Epidemiology and geography of Schistosoma mansoni in Uganda: implications for planning control

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Summary
Intestinal schistosomiasis caused by infection with Schistosoma mansoni is a widespread public health problem in Uganda. Although long known to be endemic, its current distribution within the country requires updating of parasitological data to help guide planned control. We report such data collected between 1998 and 2002 from 201 schools and 68 communities across Uganda. In accordance with epidemiological expectation, prevalence and intensity increased with age, peaking at 10–20 years and thereafter declined moderately with age, whereas intensity declined more rapidly with age, and the prevalence of infection in a school was non-linearly related to the mean intensity of infection. We used geographical information systems to map the distribution of infection and to overlay parasitological data with interpolated environmental surfaces. The derived maps indicate both a widespread occurrence of infection and a marked variability in infection prevalence, with prevalence typically highest near the lakeshore and along large rivers. No transmission occurred at altitudes >1400 m or where total annual rainfall was <900 mm; limits which can help estimate the population at risk of schistosomiasis. The results are discussed in reference to the ecology of infection and provide an epidemiological framework for the design and implementation of control efforts underway in Uganda.

keywords Schistosoma mansoni, intestinal schistosomiasis, epidemiology, geographical information systems (GIS), control programmes, Uganda

Introduction
In Africa, schistosomiasis is caused predominantly by infection with Schistosoma haematobium or S. mansoni, which cause urinary and intestinal schistosomiasis, respectively. Although estimates of schistosomiasis highlight the large numbers infected (van der Werf et al. 2003), the disease often receives less attention by health care personnel, national governments and international agencies than it merits. This is partly because not everyone infected will become ill. For example, studies show that degree of morbidity associated with S. mansoni is related to the intensity of infection (Gryseels 1992; van der Werf et al. 2002). In light infections, individuals remain asymptomatic. In mild infections, diarrhoea, bloody stool, abdominal pain and nausea can occur, while in heavier infections, extensive fibrosis of the liver may lead to hepatomegaly, splenomegaly and ascites (Lambertucci 1993). Fortunately, much of this can be reversed and prevented through early and regular chemotherapy with praziquantel (Boisier et al. 1998; Hatz et al. 1998; Frenzel et al. 1999). Thus, the current control strategies for schistosomiasis have shifted from stopping transmission to controlling morbidity, using chemotherapy, supported by health education and transmission control.

As resources available for control are often limited, it is essential to know the distribution of schistosomiasis to devise and target optimal intervention strategies. Previous approaches in describing schistosomiasis in Africa have typically been made at the national level, using data from the few studies available within a country and then extrapolating these to the country as a whole. While such an approach may be effective for advocacy, it is of limited practical relevance to the targeting of control efforts. For example, in Uganda, although S. mansoni has long been known to occur along the shores of Lake Albert and the Albert Nile (Nelson 1958; Ongom & Bradley 1972) the national situation has only been reviewed up to 1984 (Doumenge et al. 1987). Urinary schistosomiasis caused by infection with S. haematobium, has a more restricted distribution, limited to districts near Lake Kyoga, where it coexists with S. mansoni (Bradley et al. 1967).

The impetus for obtaining spatially detailed data for Uganda has recently been sharpened by the prospect of large-scale control, as the result of support from the Bill and Melinda Gates Foundation through the
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Schistosomiasis Control Initiative. Successful implementation of this control necessitates rigorous understanding of the epidemiology of schistosomiasis. However, much of the information for Uganda is more than 30 years old, and is based on varying study populations and study designs. The objective of the present study was therefore to present and analyse epidemiological data from Uganda collected since 1998, using similar survey designs and diagnostic methods, to provide a more accurate perspective on the epidemiology, ecology and control of *S. mansoni* in the country. The specific aims were to: (i) describe the epidemiology of infection by age and sex; (ii) investigate the relationship between prevalence of infection in a community and intensity of infection in a community; (iii) describe the geography of infection; (iv) investigate the large-scale ecological correlates of infection patterns; and (v) discuss the implications of the study results for the design and implementation of the planned control.

