Controlled Utilization of Induced Sputum Analysis in the Diagnosis of Pneumocystis carinii Pneumonia*

John H. Wehner, M.D.; William A. Jensen, M.D., F.C.C.P.; Carl M. Kirsch, M.D., F.C.C.P.; Frank T. Kagawa, M.D.; and Anthony C. Campagna, M.D.

We investigated the outcome and potential cost savings of a system designed to limit physician access to induced sputum analysis (ISA) for the diagnosis of Pneumocystis carinii pneumonia (PCP). Four respiratory medicine physicians screened all requests for ISA to determine the pretest likelihood of PCP. Twenty-two of 102 requests for ISA over a 1-year period were denied due to a low clinical suspicion for PCP. Seven individuals had a definitive alternative diagnosis confirmed and the remaining 15 were empirically treated for a presumptive diagnosis. All individuals were followed for at least 60 days or until death. None of the 22 individuals developed PCP during the follow-up period. We estimate that this approach saved $27,474, avoided exposure of health care workers to Mycobacterium tuberculosis, and was educational for the referring physicians.

*(Chest 1994; 105:1770-74)*

Induced sputum analysis (ISA) is recommended as the initial noninvasive test in the diagnosis of Pneumocystis carinii pneumonia (PCP). The sensitivity of ISA ranges from 56 to 95 percent.1 At our institution, the sensitivity of ISA for primary PCP or recurrent PCP is 71 percent with a negative predictive value of only 48 percent.2,3 Therefore, a negative ISA does not exclude the diagnosis of PCP and should be followed by bronchoscopy with bronchoalveolar lavage (BAL).

The current cost of medical care has sparked national interest in managed-care plans.4 These managed-care plans are designed to optimize resource allocation by controlling access to high volume and/or costly procedures. We developed an approach to control physician access to ISA in order to avoid indiscriminate and costly attempts to diagnose PCP in patients at risk. Four pulmonary medicine attending physicians evaluated all requests for ISA and performed complete consultations if requests were denied. To investigate the outcome and potential cost savings of this approach, we prospectively followed 22 individuals denied ISA over a 1-year period at the Santa Clara Valley Medical Center in San Jose, Calif.

**METHODS**

The Division of Respiratory and Critical Care Medicine

*From the Stanford University School of Medicine, Division of Pulmonary and Critical Care Medicine, Stanford, Calif, and the Santa Clara Valley Medical Center, Division of Respiratory and Critical Care Medicine, San Jose, Calif.*

Manuscript received June 23, 1993; revision accepted November 17.

Reprint requests: Dr. Jensen, Respiratory and Critical Care, Santa Clara Valley Medical Center, San Jose, Calif 95128

Key words: induced sputum analysis; managed care; opportunistic infection; Pneumocystis carinii pneumonia performs all ISA for the diagnosis of PCP at Santa Clara Valley Medical Center. All requests for ISA are screened by a respiratory medicine physician who will either agree to proceed with ISA or agree to perform a full consultation if the request is denied. All patients denied ISA were evaluated in chest clinic or on the inpatient medical ward by a pulmonary fellow and one of four pulmonary attending physicians. The evaluation included a complete history, a physical examination, selected laboratory tests, and a chest radiograph. The history focused on respiratory symptoms, including dyspnea, sputum production, and pleurisy. A history of intravenous drug abuse (IVDA), homosexual or bisexual behavior, multiple sexual partners, or blood transfusions prior to 1985 were identified as risk factors for HIV infection. The pulmonary consult attending physician interpreted the chest radiographs.

Patients were denied ISA if an alternative diagnosis was more probable than PCP. Findings suggestive of a diagnosis other than PCP included a history of purulent sputum production and/or wheezing and radiographs with focal infiltrates, pleural effusions, or adenopathy. Patients were further categorized as having either a presumptive or definitive diagnosis. Presumptive diagnoses included asthma, culture-negative pneumonia, sinusitis, or upper respiratory tract infection. A definitive diagnosis of infection required isolation of an infectious organism that corroborated a clinical diagnosis and that responded to specific antimicrobial therapy. Patients were followed up by the Respiratory Medicine Service as inpatients and later as outpatients for at least 60 days or until death.

