Human Immunodeficiency Virus Status and Delayed-Type Hypersensitivity Skin Testing in Ugandan Children

Anna Maria Mandalakas, MD*; Laura Guay, MD†; Philippa Musoke, MD§; Cindie Carroll-Pankhurst, PhD*; and Karen N. Olness, MD*

ABSTRACT. Background. In previous studies, delayed-type hypersensitivity (DTH) skin testing has been shown to be affected by several factors including nutritional status, intercurrent infection, host immune status, and previous exposure to the antigen being used.

Objective. To determine the effect of human immunodeficiency virus type 1 (HIV-1) status on DTH skin testing in a cohort of HIV-1-infected and noninfected Ugandan children followed prospectively from birth.

Design. Nested case-control study.

Setting. Primary care clinic serving study participants at Mulago Hospital, Makerere University, Kampala, Uganda.

Participants. Thirty HIV-1-infected children and 30 age-matched, HIV-1-noninfected children.

Methods. After completion of history and physical, each child underwent Mantoux skin testing with both Candida and purified protein derivative (PPD). Results of skin testing were read in 48 to 72 hours. Complete chart reviews were performed on all children. CD4 lymphocyte counts were obtained on all HIV-1-infected children at the time the skin testing was read.

Results. The average age of participants was 67 months (range, 51–92 months). HIV-1-infected children (mean CD4 lymphocyte count, 1069 mL⁻¹; range, 86–3738 mL⁻¹), compared with noninfected, age-matched peers, developed significantly smaller PPD reaction size (mean, 1.18 mm; range, 0.81–2.27 mm) than HIV-negative children (mean, 6.90 mm; range, 4.3–7.6 mm). A significant difference was not found between the two groups of children. Among HIV-1-infected children, there was a larger Candida reaction size in children who had recently received chloroquine treatment. There was no significant correlation between Candida reactivity and PPD reactivity, progressive HIV-1 disease, or CD4 lymphocyte count. The six children diagnosed clinically with active tuberculosis had lower absolute CD4 lymphocyte counts than children without tuberculosis. Lack of reaction to PPD was associated with lower CD4 lymphocyte counts and progressive HIV-1 disease.

Conclusions. In HIV-1-infected Ugandan children, DTH skin testing was influenced by the choice of antigen selected, HIV-1 infection, and recent treatment with chloroquine. Based on these findings, we believe that further prospective, longitudinal investigation into the role of chloroquine in HIV-1-infected children is needed. We emphasize the limitations of DTH skin testing in HIV-infected children as an adjunct in the diagnosis of active tuberculosis.

ABBREVIATIONS. TB, tuberculosis; HIV-1, human immunodeficiency virus type 1; BCG, bacille Calmette-Guérin; DTH, delayed-type hypersensitivity; PPD, purified protein derivative.
infections, after influenza and measles vaccination, and during periods of malnutrition.

Early diagnosis of TB has been shown to be particularly difficult in the HIV-infected population. The immunosuppression that develops with progressive HIV infection has been associated with anergy. Because of this association in HIV-infected individuals, the usefulness of the Mantoux test has been questioned. Tuberculin anergy is common in HIV-1-infected adults. In a recent study of HIV-infected adults, the prevalence of tuberculin reactivity varied directly and that of anergy indirectly with the absolute CD4 lymphocyte count. At present, limited information is available concerning DTH skin test responses in HIV-infected children. A recent case series described 12 HIV-infected children with active TB who were tuberculin anergic.

We therefore conducted a study to gather further information about the effects of HIV-1 infection on DTH skin testing in Uganda, a country with a high prevalence of HIV and TB infection. We prospectively examined purified protein derivative (PPD) DTH skin testing in a cohort of HIV-1-infected and noninfected Ugandan children followed from birth. Recently, we evaluated DTH skin testing to both PPD and Candida and examined factors associated with anergy including HIV-1 status, nutritional status, acute illness, recent chloroquine treatment, active TB, and stage of HIV-1 infection assessed by CD4 lymphocyte counts.