Materials and methods

Parasitological investigations

Between 1998 and 2002, the Vector Control Division of the Ministry of Health undertook epidemiological surveys across the country, among both school and community populations. Schools were selected based on ecological differences in rainfall, altitude and temperature. Ecological zones were identified using a combination of expert opinion and ecological zone mapping (Brooker et al. 2002a). The number of schools in each zone was calculated as a proportion of the total population of each zone. All 201 schools were visited. In each school, 30 boys and 30 girls were selected randomly. Where resources permitted, the sample size was increased. Data are also available from 28 schools in Nebbi district. However, individual level data for these schools are not available.

Community surveys were purposively selected in areas near large water bodies, where prevalence was expected to be high. The residents were informed of the study purpose and consent was obtained. Every fifth household was randomly selected and all household members were asked to provide a single stool sample.

Collected samples were examined in duplicate within 60 min using the Kato-Katz method and egg counts are expressed as arithmetic mean values. Participation was voluntary and had been approved by the school or community committee. Mass treatment of the whole study population with praziquantel (40 mg/kg) was given where the prevalence of infection exceeded 50%; otherwise infected people received individual treatment.

Environmental data

We restricted the analysis of the association between infection patterns and environmental variables to data for school-age children in either schools or communities, in order to minimize the variation by age in infection levels. In Uganda, detailed meteorological observations are available for a limited number of sites, which do not adequately capture the range of climate conditions within the country. The paucity in spatial resolution of meteorological data can be overcome by using interpolated meteorological surfaces or remotely sensed satellite sensor data, which were derived from the Pathfinder Advanced Very High Resolution Radiometer (AVHRR) sensor on-board the National Oceanic and Atmospheric Administration’s polar-orbiting meteorological satellites. To reduce cloud contamination in satellite data it is common practice in remote sensing to use long-term synoptic (long-term average) mean values, based on compositing of images (Hay 2000). The satellite data included 8 × 8 km spatial resolution Land Surface Temperature (LST) and Normalized Difference Vegetation Index derived from the AVHRR land dataset (http://daac.gsfc.nasa.gov/data/dataset/AVHRR) and processed using procedures outlined by Hay (2000). Interpolated rainfall surfaces were taken from the (http://www.brc.tamus.edu/char/) and an interpolated digital elevation model of Africa was obtained from the Global Land Information System of the US Geological Survey (http://edcwww.cr.usgs.gov/landdaac/gtopo30/). The geographical location of each school was recorded in the field by means of a hand-held global positioning system (Magellan Systems Corporation, San Dimas, CA, USA) and spatial data were displayed using ArcView (v3.3, ESRI, CA, USA).

Image processing of high-resolution satellite remote sensing data was carried out to derive thematic maps of permanent water bodies. Digital Enhanced Landsat Thematic Mapper (ETM+) data for 6 March 2000 were acquired. The ETM+ sensor measures radiation reflected from the Earth’s surface in a number of discrete spectral bands. From an ecological standpoint the most useful of these (bands 1–5 and 7) cover the visible and near infrared portions of the electromagnetic spectrum and have a spatial resolution of 30 m. Data for Uganda were geometrically corrected with reference to global positioning system ground control points using ENVI image processing software (Version 3.5; RSI Inc., Boulder, CO, USA). To produce coverages of water bodies we used a standard ‘supervised’ classification approach, where a maximum likelihood classification is carried out to allocate each image pixel to either water or non-water. Subsequently, the distance of each location to the nearest water body was
determined using standard geographical information system (GIS) functionality in ArcView.

Statistical analysis
The relationship between prevalence \( \Pr(x > 0) \) and mean intensity of infection \( M \) was modelled using logistic regression assuming a binomial distribution of prevalence, about the expected mean, with the constraint that the theoretical prevalence should be zero at zero intensity (further details given by Guyatt et al. 1994). This is given by: \( \logit[Pr(x > 0)] = \beta_0 + \beta_1 \ln(M) \). The fit of alternative models including higher order polynomials was tested by comparing residual deviances of each model, and formally tested by chi-square distribution (Venables & Ripley 1999). This model was fitted using S-PLUS 2000 (Math Soft, Seattle, WA, USA). Associations between prevalence of \( S. \) mansoni and environmental variables were investigated using the non-parametric Spearman’s rank correlation.

Results
School survey results
Individual-level data were available for 13,798 schoolchildren from 201 schools. The age range of the study population was 5–21 years, and the male-to-female ratio was 1.08:1. The mean number of children in each school was 69 (range: 27–142). The overall prevalence of \( S. \) mansoni among schoolchildren was 20.4\% (95\% CI: 19.7, 21.1\%). The prevalence among boys was 21.8\% (95\% CI: 20.9, 22.8\%) and among girls was 19.0\% (95\% CI: 18.1, 19.9\%). The age profile among schoolchildren followed the expected pattern: the prevalence and intensity of infection increased with age until 14 years and then declined (data not shown).

