ULTRASONOGRAPHIC EXAMINATION OF HAITIAN CHILDREN WITH LYMPHATIC FILARIASIS: A LONGITUDINAL ASSESSMENT IN THE CONTEXT OF ANTIFILARIAL DRUG TREATMENT

LEANNE M. FOX, BRUCE W. FURNESS, JENNIFER K. HASER, JEAN-MARC BRISSAU, JACKY LOUIS-CHARLES, SUSAN F. WILSON, DAVID G. ADDISS, PATRICK J. LAMMIE, AND MICHAEL J. BEACH

Epidemic Intelligence Service, Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Hôpital Sainte Croix, Leogane, Haiti

Abstract. To assess the clinical findings associated with detection of adult Wuchereria bancrofti worms on ultrasound, 186 schoolchildren in a filariasis-endemic area of Haiti underwent physical and ultrasonographic examinations. The filaria dance sign (FDS) of adult W. bancrofti was detected in the inguinal and crural lymphatics of 28 (15%) children. FDS detection was more common in older children \((P = 0.003)\) and in those with a history of inguinal lymph node inflammation \((P = 0.002)\) or crural lymphadenopathy on physical exam \((P = 0.01)\). Twenty-five FDS-positive children were reexamined after three annual cycles of mass treatment for lymphatic filariasis (LF). The total number of adult worm nests detected by ultrasound decreased from 29 to 4 \((P \leq 0.0001)\). FDS and lymphangiectasia were detected in the intrascrotal \((N = 3)\) and inguinal \((N = 1)\) lymphatic vessels of three postpubescent boys. This study demonstrates clinical and subclinical findings of LF in FDS-positive children.

INTRODUCTION

Lymphatic filariasis (LF) is the second leading cause of permanent disability worldwide, affecting approximately 120 million persons. Although an estimated 44 million of those infected suffer from one or more of the clinical manifestations of filarial disease, including lymphedema and elephantiasis of the limbs, hydrocele, chyluria, pneumonitis, and recurrent bacterial infections associated with damaged lymphatics, the other 76 million persons have laboratory evidence of filarial infection, but no overt signs or symptoms of disease.

Unlike other helminth infections, LF is generally considered a disease of adults and late adolescence with a higher prevalence in males. In Leogane, Haiti, about 5% of women suffer from lymphedema and up to 30% of adult males have hydrocele, both of which are clinical manifestations of filarial disease. In addition, approximately 25–30% of the adult population is microfilaremic (MF+) and 50% have evidence of circulating filarial antigen (CFA), an indicator of adult worm infection. As the chronic manifestations of disease traditionally occur after puberty or early adulthood, most clinical and epidemiologic investigations have focused on adult populations, and little is known about the pathogenesis of filarial disease in children.

Only recently has it been demonstrated that infection and disease are more common in children than previously thought. Analysis of circulating filarial antigen levels in young children in Leogane, Haiti, demonstrated that filarial infections are acquired early in life with filarial antigen prevalence greater than 30% among 4-year-old children. In addition, the finding of unexplained chronic adenopathy has been shown, both histopathologically and clinically, to be an important presentation of LF in children.

The application of ultrasonography has been a useful tool for understanding filariasis in both symptomatic and asymptomatic adults and children. It has been successfully used to assess, in vivo, the efficacy of antifilarial drugs, describe preclinical abnormalities in the lymphatic vessels of males, identify living adult worms in microfilaremic (MF−) males, and localize living adult worms in the lymphatics of the female breast. Nevertheless, there have been few published studies where ultrasound has been used in children.

The objectives of this study were to assess the feasibility of using ultrasound as a diagnostic tool for filariasis in children, to determine factors associated with a positive ultrasound finding, and, finally, to longitudinally assess, both clinically and ultrasonographically, a subpopulation of infected children.

