Absence of cervical schistosomiasis among women from two areas of north–eastern Brazil with endemic *Schistosoma mansoni*

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Genital manifestations in schistosomiasis haematobium are common and are associated with considerable morbidity. Although *Schistosoma mansoni* may also cause genital disease, the frequency of this complication is not known. Cervical biopsies (N=401) and Pap smears (N=981) were therefore collected from women living in two *S. mansoni*-endemic areas (in the states of Alagoas and Ceará, in north–eastern Brazil). The women were screened for the presence of sexually transmitted diseases and for the presence, in their cervical smears and/or biopsies, of *S. mansoni* eggs. Attempts at schistosomiasis control, which began in both study areas in 1977, have led to generally low intensities of infection (<30 eggs/g faeces in 99% of infections) and community prevalences of infection that range between 1% and 52%. As no schistosome ova were detected in any of the biopsies or smears, it appears that the risk, among women, of genital manifestations of *S. mansoni* infection is small in areas where the parasite load in the population is low (as the result of interventions to control intestinal schistosomiasis).

Genital schistosomiasis was first described more than a century ago, in Egypt (Madden, 1899). Since then, schistosome-related genital pathology, from the vulva to the ovaries, has been observed in women in almost every country where schistosomiasis is endemic (Feldmeier *et al.*, 1995). There is now convincing evidence that *Schistosoma haematobium* causes genital lesions in 50%–80% of the girls and women infected with this trematode (Renaud *et al.*, 1989; Kjetland *et al.*, 1996; Leutscher *et al.*, 1997; Poggensee *et al.*, 2000), but the frequency of genital pathology in women infected with *S. mansoni* is not known.

*Schistosoma mansoni* eggs have been observed, albeit rarely, in routine cervical smears and surgical specimens taken from African and American women (Arean, 1956; Sedlis, 1960). Among certain groups of female patients from endemic areas, the eggs of *S. mansoni* have been frequently encountered in the upper and lower reproductive tracts (Brygoo, 1968; Gelfand *et al.*, 1971; Renaud *et al.*, 1971; Berry, 1976; Bullough, 1976). In Brazil, Fróes (1957) stated that ‘the number of genital schistosomiasis cases seen by Brazilian gynaecologists increases from day to day’. Two years later, Câmara (1959) added that the
‘manifestations at the female genitals become more apparent every day in the clinical picture of this parasitic infection’.

These statements were, however, based on analyses, of case reports or hospital records, that could give little idea of the true prevalence of genital schistosomiasis among the female population from an endemic area.

Genital schistosomiasis mansoni may occur in women who do not appear to be excreting any schistosome eggs in their stools, although the detection of eggs in stools may be difficult, when few eggs are present (Feldmeier et al., 1995). Among women, the ‘gold standard’ criterion for the diagnosis of schistosomiasis of the lower reproductive tract is the observation of schistosome eggs in cervical biopsies (Feldmeier et al., 2001). The collection of such biopsies merely for a study on the prevalence of genital schistosomiasis would be ethically questionable but if such biopsies are collected for another purpose, such as the detection of cervical cancer, it should be relatively easy to check them for schistosome eggs. Here, the results of two community-based studies on women living in S. mansoni-endemic areas of north–eastern Brazil are reported. The women were examined gynaecologically during screening for sexually transmitted diseases (STD), and cervical biopsies were taken from some of them, to rule out cancer-related lesions. Most of the biopsies were checked for S. mansoni ova using the quantitative fresh compressed biopsy technique (QCBT) — currently the most sensitive method available for detecting cervical schistosomiasis (Feldmeier et al., 2001).

SUBJECTS AND METHODS

Study Areas and Subjects
The women investigated, as part of a larger study on STD in 2002, came from two municipalities in north–eastern Brazil: União dos Palmares, in the state of Alagoas, and Pacoti, in Ceará state. In both areas, participation was on a voluntary basis, with the informed consent of each subject, and virgins and pregnant women were excluded. In the study areas, women and girls use the natural waterbodies for bathing and washing clothes, and the girls also play in the water. The local populations are very stable and each subject participating in the study had lived in one of the study areas for at least 6 months. Since 1977, the Superintendência de Campanhas de Saúde Pública (SUCAM; the national agency for the control of endemic diseases) and later the Fundação Nacional de Saúde (FUNASA; the national health foundation) have run annual rounds of schistosomiasis detection and control (mainly based on selective mass chemotherapy), in both study areas.

UNIÃO DOS PALMARES
The study area and population of União dos Palmares have been described previously (De Lima Soares et al., 2003). Overall, 495 women aged 15–70 years from four villages were included in the study, of whom 341 agreed to be examined gynaecologically.

