**INTRODUCTION**

Disseminated histoplasmosis (DH) is frequently reported in disease-endemic areas of the Americas, including Colombia.\(^1,7\) Its etiologic agent is the thermally dimorphic fungus *Histoplasma capsulatum* var. *capsulatum*.\(^5,4\) Its habitat is the soil, particularly if enriched with bird and bat excrements.\(^6\) Infection is acquired during aerosol-creating activities around infected foci.\(^1,3,8\) Inhalation of *H. capsulatum* conidia from the environment leads to primary lung infection, the severity of which is related to both number of inhaled propagules and the immune response of the host.\(^1,4\) Control of the infection depends mainly on cellular immunity through the concerted action of CD4 lymphocytes, their cytokines and activated macrophages (TH\(_1\) type immunity).\(^3,4\) Thus, certain manifestations of histoplasmosis that attest to the inability of the patient to cope with the fungus, such as disseminated skin lesions, are observed in severely immunosuppressed patients infected with human immunodeficiency virus (HIV).\(^9,11\)

Histoplasmosis encompasses a spectrum of clinical forms with DH being the most severe.\(^1,4,8\) Despite the fact that the primary lung infection is frequently followed by spleen and liver invasion, DH refers only to a process of intense fungus multiplication in lungs and in extra-pulmonary organs and body sites.\(^1,4,9,11\) Disseminated histoplasmosis may occur either after recent exposure or upon endogenous reactivation of latent foci.\(^1,11,12\) In fact, HIV-infected individuals who develop DH in areas not endemic for diseases were known to have lived previously in recognized disease-endemic regions.\(^3,8,9,10,11\) Before the AIDS epidemic, risk factors for DH were immunosuppressive therapies, impaired cellular immunity, hematologic and other type of malignancies, organ transplant and dialysis, as well as extreme ages (children and old persons).\(^1,12,13\) In certain individuals, heavy exposure to infected aerosols may also give rise to DH.\(^1,3,4,8,9\) The above circumstances changed with the advent of the HIV epidemic, which transformed histoplasmosis into a common and severe fungal disease.\(^8,11\) Presently, patients with HIV have their own risk factors, such as low CD4 lymphocyte counts (< 200/µL), an epidemiologic history of exposure to the fungus, and presence of antibodies to *H. capsulatum* at the time of diagnosis.\(^13,16\)

The present study analyzes two cohorts of DH patients, those with AIDS (cohort 1) and those not infected with HIV (cohort 2). The main objectives were to determine clinical differences, effectiveness of diagnostic methods, results of antifungal therapy in connection with viral co-infection, and influence of highly active antiretroviral therapy (HAART).

**PATIENTS AND METHODS**

From 1979 to 2001, the Corporación para Investigaciones Biológicas in Medellín, Colombia established a diagnosis of DH in 62 patients, 52 of whom had prolonged follow-up observations that facilitated evaluation of their final outcome. In the 52 selected DH patients, 30 (57.7%) had AIDS (cohort 1); the remaining 22 were not co-infected with HIV (cohort 2). Databases were prepared that included demographic and clinical information, chest radiographs, as well as general laboratory (blood cell counts, erythrocyte sedimentation rate) and mycologic tests results, the latter corresponding to direct microscopic examinations (Wright stain) from exudates and biopsies (silver methenamine), cultures from the same specimens, and detection of antibodies to *H. capsulatum* (complement fixation and agar gel immunodiffusion tests with histoplasmin).\(^1,17\)