MATERIALS AND METHODS

Study design. The protocol for this study was approved by the Institutional Review Board of the Centers for Disease Control and Prevention and the Ethics Committee of Hôpital Sainte Croix. Written informed consent was obtained from the child’s parent or guardian, and written assent was obtained from children (aged 7 years or older) for participation in the study. Study participants were a subgroup \((N = 186)\) of a larger double blind, placebo-controlled study \((N = 1,292)\), evaluating single-dose combination therapy using diethylcarbamazine (DEC) and albendazole (ALB) for dual control of LF and intestinal helminths in schoolchildren (grades 1–4) attending 12 different schools in Leogane, Haiti. The placebo-controlled study began in November 1998 and concluded 6 months later in May 1999. Children were randomized to four groups: DEC only (6 mg/kg), ALB only (400 mg), DEC and ALB or placebo. At the end of the study, May 1999, those children who had received placebo or ALB only were treated with DEC and ALB, whereas those children who received DEC and ALB or DEC only received ALB. One year after initial treatment, November 1999, all children were retreated with DEC and ALB. Annual mass drug treatment (MDA) with DEC and ALB began in Leogane in October 2000.

One hundred eighty-six schoolchildren were selected from the enrollees in the drug study for clinical and ultrasonographic assessment. These included all 116 microfilaremic (MF+) children and a representative sample of 70 microfilaremic (MF−) children. The 186 children underwent laboratory, clinical, and ultrasonographic assessments in November 1998 as detailed in Table 1. All 28 FDS-positive children un-
derwent serial laboratory, clinical, and ultrasonographic examinations in March and May 1999, 3 and 6 months posttreatment, respectively.

**Long-term assessment.** Twenty-five of the 28 children who had living adult worms detected on ultrasound in 1998 were reexamined in November 2002, 4 years after their initial exam. A questionnaire, physical exam, and ultrasound examination were administered and blood was collected for measurement of circulating filarial antigen. Children who had evidence of living adult worms on ultrasound in 2002 were treated with DEC (6 mg/kg) and ALB (400 mg) after completing the ultrasound examination.

**Laboratory evaluation.** Microfilaria status was determined by microscopic examination of a Giemsa-stained 20 μL blood smear obtained by finger prick between 1900 and 2130 hours. An additional 100 μL of blood was collected in capillary tubes at the same time and serum samples were separated and frozen for later testing. The Og4C3 assay (JCU Tropical Biotechnology Pty Ltd., Queensland, Australia) for circulating filarial antigen was performed. Antigen levels were quantified against a standard curve and were highly reproducible between assays. Quantitative antigen assay results of 250 units or greater were considered positive and specimens with a response of ≥ 32,000 antigen units were assigned a fixed value of 32,000. Laboratory personnel were blinded to the infection status of the children.

**Clinical evaluation.** Medical history was collected in a single interview with children and their parents. Questions were asked regarding pain, redness, swelling, and warmth of the lower extremities and lymph nodes (axillary, crural, epitrochlear, inguinal, and popliteal) and past surgical procedures. Crural lymph nodes are located in the medial thigh area below the superficial inguinal lymph nodes. Physical examinations were also performed on each of the children concentrating on sexual maturity and lymphadenopathy of the axillary, crural, epitrochlear, inguinal, and popliteal lymph nodes. Lymphadenopathy was defined as tenderness, induration, or palpable irregularity of the lymph node on physical examination. The sexual maturity ratings (SMRs) of Marshall and Tanner were used to assess the secondary sexual characteristics of pubertal maturation. These SMRs comprise five stages for each sex and are based on breast and pubic hair development in girls and genital and pubic hair development in boys. The presence of hydrocele or spermatic cord thickening, both of which can be indicators of filarial disease in men, was also documented for boys. A single examiner (B. F.) performed physical examinations during the first 1.5 years. In 2002, two examiners (B. F. and L. F.) performed the physical examinations. Personnel performing the physical examinations were blinded to the infection status of the children on the 1998 exams.

