Clinical Aerosol Inhalation Cine-scintigraphy to Evaluate Mucociliary Transport System in Diffuse Panbronchiolitis

Teruhiko Imai, Yoshiaki Sasaki, Hajime Ohishi, Hideo Uchida, Shinsaku Ito, Keiichi Mikasa, Masayoshi Sawaki and Nobuhiro Narita

Departments of Oncoradiology and Radiology, and 2nd Department of Internal Medicine, Nara Medical University, Kashihara, Japan

This study evaluates the mucociliary transport system in patients with diffuse panbronchiolitis using aerosol inhalation cine-scintigraphy (AICS). **Methods:** Forty-one subjects, 10 healthy controls and 31 patients with diffuse panbronchiolitis, were studied. In addition, the mucociliary transport system was evaluated in 11 patients who had received erythromycin therapy for 3–8.3 yr. Following inhalation of ^{99m}Tc-human serum albumin aerosol for 3–5 min in a sitting position, the subjects were placed on the imaging table in the supine position and posterior images were obtained dynamically for 20 sec/frame over 2 hr with a gamma camera linked to a digital computer. The 360 20-sec serial frames were edited into a cinematographic presentation at 200-msec intervals. Clinical evaluation of the mucociliary transport system was based on the bolus movement of radioactive aerosol from the main bronchi to the trachea and the movement patterns, which were divided into four types using the movement in the controls as a standard (type I): type I, rapid and smooth movement; type II, slow movement; type III, stagnation at the carina; and type IV, complete stasis. **Results:** All patients with diffuse panbronchiolitis had types III and IV, indicating that mucociliary transport system was severely impaired. Of the 11 patients on erythromycin therapy, 8 had movement pattern type IV and 3 had movement pattern type III before erythromycin therapy. In eight patients (72.7%), movement pattern was improved to type I or II after therapy. **Conclusion:** Aerosol inhalation cine-scintigraphy helps evaluate the clinical usefulness of erythromycin therapy in diffuse panbronchiolitis.

Key Words: mucociliary transport system; diffuse panbronchiolitis; aerosol inhalation cine-scintigraphy; erythromycin

J Nucl Med 1995; 36:1355–1362

Diffuse panbronchiolitis is an intractable disease indigenous to Japan, as reported by Homma et al. (*1*). This chronic inflammatory disease of the respiratory bronchiolar region is characterized by dyspnea and the discharge of abundant mucus in the airway. The mechanism of its pathogenesis remains unknown. An abnormality of the defense mechanism common to the upper and lower airways is suspected, since it is frequently accompanied by chronic upper respiratory tract infection. The mucociliary transport system is an important defense mechanism for these airways. For diffuse panbronchiolitis, morphological or functional abnormality of ciliary motility has been documented in Japan (*2,3*) but not in any other countries.

Evaluation of the mucociliary transport system can be achieved by several methods. Aerosol inhalation cine-scintigraphy (AICS), which was developed in 1981 by Isawa et al. (*4,5*), permits noninvasive visual evaluation of the mucociliary transport system under physiological conditions because the movement of radiolabeled aerosol particles inhaled into the lung and deposited on the respiratory tract is serially photographed and reproduced as dynamic images. We previously used this method to evaluate the mucociliary transport system in various pulmonary diseases, including 16 cases of diffuse panbronchiolitis, and found that the mucociliary transport system was severely impaired in diffuse panbronchiolitis (*6*).

Formerly, diffuse panbronchiolitis was treated with antibiotics and steroids and produced a short-term beneficial effect, but the prognosis remained poor because airway infection usually recurred, resulting in respiratory failure due to *Pseudomonas aeruginosa* infection. In 1984, Kudo et al. (*7*) obtained successful therapeutic results treating patients with diffuse panbronchiolitis with low-dose, long-term erythromycin. Since then, many investigators have examined the effect of erythromycin on diffuse panbronchiolitis (*8–10*).

Mikami et al. (*11*) studied neutrophil elastase activity and the physical properties of sputum from patients with chronic lower respiratory tract infection, including diffuse panbronchiolitis, who were undergoing erythromycin therapy. They found that the diminished sputum viscosity observed in patients who responded to erythromycin therapy corresponded to a decrease in neutrophil counts and that the mucociliary transport system evaluated by the frog

Received May 2, 1994; revision accepted Jan. 3, 1995.

