological diagnosis was performed using standard microscopy methods on mid-morning urine specimens (i.e. 10 ml of urine were syringed through a 12 μm polycarbonate Millipore® filter and results were expressed as the number of eggs/10 ml of urine) according to WHO guidelines (Montresor et al., 1998). Eggs counts were classified into light (1–10 eggs/10 ml), medium (11–50 eggs/10 ml) and heavy (>50 eggs/10 ml) infection intensities. Visual blood in urine (macro-haematuria) and visual urine turbidity were each assessed against a colour and barcode chart as previously described (Rollinson et al., 2005). Urine-reagent strips Hemastix® (Bayer, UK) were used to detect micro-haematuria (non-visual blood in urine) as described elsewhere (French et al., 2007).

2.3. Urine-CCA strip

The urine-CCA strip tests were performed according to the protocol supplied by the LUMC, Leiden. In brief, for each urine-CCA strip, a total of 25 μl of an individual’s urine was mixed with 75 μl of CCA IDIS buffer containing carbon-labelled antibodies and then the strip was inserted into the solution. After an incubation period of 40 min, the testline for each strip was compared against that of the five quality control standards (which ranged from 0 to 10,000 ng/ml of urine CCA); a negative test criterion was based upon a testline either not visible or weaker than that of the 100 ng/ml standard, while the internal control line was visible. Further details of the development of the strip and its recent modifications thereof have been published elsewhere (Van Dam et al., 2004; Corstjens et al., 2008).

2.4. Fingerprick blood SEA-ELISA

A fingerprick blood sample from each child was collected into a 1.5 ml Eppendorf tube, transferred to the laboratory and allowed to clot at room temperature for 2 h. To collect sera, samples were then centrifuged in a bench-top microcentrifuge for 10 min at 14,000 rpm before retrieval of 3–4 μl of supernatant. Each child’s serum was then diluted 1:40 with specimen dilution buffer before a total of 100 μl was applied to respective ELISA microwells, and the test was performed according to the manufacturer’s instructions inclusive of both positive and negative control sera at the beginning and end of each batch of test samples (IVD Inc.; Carlsbad, USA). Upon completion of the SEA-ELISA test, the microtitre plate was placed on a white card and the final colour within each microwell (ranging from colourless to yellow) was recorded by visual examination by two independent observers. Positive reactions were classified...
either as positive (light yellow) or strong positive (dark yellow) upon comparison with control sera.

2.5. Data handling and statistical analysis

Data were collected from each individual using pro-forma data sheets, which were then entered onto an electronic format using Microsoft Excel™. The data thus collated were analysed using MS Excel™ and R statistical package® version 2.6.0 (Ihaka and Gentleman, 1996). For prevalence data 95% confidence intervals (CI) were estimated using the exact method as described in Armitage and Berry (1994). Responses from the four questions were treated as binary variables with 1 denoting an affirmative response, with the exception of age.

Micro-haematuria, urine turbidity, urine-CCA and SEA-ELISA diagnostic results were tested qualitatively, as alternate urinary schistosomiasis diagnosis methodologies, considering microscopy-mediated egg counting as the diagnostic ‘gold standard’. We calculated sensitivity (SS), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) for the different diagnostic approaches. Additionally, the diagnostic powers of microscopy, micro-haematuria, urine-CCA and visual turbidity were measured, this time considering SEA-ELISA as diagnostic ‘gold standard’. The diagnostic power of each test was calculated using all individuals, as well as, segregated by sex to assess for any inter-gender variability or by school to assess any heterogeneity by transmission zone.

Univariate and multivariate analyses were carried out, and models were established defining infected children as cases, i.e. infection status as a binary variable (infected and uninfected), and demographic or social factors for infection.

The Research Council of the Zanzibar Ministry of Health and Social Welfare and the NHS-LREC of Imperial College London (application 03.36) granted ethical approval for this study. All children enrolled were provided with an appropriate dose of praziquantel (40 mg/kg) and single tablet of albendazole (400 mg) regardless of their infection status and previous history of receiving school-based treatment(s).