The immune status of those patients in cohort 1 receiving HAART was determined by CD4 lymphocyte counts, both during and in some cases, at the end of antifungal treatment. All patients with DH received antifungal therapy appropriate to the severity of their clinical manifestations and more recently, observing the recommendations of Wheat and others.\(^11,18\) Treatment consisted of amphotericin B, itraconazole,
and in some cases of fluconazole, ketoconazole, or posaconazole given in the context of clinical trials. The outcome of therapy was evaluated according to a scoring system previously reported,\textsuperscript{17} in which each of the clinical abnormalities present before therapy and any mycologic findings received an arbitrary score of 2. The sum of all these scores constituted the denominator of a fraction. During treatment (3–5 months) and at the end of therapy, the above abnormalities and mycologic observations were re-evaluated. If they had resolved, each was given the same score of 2 recorded at initiation of treatment; if abnormalities had improved but not resolved, a score of 1 was assigned to each one; if they had not resolved, each received a score of 0. If a patient showed clinical and/or mycologic deterioration, a negative score equivalent to deducting 2 points for each parameter evaluated before therapy was used. These scores were aggregated to form the numerator of the fraction. The resultant equation was calculated and the results expressed as follows: 1) a negative score indicated deterioration of the clinical condition; 2) zero indicated no change in the patient’s condition; 3) a positive score indicated minor or major improvement; and 4) a score of 1 indicated complete resolution of all abnormalities observed before therapy.

The data were processed using Excel\textsuperscript{(®)} (Microsoft, Redmond, WA). Statistical analyses were done using Fisher’s exact test. The Student’s $t$-test was used for group comparisons, and the Pearson correlation test was used to evaluate response to antifungal treatment.

Appropriate informed consent was obtained from the patients and the study was reviewed and approved by the Ethics Committee of the Corporación para Investigaciones Biológicas.

### RESULTS

The male-to-female ratio was 29:1 in cohort 1 patients and 1.4:1 in cohort 2 patients ($P = 0.001$). The mean ages for cohorts 1 and 2 were 36.1 years (range = 23–59) and 33.8 years (range = 1–69), respectively, with no statistically significant differences among the cohorts. Cohort 2 included five children less than 10 years of age.

The most frequent clinical manifestations are shown in Table 1. In both cohorts, constitutional symptoms (asthenia, weight loss, anorexia, fever) predominated, being observed in more than 85% of the patients. Additional symptoms such as respiratory (cough, sputum production, shortness of breath) and gastrointestinal (nausea, vomiting, diarrhea) abnormalities were also reported. Hypertrophied lymph nodes, hepatosplenomegaly, skin lesions, and mucosal lesions were observed in a smaller proportion of patients.

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DH and HIV (n = 30)</th>
<th>DH (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (range)</td>
<td>36.1 (23–59)</td>
<td>33.8 (1–69)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>29:1</td>
<td>1.4:1</td>
</tr>
<tr>
<td>Constitutional (asthenia, weight loss, anorexia, fever)</td>
<td>90</td>
<td>86.4</td>
</tr>
<tr>
<td>Respiratory (cough, sputum production, shortness of breath)</td>
<td>80</td>
<td>59</td>
</tr>
<tr>
<td>Gastrointestinal (nausea, vomiting, diarrhea)</td>
<td>46.6</td>
<td>54.5</td>
</tr>
<tr>
<td>Hypertrophied lymph nodes</td>
<td>56.6</td>
<td>31.8</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>13.3</td>
<td>22.7</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>53.3\textsuperscript{†}</td>
<td>9\textsuperscript{†}</td>
</tr>
<tr>
<td>Mucosal lesions</td>
<td>40</td>
<td>40.9</td>
</tr>
<tr>
<td>Lung auscultation abnormalities (rales, wheezing, rhoncus, hypoventilation)</td>
<td>26.6</td>
<td>50</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Except where indicated, values are percentages.

\textsuperscript{†} $P = 0.01$.

The active co-morbidities reported in patients with disseminated histoplasmosis according to cohort are shown in Table 2. The number of patients with co-morbidities varied between the cohorts. Malignancy, mycotic diseases, bacterial diseases, viral diseases, parasitic diseases, diabetes mellitus, malnutrition, adrenal insufficiency, and alcoholism were the most common co-morbidities observed.

### Table 2

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Number of patients with co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort 1 (n = 30)</td>
</tr>
<tr>
<td></td>
<td>Previous to diagnosis</td>
</tr>
<tr>
<td>Malignancy\textsuperscript{a}</td>
<td>3</td>
</tr>
<tr>
<td>Mycotic diseases\textsuperscript{†}</td>
<td>2</td>
</tr>
<tr>
<td>Bacterial diseases\textsuperscript{‡}</td>
<td>0</td>
</tr>
<tr>
<td>Viral diseases\textsuperscript{§}</td>
<td>2</td>
</tr>
<tr>
<td>Parasitic diseases\textsuperscript{¶}</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>0</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>0</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>0</td>
</tr>
<tr>
<td>Total with co-morbidities</td>
<td>7 (23.3%)\textsuperscript{#}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Kaposi’s sarcoma and laryngeal carcinoma.