Ultrasound (US) examinations (Acuson Computer Sonogram 128XP/10C, 5.0 MHz transducer; Mountain View, CA) were performed to detect evidence of adult worm infections including adult worm nests and lymphangiectasia (lymphatic dilatation) in the lymph node areas (axillary, crural, and inguinal), the breast in postpubescent females, and the scrotum for boys. Exams were conducted for 20–30 minutes with children resting in the supine position. As with the laboratory and physical examinations, personnel performing the ultrasonographic examinations were blinded to the infection status of the children. Adult worm nests were identified based on the characteristic motility of the adult worm (filaria dance sign; FDS). Every worm nest was confirmed in B-mode, M-mode, and pulse wave Doppler-mode.

**Statistical methods.** For the purposes of data analysis, participants were allocated to one of two groups based on ultrasonographic findings; those children who had evidence of living adult worms on ultrasonographic examination (FDS-positive) and those children who had no evidence of adult worms on ultrasound (FDS-negative). Data were analyzed using Epi-Info version 6.04 (CDC, Stone Mountain, GA) and SAS version 8 (SAS Institute, Cary, NC). In univariate analyses, χ² and two-sided Fisher’s exact tests were used to compare categorical variables; continuous variables were compared using the nonparametric Wilcoxon rank sum tests.

**RESULTS**

**Initial assessment.** Of the 186 children enrolled, 90 (48%) were female, and the mean age was 8.8 years (range, 5–13 years). There was no difference in mean age between the sexes. Based on thick smear results, 116 (62%) of children were microfilaria positive (MF+) with a geometric mean microfilarial density of 4.2 mf/20 μL (range, 1 to 190 mf/20 μL). A total of 175 (94%) children had a quantitative antigen assay done, of whom 142 (81%) were circulating filarial antigen positive (CFA+) with a geometric mean filarial antigen level of 1,394.2 antigen units (range, 0 to 32,000 units, positive ≥ 250 units).

All 186 children had data collected on medical history. Only 4 (2%) children reported a history of lower extremity
problems, as defined by pain, redness, swelling, or warmth of the lower extremity. In contrast, 122 (66%) reported a history of lymph node pain, redness, swelling, or warmth. All of these children reported lymph node swelling, 119 (98%) with lymph node involvement of the inguinal area. No children complained of popliteal lymphadenopathy. Only one child reported any past surgical procedures. This 11-year-old child had a cystectomy of her left breast and axillary area 7 years earlier. Medical history of lymph node or lower extremity problems did not differ significantly by sex, microfilaria status, or antigen status.

All 186 children had physical examinations performed. Of these, 179 (96%) had a SMR stage of 1 or 2, indicating early sexual development. On physical exam, 158 (85%) children had inguinal lymphadenopathy, 44 (24%) had axillary lymphadenopathy, and 11 (6%) had crural lymphadenopathy. No epitrochlear or popliteal lymphadenopathy was detected. In males, no hydrocele or spermatic cord thickening was noted. Of children with inguinal lymphadenopathy on physical examination, 89 (56%) were boys. Physical findings did not differ significantly among SMR stages or by antigenemia or microfilaria status.

All 186 children had an US examination. Of these, 28 (15%) had ultrasonographic evidence of adult Wuchereria bancrofti nests; that is, the filaria dance sign (FDS) was detected. These children ranged in age from 8 to 11 years (Table 2). Detection of adult W. bancrofti nests was associated with microfilariaemia ($P = 0.02$), a higher geometric mean microfilarial density ($P = 0.004$), a higher geometric mean filarial antigen level ($P = 0.003$), and a greater mean age ($P = 0.003$). In the FDS-positive children, a total of 32 living adult worm nests were visualized, with a range of one to two nests per child. All of these nests were located in the inguinal (88%) or crural (12%) lymphatic vessels. The mean lymphatic diameter at the site of living adult worm nests was 4.5 mm (range 3–7 mm); a value that indicated lymphangiectasia given previous work demonstrating normal lymphatic vessel diameters of 0.5 to 1 mm in the intrascrotal lymphatic vessels of adult men.