3. Results

3.1. Statistical descriptors and urological assessments

A complete dataset was assembled from the 150 children (75 boys and 75 girls) from the five selected schools and basic statistical descriptors, pooled and at the unit of the school, are shown in Table 1. The mean prevalence of S. haematobium, as detected by microscopy, was 30.7% (95% CI = 23.4–38.7%). The range of prevalences by school varied from a minimum of 3.3% (95% CI = 0.1–17.2%) at Muyuni to maxima of 53.3% (95% CI = 34.3–71.7%) for both Mwera and Kinyasini. The infection prevalence at Kilombero was 33.3% (95% CI = 17.3–52.8%), which was similar to the aggregated mean. Using Kilombero as a comparator to ascertain relative risks for infections at other schools, risks of infection at Muyuni and Kiboje were found to be 6.9% (P = 0.014) and 22.2% (P = 0.037) of that in Kilombero, respectively. Children situated outside the known endemic zone were 12.2 times less likely to be infected with S. haematobium than those children living within it (P < 0.001). This geographical association remained statistically significant after multivariate analysis taking into consideration all data gathered from the questionnaire responses (OR = 13.0, P < 0.001).

Within this sample, it is worthy of note that origin of birth and duration of residence at the local school varied widely. Children at Mwera school appeared to have the most itinerant history with just under 25% reporting not to have been born on Unguja (e.g. Dar es Salaam in mainland Tanzania or Pemba) and the majority to have had schooling elsewhere on Unguja (e.g. Stonetown) in the preceding 3 years. These observations contrast with children in other schools, who were only 5–10% reported not to have been born on Unguja and 25% or less, to have had schooling elsewhere. Children at Kinyasini are most notable for their universal attendance at this school for the past 3 years and represent the least itinerant population. The singular case of S. haematobium encountered at Muyuni originated from a girl who reported a travel history to the north of the island and presented with gross haematuria, turbid urine and heavy infection intensity (>50 eggs/10 ml of urine). Despite not appearing significant at the univariate level, a history of previous treatment showed a positive borderline significant association with prevalence of infection at the individual level when using multivariate statistics (OR = 2.2, P = 0.059). The most parsimonious model (AIC-derived stepwise selection) included village’s endemic state (OR = 12.6, P < 0.001, baseline = non-endemic), previous treatment history (OR = 2.3, P = 0.049, baseline = absence) and duration of local schooling, for longer than 3 years, (OR = 2.0, P = 0.126) as risk factors for infection.