For correspondence or reprints contact: Teruhiko Imai, MD, Department of Oncoradiology, Nara Medical University, 840 Shijyo-cho, Kashihara City, Nara Prefecture, 634, Japan

TABLE 1
Pulmonary Function Tests of Healthy Controls

Subject no.	Age (yr)	Sex	VC (%)	FEV_1 (%)	$\dot{V}_{25}$ (%)
1	66	M	94.4	81.6	55.0
2	26	M	110.5	83.1	57.5
3	52	M	125.9	85.4	80.0
4	27	F	86.7	95.0	76.6
5	25	F	99.1	95.0	82.4
6	34	F	128.0	84.9	69.7
7	49	F	126.2	82.7	68.3
8	48	M	98.4	83.6	55.2
9	63	F	16.5	88.3	83.6
10	51	M	105.6	80.8	55.1
Mean	44.1		99.1	86.0	68.3

VC = vital capacity; FEV_1 = forced expiratory volume in 1 sec.

palate method (*12*) was thereby significantly improved in these patients.

This study was designed to evaluate mucociliary transport system by AICS in 31 patients with diffuse panbronchiolitis and to investigate the change in the mucociliary transport system in 11 patients with diffuse panbronchiolitis who had received long-term erythromycin therapy and whose clinical course could be followed. Before starting the study, patients were fully instructed about the nature of the study and informed consent was obtained from all of them.

METHODS

Subjects

A total of 41 subjects participated in the study, 10 healthy control subjects (Table 1) and 31 patients with diffuse panbronchiolitis diagnosed by transbronchial lung biopsy or open-lung biopsy (Table 2). Also included in the evaluation were 11 patients with diffuse panbronchiolitis who had received erythromycin therapy for more than 3 yr (range 3–8.3 yr; mean 6.6 yr) and whose mucociliary transport system could be followed by AICS (Table 2, Patients 1–11). For all patients except Patient 5, who almost failed to respond to the therapy, the sputum volume was decreased, dyspnea was relieved and PaO_2 was improved (Table 3).

TABLE 2
Clinical Data of Patients with Diffuse Panbronchiolitis

Patient no.	Age (yr)	Sex	VC (%)	FEV_1 (%)	$\dot{V}_{25}$ (%)	PaO_2 (torr)	Sputum volume (ml/day)	DOE (H-J)
1	18	M	83.5	76.2	30.3	69.8	20	2
2	48	M	56.9	54.0	12.5	60.0	150	3
3	56	F	39.1	66.0	17.0	69.7	50	3
4	58	M	50.5	61.2	8.3	62.2	50	3
5	59	M	72.9	54.5	13.0	65.4	70	3
6	60	M	49.5	47.5	58.7	62.7	120	3
7	60	M	97.1	70.2	16.2	72.0	80	2
8	65	M	83.3	72.7	58.3	66.3	70	3
9	67	F	66.8	70.7	2.3	67.1	120	3
10	74	F	70.5	82.6	35.2	69.9	20	2
11	84	M	60.0	71.1	54.1	65.7	30	2
12	13	M	76.2	83.3	31.1	71.5	40	2
13	79	M	67.0	50.6	28.9	87.0	50	3
14	62	M	72.7	81.6	119.2	79.5	12	2
15	73	M	54.5	78.1	55.6	78.6	16	2
16	28	M	98.8	55.9	16.8	64.2	120	3
17	59	M	45.0	71.0	23.1	67.2	30	2
18	61	F	44.4	42.0	3.8	42.3	110	4
19	24	M	41.3	66.7	6.1	63.6	50	3
20	56	M	65.7	52.0	15.2	68.3	130	3
21	19	F	67.8	60.8	12.2	77.3	290	3
22	41	M	47.0	45.3	7.9	70.0	60	3
23	38	M	44.5	34.7	2.7	59.3	40	2
24	68	F	72.4	57.3	12.2	63.5	50	3
25	72	M	84.5	46.3	7.1	68.0	30	3
26	14	M	66.3	84.7	31.0	89.3	50	2
27	47	M	78.5	29.8	5.3	69.5	60	3
28	67	F	64.0	71.0	17.0	71.0	30	2
29	55	F	54.6	59.8	15.6	64.4	60	3
30	59	M	85.4	52.7	25.5	66.4	70	3
31	31	M	81.2	65.6	17.3	76.3	40	2
Mean	52.1		65.9	61.8	24.5	68.6	68.3	2.6

DOE = dyspnea on exertion; H-J = Hugh-Jones classification. See Table 1 for other abbreviations.

