Detection of Fungi and Other Pathogens in Immunocompromised Patients by Bronchoalveolar Lavage in an Area Endemic for Coccidioidomycosis


Bronchoalveolar lavage (BAL) was performed in 51 adult immunocompromised patients (30 acquired immunodeficiency syndrome [AIDS] and 21 non-AIDS) as part of an extensive diagnostic evaluation for diffuse pulmonary infiltrates. Because multiple episodes occurred in several patients, a total of 60 BALs were performed. A diagnosis of fungal pneumonia was eventually made in 12 patients (24 percent). The organism was identified in BALs from seven of the 12, including five of seven cases of coccidioidomycosis, one of two cases of aspergillosis, and one of three cases of cryptococcus. Among the AIDS patients, only one case of coccidioidomycosis was diagnosed, whereas six such diagnoses were made from the 25 BALs performed on the 21 non-AIDS patients. This suggests that coccidioidomycosis is not as frequent an infection in AIDS patients in this endemic area as has been suggested previously. Candida-like organisms were identified in 23 BALs, but in no case were they clinically pathogenic. Their presence correlated with oral candidiasis (p = 0.01). Twenty-seven of 29 episodes related to Pneumocystis carinii were identified by Papanicolaou-stained cytocentrifuged BAL preparations, all but two of which were in AIDS patients. In addition, BALs detected six episodes of bacterial pneumonia and three of five cases of radiation pneumonitis. Overall, the diagnostic sensitivity of BAL was 52 of 60 or 87 percent. While examination of induced sputum for the presence of Pneumocystis may eliminate the need for bronchoscopy in some AIDS patients, BAL remains an excellent diagnostic procedure in the immunocompromised patient without AIDS.

**Methods and Materials**

We identified 63 consecutive BALs from 54 adult (older than 15 years old) immunocompromised patients with bilateral pulmonary infiltrates. Three patients were excluded from further study because no final diagnosis was ever determined, leaving 60 BALs in 51 patients for analysis. Alveolar sampling was achieved by bronchoscopic lavage of a portion of the lung, usually the right middle lobe, with three 50-ml aliquots of normal saline solution. The return was pooled and separate specimens were submitted for cytologic and microbiologic evaluation. Portions of the lavage were cultured for bacteria (including Legionella sp, Mycoplasma sp, and Chlamydia trachomatis, viruses, fungi, and mycobacteria). Occasional specimens were not cultured for all pathogens. Cytologic evaluation was

GMS = Grocott's methenamine silver; Pap = Papanicolaou

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Bronchoalveolar lavage (BAL) is used in many institutions as the initial diagnostic procedure to determine the cause of diffuse pulmonary infiltrates in immunocompromised patients. This procedure is particularly successful in identifying Pneumocystis carinii and various bacterial pathogens, as well as viruses, mycobacteria, and fungi. Specific experience with several pathogenic fungi, such as Cryptococcus sp, Histoplasma capsulatum, Candida sp, and Aspergillus sp, has been described. However, no study has looked systematically at the incidence and ease of detection of Coccidioides immitis, the dimorphic fungus causing coccidioidomycosis, in BAL fluid from immunocompromised hosts. Coccidioides immitis is indigenous to the southwest United States, particularly the Sonoran Desert, in a zone stretching from western Texas to the valleys of California, including northern Mexico. Tucson, Arizona, the site of the present study, is situated at the approximate geographic center of this distribution.

Coccidioidomycosis has long been recognized as an important fungal infection in this area, even in those with normal immune status. With the emergence of acquired immunodeficiency syndrome (AIDS), disseminated coccidioidomycosis has been identified as a significant contributor to mortality in this setting. The ease of identifying C immitis in bronchial secretions has been documented previously. In this report we describe the usefulness of BAL in the diagnosis of coccidioidomycosis in an immunocompromised population with diffuse pulmonary infiltrates and compare the diagnostic yield in AIDS vs non-AIDS patients. Also, we determined the relative frequency of Pneumocystis, bacterial, viral, and other fungal isolates, and other infiltrative diseases in the two patient groups.