Community survey results
Data were available for 9829 individuals from 68 communities. The age range of the study population was 1–90 years, and the male-to-female ratio was 1.22:1. The mean number of individuals in each community was 145 (range: 25–289). Among these communities the overall prevalence of \( S. \) mansoni was 47.5\% (95\% CI: 46.5, 48.5\%). The prevalence among boys was 52.9\% (95\% CI: 51.6, 54.2\%) and among females was 40.8\% (95\% CI: 39.4, 42.3\%). The age profile among schoolchildren followed the expected pattern: the prevalence and intensity of infection increased with age until 14 years and then declined (data not shown).

Relationship between prevalence of infection and intensity of infection
Previous studies demonstrate a non-linear relationship between the intensity of infection and prevalence of infection, but show that the relationship varies according to region (Guyatt et al. 1994). In order to assess this relationship in Uganda, Figure 2 depicts the relationship between the intensity of infection and prevalence of...
infection, and the relationship estimated by the logistic regression model. This suggests that the mean intensity of infection is low at low prevalence (<20%), moderate at moderate prevalence of infection (20–50%), and disproportionately high where prevalence of infection exceeds 50%.

Geography of schistosomiasis

Data aggregated at the school or community were analysed to investigate the geographical distribution of *S. mansoni* in Uganda. Figure 3 highlights an uneven distribution of infection prevalence. Prevalence appears to be highest close to the shores of Lake Albert, the Albert Nile, Lake Kyoga and the eastern shores of Lake Victoria. In the northern areas of the country, prevalences were lower (<50%), while prevalence was generally <20% in the south-west of the country away from Lake Victoria, and >50% close to Lake Victoria. Areas of zero or low prevalence are found in the north-east of the country. Prevalence is also low in much of eastern Uganda; but paddy rice cultivation here has become popular in recent years and is associated with the emergence of *S. mansoni* (Bukenya *et al.* 1994). Data are available for Lira District, north of Lake Kyoga, but because of civil unrest these data have not been mapped and not included in the present analyses, although survey results indicate prevalences of 15–75% (Vector Control Division, unpublished data). In the capital, Kampala, previous surveys report a prevalence of 4% (Kabatereine *et al.* 1996).

Investigation of the observed geographical distribution of schistosomiasis with selected large-scale environmental variables was undertaken using data of school-aged children from schools and communities only, thereby reducing the variation by age in infection levels. In areas above 1325 m above sea level, no or very little transmission of schistosomiasis was observed (Spearman’s $\rho = -0.42$, $P < 0.001$; Figure 4a). An absence or very low transmission was also observed in areas with annual total rainfall <900 mm ($\rho = 0.01$, $P = 0.78$; Figure 4b). No relationship was demonstrated between the infection patterns and temperature- or vegetation-derived variables (data not shown).

These environmental limits can help delineate areas where schistosomiasis transmission is unlikely to occur, where altitude exceeds 1325 m or rainfall is <900 mm (see Figure 4). Overlaying these limits with the 2002 national census results (http://www.ubos.org/2002census.html) enables the population not at-risk of schistosomiasis at the subdistrict (so-called county) level to be estimated: 8 million in 56 counties. Conversely, it is estimated that 16.7 million in 108 counties are estimated to be at-risk of schistosomiasis. In these areas, a wide range of prevalences are expected to occur (Figures 4a–b). However along the shores of Lake Victoria, a clear relationship was observed between distance to lakeshore and prevalence of
S. mansoni, with prevalence <15% at distances greater than 5 km ($p = -0.69, P < 0.001$; Figure 4c). In areas near the Albert Nile, although there is more scatter in the data points, prevalence also decreases with increasing distance from large water bodies ($p = -0.49, P < 0.001$; Figure 4d).

**Discussion**

The design and implementation of any parasite control requires a thorough understanding of the epidemiology and geography of infection and disease. In Uganda, although it has been known for a long time that schistosomiasis is a serious public health problem (Nelson 1958; Ongom & Bradley 1972), the current situation has not been fully described. Our study shows that intestinal schistosomiasis has a wider distribution than previously shown (Doumenge et al. 1987), and is currently endemic in at least 38 districts. The overall prevalence of infection was highest for community populations than for school populations because schools were selected to provide a cross-section of the Ugandan population, whereas communities were purposively selected near lakes, where prevalence is expected to be high.

