Analysis of Bronchoalveolar Lavage Specimens from Immunocompromised Patients with a Protocol Applicable in the Microbiology Laboratory

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Several studies have concluded that bronchoalveolar lavage (BAL) is a useful technique for diagnosing pulmonary disease in immunocompromised patients, but implementation of a protocol for obtaining, processing, and analyzing BAL specimens in a clinical microbiology laboratory has not been reported. We determined the utility of a laboratory protocol by analyzing 100 BAL specimens from 94 immunocompromised patients. Each BAL specimen was cultured quantitatively for bacteria. A concentrate of each specimen was cultured for fungi, viruses, mycobacteria, and Legionella sp. Slides of the BAL concentrate were prepared by cytocentrifugation and stained by a number of histochemical and fluorescence techniques. Overall diagnostic yields of 81% for infections, 90% for hemorrhage, and 13% for neoplasms were obtained with the patients studied. BAL analysis was incapable of diagnosing drug- or radiation-induced pneumonitis or idiopathic interstitial pneumonitis. After evaluation of the protocol was completed, it was successfully implemented in two university-based clinical microbiology laboratories as a routine diagnostic service.

Bronchoalveolar lavage (BAL), originally used as a tool for obtaining secretions and cells from the lower respiratory tracts of patients with interstitial, occupational, or both types of lung disease (18, 19), has recently been adapted for use in patients with respiratory infection, including patients with compromised host defenses (4). Performed with a fiber-optic bronchoscope, BAL can be done simply and safely. BAL has been reported to be a useful addition to transbronchial biopsy for determining the etiology of pulmonary infiltrates in immunocompromised patients (2, 3, 7, 10–12, 14, 16, 17, 21–24).

Various techniques for handling and submitting BAL samples have been described. In general, specimens have been divided and submitted to a cytology or surgical pathology laboratory for histologic examination and to one or more microbiology laboratories for culture. Ideally, a clinician should be able to submit such a specimen to a single laboratory, results of histochemical and fluorescent-antibody stains should be available within hours of specimen submission, and a report summarizing all of the information obtained from analysis should be issued from that laboratory. Several years ago, we began to study use of BAL to diagnose the etiology of pulmonary infiltrates in immunocompromised patients. From the outset, we decided to study the use of simple techniques to process BAL specimens. We chose techniques that could readily be incorporated into a protocol applicable in a clinical microbiology laboratory and would give as much information as possible bearing upon etiologies considered in differential diagnoses based on pulmonary infiltrates from these patients. We have published detailed descriptions of techniques used in key portions of this protocol and determined their utility in making specific diagnoses, namely, bacterial pneumonia (10), fungal pneumonia (11), and alveolar hemorrhage (12). However, we have not previously described the diagnostic yield to be expected when all components of the protocol are used together. Thus, in this report we describe the diagnostic yield from analysis of 100 BAL specimens from 94 patients by our protocol and describe steps in implementing the protocol in two hospital microbiology laboratories. The protocol remains in routine use at both hospitals.

MATERIALS AND METHODS

Patient population. A total of 94 immunocompromised patients underwent 100 BAL studies from 1 February 1984 to 1 February 1986. Patients were considered candidates for study if they had acquired immunodeficiency syndrome (AIDS) or hematologic malignancies, were recipients of bone marrow or solid organ transplants, or were receiving large doses of corticosteroids or other immunosuppressive drugs. All patients had radiographic evidence of new pulmonary infiltrates. A patient with these characteristics was asked to participate in the study if diagnostic bronchoscopy was planned, his hemodynamic status was stable, an arterial PO$_2$ of at least 7,333 Pa could be maintained in the patient with supplemental oxygen, and he was cooperative. Either the patient or a guardian gave informed consent for a BAL specimen to be taken. Although age was not an exclusion criterion, specimens were obtained from only four patients less than 18 years of age.