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Table 1—Final Diagnosis for 60 BALs*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>AIDS: 36 Specimens</th>
<th>Non-AIDS: 25 Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystis</td>
<td>27 (1)†</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Fungi</td>
<td>4 (2)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Bacteria</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Viruses</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>1 (1)</td>
<td>4</td>
</tr>
<tr>
<td>Radiation pneumonia</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Drug reaction</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Allograft rejection</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Adult respiratory</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>distress syndrome</td>
<td>38†</td>
<td>29†</td>
</tr>
</tbody>
</table>

*BAL = bronchoalveolar lavage; AIDS = acquired immunodeficiency syndrome.
†Numbers in parentheses indicate number of diagnoses missed by BAL.
‡Total diagnoses exceed the number of cases because of multiple diagnoses, in six cases, which were as follows: AIDS cases: Pneumocystis, C trachomatis, and S aureus; Pneumocystis and H influenza; Pneumocystis and C neoformans. Non-AIDS cases: Aspergillus and P aeruginosa; Hodgkin’s disease and L pneumophila; Hodgkin’s disease and S aureus.

performed on cytocentrifuge preparations of undiluted fluid and prepared with Papanicolaou (Pap) stain, Grocott’s methenamine silver (GMS), hematoxylin-eosin, and iron stain in 50 specimens and Pap and GMS stain only in ten.

Patient charts were reviewed to identify underlying diseases, clinical presentation, the presence of oral candidiasis (thrush), concomitant serologic tests for C immitis, and subsequent clinical course following BAL. Five patients had BALs on two occasions and two patients had three BALs; each of these represented separate episodes of disease. The diagnostic accuracy of BAL was judged by the clinical course and/or response to therapy in 44 cases and by biopsy or autopsy in 16 cases.

RESULTS

Thirty-five BALs were examined in 30 patients with a prior diagnosis of AIDS or in whom a diagnosis of AIDS was made following BAL. The 25 BALs in non-AIDS patients (21 patients) were largely in the setting of treated hematologic-lymphoid disease, including eight cases of Hodgkin’s disease, three of multiple myeloma, three of acute myelogenous leukemia, and one each of myelodysplasia and lymphoid interstitial pneumonia. Two patients had treated carcinomas, one prostate and one lung. Four were patients with organ transplants, two heart-lung and two heart. One case each of severe malnutrition, corticosteroid-treated polymyositis, and uncontrolled diabetes mellitus was noted.

Findings at BAL and final diagnoses are shown in Table 1. In general, BAL provided an accurate diagnosis of a specific process in 43 of 60 episodes that ultimately had a definite clinical or anatomic diagnosis. In nine instances a BAL that showed no abnormalities (“negative” BAL) correlated with the clinical impression and accurately ruled out infectious and/or other causes (vide infra). In these nine patients, serologic studies for coccidioidomycosis were negative at the time of BAL in seven and not done in two. Cultures of blood, sputum, and urine showed no pathogens to explain the pulmonary infiltrates. Autopsy in three cases and open lung biopsy in one case ruled out infection and neoplasm that could have been reflected in the BAL. In eight instances either Pneumocystis (two cases), lymphoma (one case), or a pathogenic fungus (five cases) was missed in the BAL. Thus, the overall diagnostic accuracy (sensitivity) of BAL in this population was 52/60 or 87 percent. There was no significant difference in sensitivity between AIDS and non-AIDS cases.

Fungi

In 12 of the 60 episodes, fungi were identified as the cause of the pulmonary infiltrates (Table 2). C immitis being found in seven cases. This fungus was grown from culture of five BALs, three of which had previously shown the organism cytologically (Fig 1).