METHODS

Study Population

In 1988, the AIDS Control Program of the Ugandan Ministry of Health, Makerere University, and Case Western Reserve University began a collaborative study of HIV-1 infection in Ugandan women and their infants. The first cohort, which focused on the natural history of HIV-1 disease, included 589 infants born to enrolled women between January 1989 and September 1990. The second cohort, which focused on the neurodevelopmental aspects of HIV-1 disease, included 530 infants born to enrolled women between November 1990 and April 1992. In the second cohort, only full-term infants without significant birth complications or neurologic or genetic impairments based on newborn physical examination were enrolled. No infants or mothers received zidovudine or other antiretroviral treatments, which were not available in Uganda.

For the current skin testing study, which was conducted during November and December of 1996, both HIV-1-infected and noninfected participants were selected from the previously established cohorts. Of the 154 HIV-1-infected children in the original two cohorts, 34 children had survived to the start of this study. All the living HIV-1-infected children who were traceable were included; 4 children could not be traced. These children were matched by age, within 3 months, to 30 randomly chosen, noninfected controls (P = .55). Written informed consent was obtained from the child’s parent or legal guardian. In cases of illiteracy, the consent form was read to the guardian. The study protocol was approved by the institutional review boards of Makerere University and Case Western Reserve University.

Immunization Schedules

All infants were immunized shortly after birth according to the United Nations Expanded Program on Immunization guidelines. The immunization schedule included intradermal BCG (0.05 mL) given in the right lower deltoid region. All children received BCG at birth or within the first month of life. The Ugandan Ministry of Health provided all vaccines, which consisted of both Pasteur and Japanese strain.

Physician History and Physical Examination

A history was obtained from each child’s parent or primary care provider with regard to any symptoms of acute or chronic illness, exposure to TB, previous TB treatment, and recent chloroquine treatment. Each child received a complete physical examination with special care given to describe any HIV-associated comorbidities.

Assessment of Nutrition and Failure to Thrive

Growth charts plotting height and weight were kept for all children from birth. Failure to thrive was defined as follows: downward crossing of at least two of the percentiles on the weight-for-age chart (excluding the 10th and the 90th percentiles), weight loss greater than 10% of baseline, or less than the 5th percentile on the weight-for-height chart.

Using EPIinfo (USD, Inc, Stone Mountain, GA), weight-for-age and height-for-age Z scores were computed on all children. Children with Z scores ≤−2 in either category were considered malnourished.

Assessment of Acute Illness

Children exhibiting two or more of the following were considered acutely ill: fever (>38°C axillary), respiratory distress (respiratory rate of >30 breaths per minute, rib retraction, nasal flaring), significant cough, gastroenteritis, anemia, and/or dehydration. Cough was considered significant if it was present throughout the day, every day, or recurrent despite medical treatment. Gastroenteritis was defined by the presence of greater than two loose, watery stools per day.

Assessment of Active Tuberculosis

Assessment of active TB disease was based on a modification of the World Health Organization criteria for the diagnosis of TB in children. The scoring system outlined by the WHO includes the following criteria: duration of illness, nutritional family history of TB, tuberculin test, malnutrition, unexplained fever and night sweats, and symptoms consistent with disseminated disease. Because the tuberculin test was one of our outcome measures, we excluded skin test results. Children were screened for significant cough of greater than 1 month duration, unexplained fever for more than 1 month, and evidence of a failure to thrive and/or a history of household exposure to a TB-infected individual. All children with two or more of the symptoms were evaluated by chest radiograph. Active TB disease was defined as the presence of two or more of these symptoms and evidence on chest radiograph consistent with pulmonary TB or physical examination findings consistent with disseminated TB. A panel of three pediatricians reviewed all chest radiographs. Chest radiographs were considered positive if they displayed hilar and/or paratracheal lymphadenopathy or infiltrates consistent with TB. Children found to have active TB disease were started on anti-TB treatment.

Delayed-Type Hypersensitivity Skin Testing

All children underwent DTH skin testing by using PPD (Tuberculin [5 TU/0.1 mL], Connaught, Swiftwater, PA) and Candida antigen (Candid, Allermed, San Diego, CA). By using standardized procedures, 0.1 mL of PPD was administered intradermally on the volar aspect of the left forearm. In a similar fashion, 0.1 mL of Candida antigen was administered to the right forearm. Candida antigen was administered undiluted. In 48 to 72 hours, the transverse diameter of induration at each injection site was measured by using the “ballpoint-pen” method.