Bronchoscopy studies. Fiber-optic bronchoscopy and bronchoalveolar lavage were performed as previously described (10–12). In patients over 18 years of age, after atropine and meperidine preanesthesia, a BF-1T (Olympus Corporation of America, New Hyde Park, N.Y.) was passed transnasally into the trachea. Topical anesthesia with 2 to 5 ml of a solution containing 10 mg of lidocaine, 7 mg of NaCl, and 1 mg of methylparaben per ml was applied, and the bronchoscope was advanced and wedged into a segmental bronchus supplying an area of radiographic abnormality. Alveolar lavage was performed by sequential instillation and suctioning of 50-ml volumes of sterile, nonbacteriostatic physiologic saline. The procedure was repeated three times, and the fluid

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TABLE 1. Diagnostic yield of BAL of 94 patients who underwent 100 BAL procedures

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>No. of diagnoses made</th>
<th>No. of positive BAL tests</th>
<th>% Yield of BAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>69</td>
<td>56</td>
<td>81</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>10</td>
<td>9</td>
<td>90</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>15</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Cardiogenic or noncardiogenic pulmonary edema</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Drug- or radiation-induced fibrosis</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Idiopathic interstitial pneumonia</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Otherb</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

* A total of 113 pulmonary diagnoses were established by clinical, bronchoscopic, open-lung biopsy, or postmortem findings.

b Fat emboli, alveolar proteinosis, bronchiolitis obliterans, and metastatic calcification.

returns were pooled. For children, an Olympus P-10 bronchoscope was used and BAL was performed by instilling 20-ml volumes of saline. Routine bronchoscopic studies including brushings, low-volume washings, and biopsies were performed after the BAL. Transbronchial biopsies were done only if prothrombin and partial thromboplastin times were within a normal range and the platelet count exceeded 50,000/mm³.

BAL studies. The protocol for analysis of BAL samples is given in Table 1. Each specimen was filtered through a sterile gauze pad. The filtrate was cultured quantitatively for bacteria as previously described (10). A BAL specimen was considered to contain a significant number of bacteria if it contained ≥10^5 CFU of a bacterial species per ml and had less than 1% squamous epithelial cells in the Giemsa-stained slide of the specimen (10). After the quantitative culture was set up, the specimen (usually 40 to 80 ml) was centrifuged at 1,500 × g for 15 min. The supernatant was decanted, and the pellet was suspended in Hanks salt solution to 20% of the original volume of the specimen (8 to 16 ml). If the specimen was grossly bloody and the pellet was predominantly erythrocytes, the latter were removed by lysis. This was accomplished by adding 10 ml of sterile, chilled (4°C) distilled water to the pellet, mixing it gently with a pipette, letting the resultant suspension sit for 10 min, and centrifuging it at 1,500 × g for 15 min. The supernatant was removed, and the pellet was suspended in Hanks solution to 20% of the original volume of the specimen. Portions of this cell concentrate were cultured for fungus, virus, mycobacteria, and legionellae. Virus cultures were performed by placing 0.5 ml of concentrate in a vial of viral transport medium which was submitted to the Wisconsin State Laboratory of Hygiene. Fungal and mycobacterial cultures were done in the laboratory of the investigators. Four to eight drops of the concentrated specimen and seven to eight drops of cytopsin collection fluid (catalog no. 999X0320; Shandon Instruments, Sewickley, Pa.) were added to each cell of the cytocentrifuge. Preliminary studies showed that the metallic salts in the collection fluid were essential for obtaining fixed slides optimal for all of the staining methods used.

Cytocentrifugation at 1,500 rpm for 15 min generated 12 slides with BAL concentrate fixed in a 5-mm-diameter circle. Slides were dried on a slide warmer (40°C) for 15 min. Two pairs of slides were stained with toluidine blue and Legionella pneumophila fluorescein-conjugated antibody, respectively. One slide was stained with each of the other techniques used. A Gram stain was read as positive for large numbers of bacteria if at least 10 organisms were seen per oil immersion field, providing that the Giemsa stain showed less than 1% squamous epithelial cells. The Giemsa-stained slide was read as positive for malignant cells only if multiple clumps of cells with obviously atypical morphology were seen. A modified toluidine blue stain which did not require use of diethyl ether in the sulfation reagent (8) was found to be superior to the standard toluidine blue staining procedure, and the modified stain was used during the last 12 months of the study. Our criteria for recognizing Pneumocystis carinii cysts or fungal hyphae in toluidine blue-stained slides (11) have been published previously. The Kinyoun modification of the Ziehl-Nielsen acid-fast stain was used. The technique for performing the Prussian blue stain for hemosiderin and for scoring the hemosiderin content of alveolar macrophages has been previously described (12). In previous work (12), we found that specimens could be placed conveniently into three groups on the basis of a low (0 to 20), intermediate (21 to 100), or high (>100) hemosiderin score. By correlation with tissue biopsies, it was shown that patients with an intermediate score had some degree of alveolar hemorrhage and those with a high score had moderate-to-severe alveolar hemorrhage. Commercially available monoclonal antibodies were used to perform Legionella (Genetic Systems, Seattle, Wash.), herpes simplex virus (Syva Co., Palo Alto, Calif.), and cytomegalovirus (CMV) (MA Bioproducts, Walkersville, Md.) direct fluorescent-antibody (DFA) stains. The monoclonal anti-Legionella monoclonal antibody was directed against an outer membrane antigen of all known serogroups of L. pneumophila. Specimens with a positive Legionella DFA stain had at least six positively stained organisms. The Gram stain was used to check for the presence of large numbers of bacteria that could produce a false-positive reaction. Specimens with a positive DFA for viral antigens had at least 10 mononuclear cells (macrophages, lymphocytes, or bronchial epithelial cells) with bright fluorescence per slide.

