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CONTENTS

ROLE OF BRONCHOALVEOLAR LAVAGE IN HOSPITALIZED PEDIATRIC PATIENTS

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Bronchoalveolar lavage (BAL) has been shown to be a rapid, relatively safe, and relatively noninvasive diagnostic procedure. Theoretically, BAL can be performed on all children hospitalized for pneumonia resistant to oral antibiotics, though practically and economically, this is not feasible. A 1-year retrospective review was conducted to define a cost-effective role for BAL in the management of hospitalized children with resistant pneumonia. The data revealed identification of at least one pathogen in 87% of sputum samples and in 95% of BAL specimens. Sputum samples provided the same information as the more invasive BAL technique in 60% of patients who had both sputum and BAL obtained for culture. Recommendations are made for the use of BAL as a diagnostic tool in the hospitalized child with resistant pneumonia.

KEY WORDS — bronchoalveolar lavage, bronchoscopy, immunocompromised child, pneumonia.

INTRODUCTION

Pulmonary processes are a major cause of morbidity and mortality in the chronically ill and immunocompromised pediatric patient.[1-3] Diffuse pulmonary infiltrates seen on radiographic evaluation are a particular diagnostic challenge, as causes may include infections, neoplasms, drug- or radiation-induced toxicity, pulmonary edema, or nonspecific pneumonitis.[2,3]

Routinely, children with pneumonia resistant to oral antimicrobials are admitted to the hospital, and empirically, broad-spectrum intravenous antibiotics are instituted. Coverage is provided to include presumptive organisms much the same as in empiric treatment for sinusitis or pharyngotonsillitis. Although intravenous therapy with broad-spectrum antimicrobials is not without potentially serious risk, the majority of children improve without untoward events.[3] In those who do not improve, a diagnosis must be confirmed. Hence, a useful diagnostic test must be identified.

Noninvasive sputum sampling, be it random or induced, requires the participation of a mature, cooperative child. Bronchoalveolar lavage (BAL) has been shown to be a rapid, relatively safe, and relatively noninvasive diagnostic procedure for the evaluation of diffuse pulmonary infiltrates.[3-9] More invasive techniques, such as open lung biopsy, are also useful in establishing a definitive diagnosis, but are associated with significant morbidity, and as such, are reserved for those patients in whom diagnoses cannot be obtained by less invasive methods.[2,7] Theoretically, BAL may be used for all pediatric patients admitted with the diagnosis of pneumonia resistant to oral antimicrobials, though practically and economically, this is not feasible. The purpose of this study is to determine a cost-effective role for BAL in the management of hospitalized children with resistant pneumonia.

METHODS

A retrospective review was performed on the charts of those children who underwent BAL during the period from April 1, 1992, to March 31, 1993, at The New York Hospital–Cornell Medical Center, a tertiary referral center. Twenty-one patients underwent BAL. Several patients underwent multiple procedures, but for the purposes of this study, only cumulative results are discussed. The patient population consisted of 9 boys and 12 girls. Ages ranged from 3 months to 17 years. All 21 patients were evaluated for diffuse pulmonary infiltrates or interstitial disease that failed to improve or worsened despite antibiotic

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therapy.

Several factors contributed to chronic illness and recurrent hospitalizations for pneumonia in 16 of the 21 patients studied. Ten patients were immunocompromised. Underlying diagnoses included chemotherapy for neoplastic disease (n = 5), steroid therapy (n = 2), human immunodeficiency virus (n = 2), and severe combined (B and T cell) immunodeficiency (n = 1). Five children had anatomic predisposing factors: 4 had gastroesophageal reflux that was documented by pH probe or milk study, and 1 had aberrant pulmonary architecture. One child was at increased risk for tuberculosis as a result of environmental exposure. The remaining 5 patients were hospitalized for pneumonia without documented underlying immunologic or anatomic disorders.

Sputum samples were obtained in 15 of the 21 patients. Sputum samples were usually obtained early in the course of hospitalization. The chart review did not reveal whether the samples were random expectorations or induced sputum specimens. To submit an induced sputum sample, the child first gargled with normal saline to reduce the colonization of normal mouth flora. Next, an ultrasonic DeVilbiss sterile water nebulizer treatment was administered. Finally, the child was instructed to cough and expectorate into a sterile cup. Chest physiotherapy was employed as an adjunctive measure.