Additionally, children were more likely to have a positive ultrasound examination if they reported a history of lymph node problems in general ($RR = 1.5, 95\% CI = 1.2 to 1.7$) or inguinal lymph node problems specifically ($RR = 1.5, 95\% CI = 1.3 to 1.8$) or had crural lymphadenopathy on physical examination ($RR = 4.7, 95\% CI = 1.5 to 14.4$). The association between a positive ultrasound examination and the presence of inguinal lymphadenopathy on physical exam was borderline significant ($RR = 1.2, 95\% CI = 1.0 to 1.3$). Boys were more likely than girls to report a history of lymph node problems ($RR = 1.4, 95\% CI = 1.2 to 1.7$) and to have crural lymphadenopathy on physical examination ($RR = 5.0, 95\% CI = 1.4 to 17.9$). These relationships were not significantly different among SMR stages.

**Posttreatment assessment.** The 28 FDS-positive children, who were randomized to four treatment groups in November 1998 (Figure 1, Treatment no. 1), underwent follow-up ultrasonographic examinations in March and May 1999, 3 and 6 months posttreatment. Twelve living adult worm nests were detected in March 1999 and eight adult worm nests were detected in May 1999; both of which were statistically fewer from the initial number of adult worm nests detected ($P \leq 10^{-5}$). The proportion of FDS-positive children belonging to each of the treatment groups is noted in Figure 1. Seventeen (71%) children demonstrated a decrease in circulating filarial antigen level from November 1998 through May 1999 and the mean percent reduction in circulating filarial antigen level among these children was 44% (range, 2–100%).

**Long-term assessment.** Twenty-five of the 28 FDS-positive children were reassessed with questionnaire, ultrasonographic demonstration of normal lymphatic vessel diameters of 0.5 to 1 mm in the intrascrotal lymphatic vessels of adult men.

---

**Table 2.** Clinical and laboratory characteristics associated with detection of living adult W. bancrofti by ultrasound (the filaria dance sign; FDS) in 186 children: Leogane, Haiti

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FDS-positive† ($N = 28$)</th>
<th>FDS-negative ($N = 158$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (range)</td>
<td>9.9 (8–11)</td>
<td>8.6 (5–13)</td>
<td>0.003</td>
</tr>
<tr>
<td>Male sex</td>
<td>16 (57%)</td>
<td>80 (51%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Microfilaria-positive (MF+)</td>
<td>23 (82%)</td>
<td>93 (59%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Geometric mean microfilarial density (mf/20 $\mu$L) (range)</td>
<td>10.8 (0–158)</td>
<td>3.5 (0–190)</td>
<td>0.004</td>
</tr>
<tr>
<td>Filarial antigen positive (CFA+)</td>
<td>25 (93%)*</td>
<td>117 (79%)†</td>
<td>0.11</td>
</tr>
<tr>
<td>Geometric mean filarial antigen level (range)</td>
<td>3,362.4 Ag units (0–32,000)</td>
<td>1,187.3 Ag units (0–32,000)</td>
<td>0.03</td>
</tr>
<tr>
<td>Mean no. of adult worm nests (total, range)</td>
<td>1.1 (32, 1–2)</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>Sexual maturity rating ≤2</td>
<td>27 (96%)</td>
<td>152 (96%)</td>
<td>1.0</td>
</tr>
<tr>
<td>History of lymph node problems</td>
<td>25 (89%)</td>
<td>97 (61%)</td>
<td>0.004</td>
</tr>
<tr>
<td>History of inguinal lymph node problems</td>
<td>25 (89%)</td>
<td>94 (59%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Inguinal lymphadenopathy on physical exam</td>
<td>27 (96%)</td>
<td>131 (83%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Crural lymphadenopathy on physical exam</td>
<td>5 (18%)</td>
<td>6 (4%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* One child did not have filarial antigen testing performed.
† Ten children did not have filarial antigen testing performed.
‡ Two children were MF-negative and CFA-negative at baseline assessment in November 1998.
Alternatively, hormonal changes may affect the localization of adult worms to different sites before and after puberty, at least in males. It is hypothesized that the hormonal changes that occur around puberty signal differing localizations of worms, especially as at least 80% of lymph node problems (80%), respectively. Compared with their physical exam findings in 1998, children were less likely to have inguinal lymphadenopathy on physical exam in 2002 (RR = 0.25, 95% CI = 0.1 to 0.5). Of note, 14 (61%) children reported having participated in all three rounds of MDA.