PACOTI
Pacoti lies in the Baturité mountains, 100 km south–west of Fortaleza, the capital of Ceará state. In 2002, 23% of the municipality’s population (of about 11,500) lived in the single urban area, and 77% in small hamlets scattered in the mountains. The cultivation of fruit and vegetables, which are sold in the markets of Fortaleza, forms the main occupation in the hamlets. The many, mostly perennial creeks and small rivers that run down the mountains support populations of Biomphalaria straminea and other snails. The 640 female residents of Pacoti who were investigated were aged 12–49 years and came either from the urban area or from one of eight hamlets (Volta do Rio, Germinal, Caititu, Holandina, Araticum, Santa Rita, Santa Quitéria and Rolador).
Gynaecological Examinations and Parasitology
Each gynaecological examination was performed, in strict privacy by a female gynaecologist, in an especially equipped room in the Padre Quiliano Hospital (Pacoti) or Women's Health Centre (União dos Palmares). The examination consisted of inspection of the vulva and the peri-anal area followed by vaginal and cervical colposcopy. During colposcopy, two smears were taken from the cervix and Pap-stained. The cervix was biopsied either only in the presence of epithelial abnormalities, to rule out cancer-related lesions (Pacoti), or in all women consenting to the procedure (União dos Palmares). Each biopsy was checked for schistosome eggs by use of the QCBT (Feldmeier et al., 2001). For this, an unfixed sample of the biopsy was pressed between two microscope slides and examined for schistosome eggs. The Pap smears were also examined for the presence of schistosome ova.

Schistosome Infection in the General Population
Data on the intensity and prevalence of S. mansoni infection in the general population (of União dos Palmares and Pacoti) and school-aged children (of União dos Palmares) were taken from the records of FUNASA. These records are based on the random selection of households and the examination of a faecal sample from each member of each selected household, as a single, Kato–Katz, thick smear.

Ethics
Ethical clearance was obtained from the Ethical Committees of the Federal University of Ceará and the Alagoas School of Medical Sciences. The information on whether a woman was pregnant or still a virgin was kept confidential. The women were given the results of the gynaecological examination, and advice on reproductive health was given by the female gynaecologist. If an STD was detected, the woman was treated according to national guidelines, and treatment for her sexual partner(s) was provided. Each biopsy was examined histopathologically for the presence of cervical intra-epithelial neoplasia. If neoplasia was suspected, the woman was referred to a specialised oncology service.

RESULTS
The demographic, gynaecological and parasitological characteristics of the two study populations are summarized in the Table. Sandy patches, the only pathognomonic sign of cervical schistosomiasis, were never observed. Polypoid lesions were present in five women. No tumours of the vulva or vagina, that might have developed from egg granulomata, were seen. No S. mansoni eggs were detected in the 401 biopsies examined by the QCBT or in the 981 Pap smears that were checked.

The intensity of infection, as measured by FUNASA in the round of random sampling in 1999, was generally very light, with 99% of infected individuals excreting fewer than 30 eggs/g faeces.

DISCUSSION
The pathology of female genital schistosomiasis is caused by the parasites' eggs and the granulomata that develop around them. The egg granulomata seem to show a predilection for the cervix, fallopian tubes, and ovaries. Of the 18 genital manifestations described in Puerto Rico by Arean (1956), for example, six (33%) occurred at the cervix and 10 (55%) in the Fallopian tubes or the ovaries. The topographic distribution of genital lesions in women from endemic areas in Brazil appears similar, with 25% of all lesions occurring at the cervix and 33% in the ovaries (Chaves, 1988; Feldmeier et al., 1998). The examination of the cervix
therefore seems to be a reasonable means of assessing the occurrence of genital schistosomiasis in an exposed population.

The present results, based on gynaecological examinations of non-pregnant, non-virgin women or girls, indicate that cervical schistosomiasis in two areas of north-eastern Brazil with endemic schistosomiasis mansoni is not a frequent event, and that the prevalence of this disease manifestation among the local women is probably <1%. In another area of north-eastern Brazil, Pernambuco, Coelho et al. (1979) only found four cases of cervical schistosomiasis among 1250 women who were excreting *S. mansoni* eggs and were screened for cervical abnormalities. The Brazilian results seem to be at odds with those from studies performed in East Africa. When, for example, Poggensee et al. (2001) examined 208 cervical biopsies from women living in an area of Tanzania where the prevalence of intestinal schistosomiasis was 35%, they found *S. mansoni* eggs in 19 (9.1%) of them. *Schistosoma mansoni* eggs were also frequently observed in genital tissue from women living in Madagascar, a country where both *S. mansoni* and *S. haematobium* prevail (Brygoo, 1968). It is unclear why cervical *S. mansoni* ova appear to be easier to detect among women from endemic areas of Africa than among women from endemic areas of Brazil. The relevant African studies have been based in areas where *S. haematobium* co-occurred and/or where the intensities of *S. mansoni* infection were relatively high. Female *S. mansoni* may perhaps mate with male *S. haematobium*. The females might then be carried to the genital plexus by the males, and there produce eggs that resemble those of *S. mansoni*. As copulating adult schistosomes have been detected in histological sections of the internal genital organs of infected women, it seems likely that the schistosome eggs found in genital tissues have been deposited there by migrating adult worms and have not simply been