TABLE 3
Follow-up of Patients with Diffuse Panbronchiolitis (n = 11)

Patient no.	Duration of EM therapy (yr)	Sputum volume (ml/day)		DOE (H-J)		PaO_2 (torr)		Response score
		Pre-therapy	Post-therapy	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy	
1	6.3	20	10	2	1	69.8	99.2	8
2	8.0	150	0	3	1	60.0	80.9	9
3	4.8	50	0	3	2	69.7	74.0	6
4	8.3	50	0	3	1	62.2	76.1	8
5	6.5	70	40	3	3	65.4	67.2	2
6	6.0	120	30	3	1	62.7	82.0	8
7	7.5	80	10	2	1	72.0	73.8	7
8	4.3	70	3	3	1	66.3	78.7	8
9	7.5	120	30	3	2	67.1	68.9	6
10	3.8	20	0	2	2	69.9	71.6	4
11	3.0	30	5	2	1	65.7	72.6	7

EM = erythromycin; DOE = dyspnea on exertion; Age = before erythromycin therapy; H-J = Hugh-Jones classification.

Aerosol Inhalation Cine-Scintigraphy

Radioaerosols (particle size, approximate aerodynamic diameter 4–6 μm; airflow rate: 6 liter/min) were generated from a nebulizer containing 100 mCi ^{99m}Tc-human serum albumin (HSA) in 5 ml saline. In a sitting position and with their noses clipped, the subjects inhaled for 3–5 min through the nebulizer mouthpiece until the total radioactivity was over 300,000 cpm (approximately 2–3 mCi deposited in the lungs) by normal tidal breathing. Immediately after inhalation, the subjects were asked to rinse their mouths with water to wash down the radioisotopes from their mouths, oropharynx and esophagus. They then assumed a supine position on the table, and posterior view images were obtained dynamically at 20 sec/frame for over 2 hr with a low-energy, general-purpose collimator and a large field of view gamma camera linked to a digital computer. After nine-point smoothing, the 20-sec stored serial frames (360 frames) were edited into a cinematographic presentation at 200 msec/frame.

Clinical Evaluation of the Mucociliary Transport System

The bolus movement of radioactive aerosol (BRA bolus) from the main bronchi to the trachea was visually examined. The patterns of the BRA were classified into four types using the movement in healthy control subjects (type I) as the standard type (Fig. 1). Types II–IV represent increasing degrees of impaired mucociliary transport system function.

Type I represents smooth and rapid movement, in which the RI bolus ascends from the bilateral main bronchi to the trachea in a continuous flow immediately after inhalation and upon reaching the larynx is swallowed unconsciously (Fig. 2). Type II movement is slower and less smooth than type I movement; the flow may be abnormal and disturbed, but the BRA ascends to the middle trachea in at least 2 hr. Type III represents stagnation of the RI bolus at the carina, although it ascends from the bilateral main bronchi. Type IV represents complete stasis except by coughing.

Response Score

The clinical effect of erythromycin therapy in 11 patients was assessed from the daily sputum volume, dyspnea on exertion and PaO_2. These parameters were scored 0 to 3, and improvement was judged from the total score (Table 4).

RESULTS

Patterns of Radioactive Aerosol Bolus Movement in Healthy Control Subjects and Patients with Diffuse Panbronchiolitis

The BRA ascended smoothly and rapidly from the main bronchi to the trachea in all healthy control subjects. Of the 31 patients with diffuse panbronchiolitis, the RI bolus movement was type IV in 29 (93.5%) and type III in the remaining 2. Thus, types III and IV accounted for 100% of this group before therapy, indicating severe impairment of their mucociliary transport system function (Table 5).

Changes in the mucociliary transport system were examined in the 11 patients who had undergone 3 to 8.3 yr of erythromycin therapy. On average, they had been given 800-1200 mg orally over 6.6 yr. Before erythromycin therapy, 8 of the 11 had type IV BRA pattern and 3 had type III. After erythromycin therapy, improvement to type I or II was obtained in eight patients (72.7%) and, thus, the

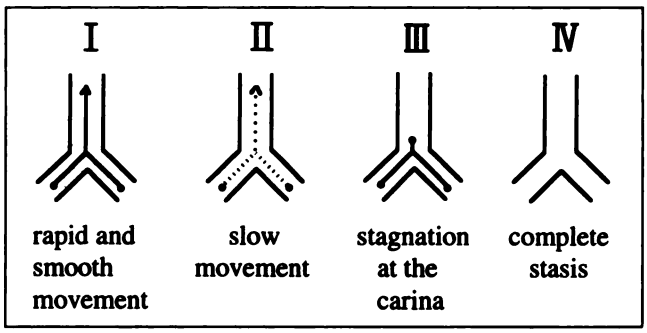

FIGURE 1. Classification of BRA from the main bronchi to the trachea.