At the end of the study period, the protocol for BAL analysis was implemented in clinical microbiology laboratories at our medical center. Details of the implementation are described below.

Ancillary bronchoscopy specimens. Bronchial washings were strained through sterile gauze and submitted for bacterial, fungal, viral, mycobacterial, and Legionella culture and stains and for cytological studies (Papanicolaou). Transbronchial biopsies were examined with hematoxylin and eosin, Gomori methenamine silver, and Ziehl-Nielsen stains. A Prussian blue stain of tissue was done when the hematoxylin-eosin stain suggested the presence of alveolar hemorrhage.

Ancillary studies. An open-lung biopsy was performed if bronchoscopic studies were nondiagnostic and the condition of the patient allowed it. In the 45 cases in which autopsies were done, results were reviewed. The results of all pertinent cultures (blood and sputum) were reviewed.

Diagnostic criteria. Etiologies of pulmonary infiltrates were established by clinical and roentgenographic findings and by studies of bronchoscopic specimens, lung biopsies, and autopsy specimens. Tissue samples for confirmation of diagnoses were available for 79 patients. All diagnoses of invasive fungal infection and viral infection were verified by histologic studies of lung biopsy or autopsy specimens. Pulmonary malignancies were diagnosed by tissue cytology, Papanicolaou cytology, or both. If a patient had the same bacterial species isolated from sputum and blood cultures or...
bacteria were seen in lung tissue at autopsy, bacterial pneumonia was diagnosed. Bacterial pneumonia was also diagnosed if an organism was isolated from the sputum and the patient responded appropriately to treatment. Cardiogenic and noncardiogenic pulmonary edema were diagnosed by clinical findings, examination of tissue, pulmonary artery (Swan-Ganz) catheterization, and response to appropriate therapy. Pulmonary hemorrhage was established by a high BAL hemosiderin score (12), examination of tissue specimens, or both. Drug or radiation toxicity was diagnosed if the patient had an appropriate exposure history, tissue showed nonspecific pneumonitis, and other potential diagnoses had been excluded. A diagnosis of idiopathic pneumonitis was made when lung tissue showed interstitial fibrosis, cellular infiltrates, or both and organisms could not be detected by stain and culture.

Analysis of data. Data were entered into a standard database (Statplan: The Futures Group, Glastonbury, Conn.) with an IBM personal computer. Files were extracted and translated into the appropriate format, and means and standard deviations were calculated. For each diagnosis (e.g., Pneumocystis pneumonia or aspergillosis), the diagnostic yield of each technique (e.g., BAL or transbronchial biopsy) was the number of times the technique yielded the diagnosis divided by the number of times the technique was applied to patients with the diagnosis times 100%. The overall diagnostic yield for each technique was the number of times the technique yielded all diagnoses divided by the total diagnoses made in patients to which the technique was applied times 100%.

RESULTS

Diagnostic yield of BAL. During the study period, 100 BAL procedures were done on 94 immunocompromised patients. The study population comprised 67 males and 27 females, ranging in age from 3 to 78 years. Underlying conditions included hematologic malignancy (30 patients), lymphoma (13 patients), bone marrow transplantation (9 patients), AIDS (5 patients), solid tumor (4 patients), and other conditions for which immunosuppressive therapy was administered (19 patients). Minor complications (cough, bronchospasm, and self-limited hemorrhage) were noted in approximately one-third of the patients. No major complications due to BAL were noted in the patients studied.