DTH skin testing and reading were performed by highly experienced personnel blinded to the subjects HIV status. Throughout the study, investigators were blinded to HIV-1 status. A positive PPD reaction was defined as greater than or equal to 5 mm induration in HIV-1-infected children and greater than or equal to 10 mm induration in HIV-1-noninfected children. A positive Candida reaction was considered any induration ≥5 mm. The presence or absence of a BCG scar was noted on all subjects. Data on previous PPD skin testing were obtained from each subject’s clinic chart.

The use of Candida antigen (Candid, Allermed) has been previously studied in adults from this same population. When compared with another commonly used preparation of Candida antigen, Candid was found to elicit a significantly larger reaction.
TABLE 1. Human Immunodeficiency Virus Type 1 (HIV-1) Clinical Staging According to the 1994 CDC Pediatric HIV Classification System

<table>
<thead>
<tr>
<th>Stage</th>
<th>No Symptoms</th>
<th>Mild Symptoms</th>
<th>Moderate Symptoms</th>
<th>AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No immunosuppression</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>2. Mild to moderate immunosuppression</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>3. Severe immunosuppression</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations: CDC, Centers for Disease Control; AIDS, acquired immunodeficiency syndrome.

size. An additional unpublished study demonstrated that anergy to Candida was associated with 22 deaths per 100 person-years compared with 10 deaths per 100 person-years in nonanergic individuals. Based on these previous findings, we were confident of our choice of Candida as our control antigen.

Lymphocyte Characterization

Peripheral blood absolute CD4 lymphocyte counts and percent CD4 lymphocytes were determined on all HIV-1-infected children by flow cytometry, using a Coulter EPIC Profile II flow cytometer (Coulter Electronics, Hialeah, FL). Assays were completed within 48 to 72 hours of skin testing, using the laboratory facilities on site at Makerere University.

HIV Serology

HIV antibody testing was performed on all infants at 12 and 18 months of age, with all positive results confirmed by western blot. HIV antibody was tested by using an enzyme-linked immunosorbent assay (Recombigen HIV-1 enzyme immunoassay, Cambridge Bioscience, Worcester, MA). Confirmatory western blots (Novapath Immunoblot Assay, Bio-Rad, Hercules, CA) were interpreted as positive if they contained any two of the following bands: gp 120/160, gp 41, or p24.

Statistical Methods

Data analysis included univariate, two-tailed significance testing with χ² and Fisher’s exact tests, when indicated by small sample size, t tests for differences in mean induration between groups, and Pearson’s correlation coefficient. Forward stepwise multivariate regression analysis also was performed to test for the combined effects of presumed predictor variables on size of skin test reaction. In all regression models, no more than four variables were tested simultaneously because of the limited sample size. Also, based on sample size, a more liberal inclusion criteria (P = .1) was used so that no indicative variables would be overlooked. All data were analyzed by using SPSS (SPSS Inc, Chicago, IL) for MS Windows, Release 6.1.

RESULTS

Description of Sample

Thirty HIV-1-infected and 30 age-matched, noninfected children were studied. All the children completed the study. Of the 30 seronegative children, 23 were seroreverters, born to seropositive mothers. The mean age was 67 months, with a standard deviation of 10.7 months and a range of 51 to 92 months.

Sixty percent of the HIV-infected and 43% of the noninfected children were females. Males and females did not differ with regard to the incidence of acute illness, malnutrition, chloroquine exposure, or active TB disease.

Based on maternal history and chart review, no child had undergone skin testing in the 36 months before enrollment. Thirteen of the children had no previous history of DTH skin testing. Of the remaining 47 children, 15 children had one previous DTH skin test, 31 children had two previous DTH skin tests, and 1 child had three previous DTH skin tests. Despite documentation of receipt in all children, BCG scars were absent in 6 HIV-1-infected and 6 HIV-1-noninfected children.

