Nonbronchoscopic Bronchoalveolar Lavage for the Diagnosis of Pneumocystis carinii Pneumonia in the Acquired Immunodeficiency Syndrome*

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We compared conventional bronchoscopic transbronchial biopsy (TBB) and bronchoalveolar lavage (BAL) with nonbronchoscopic bronchoalveolar lavage (NB-BAL) in nine patients with acquired immunodeficiency syndrome (AIDS) and bilateral lung infiltrates. NB-BAL was carried out with a control-tipped reusable catheter. In each patient, bronchoscopic procedures were performed in the right lung, followed immediately by NB-BAL in the left lung. The specimens obtained by NB-BAL confirmed the presence of P carinii pneumonia in seven of eight patients in whom the diagnosis was established by TBB or BAL. Viral cultures of NB-BAL specimens yielded cytomegalovirus (CMV) in four of five subjects with evidence of CMV via bronchoscopic technique, including two instances in which CMV was not detected by BAL. Complications were limited to right-sided pneumothorax attributable to TBB. Accuracy of NB-BAL appears to be comparable to that of conventional bronchoscopic approaches in the diagnosis of AIDS-related pulmonary infection with P carinii or CMV. NB-BAL may be a safer and more economical alternative to TBB and BAL in the diagnosis of pulmonary opportunistic infections.

P carinii pneumonia is the most common cause for hospitalization in patients with the pulmonary complications of AIDS, and is the most frequent cause of death.¹,² Larger series of AIDS cases have been confined predominately to a few urban areas, where the diagnosis and treatment of AIDS-related infections of the lung have placed large local burdens on health care resources.³,⁴,⁵ The techniques described in this report may lead to the application of safer, less expensive, and more efficient approaches to the diagnosis of lung infections in the immunocompromised host.

In patients with AIDS, and in others with immunosuppressive illnesses, an antemortem diagnosis of P carinii pneumonia is usually established from material obtained by fiberoptic bronchoscopy or open lung biopsy.⁶ Bronchoscopic approaches include bronchial washing, bronchoalveolar lavage (BAL), brush biopsy or TBB techniques, employed singly or in combination. The diagnostic strategy embodied in these approaches has been highly successful.⁷,⁸,⁹,¹⁰,¹¹ Other lung sampling techniques that have been employed with varying success include transthoracic needle aspiration of the lung,¹²,¹³ two-cuffed catheter lavage,¹⁴ trans-laryngeal aspiration,¹⁵ and the collection of hypopharyngeal material or expectorated sputum.¹⁶,¹⁷,¹⁸ These techniques were more widely employed before the flexible bronchoscope came into general use, and thus before the AIDS epidemic. Their diagnostic efficacy relative to open lung and bronchoscopic biopsy in AIDS-related P carinii pneumonia, therefore, has not been studied.

The pulmonary infections found in AIDS patients extend to infections not ordinarily considered opportunistic (including M tuberculosis and Legionella pneumonia) and can be multiple and synchronous and are often recurrent.¹⁹ Patients with AIDS not uncommonly are subjected to two or more invasive lung biopsy procedures during the course of their illness. These considerations stimulated us to seek safer, less invasive diagnostic approaches suitable for repeated application in this group of patients. In this regard, we were encouraged by the recent reports of several groups who have routinely employed BAL in the evaluation of lung infections in AIDS patients, and in other immunosuppressed hosts.²⁰,²¹,²²,²³ These published experiences, which in general parallel our own, suggest that the diagnostic efficacy of BAL is comparable to that of TBB in the diagnosis of P carinii pneumonia and other opportunistic infections.

We report here the results of our initial experience with nonbronchoscopic alveolar lavage in AIDS patients. A control-tipped, reusable catheter was chosen for its availability and ease of use (Fig 1). Originally designed for selective angiography,²⁴ the catheter was subsequently utilized to guide bronchial brushes in the sampling of peripheral lung lesions²⁵,²⁶ before being...
During a 14-week period, all patients with bilateral pulmonary infiltrates in whom *P. carinii* pneumonia was clinically suspected were considered for entry into the study. Subjects signed a consent form to participate in this study, which was approved by the University of California Committee on Human Research. Eight of nine subjects thus entered were sexually active homosexual or bisexual men. In all subjects, the diagnosis of AIDS by Centers for Disease Control criteria was established, either before entry into the study or on receipt of lung lavage and biopsy results. AIDS in the one female subject was transfusion-acquired. Subjects ranged in age from 25 to 52 years. Three patients were considered too ill to undergo bilateral bronchoalveolar lavage and were excluded from the study.