\textsuperscript{†} Pneumocystosis, candidiasis, and cryptococcosis.

\textsuperscript{‡} Tuberculosis, salmonellosis, and syphilis.

\textsuperscript{§} Cytomegalovirus, hepatitis B, and herpes virus.

\textsuperscript{¶} Toxoplasmosis and cryptosporidiosis.

\textsuperscript{#} Some patients had two or more co-morbidities.
respiratory problems and gastrointestinal alterations were also frequently recorded (59% and 46% in cohorts 1 and 2, respectively), with no significant differences. Physical examination showed enlarged lymph nodes, hepatosplenomegaly, skin and mucosal lesions, as well as lung auscultation abnormalities (Table 1). These signs were not significantly different among the two cohorts, with the exception of skin lesions, which were observed in 16 (53.3%) in cohort 1 and 2 (9%) in cohort 2 ($P = 0.001$). In 13 of cohort 1 patients (81.2%) skin lesions were widespread (face, thorax, abdomen, and upper limbs) and showed various characteristics (maculopapular, ulcerated, and/or crusted). In contrast, in cohort 2, skin lesions were nodular and less widespread.

Anemia and leukopenia were documented in 72.4% and 62.1% of the patients in cohort 1, and in 15% and 10.5% of the patients in cohort 2 ($P < 0.001$ for either parameter). No differences were noticed in platelet counts. Erythrocyte sedimentation rates were elevated in all patients in cohort and in 15 patients in cohort 2 ($P = 0.001$).

Active co-morbidities observed previous to or simultaneous with the diagnosis of histoplasmosis are shown in Table 2. They were present simultaneously with DH in 21 (70%) patients in cohort 1 with a predominance of mycotic diseases (13 of 30 patients), mostly oral candidiasis. In cohort 2, simultaneous co-morbidities were observed in 7 (31.8%) patients, with 6 showing associated conditions indicating immune response alterations (diabetes, malnutrition, and cirrhosis). Active co-morbidities observed before a diagnosis of histoplasmosis were present in 23.3% of the patients in cohort 1 and 18.2% of the patients in cohort 2.

Chest radiographs showed interstitial infiltrates in 63.3% of the patients in cohort 1 and in 45.5% of the patients in cohort 2; alveolar infiltrates were seen in 3.3% of the patients in cohort 1 and in 9.1% of the patients in cohort 2, but no significant differences were observed for either type of infiltrate. Nodules were observed only in cohort 2 (13.6%).

As shown in Table 3, DH was often diagnosed in both cohorts by direct microscopic observation (Wright stain) of *Histoplasma capsulatum* yeast cells in clinical specimens, and the fungus was also isolated in culture from these specimens. Significant differences ($P < 0.05$) were observed only for the latter procedure. In eight patients (four in each cohort), a diagnosis was established by the observation of yeast cells in hematoxylin and eosin- and/or Gomori-stained tissue biopsy specimens. Serologic test results with histoplasmin were significantly more reactive ($P < 0.05$) in cohort 2 than in cohort 1.

As shown in Figure 1, 11 patients (36.7%) in cohort 1 received HAART. In 10 of them, CD4 cell counts were available at diagnosis, with a mean value of 53 cells/$\mu$L (SD = 36.4). The remaining 19 patients did not receive HAART. In five of them, CD4 cell counts were available, with a mean value of 30 cells/$\mu$L (SD = 19.7). No significant differences were observed between these sub-groups. During antifungal therapy (mean = 9 months), the patients who received HAART had higher mean CD4 cell counts (193 cells/$\mu$L [SD = 121.4]) than patients who did not receive HAART (67 cells/$\mu$L [SD = 41]) ($P = 0.001$).