Table 2—Pathogenic Fungi in Immunocompromised Patients Undergoing BAL*

<table>
<thead>
<tr>
<th>Age, y/Sex</th>
<th>Underlying Disease</th>
<th>Organism</th>
<th>BAL Cytology</th>
<th>BAL Culture</th>
<th>How Organism Was Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>33/M</td>
<td>AIDS</td>
<td>Cryptococcus neoformans</td>
<td>+</td>
<td>+</td>
<td>BAL</td>
</tr>
<tr>
<td>39/M</td>
<td>AIDS</td>
<td>C neoformans</td>
<td>-</td>
<td>-</td>
<td>Lymph node biopsy</td>
</tr>
<tr>
<td>27/M</td>
<td>AIDS</td>
<td>C neoformans</td>
<td>-</td>
<td>-</td>
<td>Bone marrow biopsy</td>
</tr>
<tr>
<td>38/M</td>
<td>AIDS</td>
<td>Coccidioides immitis</td>
<td>+</td>
<td>+</td>
<td>BAL</td>
</tr>
<tr>
<td>84/M</td>
<td>Prostatic cancer</td>
<td>C immitis</td>
<td>-</td>
<td>-</td>
<td>Blood culture</td>
</tr>
<tr>
<td>30/M</td>
<td>Uncontrolled diabetes</td>
<td>C immitis</td>
<td>+</td>
<td>+</td>
<td>BAL</td>
</tr>
<tr>
<td>23/F</td>
<td>Hodgkin’s disease</td>
<td>C immitis</td>
<td>-</td>
<td>-</td>
<td>BAL</td>
</tr>
<tr>
<td>78/M</td>
<td>Myelodysplasia</td>
<td>C immitis</td>
<td>-</td>
<td>-</td>
<td>Autopsy</td>
</tr>
<tr>
<td>88/F</td>
<td>Treated polymyositis</td>
<td>C immitis</td>
<td>-</td>
<td>+</td>
<td>BAL</td>
</tr>
<tr>
<td>24/M</td>
<td>Hodgkin’s disease</td>
<td>C immitis</td>
<td>+</td>
<td>+</td>
<td>BAL, skin biopsy</td>
</tr>
<tr>
<td>67/M</td>
<td>Leukemia</td>
<td>Aspergillus sp</td>
<td>-</td>
<td>-</td>
<td>Open lung biopsy</td>
</tr>
<tr>
<td>67/M</td>
<td>Malnutrition</td>
<td>Aspergillus terreus</td>
<td>+</td>
<td>+</td>
<td>BAL, transbronchial biopsy</td>
</tr>
</tbody>
</table>

*BAL = bronchoalveolar lavage; AIDS = acquired immunodeficiency syndrome.
One additional case was diagnosed at autopsy and the other was diagnosed from blood and bronchial brushings. Only one of the seven cases of coccidioidomycosis occurred in an AIDS patient. Serologic studies for coccidioidomycosis were obtained during 46 of the 60 episodes, including all seven of those in which such a diagnosis was ultimately confirmed. Five of the seven were positive, with complement-fixing antibody titers (four patients) that ranged from 1:4 to 1:256. In one patient, precipitating antibody was present with a negative complement-fixing titer, and in two others, the titer was positive with a negative precipitating reaction. Serologic studies in the patient whose condition was diagnosed at autopsy were negative two weeks prior to his death. Among the 39 other samples tested, two were positive. In neither case was there evidence of significant active infection.

The three episodes of cryptococcal pneumonia all occurred in AIDS patients; the organism was seen cytologically and cultured in one BAL but it was absent in the two others. Disseminated cryptococcal infection was eventually demonstrated in these latter two patients by lymph node or bone marrow biopsy specimen. Invasive aspergillosis was diagnosed in two non-AIDS patients. Hemorrhagic necrotizing aspergillosis was diagnosed both cytologically and by culture from a BAL and confirmed by transbronchial biopsy. However, a case of granulomatous aspergillosis was not detected by BAL, but it was diagnosed subsequently by open lung biopsy. Aspergillus sp was also grown from a BAL in one AIDS patient with Pneumocystis pneumonia, but there was no evidence of pulmonary infection clinically or in a transbronchial biopsy specimen.

Fungi consistent with Candida sp, including *Torulopsis glabrata* and yeast not otherwise identified (not *Cryptococcus*) were detected cytologically in nine BALs and cultured in 23. The ability to culture the Candida-like organism from BAL was positively correlated with the presence of thrush ($X^2 = 6.61; p = 0.01$). However, in no case was it apparent, clinically or pathologically, that Candida was a cause of lower respiratory tract infection.

**Pneumocystis carinii**

*Pneumocystis carinii* was the most frequent pathogen isolated from BAL fluid. The organism was seen cytologically in 27 of the 60 specimens, 26 of which were from the AIDS population. In one AIDS patient with a negative BAL, Pneumocystis pneumonia was diagnosed clinically by lack of other identifiable causes for pulmonary infiltrates coupled with complete response to trimethoprim-sulfamethoxazole. Although this drug may be therapy for other infections as well, we would regard the case as one of Pneumocystis because of the high likelihood of this organism being present. One non-AIDS patient had a negative BAL but sputum positive for Pneumocystis. In each case.