A total of 113 diagnoses were established in the 94 patients who underwent BAL (Table 1). Infection predominated (69 diagnoses), followed by pulmonary neoplasia (n = 15), hemorrhage (n = 10), cardiogenic or noncardiogenic pulmonary edema (n = 9), drug- or radiation-induced fibrosis (n = 4), idiopathic pneumonia (n = 2), and other diagnoses (n = 4). BAL was most useful for diagnosing infection and alveolar hemorrhage, had modest utility for diagnosing neoplasm, and was incapable of determining a number of other diagnoses (Table 1). The diagnostic yield was variable, depending on the underlying conditions, being 82% for bone marrow transplant recipients but only 20% for patients with lymphoma (Table 2). The low diagnostic yield for BAL in lymphoma patients may be accounted for by the fact that 8 of the 13 patients had pulmonary involvement with lymphoma and 2 had drug-related fibrosis, diagnoses that we found difficult to establish by BAL techniques.

BAL compared with other techniques for diagnosis of pulmonary infections. Sixty-nine pulmonary infections were established in the patient population (Tables 2 and 3). The overall diagnostic yield of BAL (81%) was similar to that obtained by transbronchial biopsy (80%). It happened that all open-lung biopsies were done on patients infected with P. carinii or Aspergillus sp. When either of these was present, BAL had a diagnostic yield of 72%, which compared favorably with the 88% value observed for open-lung biopsy.

P. carinii was identified in 17 of 22 instances (77%) by toluidine blue staining of BAL specimens. BAL stains were positive in 10 (56%) of 18 samples from patients with invasive fungal infection, whereas cultures were positive in 5 (28%) of 18 samples. Overall, BAL stains, cultures, or both were diagnostic of fungal infection in 12 (66%) of 18 patients. Although examination of stained preparations detected more infections than did cultures, there were two instances in which the culture was positive and the stains were negative for the fungus. Fungal infections were due to Aspergillus sp., except in one patient, who had mucor mycosis. Although BAL cultures were positive for virus in the 11 patients with pneumonitis due to either CMV or herpes simplex virus, DFA stains were diagnostic in four (50%) of eight and one (33%) of three BAL samples from patients with CMV and herpes simplex virus infections, respectively.

Quantitative BAL cultures grew significant numbers of a bacterial pathogen (>10^7 CFU/ml; mean, 5 x 10^6 CFU/ml) in all seven patients with bacterial pneumonia. Organisms isolated included Pseudomonas aeruginosa (four isolates), Citrobacter freundii (one isolate), Streptococcus pneumoniae (one isolate), and Staphylococcus aureus (one isolate). In 4 of 87 patients without evidence of bacterial infection, BAL contained >10^3 CFU of bacteria per ml; however, oropharyngeal contamination of these samples was indicated by a high percentage of squamous epithelial cells.

Cell types present in BAL. We had already shown that determining the percentage of squamous epithelial cells in the differential count of a Giemsa-stained slide of a BAL specimen was useful in judging whether or not it had been contaminated significantly with oropharyngeal flora (10). Approximately 90% of cells recovered in BAL specimens from normal subjects are alveolar macrophages (19). Data regarding the cell differentials seen in specimens from immunocompromised hosts with various infections are compiled in Fig. 1. A predominance of polymorphic neutrophils was seen in specimens from patients with bacterial infections, most notably in those from patients with L. pneumophila pneumonia. Specimens from patients with fungal, viral, or Pneumocystis infections tended to have increased percentages of lymphocytes.

In five patients, an excess of BAL eosinophils was noted, ranging from 3 to 30% of the total cell differential. Diagnoses for these inpatients included P. carinii (two patients), asper-
gilliosis (one patient), Hodgkin’s disease (one patient), and leukemic lung infiltration (one patient).

Implementing BAL analysis as a routine laboratory procedure. At the end of the study period, microbiology technicians at the Middleton Memorial Veterans Administration Hospital and the University of Wisconsin Hospital were trained to perform BAL analyses. In both locations, we began by training one technician, who in turn trained additional technicians. Approximately 2 months was required to complete training. The BAL analysis was then made available as a routine clinical procedure. For the first 2 months after the analysis became routine, the readings of the slides were double checked by one of the investigators. At the University Hospital laboratory, portions of the BAL concentrate were sent to the microbiology laboratory to the State Laboratory of Hygiene in appropriate containers for cultures of virus, mycobacteria, fungi, and legionellae. At the VA Hospital, a portion was sent to the State Laboratory for viral culture and all other cultures were done in the hospital laboratory. Because the service was viewed so positively by physicians and the technician time required to process specimens was significant, it was necessary to establish rules for submission of specimens. For specimens submitted before 1 p.m. on a regular work day, results were available for histochemical and DFA stains by the end of the work day. For specimens submitted between 1 and 3 p.m., specimens were processed but cytospin-prepared slides were not stained until the following morning. The Infectious Diseases Consultation Service had to approve processing of specimens after 3 p.m. on regular workdays, weekends, and holidays. With education of physicians, it was possible to limit greatly the number of specimens processed during the latter periods. From 1 May 1986 to 31 January 1987, 134 BAL specimens (about 15 per month) were analyzed by the microbiology laboratories at our medical center.