Table 1

<table>
<thead>
<tr>
<th>Village</th>
<th>Kilombero</th>
<th>Kinyasini</th>
<th>Mwera</th>
<th>Kiboje</th>
<th>Muyuni</th>
<th>All population</th>
</tr>
</thead>
<tbody>
<tr>
<td>District</td>
<td>North</td>
<td>Centre</td>
<td>South</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years (mean/range)</td>
<td>10.7 (9–14)</td>
<td>10.2 (8–14)</td>
<td>10.0 (8–12)</td>
<td>10.4 (8–14)</td>
<td>10.1 (9–12)</td>
<td>10.3 (8–14)</td>
</tr>
<tr>
<td>Reported previous treatment in % (95% CI)</td>
<td>43.3 (25.5–62.6)</td>
<td>30.0 (14.7–49.4)</td>
<td>40.0 (22.7–59.4)</td>
<td>73.3 (54.1–87.7)</td>
<td>10.0 (2.1–26.5)</td>
<td>39.3 (31.5–47.6)</td>
</tr>
<tr>
<td>Proportion in % (95% CI) of individuals who:</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Were born on Unguja island</td>
<td>90.0 (73.5–97.9)</td>
<td>93.3 (77.9–99.2)</td>
<td>76.7 (57.7–90.1)</td>
<td>90.0 (73.5–97.9)</td>
<td>96.7 (82.8–99.9)</td>
<td>89.3 (83.3–93.8)</td>
</tr>
<tr>
<td>Were attending the school for &gt;3 years</td>
<td>73.3 (54.1–87.7)</td>
<td>100.0 (88.4–100.0)</td>
<td>43.3 (25.5–62.6)</td>
<td>86.7 (69.3–96.2)</td>
<td>90.0 (73.5–97.9)</td>
<td>78.7 (71.2–84.9)</td>
</tr>
<tr>
<td>Diagnostic parameters in % (95% CI):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micro-haematuria</td>
<td>0.00 (0.00–11.6)</td>
<td>16.7 (5.6–34.7)</td>
<td>20.0 (7.7–38.6)</td>
<td>0.00 (0.00–11.6)</td>
<td>3.3 (0.1–17.2)</td>
<td>8.0 (4.2–13.6)</td>
</tr>
<tr>
<td>Micro-haematuria (Hemastix®)</td>
<td>33.3 (17.3–52.8)</td>
<td>70.0 (50.6–85.3)</td>
<td>63.3 (43.9–80.1)</td>
<td>6.7 (0.8–22.1)</td>
<td>3.3 (0.1–17.2)</td>
<td>35.3 (27.4–41.5)</td>
</tr>
<tr>
<td>Serology positive (SEA-ELISA)</td>
<td>43.3 (25.5–62.6)</td>
<td>86.7 (69.3–96.2)</td>
<td>66.7 (47.2–82.7)</td>
<td>26.7 (12.3–45.9)</td>
<td>13.3 (3.8–30.7)</td>
<td>48.0 (39.8–56.1)</td>
</tr>
<tr>
<td>Urine-CCA positive</td>
<td>6.7 (0.8–22.1)</td>
<td>6.7 (0.8–22.1)</td>
<td>0.00 (0.00–11.6)</td>
<td>6.7 (0.8–22.1)</td>
<td>0.00 (0.00–11.6)</td>
<td>4.0 (1.5–8.5)</td>
</tr>
<tr>
<td>Urinary schistosomiasis* in % (95% CI)</td>
<td>33.3 (17.3–52.8)</td>
<td>53.3 (34.3–71.7)</td>
<td>53.3 (34.3–71.7)</td>
<td>10.0 (2.1–26.5)</td>
<td>3.3 (0.1–17.2)</td>
<td>30.7 (23.4–38.7)</td>
</tr>
</tbody>
</table>

* Based upon egg counts.
Across the sample, the prevalence of gross haematuria was 8.0% (95% CI = 4.2–13.6%) but this sign was confined to children attending either Mwera or Kinyasini, with one exceptional case encountered at Muyuni. Upon visual examination of the urine specimens, gross-haematuria was notably different in children from Mwera compared to those from Kinyasini; typically urine turbidity was much less common and ‘pebble-like’ tissue blood clots were much more apparent. By contrast, urine turbidity was very common at Kinyasini, the majority being visually opaque and no ‘pebble-like’ tissue clots were seen even in samples with gross-haematuria. Infection intensities at Mwera and Kinyasini did not differ significantly ($\chi^2 = 0.83$, degree of freedom (df) = 2, $P = 0.659$) and broadly conformed to the following: light (18.8%), medium (43.8%) and heavy (37.4%) infections. Using reagent strips, the levels of micro-haematuria were highest at these two schools; Kinyasini (70.0%, 95% CI = 50.6–85.3%) and Mwera (63.3%, 95% CI = 43.9–80.1%) with a mean prevalence of micro-haematuria being 35.3% (95% CI = 27.7–43.5%).

### 3.3. Fingerprick blood SEA-ELISA

All sera samples were tested with the SEA-ELISA on the same day as collection. Table 1 shows that, based on the 150 tests performed, the mean prevalence of putative schistosomiasis was 48.0% (95% CI = 39.8–56.3%). Prevalence of positive SEA-ELISA children at the unit of the school ranged from a minimum of 13.3% (95% CI = 3.8–30.7%) at Muyuni to a maximum of 86.7% (95% CI = 69.3–96.2%) at Kinyasini. No significant difference was detected in the frequency distribution of graded SEA-ELISA positive reactions (i.e. positive and strong positive) between Mwera and Kinyasini ($\chi^2 = 1.24$, df = 1, $P = 0.266$).

The positive association between SEA-ELISA and increasing egg count is shown in Fig. 1A. Children with positive or strong positive SEA-ELISA responses were 8.3 and 42.3 times (both $P < 0.001$), respectively, more likely have $S. \text{haematobium}$ eggs in urine than those without although it should be noted that there were a total of five children who had eggs in urine yet were found to be SEA-ELISA negative. The relationship between positive SEA-ELISA and children with micro-haematuria is shown in Fig. 1B. Children with positive or strong positive SEA-ELISA responses were 30 and 114 times (both $P < 0.001$), respectively, more likely to have micro-haematuria than those children without.