In 2002, only three (12%) children, all males, had detectable FDS on follow-up ultrasonographic examination. Four adult worm nests were identified (Table 4), all but one in the intrascrotal lymphatics. One child (Patient no. 3), with high circulating filarial antigen levels in both 1998 and 2002, had worms localized to either the crural or inguinal areas. In contrast, 4 years later, in November 2002, only three (12%) children, all males, had detectable FDS on follow-up ultrasonographic examination. Four adult worm nests were identified (Table 4), all but one in the intrascrotal lymphatics. One child (Patient no. 3), with high circulating filarial antigen levels in both 1998 and 2002, had worms localized to either the crural or inguinal areas.

**DISCUSSION**

Little is known about the clinical manifestations or the natural history of LF in the pediatric population. We correlated medical history and physical examination findings with the detection of adult worms by ultrasound and longitudinally assessed a cohort of FDS-positive children over time. These data highlight the role of medical history and physical examination findings in FDS-positive children, demonstrate subclinical filarial disease in children and suggest a role for mass drug administration in decreasing adult worm burden in children.

In this study, key history and physical exam findings were associated with the detection of living adult worms on ultrasonographic examination. FDS-positive children reported lymph node pain, redness, swelling, or warmth, specifically in the inguinal region, and inguinal and crural lymphadenopathies were found on physical exam. As adult worms in prepubescent children localize to the lymph nodes, they can cause lymph node hypertrophy. The presence of crural lymphadenopathy and, to a lesser extent, inguinal lymphadenopathy might indicate early filarial disease, particularly in prepubescent children. After puberty, the children in this cohort were less likely to have either inguinal or crural adenopathy; whether this is due to the older age of these children and fewer non-parasitic causes of adenopathy, localization of adult worms to other sites, or antifilarial drug treatment is unknown. Additionally, the clinical findings of lymphadenopathy have been seen in human experimental infections with *Brugia malayi* as well as in early clinical observations of filariasis in American troops returning from the Pacific islands. Although the specificity of lymphadenopathy for LF may be low, these results support the consideration of filarial disease in the differential diagnosis for lymphadenopathy in children from LF-endemic countries.

The ultrasonographic findings in this study demonstrating lymphangiectasia provide further evidence for subclinical filarial disease in infected children. In this cohort, lymphatic dilatation (lymphangiectasia) at the site of living adult worm nests ranged from 2 to 9 mm. Detection of living adult worms in children was associated with older age as well as both higher microfilarial density and a higher circulating filarial antigen level suggesting that the probability of a positive ultrasonographic examination is associated with these measures of infection intensity. This is similar to previous work by Dreyer and others from Recife, Brazil, where FDS detection was more common in older children, in boys and in children with microfilaraemia.