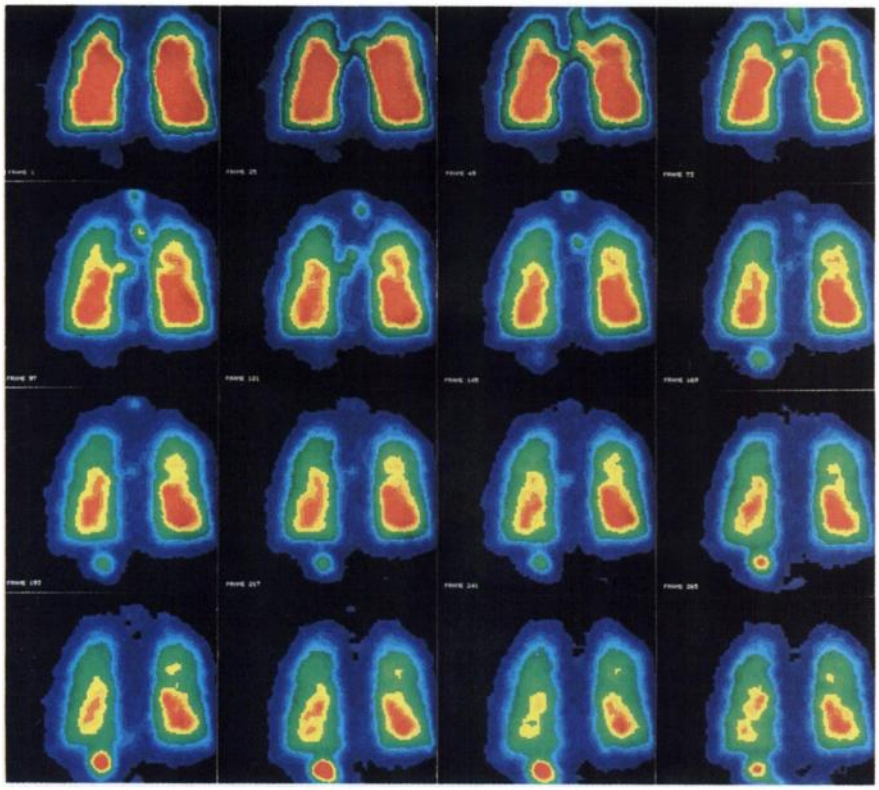

FIGURE 2. Aerosol inhalation cine-scintigraphy in a healthy control subject (type I). Since it was impossible to show 360 frames in this report, 16 frames were presented, 1 for every 24. The BRA ascended smoothly and rapidly in a continuous flow from bilateral main bronchi to the trachea. After reaching the larynx, it was swallowed into the stomach.

mucociliary transport system was significantly improved (Fig. 3).

Relationship between Response Score and Radioactive Aerosol Bolus Movement

The improvement in the mucociliary transport system after erythromycin therapy was correlated to the response score (Fig. 4). Mucociliary transport system impairment, however, persisted in two patients despite high response scores: an 84-yr-old man who had the shortest history of erythromycin therapy, and an 18-yr-old boy who was the youngest patient in the series.

Case Report

Chest Radiograph and AICS before and after Erythromycin Therapy. Patient 8 had obstructive ventilatory disturbance, with a daily sputum volume of 70 ml and respiratory dysfunction (VC = 83.3%, FEV_1 = 72.7%). Arterial blood gas analysis revealed hypoxemia with a PaO_2 of 66.3 torr. The patient also had dyspnea on exertion. Chest radiographs showed overinflation of both lungs due to a structure caused by edematous hypertrophy of the respiratory bronchiolar region. Diffuse granular shadows dominated the middle to lower lung fields caused by centrolobular inflammation. Aerosol inhalation cinc-scintigraphy revealed a highly irregular distribution of aerosol and the formation of multiple hot spots in both lungs immediately after inhalation. Diffuse obstructive ventilatory disorder in both lungs was confirmed.