The prevalence of PCP and sensitivity of ISA for PCP during the study period were determined as previously reported by Glenny and Pierson.1

**RESULTS**

From February 1, 1992 to January 31, 1993, 22 (22 percent) of 102 requests for ISA were denied. Twenty of the 22 patients denied ISA were male. The ages ranged from 25 to 53 years with a mean of 35 years. Nineteen (86 percent) of 22 patients were known to be HIV positive or to have AIDS at the time of con-
consultation. The remaining three patients had risk factors for HIV and two eventually had negative HIV serologic tests. Five (23 percent) patients had a history of IVDA and five had at least one prior episode of PCP. Six patients (27 percent) were taking PCP prophylaxis, including trimethoprim-sulfamethoxazole (n=1), dapsone (n=3), and aerosolized pentamidine (n=2).

The most frequent symptom was a productive cough of yellow-green sputum or hemoptysis (55 percent) for a duration of 1 day to 3 weeks. An additional three patients complained of pleuritic chest pain. Two of these three patients had an ipsilateral focal infiltrate with a pleural effusion on chest radiograph. Dyspnea, at rest or with exertion, occurred in nine (41 percent) patients while a history of fever was elicited in 11 patients (50 percent). Physical examination revealed focal rales or diminished breath sounds in seven (32 percent) patients, multilobar rales in three (14 percent), and wheezing in four (18 percent). Eight (36 percent) patients had normal results of chest examination.

Ten (45 percent) patients had focal infiltrates, with or without pleural effusions, on their chest radiographs. One additional patient developed a pleural effusion during hospitalization. Three (14 percent) patients had multilobar infiltrates while another two revealed peribronchial cuffing. Six patients had normal chest radiographs.

Whole blood helper T-cell counts and serum lactate dehydrogenase (LDH) levels were available in 16 and 21 patients, respectively. The mean helper T-cell count was 160×10^6 cells per liter with a range of 5 to 672×10^6 cells per liter. The mean serum LDH level was 323 U/L (normal, 112 to 227 U/L) while the range was 173 to 1,060 U/L. Five of the highest serum LDH levels had accompanying significant increases in either serum transaminases or serum creatine phosphokinase. Thus, the diagnostic utility of these elevated serum LDH levels as a marker for PCP is ambiguous.\(^5\) The white blood cell count, obtained in 21 patients, showed a mean of 7.9×10^9 cells per liter with a range of 2.3 to 13.7×10^9 cells per liter. Nineteen (86 percent) patients had an arterial blood gas value with a mean alveolar-arterial oxygen tension (P(A-a)O\(_2\)) difference of 30 mm Hg (range, 3 to 67 mm Hg).

Induced sputum analysis was denied in 12 (55 percent) patients with a history of purulent sputum production or hemoptysis, in three (14 percent) patients with pleural effusions, and in three (14 percent) patients with wheezing and no apparent pneumonia. One patient, who denied dyspnea and cough, presented with cervical lymphadenopathy and a normal chest radiograph. A fine-needle aspiration of a prominent cervical lymph node was 4+ smear positive for acid-fast bacilli. A second patient who presented with a 9-kg weight loss, fever, history of a positive tuberculin skin test, and bibasilar interstitial infiltrates, was refused ISA due to a clinical suspicion of tuberculosis. He also eventually tested negative for HIV infection. Finally, two patients with a history of cough without dyspnea were denied ISA due to a lack of signs and symptoms for PCP.

Seven (32 percent) patients denied ISA had a definitive non-PCP diagnosis (Table 1). Pneumococcal and Acinetobacter bacteremia occurred in one patient each while a sputum culture grew Klebsiella pneumoniae in a third patient. Pansinusitis with otitis media secondary to Pseudomonas aeruginosa occurred in one patient. A patient with profound weight loss and bibasilar interstitial infiltrates was subsequently diagnosed as having aspiration pneumonia due to esophageal dysfunction secondary to