Patients who were mechanically ventilated underwent flexible fiberoptic bronchoscopy using the Olympus BF3C20. Examination of the airway to rule out structural abnormalities, as well as to obtain the culture material, was accomplished. Premedication consisted of bolus doses of fentanyl citrate (1 to 2 μg/kg), midazolam maleate or lorazepam (0.05 to 0.10 mg/kg), and vecuronium bromide (0.10 mg/kg). The bronchoscope was passed directly into the endotracheal tube via a Bodai adapter so as to permit concurrent ventilation during the procedure. Electrocardiographic and oxygen saturation measurements were monitored throughout the procedure. The bronchoscope was passed into the trachea, and initially the entire tracheobronchial tree was examined. Next, the area of concern was localized and lavaged with a total of 20 to 40 mL of sterile saline. The specimens were aspirated separately by vacuum suctioning in 3- to 6-mL aliquots and then pooled.

Patients who were on supplemental oxygen by nasal cannula or face mask underwent flexible or rigid bronchoscopy and lavage under general anesthesia. Similarly, the entire tracheobronchial tree was examined. Next, the bronchoscope was placed into the areas of greatest clinical and/or radiographic concern. Lavage was performed in an identical fashion.

Specimen Studies. The pooled lavage fluid was apportioned for the individual laboratories within 3 hours of collection.

In the microbiology laboratory, BAL fluid was centrifuged for 5 minutes at 3,000 rpm. The supernatant was discarded and the sediment was used for Gram's stain in the customary manner. Cultures were incubated and read accordingly.

In the virology laboratory, the pooled lavage fluid was immediately transferred to viral Hanks' balanced salt solution with antibiotics. It was then placed in one of two tissue cell culture lines: human embryonic lung, or primary monkey kidney. It was placed in incubation in cell culture maintenance medium (2% fetal calf serum; Biowhittaker Co, Walkersville, Md) and evaluated after 2 to 3 weeks for cytopathic changes.

Respiratory syncytial virus was evaluated by nasopharyngeal swab and BAL using direct fluorescent monoclonal antibody staining with fluorescein isothiocyanate–labeled mouse monoclonal antibody against respiratory syncytial virus internal capsid protein and envelope surface glycoprotein.[6] Cytomegalovirus (CMV) was detected by cytopathic changes in cell culture. Additionally, a rapid fluorescent evaluation was performed on specimens incubated on coverslips for 48 hours. Finally, some specimens were evaluated by polymerase chain reaction.[8,9]

To evaluate for mycobacteria, a solution of N-acetyl-L-cysteine in sodium hydroxide and sodium citrate solution was added to the specimen and centrifuged for 15 minutes at 3,000 rpm. The supernatant was discarded and the sediment was resuspended in 1 mL of buffer to enhance growth. A Lowenstein, Jensen, and Middlebrook 7H11 plate was inoculated and incubated for 2 weeks in 5.1% carbon dioxide at 35°C with the cap slightly ajar to facilitate evaporation. After 2 weeks, the culture was transferred to a standard incubator, where it remained for 6 weeks. The cultures were surveyed weekly for contamination and growth. Once growth was seen, a Kinnion acid-fast smear was made. A Gen-Probe (Gen-Probe, Inc) was used for rapid identification, and sensitivities were prepared. Additionally, auramine O fluorescent evaluation was performed on the fluid on the day of processing as a preliminary method of screening.

For mycology, the BAL fluid was inoculated on three media: Sabouraud, Mycosel, and inhibitory mold agars. They were incubated for 3 weeks at 30°C and evaluated weekly. A KOH-Calcafluor potassium hydroxide and fluorescent brightener (28 Calca-

TABLE 1. SPUTUM ISOLATES (N = 15)

	RSV	Bact	PMN	PCP	AFB	CMV	Fungus	Yeast	Pert	Leg	Cand
Positive	2	9	9	0	2	0	0	0	1	0	4
Negative	10	5	4	7	9	1	3	4	4	5	0
N/A	3	1	2	8	4	14	12	11	10	10	11

Percent yield was 13 of 15 or 87%.

N/A — culture not obtained, RSV — respiratory syncytial virus, Bact — bacteria, PMN — polymorphonuclear cells, PCP — *Pneumocystis carinii*, AFB — acid-fast bacteria, CMV — cytomegalovirus, Pert — *Bordetella pertussis*, Leg — *Legionella*, Cand — *Candida albicans*.

fluor M2R fluorescent stain, Sigma Chemical Co, St Louis, Mo) was also used on the BAL fluid. It was mixed on a coverslip and examined under the microscope.