In accordance with epidemiological expectation (Jordan & Webbe 1993), our results show that infection is acquired early in life and prevalence and intensity increase with age, peaking at 10–20 years and declining.
moderately with age, whereas intensity declines more rapidly with age. Among older children and adults, infection is more prevalent and intense among males than females. This sex difference resembles those from several other populations in Africa (Smith et al. 1979; Butterworth et al. 1984; Lwambo et al. 1999; Naus et al. 2003) but differs from other populations (de Clercq et al. 1985; Adekolu-John & Abolarin 1986). Such sex differences are generally presumed to reflect differences in exposure to infection, which are often occupationally related. However, this is not always the case. For example, in Kenya, the prevalence of S. mansoni is higher in men than in women, yet detailed water contact studies indicate that women have longer and more frequent contact with infected water bodies during the collection of water and the washing of clothes (Butterworth et al. 1984). However, although the duration of water contact on a daily basis may be similar in the two sexes, they are involved in different activities that may carry different risks of infection (Kabatereine et al. 1999). Alternatively, Webster et al. (1997) suggest that hormonal differences between males and females may account for higher infection rates in males than females, but further studies are required to ascertain this suggestion.

Our analysis also sheds light on the ecology of S. mansoni in Uganda, and shows that S. mansoni only represents a public health problem of major concern under certain environmental conditions, presumably those conditions favourable for the snail hosts. The main intermediate hosts of intestinal schistosomiasis in Uganda are Biomphalaria stanleyi in Lake Albert and the Albert Nile and B. sudanica in the swampy lake margin of Lakes Victoria, Albert and Kyoga (Prentice 1972; Kabatereine 2000). Further away from the lakeshore, seasonal transmission takes place through B. pfeifferi, which inhabits temporary water bodies (Prentice 1972). Climatic conditions, primarily rainfall and temperature, influence the distribution and density of snails and the rate of schistosomal development in the snail host (Appleton 1978; Sturrock 1993), and probably influence the distribution of schistosomiasis in Uganda.

Absence of schistosomiasis transmission was associated with annual rainfall <900 mm. This influence of rainfall is inherently linked to availability of water bodies. The relative regularity and abundance of rainfall in areas where annual rainfall exceeds 900 mm provides ideal conditions for the occurrence of snail intermediate hosts. By contrast, in areas where rainfall is <900 mm, the temporary nature of water bodies may not be suitable for the growth of floating and submerged vegetation, habitats of Biomphalaria spp. snail populations.

Altitude is related to the distribution of schistosomiasis, with no or very little transmission occurring above 1325 m. Previously, Schwetz (1951) reported prevalences of <5% in communities adjacent to Lake Bunyonyi in south-western Uganda, at an altitude of 1900 m. However, no recent surveys have been undertaken to confirm this and it is possible that these, generally light, infections were acquired at lower altitude elsewhere. Elsewhere in Africa, the relationship between patterns of S. mansoni and altitude is well established: the upper altitudinal limit of S. mansoni is 2000–2200 m in Ethiopia (Kloos et al. 1988) and 1800 m in Kenya (Diesfeld 1969). At these altitudes, low temperatures (<16 °C) cause snails to die before the cercariae mature from sporocysts, limiting transmission (Pflüger 1980; Joubert et al. 1986). In Ethiopia, Malone et al. (2001) found that annual composite maximum satellite-derived LSTs of 20–33 °C and wet season values of 18–29 °C defined the distribution of S. mansoni prevalence >5%. In Uganda, by contrast, no association was observed between S. mansoni prevalence and temperature-derived variables. This lack of association is explained in part by the small thermal range (23.8–37.7 °C) evident among survey locations, and thus, low temperature cannot explain the apparent altitude threshold of 1325 m observed in Uganda. The reason for this threshold is unclear and further study is recommended to investigate the influence of vegetation and other factors.