<p>| Table 1—Characteristics of Patients With a Definitive Diagnosis* |
|-----------------|------------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Patient</th>
<th>Reasons ISA Denied</th>
<th>Definitive Diagnosis</th>
<th>Confirmation</th>
<th>Follow-up, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Focal infiltrate with effusion and pleurisy</td>
<td><em>S pneumoniae</em> pneumonia</td>
<td>+Blood culture</td>
<td>298</td>
</tr>
<tr>
<td>2</td>
<td>Productive cough, focal infiltrate</td>
<td>Acinetobacter pneumonia</td>
<td>+Blood culture</td>
<td>77 (died)</td>
</tr>
<tr>
<td>3</td>
<td>Productive cough, focal infiltrate</td>
<td>Klebsiella pneumonia</td>
<td>+Sputum culture</td>
<td>45 (died)</td>
</tr>
<tr>
<td>4</td>
<td>Productive cough, postnasal drip, focal infiltrate</td>
<td>Pseudomonas pansinusitis, otitis</td>
<td>Sinus CT scan, +sputum and auricular culture</td>
<td>119</td>
</tr>
<tr>
<td>5</td>
<td>Cervical adenopathy, no dyspnea, normal chest radiograph</td>
<td><em>M tuberculosis</em></td>
<td>Lymph node FNA +M tuberculosis</td>
<td>74</td>
</tr>
<tr>
<td>6</td>
<td>Pleural effusion, +PPD, LDH=232 U/L</td>
<td><em>M tuberculosis</em></td>
<td>+Sputum culture</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>9-kg weight loss, +PPD, NS, HIV negative</td>
<td>Aspiration pneumonia, esophageal dysfunction, polymyositis</td>
<td>Chest CT scan, muscle biopsy, CPK=6,915 U/L</td>
<td>100</td>
</tr>
</tbody>
</table>

*FNA=fine-needle aspiration; NS=night sweats; CT=computed tomographic; CPK=creatine phosphokinase.
†Also grew *M tuberculosis* from sputum culture.
polymyositis. One patient had tuberculous lymphadenitis, and another patient developed a new pleural effusion in association with a 20-mm positive tuberculin skin test. Induced sputum was positive for acid-fast bacilli that subsequently grew *Mycobacterium tuberculosis*. The remaining 15 (68 percent) patients had a presumptive diagnosis (Table 2). Eight patients had culture-negative pneumonia or bronchitis. Four additional patients had asthma without apparent pneumonitis. The remaining three patients were diagnosed as having sinusitis (n=1) and a nonspecific upper respiratory tract infection (n=2). All patients demonstrated clinical improvement while receiving nonpneumocystis antimicrobial therapy when indicated. Of note, two additional patients eventually had growth of *M tuberculosis* from sputum cultures. Thus, four (18 percent) patients were ultimately diagnosed as having tuberculosis.

All patients denied ISA were followed up an average of 112 days with a range of 45 to 298 days. During follow-up, two patients died. One patient was subsequently found to have PCP by ISA 151 days after the initial evaluation. The other patient was hospitalized for aspiration pneumonia, upper gastrointestinal tract bleeding, and alcohol intoxication 75 days after the initial evaluation and died 2 days later while receiving supportive care. No postmortem examination was performed.

Of the 102 requests for ISA, 80 (78 percent) proceeded to ISA. Fourteen patients with negative ISA refused follow-up bronchoscopy. Eight of the 14 patients were successfully treated with nonpneumocystis therapy without sequelae for at least 60 days. Four patients were treated empirically with antipneumocystis therapy (pentamidine, n=3; dapsone-trimethoprim, n=1); three clinically responded and one died. These four patients are not included in the calculation of the sensitivity of ISA during the study period since they did not proceed with bronchoscopy and BAL. However, they are included in the calculation of the prevalence of PCP during the study period. One patient was diagnosed as having PCP 45 days later with a repeated ISA. His original ISA was therefore considered to be a false negative. Lastly, one patient was unavailable for follow-up.

Induced sputum analysis or BAL was positive for PCP in 49 patients (60 percent). Of the 49 patients with documented PCP, the conditions of 34 were diagnosed with ISA, yielding a sensitivity of 69 percent for ISA during the study period. Screening all ISA requests led to an increase in PCP prevalence from 52 percent (n=102) without screening to 66 percent (n=80) with screening. The cost of a pulmonary consultation was $166.

The cost of ISA and bronchoscopy with BAL, including supplies, technician, and professional fees, was $298 and $1,131 per patient, respectively. If referring physicians had been given direct access to ISA during the study period, the total cost for evaluation and diagnosis would have amounted to $100,454 (Fig 1). In comparison, screening of all ISA requests generated 24 extra consults which prevented 22 unnecessary sputum inductions and bronchoscopies for a total cost of $72,960, a cost savings of $27,474 (Fig 1 and 2).