Following an eight-hour fast, each subject received intramuscular morphine and promazine, with supplemental intravenous diazepam, if needed during the procedure. All subjects were initially studied in a supine position. Following preparation with topical anesthesia and orotracheal intubation with an 8.5 mm endotracheal tube, each patient underwent fiberoptic bronchoscopic examination with a Pentax FB/9D bronchoscope (Pentax Instrument Corporation, Orangeburg, NY, USA). After routine examination of the airways, the tip of the bronchoscope was wedged in an anterior subsegment of the right middle lobe. Up to 120 ml of normal saline solution was lavaged in 20 ml aliquots and aspirated into a trap by means of a suction pump. Lavage was discontinued as soon as 50 ml of fluid returned. A right lower lobe brush biopsy specimen (in seven of the nine subjects) and four to ten right lower lobe TBB specimens (in six of the nine subjects) were then obtained under single-plane fluoroscopic control. After the suction traps and lines had been changed, a Medi-Tech B/13/85 bronchial catheter (Medi-Tech, Inc, Watertown, MA, USA) was passed via the endotracheal tube into the contralateral (left) lung under fluoroscopic guidance. The tip of the catheter was passed into a distal bronchus (usually in the left lower lobe) until it could pass no farther. In this presumably wedged position, 100 to 150 ml of normal saline solution in 20 to 50 ml aliquots were injected into the lung and aspirated into a suction trap. With experience, we found that better returns of injected saline solution were associated with use of continuous pump suction rather than manual aspiration, and with use of larger aliquots of saline (50 to 60 ml). The return also could be augmented on occasion by having the patient adopt the decubitus position, with the lavaged lung up. Occlusion of the catheter by bronchial mucosa sucked into the distal opening could be prevented by manipulation of the movable tip.

Immediately following lavage, bronchoscopic and catheter lavage fluid samples were each pooled and divided. Approximately half of each fluid specimen was reserved for stain and culture of aerobic pyogenic bacteria as well as mycobacteria, Legionella (direct immunofluorescent assay and culture on charcoal yeast extract), fungi, and viruses (CMV, herpes simplex, varicella-zoster, adenovirus). The remainder of the fluid was subjected to centrifugation at approximately 3,000 rpm for 5 min. The pellet material was smeared on glass slides and fixed immediately in 95 percent ethanol solution and subjected to Papanicolaou and silver methenamine staining. Bronchial brushes were severed into capped sterile tubes and submitted for Legionella and viral studies as above. Formalin-fixed, paraflin-embedded TBB specimens underwent routine hematoxylin and eosin, Zielh-Neelsen, and silver methenamine staining.

Following bronchoscopy, the bronchoscope was washed manually in warm soapy water, then rinsed in tap water. A stream of O2 was used to dry the inner channel. The instrument was then subjected to ethylene oxide gas sterilization for five hours, followed by aeration at approximately 37°C for approximately 12 hours. The Medi-Tech lavage catheter was cleaned and gas sterilized in similar fashion. The metal grip was detached and steam sterilized in an autoclave.

## RESULTS

### P carinii

The diagnosis of PCP was established in eight of nine subjects by a bronchoscopic technique (Table 1). In each case in which *P. carinii* pneumonia was noted on TBB, the diagnosis was confirmed by bronchoscopic BAL (BAL). Nonbronchoscopic BAL (NB-BAL) confirmed the presence of *P. carinii* in seven of the eight cases established by either BAL or TBB. Although in one subject NB-BAL gave falsely negative results, in another subject both BAL and NB-BAL detected *P. carinii* not demonstrated by TBB.

### Viral Pathogens

CMV was the only viral pathogen identified in these subjects (Table 1). Culture evidence of CMV was obtained in five of nine subjects overall, three by BAL and four by NB-BAL. BAL failed to detect CMV in two subjects in whom the virus was identified by NB-BAL. Histopathologic evidence of CMV infection (eg, cytomegalic inclusion bodies) was noted in TBB specimens from four of six subjects, and was corroborated by the results of both lavage techniques in all but one instance. Culture of brush biopsy specimens yielded CMV in only one subject.

#### Table 1—Comparison of Bronchoscopic with Nonbronchoscopic Techniques in the Diagnosis of AIDS-related Opportunistic Lung Infections

<table>
<thead>
<tr>
<th>Patient</th>
<th>BAL</th>
<th>NB-BAL</th>
<th>TBB</th>
<th>Brush</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PCP*, CMV</td>
<td>PCP*, CMV</td>
<td>PCP*, CMV</td>
<td>—</td>
</tr>
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<td>PCP*, CMV</td>
<td>PCP*, CMV</td>
<td>NA†</td>
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<td>4</td>
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<td>NA†</td>
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<td>PCP*, CMV</td>
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<tr>
<td>9</td>
<td>PCP*, CMV</td>
<td>NA†</td>
<td>PCP*, CMV</td>
<td>CMV</td>
</tr>
</tbody>
</table>

*P carinii pneumonia.
†Not available.