Ultrasonographic exam findings in this population confirm the different location of adult worms in children associated with puberty. In 1998, all 16 boys who had a positive ultrasonographic examination were prepubescent (SMR 1–2) and had worms localized to either the crural or inguinal areas. There were no nests located in the intrascrotal lymphatic vessels and no hydrocele on ultrasonographic examination. Similarly, neither hydrocele nor spermatic cord thickening was noted on physical examination. In contrast, 4 years later, three postpubescent not consistent with earlier writing of postpubescent boys (SMR 3–4) all demonstrated adult worms in the intrascrotal lymphatics, as has been reported previously for adult males and adolescent boys. In addition, one of the three FDS-positive boys had both hydrocele and spermatic cord thickening on ultrasonographic and physical exam, respectively. These results imply that worms tend to localize to different sites before and after puberty, at least in males. It is unknown why there is an apparent difference in adult worm tropism with advancing age in boys. Perhaps the hormonal changes that occur around puberty signal differing localization of worms, especially as at least 80% of *W. bancrofti* worms nests in adult men that are detectable by ultrasound are found in the intrascrotal area. In the animal literature, changes in the localization of worms have been seen at the onset of puberty. Alternatively, hormonal changes may stimulate development of lymphatic vessels, which allows the worm movement to be visualized.

The proportion of children with adult worm nests detected by ultrasound was similar for prepubescent boys and girls (16.7% versus 13.3%), but in postpubescent children, only males were found to be FDS-positive. Although other investigators have localized living adult worms in postpubescent females and adult women, no worm nests were found on our 2002 assessment of a relatively small number of adolescent
females (N = 11), suggesting that adult worms are more easily detected in boys, particularly once they reach puberty.\textsuperscript{12,18}

Although adult worms were detected by ultrasound in microfilaremic and filarial antigen negative individuals (N = 2), only 20% (23/115) of MF+ children and 18% (26/142) of CFA+ children had adult worms detected by ultrasound. This is similar to a previous report by Dreyer and others where 14.1% of children in her pediatric population demonstrated the characteristic movements of adult worms.\textsuperscript{12} The sensitivity of adult worm detection appears to be much lower than that reported in adult men, where adult \textit{W. bancrofti} worms can be visualized in 80% of microfilaremic men and 37% of amicrofilaremic men.\textsuperscript{15,17} This may be due, in part, to the lack of a single preferred location of adult worms in prepubescent children, making ultrasound examinations more difficult and time-consuming and suggests that ultrasound may not be the primary diagnostic tool in children.


d| Longitudinal assessment of this cohort of FDS-positive children demonstrates a decrease in the number of detectable living adult worm nests over time (Figure 1). This decrease is greater in the group of children who received DEC alone or DEC and ALB in the randomized placebo-controlled study. In these children, the number of living adult worm nests decreased within 6 months from seven to zero and nine to three, respectively; whereas the ALB only and placebo groups demonstrated a decrease from five to three and four to two nests, respectively, during the same period of time. Ultrasonographic follow-up of these children demonstrated a continued decrease in total living adult worm burden; with 12 worm nests detected in March 1999, 8 detected in May 1999 and 3 detected in November 2002. The decreased ability to find FDS-positive children by ultrasound on follow-up suggests that mass drug administration may have killed some adult worms and, by decreasing transmission, prevented the establishment

TABLE 3

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FDS-positive</td>
<td>25 (100%)</td>
<td>3 (12%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Filarial antigen positive</td>
<td>22 (92%)</td>
<td>18 (72%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Geometric mean filarial antigen level (range)</td>
<td>3,113.0 Ag units (0–32,000)</td>
<td>1,017.6 Ag units (0–32,000)</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean no. of adult worm nests (total, range)</td>
<td>1.2 (29, 1–2)</td>
<td>0.2 (4, 1–2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sexual maturity rating ≤ 2</td>
<td>24 (96%)</td>
<td>3 (12%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>History of lymph node problems</td>
<td>22 (88%)</td>
<td>21 (84%)</td>
<td>1.0</td>
</tr>
<tr>
<td>History of inguinal lymph node problems</td>
<td>22 (88%)</td>
<td>20 (80%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Inguinal lymphadenopathy on physical exam</td>
<td>24 (96%)</td>
<td>6 (24%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Crural lymphadenopathy on physical exam</td>
<td>4 (16%)</td>
<td>2 (8%)</td>
<td>0.7</td>
</tr>
<tr>
<td>History of participation in mass drug administration</td>
<td>N/A</td>
<td>23 (92%)</td>
<td>—</td>
</tr>
</tbody>
</table>