Apart from helping to exclude areas where S. mansoni is unlikely to be a problem, the results also highlight where the problem of S. mansoni is greatest. It has been known for some time that schistosomiasis is concentrated along the shores of large water bodies and rivers in Uganda (Nelson 1958). Children living on or near the shore are more prone to undertake risky water contact behaviour. Children are also exposed to more intense transmission because of the differential distribution of snail species in large water bodies (Nelson 1958; Gryseels et al. 1987; Kabatereine et al. 1996; Lwambo et al. 1999). We saw a clear relationship between distance to lakeshore and prevalence of S. mansoni along Lake Victoria, with prevalence <15% at distances >5 km. However, in north-west regions near the Albert Nile, relatively high infection rates (>40%) existed along small rivers and streams, and there was no clear relationship between prevalence and distance from water bodies. A practical implication of these results is that distance to lakeshore can be used as a tool for the rapid identification of high prevalence areas near Lake Victoria and possibly Lake Albert, and 5 km serves a useful threshold. However, near the Albert Nile, such a geographical tool is less applicable, and in these areas, parasitological diagnosis will typically remain the preferred option for targeting control.
Until now, no large-scale schistosomiasis control has been undertaken in Uganda. However, in 1992, the Ministry of Health drafted a national plan of control, and recent funding from the Gates Foundation through the Schistosomiasis Control Initiative (http://www.schisto.org) has enabled implementation of the plan. Our findings provide an epidemiological framework for the design and implementation of planned control interventions. First, the age profiles confirm that infection is most prevalent and intense among schoolchildren, supporting the need for a school-based strategy. Among adults, although prevalence declines only moderately with age, intensity of infection declines more rapidly. The practical implication of this is that in lakeshore areas school-based treatments may be insufficient and community treatment is preferable.

Secondly, the quantification of the relationship between prevalence of infection and mean intensity is of practical relevance to predict the potential impact of treatment. It can be used to predict mean intensity of infection on the basis of infection prevalence for areas where only prevalence data are available. Such predictions can help estimate the potential impact of treatment with varying timings and degrees of population coverage on the basis of mathematical models of transmission dynamics (Chan et al. 1995) as mean intensity is the key parameter in determining transmission dynamics. Dynamic models predict rates of re-infection over fixed time intervals, and provide estimates of infections, heavy infections and morbidity cases prevented each year. These predictions, which will require validation, will assist in quantifying the impact of control on disease burden, and thereby in evaluating the cost-effectiveness of control (Guyatt 1998).

Thirdly, the mapping of *S. mansoni* describes the geographical variation in the country and helps to characterize areas directly relevant to targeting control. In particular, GIS allows policy makers to easily visualize the extent of the problem in relation to the natural environment and population. The rainfall and altitude limits of transmission are of use in excluding areas where schistosomiasis is unlikely to be a public health problem, and so help focus on priority areas, such as near lakeshores. This information can aid estimation of the population at risk and stratify areas by risk, guiding implementation of the various intervention strategies, and so more effectively target resources (Brooker et al. 2002a).

While the potential uses of GIS for predictive modelling are attractive research objectives (Mukaratirwa et al. 1999; Brooker et al. 2001, 2002b; Malone et al. 2001), at present the approaches require intensive investments in digital data, database management and statistical modelling, which is typically accessible only to Western researchers or international organizations, and which would be expensive for national control programmes to develop and implement without external funding. However, used appropriately, GIS can provide us with a tool for standardizing programme surveillance and monitoring indicators across different countries, and can promote collaboration between disease control programmes. GIS has the potential to promote data-driven priority setting and could result in careful targeting of finite financial resources. With the recent influx of major new sources of funding for large-scale parasite control programmes, we now have the opportunity to test the usefulness of GIS for public health.

**Acknowledgements**

We thank our fieldworkers and our data manager Jackson Rwaheru for their hard work and enthusiasm, and extend sincere thanks to the schoolchildren, teachers and community members who participated in the study. We thank Neal Alexander, Simon Hay, Jon Cox and Diarmid Campbell-Lendrum for input on statistical analysis and remote sensing. We thank David Bradley and two anonymous reviewers for helpful comments on earlier drafts.

Support for the work was received from the Danish Bilharziasis Laboratory, World Health Organization, Uganda Fisheries Research Institute (FIRI), World Food Programme and the Schistosomiasis Control Initiative, which receives support from the Bill and Melinda Gates Foundation. SB was funded by a Wellcome Trust Fellowship (062692). Finally, we thank the Director General of Health Services for giving us permission to publish the results.

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