To evaluate for *Pneumocystis carinii*, BAL fluid was centrifuged for 3 to 5 minutes at 1,200 rpm. The sediment was smeared and stained with Gram-Weigert stain and read under the microscope on high power.

RESULTS

Characteristics of Patient Population. The sample consisted of 21 children: 9 boys (43%) and 12 girls (57%). They ranged in age from 3 months to 17 years. All had diffuse pulmonary infiltrates or interstitial disease that failed to improve or worsened despite therapy. All (100%) were on broad-spectrum antimicrobials; 2 (10%) were on antiviral therapy at the time of BAL; most patients had completed 10 to 14 days of therapy prior to BAL. Ten of 21 (48%) had documented causes of immunosuppression. An additional 5 of 21 (24%) had anatomic abnormalities identified as causative or contributing factors leading to recurrent pneumonia requiring repeat hospitalizations. One of 21 (5%) had documented exposure to pulmonary tuberculosis. The remaining 5 of 21 (24%) had no documented immunologic disorder.

Isolates in Sputum. Fifteen of 21 (71%) children had sputum samples sent for microbial evaluation. The identification of one or more organisms was determined to be a "positive yield." No identification or identification of normal mouth flora only was labeled a "no yield." The overall yield for isolation of any pathogen in sputum was 13 of 15 (87%) children. However, there were a total of 69 tests performed, ie, cultures inoculated. Forty-two of 69 (61%) of cultures revealed no growth. Isolates were identified in 27 of 69 (39%; Table 1).

Isolates in BAL. Similarly, the isolates obtained from BAL can be examined. All 21 (100%) children underwent BAL. The identification of one or more organisms was determined to be a "positive yield." No identification or identification of normal mouth flora only was labeled a "no yield." The overall yield for isolation of any pathogen in BAL was 20 of 21 (95%) children. However, there were a total of 165 tests performed, ie, cultures inoculated. One hundred twenty-five of 165 (76%) cultures showed no growth. Isolates were identified in 40 of 165 (24%; Table 2).

Comparison of BAL to Sputum. In comparing BAL to sputum isolates, results were concordant in 6 of 15 (40%). In 9 of 15 (60%) there were discordant yields. Of the 60% in which discrepancy was noted, in 20% (n = 3) the sputum yield was greater, in 20% (n = 3) the BAL yield was greater, and in 20% (n = 3) a difference was noted; ie, additional information was obtained from BAL, but organisms isolated from sputum cultures were not confirmed. Therefore, in 9 of 15 (60%) children, noninvasive sputum sampling provided all the same data as the more invasive BAL technique.

DISCUSSION

Overall, for any given patient, identification of at least one pathogen occurred in 87% (n = 13 of 15) of sputum samples and 95% (n = 20 of 21) of BAL specimens. These data conform to the range of values noted in the literature of 71% to 95%.[4,6]

Of those patients who had sputum sent for culture (n = 15), 69 cultures were inoculated and only 27 (39%) demonstrated growth. Similarly, in those patients who underwent BAL (n = 21), 165 cultures were inoculated and only 40 (24%) revealed growth.

TABLE 2. BRONCHOALVEOLAR LAVAGE ISOLATES (N = 21)

	RSV	Bact	PMN	PCP	AFB	CMV	Fungus	KOH	Pert	Leg	Cand
Positive	4	10	10	0	1	4	1	1	0	0	9
Negative	13	11	8	15	18	10	11	12	16	11	0
N/A	4	0	3	6	2	7	9	8	5	10	11

Percent yield was 20 of 21 or 95%.

N/A — culture not obtained, RSV — respiratory syncytial virus, Bact — bacteria, PMN — polymorphonuclear cells, PCP — *Pneumocystis carinii*, AFB — acid-fast bacteria, CMV — cytomegalovirus, KOH — yeast, Pert — *Bordetella pertussis*, Leg — *Legionella*, Cand — *Candida albicans*.

This suggests that the majority of cultures inoculated show no growth. In 9 of 15 (60%) patients who had both sputum and BAL obtained for culture, sputum sampling provided the same information as BAL, or more.