**Discussion**

*Pneumocystis carinii* pneumonia is the most frequent pulmonary complication in patients with HIV

**Table 2—Characteristics of Patients With a Presumptive Diagnosis**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Reasons</th>
<th>Presumptive Diagnosis</th>
<th>Confirmation</th>
<th>Follow-up, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6</td>
<td>Productive cough (n=4) or hemoptysis (n=1) and focal infiltrate; focal infiltrate with effusion (n=1)</td>
<td>Bacterial pneumonia†</td>
<td>Improved with antibiotics</td>
<td>64-167 mean=112</td>
</tr>
<tr>
<td>7</td>
<td>Productive cough, alcohol intoxication with LOC</td>
<td>Aspiration pneumonia</td>
<td>Improved with antibiotics</td>
<td>65</td>
</tr>
<tr>
<td>8</td>
<td>Productive cough, normal CXR, normal LDH</td>
<td>Bacterial bronchitis</td>
<td>Improved with antibiotics</td>
<td>165</td>
</tr>
<tr>
<td>9-12</td>
<td>Wheezing; with cough (n=2), otitis media (n=1), exudative pharyngitis (n=1)</td>
<td>Asthma</td>
<td>Improved with antibiotics and bronchodilators</td>
<td>67-257 mean=152</td>
</tr>
<tr>
<td>13</td>
<td>Productive cough, postnasal drip</td>
<td>Sinusitis</td>
<td>Improved with antibiotics</td>
<td>65</td>
</tr>
<tr>
<td>14</td>
<td>Cough, no dyspnea, normal arterial blood gas</td>
<td>Viral URI</td>
<td>Improved with no therapy</td>
<td>69</td>
</tr>
<tr>
<td>15</td>
<td>Cough, malaise, normal CXR, normal LDH</td>
<td>Viral URI</td>
<td>Improved with no therapy</td>
<td>87</td>
</tr>
</tbody>
</table>

*LOC=loss of consciousness; CXR=chest radiograph; URI=upper respiratory tract infection.
†One patient eventually grew *M tuberculosis* from sputum culture.
*All patients received only nonpneumocystis antimicrobial therapy.

Induced Sputum Analysis in PCP (Webner et al)
infection. Investigators have suggested that exercise testing either alone or in combination with clinical predictors can help determine the need for diagnostic testing to rule out PCP. In order to optimize resource utilization, we developed a clinical evaluation for each ISA request. Based on a constellation of signs, symptoms, and specific laboratory data, we determined whether PCP was likely or unlikely. If PCP was likely, we subsequently performed ISA and then bronchoscopy with BAL if ISA was negative. If PCP was unlikely, we denied the request for ISA and performed a full consultation. Over a 1-year period, we denied 22 percent of requests for ISA. Presumptive diagnoses of non-PCP disease were supported by appropriate clinical and microbiologic follow-up, including response to empiric therapy. Except for one patient who had PCP 151 days after the ISA request, no new cases of PCP were documented following ISA denial. The denial of 22 requests for induced sputum analyses saved $6,556 in sputum costs and probably avoided another $24,882 in expenses for bronchoscopy of patients with negative ISA (Fig 1 and 2). The incremental cost of pulmonary consultation due to screening of ISA requests amounted to $3,984 (24X$166). However, those patients required consultation since they proved to have a non-PCP lung disorder that required further evaluation. In addition, reducing physician access to ISA led to an unexpected health benefit, since M tuberculosis eventually grew from sputum cultures in three patients. Thus, not only did a screening evaluation provide a monetary savings, but such screening prevented exposure of respiratory personnel to aerosolized M tuberculosis during sputum induction.

The cost of diagnosing PCP by ISA has been shown to depend on the prevalence of PCP in the population studied and the sensitivity of ISA. This study reinforces the importance of careful screening to enhance the pretest probability of PCP and thereby maintain a cost-effective diagnostic tool. By controlling physician access to ISA, we succeeded in increasing the prevalence of PCP from 52 to 66 percent.

In an era of increasing health care expenditures and limited resources, guidelines to maintain quality and decrease the cost of medical care continue to be explored and developed. We present an approach for avoiding indiscriminate utilization of ISA in the diagnosis of PCP. Our study shows that controlled utilization of ISA targets the appropriate patients for PCP evaluation while avoiding exposure of medical personnel to infectious aerosols.
REFERENCES

Second International Conference on Geriatric Oncology; Cancer in the Elderly

In collaboration with the University of South Florida, Tampa, the National Institute on Aging, and Brown University, this conference will be held in Genova, Italy, September 19-21. For information, contact Colin Cuervo Henderson, Florida Policy Exchange Center on Aging, University of South Florida, Box 3208, Tampa 33620 (813:974-3468).

1774

Induced Sputum Analysis in PCP (Wehner et al)