TABLE 4

<table>
<thead>
<tr>
<th>Year</th>
<th>Characteristic</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>Gender</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>9</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Sexual maturity rating</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>FDS size and location</td>
<td>5 mm right inguinal</td>
<td>7 mm left inguinal</td>
<td>5 mm left inguinal</td>
</tr>
<tr>
<td></td>
<td>CFA (Ag units)</td>
<td>1,565</td>
<td>32,000</td>
<td>32,000</td>
</tr>
<tr>
<td></td>
<td>Physical exam</td>
<td>Lymphadenopathy</td>
<td>Inguinal</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crural</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydrocele</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spermatic cord thickening</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1999</td>
<td>FDS size and location</td>
<td>—</td>
<td>—</td>
<td>6.5 mm left inguinal</td>
</tr>
<tr>
<td></td>
<td>CFA (Ag units)</td>
<td>692</td>
<td>32,000</td>
<td>32,000</td>
</tr>
<tr>
<td>2002</td>
<td>Age</td>
<td>13</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Sexual maturity rating</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>FDS size and location</td>
<td>2.3 mm right supratesticular</td>
<td>2.8 mm right infratesticular</td>
<td>9 mm left inguinal and 4 mm left infratesticular</td>
</tr>
<tr>
<td></td>
<td>CFA (Ag units)</td>
<td>242</td>
<td>2,817</td>
<td>32,000</td>
</tr>
<tr>
<td></td>
<td>Physical exam</td>
<td>Lymphadenopathy</td>
<td>Inguinal</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crural</td>
<td>—</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydrocele</td>
<td>—</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spermatic cord thickening</td>
<td>—</td>
<td>+</td>
</tr>
</tbody>
</table>

FDS, filaria dance sign; N/A, not available.
of new worms in these children. Nevertheless, it is intriguing
to note that of the four worm nests visualized on ultrasound
in November 2002, three nests, all located in the intrascrotal
lymphatics of adolescent boys, were not detected on previous
ultrasound exams. This finding suggests that new infections
occurred in these boys during the 3-year period. Another
possibility is that these worms were already present, but be-
low the limit of detection by ultrasound. Alternatively, it is
conceivable that existing adult worms migrated to the scrotal
area, but this seems less likely given the remarkable stability
of adult worm nest location.26

Of the 32 worm nests initially noted on ultrasonographic
examination in November of 1999, only one, a worm nest in
the left inguinal area, was found in the same location 4 years
later. This boy reported having participated in three rounds
of MDA with DEC and ALB but continued to have high levels
of circulating filarial antigen and inguinal and crural lymph-
adenopathy both in 1998 and 2002. He also had a second
worm nest in the left infratesticular location. The lymphatic
vessel dilatation seen at the site of the living adult worm
continued to progress, increasing in diameter by 4 mm in 4
years, which is consistent with previously published data on
the rate of lymphatic vessel dilatation over time in adult
men.20 This finding suggests the continuous presence of adult
worms at this site.

This study has several limitations. First, due to the fact that
participation in mass drug administration was self-reported,
we are unable to assess whether any individual child actually
participated in the MDAs. Overall drug coverage during the
Leogane MDA was 72%, 55%, and 78%, in 2000, 2001, and
2002, respectively (Mathieu E. and others, unpublished ob-
servations).30 Second, the small number of FDS-positive chil-
dren who were longitudinally evaluated made it difficult to
distinguish between the effects of age and other factors such
as drug treatment on physical and ultrasonographic findings.