When the analysis became available in the University Hospital clinical microbiology laboratory, it became possible to determine the cost for the BAL analysis relative to those of other procedures that could be used for diagnosis of pneumonia in immunocompromised hosts. We determined costs for procedures (medications and blood products, equipment use, anesthesia time, and professional fees) and analysis of BAL specimens or tissue biopsies (histochemical stains, DFA stains, and cultures) as of April 1986. The BAL analysis, including cultures and stains, cost $248. Bronchoscopy with BAL analysis cost $606, bronchoscopy with BAL and transbronchial biopsy cost $1,033, and open-lung biopsy cost $2,140. The latter did not include costs for observation in an intensive care unit or management of a chest tube for several days, which was required for many patients undergoing open-lung biopsy.

**DISCUSSION**

Bronchial washings and transbronchial biopsies obtained with a flexible bronchoscope have been widely used during the past decade as a method for diagnosing pneumonitis in immunocompromised hosts. However, the presence of coagulopathies limits our ability to obtain transbronchial biopsies from patients with hematological malignancies. It has been shown that in many instances bronchial washings are composed largely of the local anesthetic used to assist

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**TABLE 3. Ability of BAL to diagnose infections compared with other procedures**

<table>
<thead>
<tr>
<th>Infection diagnosed</th>
<th>No. of specimens positive/total no. (% diagnostic yield) by:</th>
<th>BAL</th>
<th>Stain</th>
<th>Culture</th>
<th>Stain, culture, or both</th>
<th>Bronchial washings</th>
<th>Transbronchial biopsy</th>
<th>Open-lung biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. carini</em></td>
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<tr>
<td>Filamentous fungi</td>
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<td>CMV</td>
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<td>Herpes simplex virus</td>
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<td>Other viruses</td>
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<td></td>
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<tr>
<td><em>Legionella sp.</em></td>
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<td><em>Mycobacterium sp.</em></td>
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<tr>
<td>Other bacteria</td>
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<td></td>
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<td></td>
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<tr>
<td>All infections</td>
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</tr>
</tbody>
</table>

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*Infections produced by filamentous fungi included aspergillosis (17 patients) and mucormycosis (1 patient). Other viruses included influenza virus (one patient) and BK virus (one patient). The latter patient was a bone marrow transplant recipient with interstitial pneumonia. The BK virus was isolated from urine by Duad Walker, Medical Microbiology Department, University of Wisconsin-Madison. Indirect fluorescent-antibody staining of the BAL specimen was positive for BK virus. The significance of BK virus infection in this patient’s pneumonia is unknown, but this information is provided for the sake of completeness. —. Either specimens were not obtained or the technique was incapable of diagnosing the infection. Bacterial infections could not be diagnosed without quantitative cultures.

* A positive result was obtained by stain, culture, or both techniques.
positioning of the bronchoscope (1). One would not expect washings to sample alveoli well. At the inception of our study, these were our major reasons for studying the use of BAL as a diagnostic technique. However, the high frequency of pulmonary infections in patients with AIDS has provided a more potent impetus to studying the use of BAL at medical centers where large numbers of these patients are treated. Thus, most published accounts have dealt exclusively with the use of BAL in diagnosing infections in patients with AIDS and have centered mainly on its utility in diagnosing Pneumocystis pneumonia in these patients (2, 7, 14, 16, 22).