**Figure 1.** Photomicrographs of spherules of *Coccidioides immitis* in bronchoalveolar lavage (BAL) fluid: A. Small spherule (arrow) phagocytized by a macrophage. B. Mature spherule with endospores, slightly folded. C. Collapsed empty spherule surrounded by inflammatory cells (all Papanicolaou stain, ×1135).
positive by Pap stain, the presence of the organism was confirmed by GMS stain, and in no case was an additional identification of Pneumocystis made with this special stain.

**Viruses**

Cytomegalovirus was demonstrated by direct immunofluorescence with monoclonal antibodies and/or culture in 21 of the 59 BALs studied. Likewise, herpes simplex virus was identified in five specimens and parainfluenza type 3 was identified in one. Intranuclear viral inclusions were seen cytologically in only two cases, one of cytomegalovirus and one of herpes. In only one patient who had treated acute myelogenous leukemia was cytomegalovirus believed clinically to be a cause of progressive pneumonia. In 13 cases, cytomegalovirus was isolated from AIDS patients with Pneumocystis pneumonia, but clinically it was not responsible for disease. In four patients (one each with malnutrition, Hodgkin's disease, heart-lung transplant, and acute myelogenous leukemia) either biopsy specimen or autopsy failed to show cytomegalovirus as a pathogen. A heart transplant patient with Pneumocystis pneumonia and cytomegalovirus cultured from a BAL recovered after therapy for Pneumocystis; blood, throat, and urine cultures were negative for cytomegalovirus. The remaining two patients, one with multiple myeloma and a drug reaction, the other with coccidioidomycosis complicating corticosteroid-treated polymyositis, had no clinical evidence of cytomegalovirus pneumonia.

**Bacteria**

Of the 57 of 60 BALs cultured for bacteria, bacterial pathogens grew from eight: these included three cases of coagulase-positive *Staphylococcus aureus*, and one each of *Streptococcus pneumoniae*, *Chlamydia trachomatis*, *Legionella pneumophila*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa*. Of the three isolates of *S. aureus*, one was regarded clinically as a pathogen in an elderly man with severe chronic obstructive pulmonary disease and AIDS; the patient was treated for this infection but died shortly thereafter; an autopsy was not performed. In another patient with AIDS and Pneumocystis, *C. trachomatis* was regarded as a pathogen and treated while the *S. aureus* isolated was not treated. A patient with Hodgkin's disease and *S. aureus* was treated for this infection; autopsy showed pneumonia that could have been staphylococcal. *Legionella pneumophila* pneumonia was confirmed at autopsy. *Streptococcus pneumoniae* was treated as a pathogen in an AIDS patient who had prompt response to antibiotic therapy, but therapy against *Pneumocystis* was not given. *Pseudomonas aeruginosa* isolated in a patient with invasive aspergillosis was treated but *H. influenzae* from a patient with Pneumocystis was believed to be a nonpathogen. Colony counts were not done on bacterial pathogens isolated from BALs. None of these bacteria was isolated from blood cultures done at approximately the same time or from urine or sputum cultured in some cases. Twelve cultures were sterile, and a variety of organisms, including *Streptococcus viridans*, non-hemolytic streptococci, coagulase-negative staphylococci, diphtheroids, and Neisseria sp, grew from the remainder. All of these were clinically nonpathogenic.

No mycobacteria were cultured or seen by smear in any of the 59 BALs examined for these pathogens. Similarly, no Mycoplasma sp were identified in the 50 BALs examined for this organism.

**Noninfectious Causes of Infiltrates**

Radiation pneumonitis was an eventual diagnosis in five patients by open lung biopsy in two patients, autopsy in one, and clinical course in the remaining two. In three of these, BAL cytologic study demonstrated reactive atypia of epithelial cells consistent with radiation. In two other cases, the final diagnosis was rejection of transplanted lungs, and the "negative" BAL was clinically important in making this distinction. The BAL was also appropriately negative in two cases of adult respiratory distress syndrome and three cases of pneumonitis due to drug toxicity. Two cases of pulmonary infiltrates due to drug reaction responded quickly to corticosteroid therapy and drug withdrawal alone, while another with a skin rash as well cleared rapidly following discontinuance of the drug therapy. A patient with treated lymphoid interstitial pneumonia who subsequently developed adult respiratory distress syndrome had a "negative" BAL; autopsy showed diffuse alveolar damage but no lymphoid interstitial pneumonia. A case of clinically disseminated Kaposi's sarcoma was manifest in the lung by the presence of many hemosiderin-laden macrophages in the BAL fluid. One patient with pulmonary involvement by lymphoma, subsequently proven by lymph node biopsy, had an unremarkable BAL. The pulmonary lesions were believed to be lymphoma because they were mass-like, occurred in a setting of disseminated (liver, spleen, lymph node) disease, and disappeared with chemotherapy directed against the lymphoma. Three cases of Hodgkin's disease involving the lungs, malignant lymphoreticular cells, were present in the lavage.