### 3.4. Diagnostic comparisons and predictors of prevalence

For the urine-CCA strip, the diagnostic scores in this evaluation were as follows: $SS = 9\%$ (95% CI = 2–21%), $SP = 98\%$ (95% CI = 93–100%), $PPV = 67\%$ (95% CI = 22–96%) and $NPV = 71\%$ (95% CI = 63–78%). The urine-CCA strip could not be used as a predictor of general prevalence by school.

For the SEA-ELISA, the diagnostic scores are shown in Table 2 for all data and those obtained for boys and girls alone assuming either microscopy or SEA-ELISA to be the diagnostic ‘gold standard’, respectively. When microscopy was considered the diagnostic standard, the diagnostic scores were as follows: $SS = 9\%$ (95% CI = 2–21%), $SP = 98\%$ (95% CI = 93–100%), $PPV = 67\%$ (95% CI = 22–96%) and $NPV = 71\%$ (95% CI = 63–78%).

### Table 2

<table>
<thead>
<tr>
<th>Diagnostic parameter</th>
<th>SEA-ELISA vs. microscopy</th>
<th>Microscopy vs. SEA-ELISA</th>
</tr>
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<tbody>
<tr>
<td><strong>Total population</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$SS$</td>
<td>89 (76–96)</td>
<td>57 (45–69)</td>
</tr>
<tr>
<td>$SP$</td>
<td>70 (60–79)</td>
<td>94 (86–98)</td>
</tr>
<tr>
<td>$PPV$</td>
<td>57 (45–69)</td>
<td>89 (76–96)</td>
</tr>
<tr>
<td>$NPV$</td>
<td>90 (86–98)</td>
<td>70 (60–79)</td>
</tr>
</tbody>
</table>
1998; Ayele et al., 2008). However, the results obtained in this study revealed a very strong positive association between microscopy and the putative prevalence of *S. haematobium* at the school level. The fitted trend line (i.e., y = 0.760x – 0.053) gave a very good representation of the relationship with a high R² value (i.e., >0.90 is regarded as a very good fit), which is demonstrative of strong proportionality (~75%) between microscopy and SEA-ELISA methods. Of particular note is the correlation coefficient, which was 0.9297.

**4. Discussion**

Developing better diagnostic protocols with increased sensitivity and specificity is central within the ethos of the monitoring and surveillance programme of *P. haematobium* infections, while CCA ELISA-based protocols can (Kahama et al., 1998). It is known that ELISA is more sensitive than lateral flow devices (Van Lieshout et al., 2000) and plausible explanations have already been advanced, such as, differences in *S. haematobium* populations between regions (Stothard et al., 2006). However, it is evident that levels of excreted schistosome CCA in the urine of children with patent urinary schistosomiasis presently fall below the detection threshold of the reformulated strip, whereas excreted levels of CCA in children with patent intestinal schistosomiasis do not. Given that the diagnostic scores of Hemastix® have been shown to be favourable throughout the duration of the *P. haematobium* infection, it is unlikely that any future antigen detection strip could either perform better or be more affordable within a context of large-scale operations against urinary schistosomiasis.

**4.2. The SEA-ELISA**

Despite the advantages of serological tools (Doenhoff et al., 2004), to date, such methods have found little application in schistosomiasis control programmes carried out in sub-Saharan Africa unlike those operating in China (Zhu, 2005). A common criticism of assays based upon anti-schistosome antibody titres has been that excreted antigens are not problematic and patient compliance was excellent. In our hands we have found the field performance of this SEA-ELISA kit to be straightforward to use, robust and reliable. Indeed, the diagnostic scores obtained in this evaluation were good (Table 2) and the positive association between increasing egg count and raised antibody titre was strong (Fig. 1). It is also worth mentioning that children with positive or strong positive SEA-ELISA titres were 30 and 114 times (both P < 0.001) more likely to have micro-haematuria than those children without. Unravelling cause and correlation precisely in this instance will be difficult as both are proportional with egg counts, but it may be that an increasing SEA-ELISA titre could also be related with an increasing immuno-modulated inflammation reaction. If so, then this could further promote the increased release of blood in those with bladder inflammation as eggs are voided.