In cohort 1, itraconazole was given at a dose 400 mg/day for 3.4 months (range = 0.5–13 months), with maintenance treatment of 200–400 mg/day for a mean of 28.4 months (range = 1–78 months). Amphotericin B was given for 12.3 days (range = 1–15 days) and other azole compounds were given for 6.9 months. None of the latter two groups of medications were used for maintenance therapy. As shown in Table 4, three of the patients who received HAART were also treated with amphotericin B, seven with itraconazole, and 1 with posaconazole; nine of these patients received itraconazole maintenance therapy. In patients who did not receive HAART, 2 were also treated with amphotericin B, 13 with itraconazole, and 4 with other azole compounds (fluconazole and itraconazole): 7 of these patients received itraconazole maintenance therapy. Therapy with amphotericin B was given to 5 patients (16.7%), itraconazole to 20 patients (66.7%), and ketoconazole, fluconazole or posaconazole to 5 patients (16.7%). Maintenance treatment was given to 16 (53.3%) patients in cohort 1. Six (20%) of 30 patients in cohort 1 died before initiating the second stage of treatment; mean time to death was 3.4 months (range = 2 days to 12 months). Eight (26.6%) patients were lost for follow-up after the initial treatment.

In cohort 2, treatment was continuous. Due to severe illness, an adult patient received amphotericin B initially for 15 days and was then treated with itraconazole. This triazole was given to 13 other patients (59%) as the only medication at doses of 100 (children) to 400 mg/day for a mean of 8.7 months (range = 3–13 months). One child died soon after initiating therapy. The remaining eight patients were treated with other azole-derived compounds such as ketoconazole, itraconazole, or fluconazole.

The scores of the point system evaluation were condensed into two groups (Figure 2): patients responding adequately (complete resolution or major improvement), and patients not responding (minor improvement, worsening, or death). This system was applied during and at the end of therapy. During treatment (three months in cohort 1 and five months in cohort 2), 53.4% of cohort 1 patients showed complete resolution or major improvement. In contrast, 86.4% of cohort 2 patients showed an adequate response ($P = 0.012$) (Figure 2a). At the end of therapy, the scores indicated complete resolution or major improvement in 66.7% of the patients in cohort 1 versus 95.5% of the patients in cohort 2 ($P < 0.05$) (Figure 2b).

As shown in Table 5, there were significant differences in
We observed that cohort 2 distribution of highly reactive retroviral therapy (H/11505) Itraconazole No skin lesions were observed upon AIDS (1,4,8) < 0.05). Age distribution was similar in the two cohorts (young adults) as reported by others, 15,21,22 but the age range of cohort 2 patients extended from childhood to old age. This indicated that in individuals not infected with HIV, DH may occur at any age, whereas in those with AIDS, a rather restricted age range is to be expected. 15,21–23 We found few significant differences in the clinical manifestations of histoplasmosis among the two cohorts. Fever appeared to be a common symptom (more than 90% of the cases) in both DH patients with AIDS and in those not co-infected with HIV. 9,10,13,21,23 Skin lesions, mostly widespread, predominated (53.3%) in cohort 1 patients and were uncommon in cohort 2 cases (P = 0.001). Such lesions were also more frequent (66%) in Brazilian DH patients co-infected with HIV compared with those in North America (7%). 21 In another series of Brazilian patients, skin lesions had an intermediate (47.6%) frequency. 24 No skin lesions were observed in a large multi-center study in the United States of HIV-infected histoplasmosis patients. 11 We observed that cohort 2 patients differed significantly from cohort 1 only in their lower proportion of skin lesions (9%). It is interesting to note that in HIV-infected Latin American patients, the skin constitutes a more important target organ for H. capsulatum than in North American patients; however, no explanations for this can be given unless a late diagnosis or inadequate diagnostic facilities were considered.

Gastrointestinal involvement was observed in similar proportions in both cohorts, but was more frequent in Brazilian HIV-infected patients with histoplasmosis than in cases in the cohort 1 patients than in cohort 2 patients. Additionally, response to antifungal therapy was less in the former group. Prognosis also depended on the immune status of the patient because all DH patients treated with HAART improved, whereas less than 53% of those not receiving this medication responded to antifungal treatment.