TABLE 4
Response Score*

Parameters	Score
Daily volume of sputum	
Improved markedly (almost no sputum)	3
Improved (volume decreased by 1/3 or more)	2
Improved slightly (decreased slightly)	1
No change	0
Dyspnea on exertion (Hugh-Jones classification)	
Improved markedly (almost no dyspnea)	3
Improved (decreased more than 1 grade)	2
Improved slightly	1
No change	0
PaO_2	
Improved markedly (increased more than 20 torr)	3
Improved	2
Improved slightly	1
No change	0

*Response score: assessed by total score of three parameters.

TABLE 5
Patterns of Radioactive Bolus Movement in Healthy Controls and Patients with Diffuse Panbronchiolitis

Subjects	Number	Patterns of bolus movement			
		Type I	Type II	Type III	Type IV
Healthy controls	10	10			
DPB	31			2	29

HC = healthy control; DPB = diffuse panbronchiolitis.

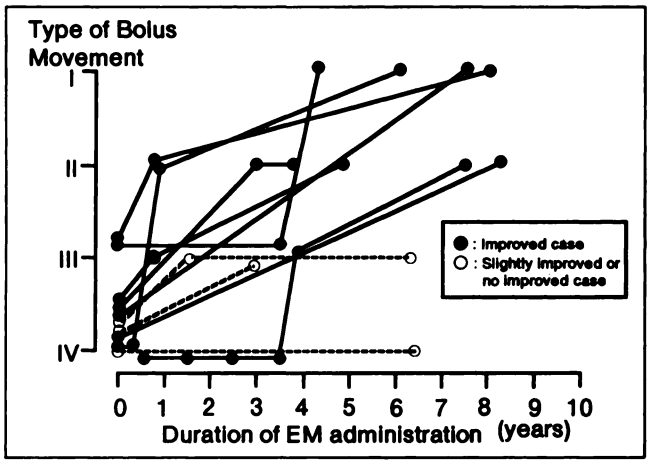

FIGURE 3. Changes in BRA.

After 4.3 yr of erythromycin therapy, sputum almost disappeared. Respiratory function was improved (VC = 124.3%, FEV_1 = 78.3%). PaO_2 was 78.7 torr in arterial blood gas analysis. Dyspnea on exertion was remitted. Chest radiographs confirmed the disappearance of the granular shadows. Pulmonary overinflation was also improved. Upon AICS evaluation, the previously seen hot spots were no longer observed and aerosol was evenly distributed in peripheral parts of the airway (Fig. 5).

AICS before and after Erythromycin Therapy. Before erythromycin therapy, the RI bolus ascended slightly from the main bronchi to the carina but ceased to move any further (type III) (Fig. 6A), indicating that the mucociliary transport function was severely impaired. After erythromycin therapy, immediately after inhalation, the BRA rapidly ascended from the bilateral main bronchi to the trachea and was unconsciously swallowed when it reached the larynx (type I) (Fig. 6B). Mucociliary transport system function was thus restored to normal.

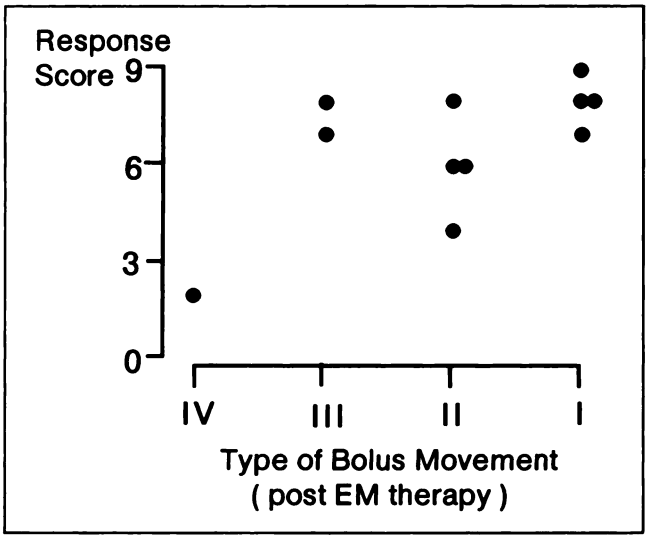

FIGURE 4. Relation between response score and BRA.