**TABLE. Demographic, gynaecological and parasitological data on the two study populations**

<table>
<thead>
<tr>
<th>Study site</th>
<th>União dos Palmares</th>
<th>Pacoti</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PREVALENCE OF <em>Schistosoma mansoni</em> INFECTION IN 2001 (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Among school-age children</td>
<td>58</td>
<td>ND</td>
</tr>
<tr>
<td>Among total population</td>
<td>52</td>
<td>1–20*</td>
</tr>
<tr>
<td>No. of women examined gynaecologically</td>
<td>341</td>
<td>640</td>
</tr>
<tr>
<td>Median age of subjects and (range) (years)</td>
<td>33 (15–70)</td>
<td>31 (13–49)</td>
</tr>
<tr>
<td><strong>NO. SHOWING CERVICAL ALTERATIONS SUGGESTIVE OF SCHISTOSOMIASIS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sandy patches</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Inflammation</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Polypoid lesions</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nodular hypertrophy/cauliflower-like growth</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>NO. OF CERVICAL BIOPSIES:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taken</td>
<td>341</td>
<td>98</td>
</tr>
<tr>
<td>Checked by QCBT</td>
<td>341</td>
<td>60</td>
</tr>
<tr>
<td>Found positive for schistosome eggs</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>NO. OF PAP SMEARS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taken</td>
<td>341</td>
<td>640</td>
</tr>
<tr>
<td>Examined</td>
<td>341</td>
<td>640</td>
</tr>
<tr>
<td>Found positive for schistosome eggs</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Prevalence varied considerably between the different hamlets but the mean community prevalence was 3.7%. ND, Not determined; QCBT, quantitative compressed biopsy technique.
carried there, in the bloodstream, from other sites (Fröes, 1957).

Abnormal migration patterns of adult worms might be triggered by crowding in heavily infected individuals. Feldmeier et al. (1982) showed that, in children co-infected with S. mansoni and S. haematobium, the number of S. mansoni eggs in the urine was directly related to the number of S. mansoni eggs excreted in the stool. If, as seems likely, the number of eggs excreted per unit of stool or urine is correlated with the number of worm pairs dwelling in the relevant organs, this observation indicates that, when overcrowded, adult S. mansoni in the haemorhoidal veins tend to migrate through the recto-vesical anastomoses, eventually to reach the plexus vesicalis. A similar phenomenon may trigger the migration of overcrowded S. mansoni worms to the genital organs of infected women.

It may be such a response to overcrowding that explains why, in Brazil, there were many case reports of genital schistosomiasis between 1936 and the early 1950s, when intensities of infection were high in endemic areas (Coutinho, 1935; Ribeiro, 1936; Coutinho and Coelho, 1940; Fernandes and Lapa, 1940; Luz, 1940; Werneck and Junqueira, 1941; Motta and Elejalde, 1943; Gaiaño and Gueiros, 1945; Junqueira, 1946; Armbrust, 1950; Galluci et al., 1951; Schmitt, 1954), but relatively few since regular, nation-wide control of schistosomiasis began in 1977. In rural Alagoas, although the prevalence of intestinal schistosomiasis is still high, the intensity of infection is generally low. In the endemic areas of Ceará, the intensity of infection has never been high since 1977, and community prevalences are <5%.

In the present study, no evidence of cervical schistosomiasis was detected in almost 1000 women and girls from areas with a low intensity of infection. At the population level, therefore, the occurrence of genital lesions is probably determined by the number of worms parasitising an individual. The schistosomiasis control since 1977 will not only have reduced the frequency of liver complications, such as fibrosis, ascites and the formation of collaterals (which may eventually lead to gastro-intestinal haemorrhage and death), but also have reduced the incidence of the genital manifestations. The genital disease may still develop in individual women, even when the intensity of infestation is low (Marago et al., 2004), however, and must remain an important differential diagnosis in gynaecological patients from endemic areas.

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REFERENCES