**DISCUSSION**

Sub-clinical infection with H. capsulatum is common in persons residing in disease-endemic areas, whereas clinically manifested disease was not, at least not until the onset of AIDS, when HIV-infected individuals were shown to develop rapidly progressive and often fatal histoplasmosis. 1,4,8–10 This was also the case in Colombia where infection, as detected by skin tests, was demonstrated in approximately 12% of the population, 19 with various clinical forms of histoplasmosis, including outbreaks, reported sporadically. 6–8,20 Once AIDS appeared, DH became more apparent, and showed a high morbidity rate. 6

We conducted a retrospective study of 52 DH patients and divided them in two cohorts, 30 with AIDS and 22 not co-infected with HIV. Patients in cohort 1 were diagnosed from 1988 to 2004, whereas patients in cohort 2 were diagnosed for a longer period (1979–2001). The aim of this comparative study was to detect significant differences between the two cohorts to facilitate early recognition and treatment of DH in HIV-infected patients.

As previously reported in other series, 6,21–23 males predominated (80.7%) in cohort 1 with a male to female ratio of 29:1; in cohort 2, the sex distribution was not so markedly different (P < 0.05). Age distribution was similar in the two cohorts (young adults) as reported by others, 15,21,22 but the age range of cohort 2 patients extended from childhood to old age. This indicated that in individuals not infected with HIV, DH may occur at any age, whereas in those with AIDS, a rather restricted age range is to be expected. 15,21–23

We found few significant differences in the clinical manifestations of histoplasmosis among the two cohorts. Fever appeared to be a common symptom (more than 90% of the cases) in both DH patients with AIDS and in those not co-infected with HIV. 9,10,13,21,23 Skin lesions, mostly widespread, predominated (53.3%) in cohort 1 patients and were uncommon in cohort 2 cases (P = 0.001). Such lesions were also more frequent (66%) in Brazilian DH patients co-infected with HIV compared with those in North America (7%). 21 In another series of Brazilian patients, skin lesions had an intermediate (47.6%) frequency. 24 No skin lesions were observed in a large multi-center study in the United States of HIV-infected histoplasmosis patients. 11 We observed that cohort 2 patients differed significantly from cohort 1 only in their lower proportion of skin lesions (9%). It is interesting to note that in HIV-infected Latin American patients, the skin constitutes a more important target organ for H. capsulatum than in North American patients; however, no explanations for this can be given unless a late diagnosis or inadequate diagnostic facilities were considered.

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**FIGURE 1.** Distribution of highly reactive retroviral therapy (HAART) and CD4 cell counts in patients with disseminated histoplasmosis in cohort 1.

**TABLE 4**

Treatment of disseminated histoplasmosis in cohort 1 patients according to highly active antiretroviral therapy (HAART)

<table>
<thead>
<tr>
<th>Antiviral therapy (n)</th>
<th>Antifungal therapy no. (%)</th>
<th>Maintenance therapy no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amphotericin B* Itraconazole† Other azoles Itraconazole</td>
<td></td>
</tr>
<tr>
<td>HAART (11)</td>
<td>3 (27.3)</td>
<td>7 (63.6) 1 (9.1) 9 (81.8)</td>
</tr>
<tr>
<td>No HAART (19)</td>
<td>2 (10.5)</td>
<td>13 (68.4) 4 (21.1) 7 (36.8)</td>
</tr>
<tr>
<td>Total (30)</td>
<td>5 (16.7)</td>
<td>20 (66.7) 5 (16.7) 16 (53.3)</td>
</tr>
</tbody>
</table>

* Mean = 12.3 days, range = 1–15 days.
† Mean = 3.4 months, range = 0.5–15 months.
‡ Mean = 28.5 months, range = 1–78 months.
United States, a finding that has been confirmed in different series. The frequency of abdominal problems was similar in this study (46.6%) and in those of Hajjeh and others (24%) and Karimi and others (33%). Other differential findings were observed for lung lesions, with significantly more interstitial infiltrates observed in cohort 1 (63.3%). Interstitial infiltrates were also observed in half of the patients reported by Hajjeh and others, in 63% of the Brazilian patients studied by Karimi and others, and in 53.3% of French Guyana patients. This involvement suggests the existence of a primary lung infection that was not noticed.