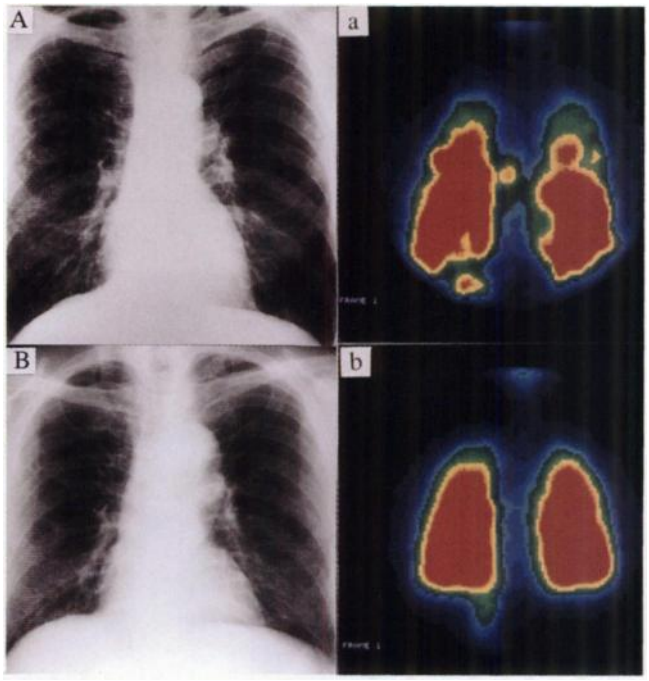

FIGURE 5. Chest radiograph and aerosol inhalation cine-scintigram before and after erythromycin therapy in Patient 8, a 65-yr-old man with a response score of 9. Inhomogeneous pulmonary distribution of radioactive aerosols equalized, hot spots disappeared and chest radiographic findings improved.

DISCUSSION

Measurement of the Mucociliary Transport System

In vivo observation of the mucociliary transport system in the airway can be achieved by an invasive or noninvasive method. Invasively, a marker such as a Teflon disc is placed on the airway under bronchofiberscopic guidance, and its movement is observed by a bronchofiberscope (*13*) or a fluoroscopic image intensifier (*14*). In the noninvasive method, radioactive aerosol is introduced into the lung, and its movement (*15*) or clearance (*16*) is observed at regular time intervals. Many investigators have studied mucociliary transport system noninvasively, since it permits observation under physiologic conditions.

Clearance from the lung involves both mucociliary and alveolar clearance. Aerosol particles deposited on cilia in the respiratory tract are completely excreted within 24 hr. For strict calculation of mucociliary clearance, it is necessary to subtract the amount of alveolar deposition of particles at 24 hr from total clearance from the lung. Since the alveolar deposition of particles should be measured repeatedly at 24 hr, this method is too complicated. In addition, coughing is an interfering factor that may disturb clearance quantification. Furthermore, in severe chronic obstructive pulmonary diseases such as diffuse panbronchiolitis, intrapulmonary deposition of radioactive aerosol particles immediately after inhalation may be distributed diffusely and irregularly in both lungs, or may form numerous hot spots. This has been estimated to have a non-negligible effect on the quantification of mucociliary clearance (*17*).