This is one of the first studies to longitudinally evaluate a
cohort of FDS-positive children using a combination of past
medical history, physical examination findings, laboratory as-
say results, and ultrasound examination findings. These ultras-
onographic data demonstrate the change in location of adult
worms that occurs around puberty in males and confirm the
utility of ultrason in better understanding the natural his-
tory of bancroftian filariasis in the pediatric population. They
suggest a role for pertinent physical exam findings, specifi-
cally crural and inguinal lymphadenopathy, as signs of FDS-
positivity in young children. Further longitudinal and popu-
lation-based studies that delineate LF pathogenesis and eval-
uate macrofilaricidal efficacy of antifilarial drugs in chil-
dren are needed to determine the optimal management and
prevention of filarial disease in the pediatric population.

Received May 28, 2004. Accepted for publication August 22, 2004.

Acknowledgments: We would like to thank Amanda Freeman,
Marie-Denise Milord, Jack Lafontant, and the Hôpital Sainte Croix
Filariasis Team for their assistance with the project. We are especially
indebted to the children of Leogane who participated in this study,
their parents, and the headmasters and staff of the participating
schools.

Authors’ addresses: LeAnne M. Fox, Center for International Health
and Development, Boston University School of Public Health, Bos-
ton, MA 02118, Telephone: 617-414-1209, Fax: 617-414-1261, Bruce
W. Furness, STD Control Program, Washington, DC, 20005, Tele-
Health & Science University (OHSU), Portland, OR 97239, Tele-
phone: 503-494-8428, Fax, 503-494-8120, Jean-Marie Brissau, Filariasis
Program, Hôpital Sainte Croix, Leogane, Haiti, Telephone, 509-557-
6424, Fax, 509-235-1845, Jacky Louis-Charles, Filariasis Program,
Hôpital Sainte Croix, Leogane, Haiti, Telephone, 509-512-1868, Fax:
509-235-1845. Susan F. Wilson, New Jersey Medical School, Newark,
NJ 07101, Telephone, 973-220-8547. David G. Addiss, Division of
Parasitic Diseases, National Center for Infectious Diseases, Centers
for Disease Control and Prevention, Atlanta, GA 30341-3724, Tele-
phone 770-488-7760, Fax: 770-488-7761. Patrick J. Lammie, Division of
Parasitic Diseases, National Center for Infectious Diseases, Centers
for Disease Control and Prevention, Atlanta, GA 30341-
3724, Telephone, 770-488-7760, Fax, 770-488-7761.

Reprint requests: LeAnne M. Fox, Center for International Health
and Development, Boston University School of Public Health, 85
East Concord Street, Boston, MA 02118, Telephone: 617-414-1209,
Fax: 617-414-1261, E-mail: fox@bu.edu.

REFERENCES


egies and tools for the control/ elimination of lymphatic filari-

global prevalence and distribution of lymphatic filariasis.
Parasi
tology 112: 409–428.

survey of knowledge, attitudes, and perceptions (KAPs) of
lymphatic filariasis, elephantiasis, and hydrocele among resi-
dents in an endemic area in Haiti. Am J Trop Med Hyg 54:
299–303.

specific prevalence of antigenemia in a Wuchereria bancrofi-

7. Lammie PJ, Reiss MD, Dimock KA, Streit TG, Roberts JM,
Eberhard ML, 1998. Longitudinal analysis of the development
of filarial infection and antifilarial immunity in a cohort of

lymphadenopathy: a histopathologic study of fifty-eight cases

EA, 2001. Lymphatic filariasis in children: adenopathy and its evo-

10. Amaral F, Dreyer G, Figueredo-Silva J, Noroese J, Cava
detected by ultrasonography in human bancroftian filariasis.

11. Chau
bal NG, Pradhan GM, Chau
Dance of live adult filarial worms is a reliable sign of scrotal

12. Dreyer G, Noroese J, Addiss D, Santos A, Medeiros Z, Figueredo-
Silva J, 1999. Bancroftian filariasis in a paediatric population:
an ultrasonographic study. Trans R Soc Trop Med Hyg 93:
633–636.

Addiss D, 1995. Direct assessment of the adulticidal efficacy of
a single dose of ivermectin in bancroftian filariasis. Trans R

vessels in young men with adult Wuchereria bancrofti infection