From a disease monitoring perspective, identifying the strong positive linear correlation of estimated prevalence by school using the reformulated urine-CCA strip was only slightly better than those originally reported from Zanzibar when the EVL manufactured test was used (Stothard et al., 2006). It can thus be firmly concluded that the reformulated urine-CCA strip does not perform at a satisfactory level for diagnosis of urinary schistosomiasis on Unguja. Confirmation that our observations made in Zanzibar were not artefactual was obtained when the remaining strips and test reagents were later used within a *S. mansoni* endemic area of Tanzania (i.e. Lake Victoria shoreline of Mwanza district). The strips performed well with the following diagnostic scores: SS = 95% (95% CI = 84–99%), SP = 80% (95% CI = 44–97%), PPV = 95% (95% CI = 84–99%) and NPV = 80% (95% CI = 44–97%) for intestinal schistosomiasis, marginally better than those originally reported for the EVL manufactured test (Stothard et al., 2006).
SEA-ELISA is important to show that the method performs well across a range of endemic settings (Fig. 2). Since our diagnostic ‘gold standard’ of microscopy, however, is based upon a single urine sample, no doubt some infections will have been missed, i.e. created false negatives, thus it might not be surprising that some additional 27 children (18%) were found to be SEA-ELISA positive while no eggs were observed within a single mid-morning urine sample. If such cases represent ‘true’ infections whose egg excretion has been sporadic, the diagnostic scores of microscopy against this new ‘gold standard’ of SEA-ELISA were very reasonable, only lacking in SS (we found 57% (95% CI = 45–69%) which is a known failing of parasitological methods) (see Hamilton et al., 1998).

4.3. Further work and future applications

The longer term dynamics of SEA-ELISA titres within this Unguja population presently remain to be determined. In so doing it would be important to interview children in greater detail to ascertain not only their immediate treatment history but also their duration of residence and water contact rates. It is particularly interesting that origin of birth and length of time attending the local school varied widely (Table 1). For example, children from Mwera have the most peripatetic travel history, while those at Kinyasini represent the least. From other studies it is evident that duration of residence is an important factor determining probabilities of schistosome infection and infection intensity in addition to specific water contact factors (Rudge et al., 2008). This subtle heterogeneity may partly explain that while prevalence of infection at Mwera and Kinyasini was equivalent a greater proportion of children at Kinyasini were SEA-ELISA positive, as is illustrated in Fig. 2. It therefore seems reasonable to speculate that anti-SEA antibody titres in children from Kinyasini will have had a longer time to accrue progressively upon comparison with those at Mwera as infections in these latter children will have had a shorter disease evolution.

To develop better disease monitoring and surveillance, consideration of the cost-effectiveness of the diagnostic method is needed, not only in cost per individual test but also ancillary budget allocations, e.g. associated consumables, equipment and staff time. The application of an expensive test may be justified when set against the value of novel information to be gained but more usually the level of implementation reflects financial constraints. For example, although urine-albumin assays are best applied within a targeted surveillance setting, since cost per test is relatively expensive, they have provided a detailed insight into the dynamics of urinary tract damage and its reversion post-treatment (Rollinson et al., 2005) which is important as kidney and bladder disease may involve different mechanisms of pathogenesis (Kouriba et al., 2005). Even though much of the morbidity of schistosomiasis is immunemediated (Vennervald and Dunne, 2004), it is perhaps surprising that large-scale control programmes have not, as yet, routinely monitored immuno-dynamics within sentinel settings. The availability of the SEA-ELISA may therefore facilitate such future studies. Presently the cost per ELISA test has yet to be set by the manufacturer but is likely to be between US$ 1.0 and 1.5 making this method affordable and attractive. The novel information to be gained from its use will bolster parasitological methods.

Conflicts of interest

The authors have no conflicts of interest concerning the work reported in this paper apart from G.J.D./A.M.D., whom as part of their research activities at LUMC, have developed the urine-CCA strips that were used in the current report. G.J.D. also has been involved in a starting spin-out business enterprise focusing on making these strips available at cost-price for health care use in developing countries.

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