Among the HIV-1-infected children, the clinical stages varied greatly (Table 1). Lymphocyte subsets were available for 27 HIV-infected children; the parents of 2 children refused phlebotomy and 1 sample was inadequately processed.

Mantoux Skin Test Reactions

Mantoux skin test reactions to PPD and Candida for all children are shown in Fig 1. Six children were anergic, ie, 2 HIV-1 noninfected and 4 HIV-1 infected.

Ten children were PPD-positive, ie, 8 HIV-1 noninfected and 2 HIV-1 infected children. The mean PPD size was 1.2 ± 4.3 mm among HIV-1-infected children and 4.6 ± 7.6 mm among HIV-1-noninfected children (P = .035). To accommodate the high proportion of children who had no PPD reaction, dichotomous analyses were also performed by using the previously defined guidelines for anergy. This approach yielded similar, but only marginally significant, differences between HIV-1-infected and noninfected children (Fisher’s exact test, P = .08). There was no significant difference in PPD size because of acute illness, malnutrition, chloroquine exposure, BCG scar presence, BCG scar size (data not shown), or active TB disease (Table 2). There was no correlation between PPD reaction size and CD4 lymphocyte count or Candida reaction size.

Two HIV-1-infected children mounted reactions to PPD that were less than 5 mm. One of these children had no history of TB exposure and an HIV clinical stage of N. No CD4 count was obtained. Although he was diagnosed with malnutrition, he had no other
TABLE 2. Difference in Mean Induration

<table>
<thead>
<tr>
<th></th>
<th>PPD (mm)</th>
<th>Candida (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>3.5*</td>
<td>1.8</td>
</tr>
<tr>
<td>Active TB</td>
<td>1.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Acute illness</td>
<td>2.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>1.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Recent chloroquine exposure</td>
<td>1.6</td>
<td>3.9t</td>
</tr>
</tbody>
</table>

Abbreviations: PPD, purified protein derivative; HIV, human immunodeficiency virus; TB, tuberculosis. *P < .05; †P < .01.

active clinical problems. The second child had been diagnosed and treated for TB 5 years before study enrollment. He was also malnourished with an HIV clinical stage of C2 and a CD4 count of 352.

When comparing HIV-1-infected versus HIV-1-noninfected children, there was no significant difference in mean Candida reaction size (9.1 ± 5.0 vs 10.9 ± 3.9, respectively; P = .14). The same dichotomous strategy noted above was used to examine reactions to Candida. This analysis produced similar results. There was no significant difference in Candida reaction based on HIV-1 status (P = .47). There was no significant difference in Candida size because of acute illness, malnutrition, or active TB (see Table 2). There was no correlation between CD4 lymphocyte count and size of Candida reaction.

When examining the total sample (n = 60), children who had received chloroquine within the 6-week period before study enrollment had significantly larger Candida reactions than those who had not recently been treated with chloroquine (12.9 vs 9.0 mm, respectively; P = .004) (see Table 2). By using a stratified approach to explain the potential confounding by HIV-1 status, we demonstrated that among the HIV-1-infected children there was a significantly larger Candida reaction in children who had been treated with chloroquine in the 6-week period before study enrollment (12.8 vs 7.8 mm; P = .012). Conversely, the HIV-1-noninfected children had no significant difference in Candida reaction size with regard to chloroquine exposure. There was no significant difference in the incidence of chloroquine exposure (P = .77) associated with HIV-1 infection. Within the HIV-1-infected children, there was no significant difference in mean CD4 lymphocyte count associated with recent chloroquine treatment.

Between the HIV-1-infected and HIV-1-noninfected children, there were no significant differences in the incidence of concomitant acute illnesses or malnutrition. Within the group of HIV-1-infected children, there were no significant associations between mean CD4 lymphocyte count and malnutrition, acute illness, or chloroquine treatment. Examining the entire group of children revealed no significant association between size or presence of BCG scar and Candida or PPD reactions.