**Discussion**

The differential diagnosis of diffuse pulmonary infiltrates in the immunocompromised patient is difficult at best. In addition to a large variety of infectious agents, one must also consider that recurrence of the primary disease, drug toxicity, the adult respiratory distress syndrome, and toxic reactions to radiation...
therapy that may produce similar clinical and roentgenographic findings. Even when all these possibilities have been exhausted, one is often left with a small number of patients with interstitial disease of unknown cause. The present study examined the BAL findings in two groups of such immunocompromised patients in an area that is endemic for coccidioidomycosis. In keeping with the findings of several recent reports,10,21,22 the most common finding among AIDS patients was Pneumocystis pneumonia. Among the 35 BALs in 30 such patients examined, 26 were cytologically positive for this organism. All identifications were made with Pap stains prepared within 1 h of the bronchoscopic procedure, similar to previous reports.23 No additional diagnoses were made with GMS preparations, although the initial diagnosis was confirmed in each instance. The ease of the Pap preparation and the fact that identification was made by pathology residents on nights and weekends with 100 percent accuracy was an additional positive factor in the use of the Pap stain. Another advantage of this stain was the fact that a number of other organisms could be identified simultaneously. Fungi such as C. immitis, cryptococci, and some species of Candida were frequently seen. Also, it was possible to recognize atypical or neoplastic cells, old hemorrhage, and other cytologic changes that contributed to the diagnostic conclusions. The GMS stains are still used to identify some fungi that may be missed with Pap staining and to confirm results.

The 12 cases (20 percent) of fungal infection in 60 BALs in the current series is higher than has been reported previously (see Table 3). This is primarily due to the seven cases of coccidioidomycosis, a number that was not surprising in view of the fact that the patient population comes from the endemic area for this disease. In five of the seven cases, the diagnosis was made by BAL, either immediately, by cytologic examination of the Pap-stained BAL, or several days later, by culture. In one instance in which the diagnosis was missed, the BAL fluid was of small quantity and contained few alveolar macrophages, indicating a somewhat inadequate specimen. The other case involved a patient with myelodysplasia who died shortly after the bronchoscopy with pneumonia and pulmonary hemorrhage. Cultures of blood and urine were also negative, as was the serologic test. The diagnosis was made only at autopsy, with the identification of fibrotic granulomas that were limited in extent and only minimally active. Among those patients with active pulmonary involvement in whom an adequate BAL specimen is obtained, the diagnostic yield of this procedure approaches 100 percent. The yield from serologic studies for coccidioidomycosis was similar to that of BAL (five to seven). Unfortunately, serologic results are often not available for up to seven days at a time when immediate therapeutic intervention is required. Thus, the fact that the BAL Pap-stained cytologic test result is available within hours from the time of collection represents a distinct clinical advantage. Of particular interest in this series was the fact that only one of the 31 AIDS patients (36 BALs) was found to have coccidioidomycosis. This contrasts sharply with a previous report of a 25 percent prevalence of this disease in AIDS patients living in this area.

Although others6,9,13 have described invasive candidal pneumonia in some patients in whom Candida sp were isolated from BALs, we found no clinical or pathologic evidence that Candida sp were respiratory pathogens in our series. The positive correlation between oral candidiasis and a positive BAL culture