Our protocol for BAL analysis was applied to a population of immunocompromised patients with a variety of underlying diseases. Thus, our findings should predict the utility of a standardized BAL analysis as a routine diagnostic tool at a tertiary care hospital. For patients with hematologic malignancy and AIDS, the diagnostic yield for infections with our protocol (e.g., 75 to 82%) was similar to those reported by other investigators (4, 5, 8–13). Among all patients who underwent bronchoscopy, approximately two-thirds (66%) of pulmonary infections were diagnosed by BAL. It was possible to obtain a transbronchial biopsy from only a fraction of patients in whom an infection was diagnosed by BAL. Because of the limited number of transbronchial biopsies obtained from the patients in the study, the diagnostic yield of this technique for the various infections listed in Table 3 may not be truly representative. For example, in a previous study, we reviewed experience with the transbronchial biopsy to diagnose aspergillosis at our medical center and found that it had a diagnostic sensitivity of only 18% (11). In any event, it is clear that obtaining BAL specimens from all immunocompromised patients who undergo bronchoscopy would increase the likelihood of diagnosing infections by bronchoscopy.

BAL analysis was also useful in diagnosing alveolar hemorrhages that occurred either de novo or associated with aspergillosis (12). Our protocol was not very useful in diagnosing neoplasm, pulmonary edema, drug- or radiation-induced pneumonitis, or interstitial pneumonia. However, negative results from BAL could stimulate active pursuit of the underlying diagnoses.

There were several problems that had to be overcome in making BAL analysis available as a routine procedure. The first was simplifying submission of the specimen. If a specimen has to be divided by a clinician into aliquots and sent to various laboratories, part of the specimen may not be submitted to the appropriate laboratory and the task of tracking down information and correlating it is magnified. It was necessary to identify a laboratory unit that could be readily trained to set up the required tests and would be able to produce results in a timely manner. We felt that the clinical microbiology laboratory fulfilled these criteria. The second problem was designing a protocol for BAL analysis that would yield information that discriminates between the diagnoses of most interest in evaluating immunocompromised patients with pulmonary infiltrates of recent onset, namely, bacterial pneumonitis, fungal pneumonitis, Pneumocystis pneumonia, viral pneumonitis, and alveolar hemorrhage. The third was establishing a protocol that would be simple and allow use of instruments and reagents readily available commercially. In all published studies of the use of BAL, stains were done by a cytopathology or pathology laboratory using procedures that were complex and time consuming, i.e., Papanicolaou and Gomori methenamine silver stains (2, 3, 7, 14, 16, 17, 21–24). Reagents available only in the research laboratory where the studies described were done have been used in many instances (5, 21).

The panel of cultures and stains we chose worked well; however, certain limitations and technical difficulties were unavoidable. For example, although the cell differential from the Giemsa-stained slide was essential in excluding significant oropharyngeal contamination of the specimen, it did not contribute greatly to a diagnosis. The most difficult stain to interpret was the DFA for detecting CMV. The monoclonal antibody we used nonspecifically stained granules in neutrophils, and staining of at least 10 mononuclear cells was required for a slide to be considered positive. This may have decreased the sensitivity of this stain greatly. Researchers continue to seek polyclonal or monoclonal anti-CMV antibodies that will more specifically detect CMV antigens in clinical specimens (5, 9, 20). Detection of CMV in clinical specimens by DNA hybridization is under investigation (13, 15), but we do not believe that this method has been simplified sufficiently for routine application in a clinical laboratory. Shell vial techniques for CMV culture, in which infection of the cell culture substrate can be detected within 24 h of inoculation with the specimen (6, 20), may be more sensitive and specific than DFA staining for demonstrating the presence of CMV in BAL specimens. However, interpretation of a positive BAL culture for CMV is difficult (5) and other causes of pneumonitis must be excluded before CMV can be accepted as the cause of pneumonitis.

We feel that the cost for BAL analysis at our medical center is very reasonable, considering the results obtained. Because of the complexity of the patients studied, we could not assess the impact that BAL analysis had on their morbidity or mortality. At our medical center, we recommend that bronchoscopy be performed expeditiously on any immunocompromised patient with pulmonary infiltrates of unknown etiology who does not respond to his present treatment regimen. A BAL and, if possible, a transbronchial biopsy should be done. If stains are not diagnostic, the clinician may await cultures and continue treatment with an empirical regimen that best fits all of the available data or proceed to an open-lung biopsy, depending upon that patient’s course.

ACKNOWLEDGMENTS

This work was supported in part by the Veterans Administration and by Public Health Service grant AI15682 from the National Institute of Allergy and Infectious Diseases.

We thank Elizabeth Smith and James Stephens for technical assistance. We thank Elsie M. Lapinski (Middleton Veterans Administration Hospital), Carol A. Spiegel (University of Wisconsin Hospital), and the technicians in the microbiology laboratories under their direction for their cooperation in implementing BAL analysis in these clinical laboratories.

LITERATURE CITED