By using multiple-regression analysis to simultaneously control for the variables of interest (malnutrition, acute illness, chloroquine treatment, CD4 lymphocyte count, and HIV-1 status), we showed similar results. There was a significance association between HIV-1 infection and a smaller PPD reaction size (P = .01) while controlling for acute illness, which was the only marginally significant variable (P = .08). As shown by the same analysis strategy for evaluating the size of the Candida reaction, the only variable that predicted induration size was chloroquine treatment. Chloroquine exposure was associated with a larger mean induration to Candida (P = .003) while controlling for HIV-1 status, which was not significant at the 0.05 level (P = .09). Within each group, HIV-1 infected and HIV-1 noninfected, there was no significant association between any of the factors.

Outcome Relative to Active Tuberculosis

The incidence of active TB disease was found to be higher in the HIV-1-infected children. Six HIV-1-infected children had active TB compared with none of the HIV-1-noninfected children (P = .01). The clinical description of the children diagnosed with TB is summarized in Table 3. There were no cases of disseminated TB diagnosed. Of these 6 children, 3 had previously been diagnosed with active TB disease from 12 to 24 months before the current study (Table 4). One child had completed an adequate course of TB treatment. The families of the remaining 2 children were unsure of treatment completion. Five of 6 children with active TB were nonreactive to PPD. Only 1 of these 5 children was nonreactive to Candida. The single child who was reactive to both Candida and PPD had the least advanced clinical stage (B1) of the children with active TB. Within the HIV-1-infected children, the mean absolute CD4 lymphocyte count of the children diagnosed with active TB disease was significantly lower than the children with no active TB disease (624 ± 448 and 1196 ± 815, respectively; P = .04) (see Table 4). The proportion of children with severe, moderate, or no evidence of immunosuppression was not significantly different between the children with active TB and those without (P = .16), reflecting the small sample size.

**DISCUSSION**

When examining DTH skin testing responses in HIV-1-infected and noninfected Ugandan children, we found that the response mounted by the immune system varied significantly based on the antigen used. The difference in the mean PPD reaction size in HIV-1-infected and HIV-1-noninfected groups (1.18 and 4.65, respectively) was statistically significant (P < .035), whereas Candida reaction size was not different statistically. With regard to Candida, these findings are similar to the study completed by Raszka et al in which analysis was completed on
both the number of positive skin reactions and the size of mean induration. In their study of 27 HIV-infected and 14 noninfected children, no significant difference was found in the number of positive skin reactions to a different *Candida albicans* antigen at a dilution of 1:10 or in the size of mean induration to *C albicans* at dilutions of both 1:10 and 1:100. There was a significant difference in the number of positive reactions to *C albicans* at a dilution of 1:100.

Our study is the first to be completed in HIV-1-infected children from sub-Saharan Africa, comparing DTH skin testing of *Candida* and PPD. Our results clearly show that HIV-1-infected children have a greater reaction elicited by *Candida* than 5-TU PPD. In addition, there was no statistical difference in *Candida* reaction size between HIV-1-infected and noninfected children. HIV-1-infected children have a higher incidence of mucocutaneous candidal infections. Theoretically, this increases *Candida* sensitization. This is one potential explanation for the larger reaction size to PPD and a lack of reactivity to *Candida* in HIV-1-infected children with TB (see Table 4).

As postvaccination tuberculin sensitivity diminishes, induration associated with PPD is more likely to be representative of TB infection or active TB disease. TB is highly endemic in eastern Africa. In an earlier national survey in 1970, 58% of Ugandan adults older than 15 years were tuberculin positive.30 In our study, PPD reactivity proved to be a poor predictor of TB in HIV-1-infected children. Ten children were PPD positive; 9 of these children were asymptomatic with normal chest radiographs and no signs of disseminated TB on physical examination. Of the 9 PPD positive children without TB, 1 was HIV-1 infected (see Fig 1). Six children were diagnosed with active TB disease and 1 of these children had a positive PPD (see Table 4). Of note, all children with active TB were HIV-1 infected. The lack of reaction to PPD in HIV-1-infected children with active TB is consistent with the cases described by similar *Candida* reactions. If the HIV-1-infected and noninfected children were able to mount reactions similar to 5-TU PPD, we anticipate similar PPD reaction size because of natural TB infection. This was not the case. In the HIV-1-infected group of children, there was a statistically smaller mean PPD induration and a greater proportion of children nonreactive to PPD.