In evaluating our results, one may note several findings. Cytomegalovirus was only isolated from BAL specimens. *Candida albicans* had a greater yield in our cultures from BAL than sputum. No *P carinii* or *Legionella* was identified from BAL or sputum samples. The remainder of our data demonstrate that various organisms were not remarkably better isolated from either sputum or BAL.

One possible variable affecting culture results is that of oral contamination in the samples. Generally, random sputum specimens are believed to have a higher incidence of oral contaminants than induced samples. In health, the lower respiratory tract is sterile. Contaminants may be introduced on intubation for mechanical ventilation and/or diagnostic intervention.

The differentiation of pathogen from contaminant is nearly impossible. One cannot rely on an elevated neutrophil count to diagnose acute infection, because counts may be elevated in such conditions as active pulmonary fibrosis or adult respiratory distress syndrome, and they may be depressed in immunocompromised patients.[10] Attempts to distinguish pathogens from contaminants may be aided by the use of quantitative bacteriologic studies (ie, samples with $\geq 10^5$ colonies and <1% squamous epithelial cells are less likely to be contaminated).[10,11] In addition, protected brushings can be used during BAL in adults, but are not often feasible in children, secondary to technical limitations in a significantly smaller airway.

There is an 83% isolation rate of fungus through BAL reported in the literature.[8] There is, however, a low rate of isolation of acid-fast bacilli with BAL in children, as was noted in our patient population. This low isolation rate utilizing BAL has been attributed to the observation that children with primary pulmonary tuberculosis have closed, caseous lesions with smaller numbers of mycobacteria in comparison to adults, and that the use of lidocaine in awake patients may reduce the yield for recovering mycobacteria.[12,13] Abadco and Steiner,[12] in a 1992 study, compared BAL to gastric lavage for the diagnosis of *Mycobacterium tuberculosis* in children. They found gastric lavage performed on three consecutive mornings to be superior to BAL in diagnosing acid-fast bacilli. Our results, as well as a review of the literature, would support the initial use of gastric lavage in those patients with suspected *M tuberculosis*.

A review of the literature confirms *P carinii* pneumonia to be the most common isolate from BAL in immunosuppressed hosts, regardless of the cause of the immunocompromise.[1,2,8,10,14-16] Yet, in this retrospective review, no *P carinii* was isolated. None of the patients with human immunodeficiency virus (n = 3) were found to be infected with *P carinii*. A possibility for the low yield in the isolation of *P carinii* in this study may be that BAL was selectively not performed in patients with *P carinii* pneumonia. *Pneumocystis carinii* is readily isolatable with routine suctioning; therefore, the diagnosis may have been made without the need for BAL.

Identification of acute CMV infection has been described as technically difficult, because the mean culture time is 27 days and a wide spectrum of genetic and structural variability makes monoclonal antibody detection challenging. Cytomegalovirus has the ability to create multifocal infection with uneven distribution among cells. Hence, the number of CMV isolates does not reliably predict the severity of disease or differentiate acute infection from colonization or shedding.[14,15]

CONCLUSION

The data in this study support the utility of BAL in the armamentarium of tools available for the diagnosis of diffuse pulmonary infiltrates. Yet, the operative and laboratory expenses of both sputum sampling and BAL seem excessive. In light of the present-day political agenda to limit medical expenditures, what is the role of BAL in hospitalized pediatric patients? It may be an acceptable and economically plausible alternative to begin broad-spectrum intravenous antimicrobials for pneumonia (without sample for culture), as we might for sinusitis or pharyngotonsillitis, and reserve diagnostic intervention for those who fail.

Based on this 1-year retrospective review at The New York Hospital–Cornell Medical Center, the following recommendations are suggested.

1. Broad-spectrum intravenous antimicrobials should be instituted in patients not responding to oral agents.

2. Noninvasive sputum samples should be obtained on all patients who do not improve or worsen with institution of broad-spectrum intravenous antimicrobials. In those patients who are mechanically ventilated, deep suction lavage may be obtained.

3. Bronchoalveolar lavage should be reserved for those patients in whom *Candida*, CMV, or *Bordetella pertussis* is suspected. Bronchoalveolar lavage is

also indicated for those patients in whom sputum cannot be obtained, or when the presence of structural abnormalities must be evaluated.

4. Gastric lavage should be utilized in children suspected of having tuberculosis.

5. Cultures ordered should be limited by such variables as immune status and the time of year in which the infection occurs.

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