Anemia and leukopenia were the most common hematologic abnormalities and differed significantly between cohorts 1 and 2 (P < 0.001 for either parameter). Sedimentation rates were elevated in all cohort 1 patients but only in half of cohort 2 patients (P = 0.001). These results should considered when HIV infection in a patient with histoplasmosis is suspected.

Although DH can be diagnosed by observation of H. capsulatum yeast cells in clinical specimens, isolation of the fungus in culture varied in the two cohorts, with nearly all (96.3%) patients in cohort 1 showing positive results, but only 73.6% in cohort 2 (P < 0.05). Conversely, detection of antibodies in sera by either immunodiffusion or complement fixation was significantly lower in cohort 1 patients than in cohort 2 patients (P < 0.05). These findings have been previously demonstrated by Wheat and by Karimi and others in the Brazilian cohort.

The number of CD4 lymphocytes in cohort 1 patients was low (30–53 cells/μL) in those receiving HAART and in those not receiving HAART, suggesting that histoplasmosis occurs when the immune response is markedly impaired, as demonstrated by McKinsey and others, who found that the annual incidence of histoplasmosis in AIDS patients increases when CD4 lymphocyte counts are less than 50 cells/μL. This finding has also been reported in patients in the United States.

In our patients HAART significantly increased CD4 lymphocyte counts (to more than 150/μL), but most importantly, improved the response to antifungal therapy, as shown by the fact that all patients thus treated achieved complete resolution or major improvement of their pre-therapy abnormalities in a manner similar to those patients not co-infected with HIV (cohort 2). In contrast, patients not receiving HAART did not respond as well (P = 0.003) to antifungal treatment. Despite the fact that antiretrovirals are known to improve defense mechanisms, thus allowing AIDS patients to overcome opportunistic infections, their positive influence in histoplasmosis has been recognized only recently, as shown by one case report from the Phillipines, and by a series of cases from Argentina, which indicate that HAART immune restoration effectively cooperates with antifungal therapy in controlling the mycosis.

Due to its retrospective character, this study had several limitations, among them lack of information on CD4 lymphocyte counts in the HIV-infected population both before and

Table 5

Effect of highly active antiretroviral therapy (HAART) on the efficacy of antifungal therapy in patients with disseminated histoplasmosis in cohort 1: comparison with cohort 2 patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cohort 1 (n = 30)</th>
<th>Cohort 2 (n = 22)</th>
<th>P HAART (HAART vs. no HAART)</th>
<th>P vs. HAART</th>
<th>P vs. no HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete resolution or major improvement</td>
<td>HAART n = 11 (%)</td>
<td>No HAART n = 19 (%)</td>
<td>0.03</td>
<td>21 (95.5)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Minor improvement, worsening, or death</td>
<td>0</td>
<td>10* (52.6)</td>
<td>0.03</td>
<td>1 (4.5)</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

* There were 7 (36.8%) deaths in this group.
after therapy. Additionally, variations in treatment modalities during the course of the study interfered with a more precise evaluation of the clinical responses, especially in the DH patients co-infected with HIV, whose treatment is currently defined by expert guidelines.8,18 However, the extended period of the study (1979–2001) did not alter the way in which diagnosis was established in our laboratory since newer modalities (e.g., antigenemia) have not been used regularly in our institution and have been previously used only for standardization purposes, not for diagnosis.18

This study shows that the prognosis of DH is greatly influenced by co-infection with HIV since response rates to antifungal treatment were lower in co-infected patients. Nonetheless, HAART appears to improve this unfavorable condition by restoring the immune response so that even in the presence of AIDS, antifungal therapy can be successful. Therefore, it is mandatory to suspect mycosis as early as possible and initiate antifungal and antiretroviral therapies promptly to improve the prognosis of DH patients co-infected with HIV.

Received February 24, 2005. Accepted for publication May 17, 2005.

Acknowledgments: We thank the patients for participating in the study and the physicians for referring their cases to our institution. We also thank Dr. Elizabeth Castañeda (Instituto Nacional de Salud, Bogotá, Colombia) for cooperation.

Financial support: This study was supported by the Corporación para Investigaciones Biológicas (Medellín, Colombia).

Disclosure: None of the authors have any conflicts of interest.

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