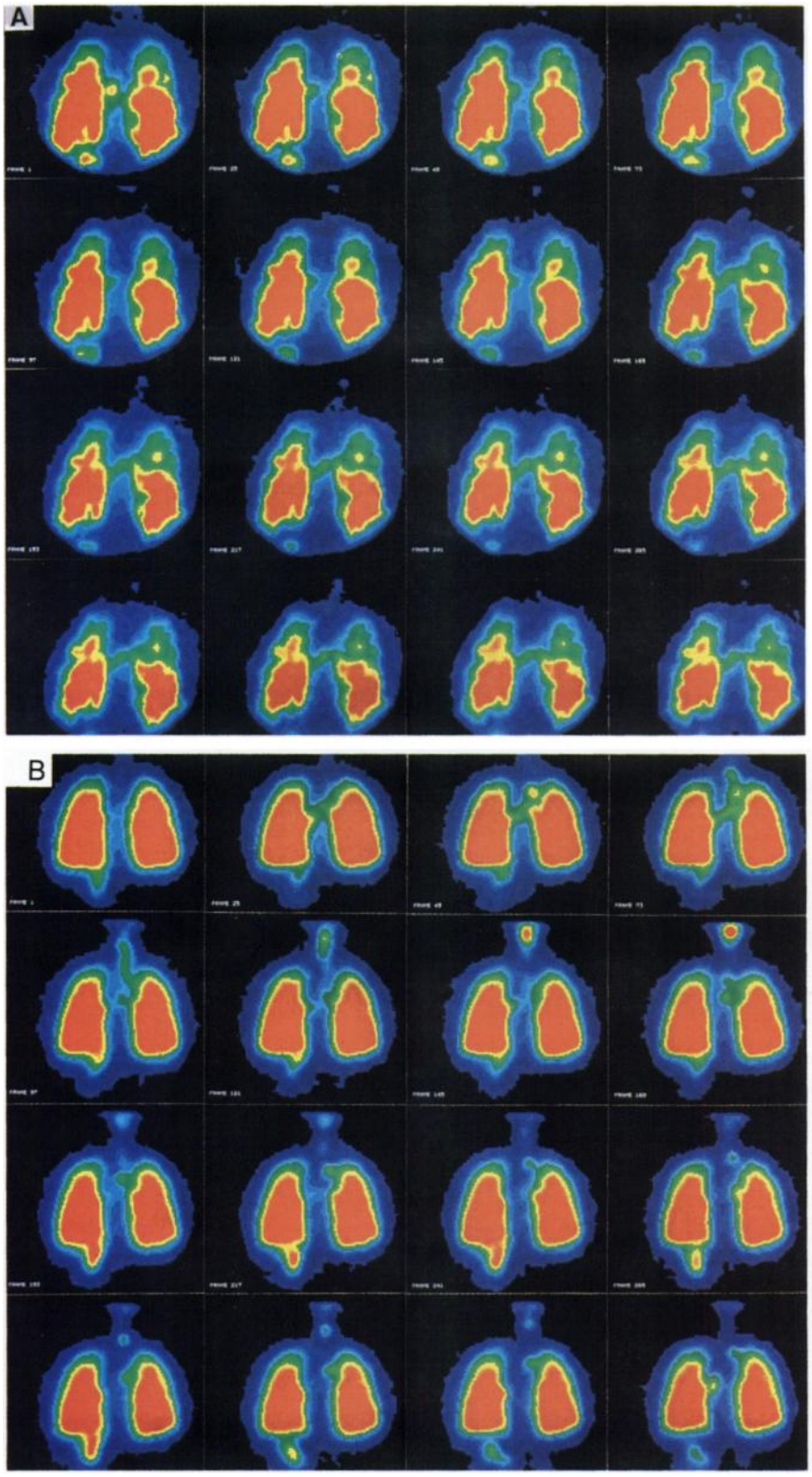

FIGURE 6. Aerosol inhalation cine-scintigraphy in Patient 8. (A) Before erythromycin therapy, the RI bolus ascended only slightly from the main bronchi to the carina but ceased to move any further, suggesting advanced impairment of the mucociliary transport system (type III) (B) After therapy, immediately after inhalation the RI bolus rapidly ascended from the bilateral main bronchi to the trachea (type I).

The rate of BRA in the airway can be measured by the method of Yeates et al. (*15*). In our previous study of 116 patients with various pulmonary diseases (*6*), the measurement of RI bolus was frequently precluded due to a diversity of abnormal movement patterns such as spiral movement, regurgitation and stasis, while the rate was relatively stable (3.2–10.9 mm/m; mean 8.0 mm/m) in healthy control subjects. In this study, we therefore decided to classify the BRA from the main bronchi to the trachea into four major patterns, as observed by several nuclear medicine specialists. We allowed a full 2 hr for such observation. We saw no reason to shorten the observation time since we basically adopted the method of Isawa et al. (*4,5*) and because the BRA that might not be visualized during the first half of

observation was expected to appear during the latter half. During the observation period, the patients assumed a supine position on the table and the chest was immobilized. We have performed AICS without any problems on more than 200 patients. The patients were requested to refrain from coughing, but even if they did, any RI bolus movement induced by coughing could be easily distinguished when carefully observed in cine-scintigraphy.