Table 3—Identification of Fungi in BAL Fluid*

<table>
<thead>
<tr>
<th>Source, yr</th>
<th>Number of BALS</th>
<th>Type of Patient</th>
<th>% of BALs with Pathogenic Fungi</th>
<th>Aspergillus sp</th>
<th>Candida sp</th>
<th>Coccioides immitis</th>
<th>Cryptococcus neoformans</th>
<th>Other</th>
<th>Cases Missed by BAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stover et al, 1984</td>
<td>97</td>
<td>Non-AIDS</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stover et al, 1984</td>
<td>72</td>
<td>AIDS</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Young et al, 1984</td>
<td>30</td>
<td>Non-AIDS</td>
<td>20</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Broaddus et al, 1985</td>
<td>276</td>
<td>AIDS</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Orenstein et al, 1986</td>
<td>78</td>
<td>AIDS</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Francis et al, 1987</td>
<td>120</td>
<td>AIDS</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Linder et al, 1987</td>
<td>604</td>
<td>Non-AIDS</td>
<td>—</td>
<td>5</td>
<td>167</td>
<td>0</td>
<td>1</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>Martin et al, 1987</td>
<td>100</td>
<td>Mostly non-AIDS</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Present study</td>
<td>60</td>
<td>60% AIDS</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>24</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*BAL = bronchoalveolar lavage; AIDS = acquired immunodeficiency syndrome.
†Mucor species.
‡Number in parentheses indicates identified but not a pathogen.
§Histoplasma capsulatum.
†167 Candida sp isolated, 26 Alternaria sp isolated; pathogenic vs nonpathogenic not specified.
for Candida sp suggests that many instances of Candida in BALs represent contamination from the upper respiratory tract. Aspergillus sp similarly can colonize the tracheobronchial tree, as was the case in one AIDS patient whose BAL showed growth of Aspergillus sp and contained Pneumocystis. Transbronchial biopsy specimen showed only Pneumocystis and the clinical course was that of Pneumocystis pneumonia. The recovery of Aspergillus sp from BAL does not indicate invasive disease, and a tissue biopsy specimen may be necessary to evaluate its role as a pathogen.

The recovery of a potentially pathogenic virus, either cytomegalovirus or herpes simplex virus, in more than one third of the cases is a higher percentage than reported by others and underscores the problem cited by Broad du et al that not all positive viral cultures imply disease. Detection of either cytomegalovirus or herpes simplex virus in BALs by monoclonal antibody staining or culture was far more sensitive in detecting the presence of virus than cytologic study, as others have shown. In 20 instances cytomegalovirus or herpes simplex virus was identified in association with another known pathogen, usually Pneumocystis. It is possible that in some cases the virus was contributing to the patient's pneumonia. Nevertheless, in all such cases the pneumonia was effectively treated without therapy directed toward the virus. Also, autopsies on five patients who had cytomegalovirus cultured from their BAL failed to reveal histologic changes consistent with cytomegalovirus pneumonia or viral inclusions in lung tissue. However, most of the cytomegalovirus was in AIDS patients with Pneumocystis (13/21), and the two transplant patients with cytomegalovirus had no Pneumocystis attributed to this virus.

Our inability to detect Mycoplasma sp in any case studied is curious in view of a previous report from the same city that preceded the present study. In that report approximately 20 percent of the immunocompromised patients had Mycoplasma recovered from BAL fluid. We are unable to explain the absence of Mycoplasma in the present series, even though the same culture methods were employed. Mycobacterium tuberculosis and Mycobacterium avium-intracellulare have been reported in BALs from other institutions, and we have seen M avium-intracellulare infection at autopsy in several AIDS patients. The incidence of mycobacteria in BALs of immunocompromised patients without AIDS has been reported to be 3 to 4 percent and 9 to 12 percent in AIDS patients. However, no patient in the present series had this organism demonstrated by smear or culture. Since the present report includes only patients with diffuse radiologic infiltrates, we excluded two cases of M avium-intracellulare presenting with localized infiltrates during the period of study.

More recently we have begun to examine induced sputum for the presence of Pneumocystis in AIDS patients using both Pap- and GMS-stained cytologic preparations and fluorescein labeled monoclonal antibodies against Pneumocystis. This approach, as shown by others, may decrease the number of patients that require diagnostic BAL, although one study suggests that in areas with only a moderate incidence of AIDS, BAL may be a better diagnostic approach. Since C immitis can also be diagnosed by sputum examination, this approach may enable the diagnosis of coccidioidomycosis to be made in a portion of patients with that infection as well. However, the present study suggests that non-AIDS patients are less likely to have diseases, such as Pneumocystis pneumonia, that can be detected by sputum examination alone. The diagnosis of noninfectious pulmonary infiltrates in these immunocompromised patients usually requires BAL examination rather than sputum cytologic study.

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