In contrast to previous studies, we were unable to show an association between a lack of reaction to *Candida* and the degree of HIV-related immunosuppression. Among HIV-1-infected children, there was no significant association between the size of *Candida* reaction and the absolute CD4 lymphocyte count. We found no correlation between a lack of reactivity to *Candida* and a lack of reactivity to PPD. Although five HIV-1-infected children with TB had no reaction to PPD, all but one of these children displayed reactions to *Candida* (see Table 4).

When comparing the characteristics of the HIV-1-infected children with TB (see Table 4), we found that a lack of reaction to PPD was associated with progressive HIV-1 disease and lower CD4 lymphocyte counts. When comparing HIV-1-infected children with active TB disease with those without active TB disease, the mean CD4 lymphocyte counts were significantly lower in those with active TB disease (P = .04). These findings are consistent with those of several studies that have shown a significant association between anergy and advanced HIV-related immunosuppression. In a large multicenter US study involving 1353 adults, Markowitz et al18 found that patients with HIV infection and less than 400 CD4 lymphocytes/mm³ had a lower prevalence of PPD reactivity than HIV-1-noninfected controls. In the study by Raszka et al,28 absence of any induration of more than 5 mm to a panel of at least four antigens was shown to be associated with symptomatic disease, evidence of clinically advanced HIV infection, or a CD4 percentage of 15% or less.

In our study, PPD reactivity proved to be a poor predictor of TB in HIV-1-infected children. Ten children were PPD positive; 9 of these children were asymptomatic with normal chest radiographs and no signs of disseminated TB on physical examination. Of the 9 PPD positive children without TB, 1 was HIV-1 infected (see Fig 1). Six children were diagnosed with active TB disease and 1 of these children had a positive PPD (see Table 4). Of note, all children with active TB were HIV-1 infected. The lack of reaction to PPD in HIV-1-infected children with active TB is consistent with the cases described by

### TABLE 4. Children With Active Pulmonary Tuberculosis

<table>
<thead>
<tr>
<th>HIV-1 Status</th>
<th>PPD (mm)</th>
<th><em>Candida</em> (mm)</th>
<th>Absolute CD4</th>
<th>CD4 (%)</th>
<th>HIV Stage</th>
<th>Previous History of TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>0</td>
<td>11</td>
<td>726</td>
<td>13.2</td>
<td>C2</td>
<td>Yes</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>14.5</td>
<td>196</td>
<td>8.9</td>
<td>C3</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>23</td>
<td>10</td>
<td>1325</td>
<td>28.2</td>
<td>B1</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>10</td>
<td>624</td>
<td>26.0</td>
<td>B2</td>
<td>Yes</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>3</td>
<td>86</td>
<td>1.9</td>
<td>C3</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>11.5</td>
<td>790</td>
<td>14.1</td>
<td>C2</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Abbreviations: HIV-1, human immunodeficiency virus type 1; PPD, purified protein derivative; TB, tuberculosis.
In many countries where endemic malaria exists, such as Uganda, it is common practice to self-medicate with chloroquine as a treatment for non-specific fever. The effects of chloroquine on DTH skin testing in HIV-1-infected children have never been previously examined. Assuming that study participants had equal Candida exposure within their respective HIV-1 status groups, any significant difference in Candida reaction size was caused by host factors. In our study, HIV-1-infected children recently treated with chloroquine had significantly larger Candida reaction size than HIV-1-infected children without recent chloroquine exposure. These findings are consistent with studies completed in HIV-1-infected adult populations. After treatment of HIV-1-infected cells with chloroquine, there was a significant reduction in cell size, virus associated with glycoprotein, gp 120 of HIV-1, and total virus yield. Also, most virions released were noninfectious. In a randomized, double-blind, placebo-controlled study, hydroxychloroquine or placebo was given to 40 HIV-1-infected adults for 2 months. Not only was chloroquine or hydroxychloroquine or placebo was given to 40 HIV-infected children, reactivity to tuberculosis antigens, may provide a greater predictive value when testing for anergy. As an adjunct to the diagnosis of active TB in HIV-1-infected children, PPD skin testing is most useful when positive. A non-reactive PPD skin test gives little conclusive information.

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REFERENCES


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