### Footnotes

- **Figure 1.** Medi-Tech B/13/85 bronchial catheter.
Bacterial and Fungal Pathogens

Potential pyogenic bacterial pathogens (eg, Strep pneumoniae, Staphylococcus and Pseudomonas species) were cultured from the BAL and NB-BAL specimens of several subjects. None of these subjects, however, had clinical evidence (eg, purulent sputum, lobar lung consolidation) to suggest a role for these bacteria in the subjects’ symptoms. No positive evidence by stain or culture was found for infection by acid-fast bacilli or Legionella species by any technique. Candida albicans was cultured in one subject by BAL and NB-BAL, and in an additional subject by NB-BAL alone, but in neither of the two cases was there evidence on TBB to suggest that the organisms were of pathogenic importance in the lung.

Histopathology

With the exception of one subject who had interstitial fibrosis on TBB despite the demonstration of P carinii pneumonia by both lavage techniques, all subjects undergoing TBB had pulmonary histologic findings typical of CMV and/or P carinii lung infection in AIDS.6

Complications

After TBB and lavage studies, one subject developed a right-sided pneumothorax requiring thoracostomy tube evacuation. No complication attributable to the lavage procedures was noted.

DISCUSSION

Our preliminary experience with catheter lavage in the diagnosis of AIDS-related P carinii pneumonia leads us to propose NB-BAL as a possible alternative to a biopsy-based bronchoscopic procedure. Catheter lavage appears to be safe; it is tolerated well and the risk of pneumothorax or bleeding associated with biopsy techniques is presumably avoided. There was no evidence of pneumonia caused by the bronchoscopic procedures or NB-BAL in this study; therefore, the expected incidence (about 5 percent) of this complication can only be extrapolated from the published experience with BAL.5,53,57

For physicians involved directly in the diagnosis of pulmonary infections in the AIDS population, the catheter lavage approach has an additional advantage in that it allows one to avoid exposing the fiberoptic bronchoscope to the stringent sterilization conditions recommended for lensed instruments exposed to the blood or secretions of patients with known or suspected AIDS.1,4,56 Prolonged sterilization diminishes instrument availability and, in our experience, also shortens the useful life of the bronchoscope.

Our study design called for BAL of the right lung to precede NB-BAL of the left lung in intubated subjects with bilateral infiltrates. Following BAL, care was taken to change the lines and traps and to evacuate saline-enriched secretions from the right lung prior to introduction of the steerable catheter into the left lung. Given these precautions and the diffuse nature of the pulmonary infiltrates, it is unlikely that BAL significantly affected the results of NB-BAL. Lung sampling techniques, whether directed by the bronchoscope or not, can be expected to be less effective diagnostically in patients for whom pulmonary infection is highly localized or roentgenographically occult. Used under fluoroscopic control, however, the catheter may be directed to specific regions of lung involvement for the purpose of selective lavage. Indeed, experience with the control-tipped catheter as a selective guide for the bronchial brush in the sampling of peripheral lung lesions is considerable.7,28 In the immunocompromised host with localized pulmonary infiltrates, the catheter could serve as a conduit for a sheathed catheter for selective sampling of secretions free of contamination by organisms from the upper respiratory tract. We find culturing for aerobic pyogenic bacteria in secretions aspirated directly through the catheter or bronchoscope to be of little practical value.

For their safety and comfort during bilateral lung sampling by bronchoscopic and nonbronchoscopic techniques, the subjects in this study underwent orotracheal intubation. The catheter, however, is readily introduced and manipulated without an endotracheal tube, and it is our bias that intubation before NB-BAL will be unnecessary for most patients. In the patient with diffuse pulmonary involvement, fluoroscopy, too, may be unnecessary. But as a guide to segmental catheterization of patients with localized disease, fluoroscopy remains indispensable.

Although experience with bronchoscopic BAL suggests that the diagnostic accuracy of lavage does not differ significantly from that of TBB in opportunistic lung infections, further experience with AIDS-related lung infections is necessary before the accuracy of NB-BAL can be similarly validated. This is particularly true of opportunistic infections other than P carinii pneumonia and CMV, since among the AIDS patients we studied, no additional pulmonary opportunistic infection (eg, mycobacteria, fungi, Legionella) was detected. Based on our encouraging preliminary experiences with non-bronchoscopic BAL, we are now attempting to extend our observations beyond P carinii pneumonia and CMV to encompass the less common AIDS-related opportunistic infections of the lung, and are investigating catheter techniques which may permit bedside lavage without conventional bronchoscopy, orotracheal intubation, or fluoroscopy.
REFERENCES

3 Gottlieb MS, moderator. The acquired immunodeficiency syn-
4 Centers for Disease Control. Acquired immunodeficiency syn-
5 Hopewell PC, Luce JM. Pulmonary involvement in the acquired immunodeficiency syndrome. Chest 1985; 87:104-12
11 Drew WL, Finley TN, Mintz L, Klein HZ. Diagnosis of Pneumocystis carinii pneumonia by bronchopulmonary lavage. JAMA 1974; 230:713-15
29 Simmons BP. Guidelines for hospital environmental control. Atlanta: Centers for Disease Control, 1981

Nonbronchoscopic BAL in Diagnosis of PCP (Caughey et al)