Mucociliary Transport System in Diffuse Panbronchiolitis

Because diffuse panbronchiolitis is a disease indigenous to Japan, diffuse panbronchiolitis in the mucociliary transport system has not been documented in other countries. Our earlier study using AICS (*6*) showed that the mucociliary transport system in chronic lower respiratory diseases such as bronchiectasis, chronic bronchitis and diffuse panbronchiolitis is impaired by various abnormalities and that the mucociliary transport system is most severely impaired in diffuse panbronchiolitis. In this study, the mucociliary transport system before erythromycin therapy in the 31 patients with diffuse panbronchiolitis was extremely impaired (type IV in 29/31 [93.5%] and type III in 2). In diffuse panbronchiolitis, the concentration or activity of neutrophil elastase in the airway has been found to be elevated because of persistent infection of the lower airway (*18*). Elastase has a strong proteolytic action and is known to induce airway epithelial injury (*19*), to inhibit cilia movement (*18,20*) and to increase airway mucus discharge. Abnormality of both mucus and cilia results in mucociliary transport system impairment.

Efficacy of Erythromycin Therapy in Diffuse Panbronchiolitis

Compared to other lower respiratory tract diseases, diffuse panbronchiolitis had been considered an intractable disease with poor prognosis leading to respiratory failure with a large amount of sputum in the airway. Recently, the effectiveness of low-dose, long-term erythromycin therapy has been established, and the prognosis has been dramatically improved. Earlier studies have suggested that erythromycin augments the host's defense by suppressing the development of infection through inhibition of bacterial attachment, by inhibiting elastase and protease production, by elevating the activity of natural killer cells or by increasing the production of various cytokines (*21–23*).

In all patients except Patient 2, the clinical symptoms (sputum volume, dyspnea on exertion and PaO_2) and mucociliary transport system function were improved and, in some patients, recovery to a normal condition was obtained. In one of the two patients whose mucociliary transport system remained impaired despite improved clinical conditions, the history of erythromycin therapy was short (3 yr), but the symptoms were expected to improve with continuation of this therapy; many patients have responded to the therapy after receiving it for 3 yr. For the other patient, erythromycin therapy was administered for 6.3 yr. Although the total response score in this patient was 8, which is high enough to be interpreted as markedly responsive, the mucociliary transport system impairment remained unimproved. Both mucus and cilia are mutually involved in the mucociliary transport system. As the patient is only 18 yr old, this is a case of early onset of mucociliary transport functional disorder. Therefore, morphological or functional abnormality of the ciliary motility itself is suspected. Electron-microscopic evaluation or examination of ciliary function would be required if the current condition persists.

The clinical effect of erythromycin therapy is characterized by the improvement of both subjective symptoms and objective symptoms. In patients highly responsive to erythromycin therapy, mucociliary transport function has been estimated to reach a plateau in approximately 6 mo. In patients with progressive pulmonary disease, the symptoms have been estimated to improve 1 or 2 yr after erythromycin therapy. Even after 17 mo of treatment, the mucociliary transport system was only slightly restored in these patients despite considerable improvement of the clinical symptoms (*24*). Of the present series of patients who had undergone erythromycin therapy for more than 3 yr, however, clinical symptoms and mucociliary transport function were simultaneously improved in those who responded well to the therapy. Interestingly, in some of the patients, mucociliary transport system impairment persisted while clinical symptoms improved; yet, mucociliary transport function did eventually improve, although in a delayed manner, with continued erythromycin therapy. This fact demonstrates that mucociliary transport system evaluation by AICS is important as a subjective assessment of the effect of erythromycin therapy on mucociliary transport system in diffuse panbronchiolitis. It also suggests that mucociliary transport system evaluation by AICS may help in determining the time of erythromycin therapy withdrawal or the posttherapeutic course.

We previously used AICS to evaluate the effects of drugs on mucociliary transport system (*25*). More extensive AICS application to clinical research is expected, such as assessing mucociliary transport system impairment by radiotherapy and analyzing the pathology of pulmonary atypical mycobacteriosis, which may be related to mucociliary transport system impairment.

CONCLUSION

The mucociliary transport system in 10 healthy control subjects and 31 patients with diffuse panbronchiolitis was evaluated using AICS. In addition, mucociliary transport system was evaluated in 11 patients who had received erythromycin therapy before participating in this study. The mucociliary transport system, severely impaired in patients with diffuse panbronchiolitis before therapy, was improved significantly after therapy. AICS is a useful method for evaluating the clinical effectiveness of erythromycin therapy in patients with diffuse panbronchiolitis.

REFERENCES

1. Homma H, Yamanaka A, Tanimoto S, et al. Diffuse panbronchiolitis: a disease of the transitional zone of the lung. *Chest* 1983;83:63–69.
2. Atushi N. Ultrastructural characteristics of bronchial cilia in patients with respiratory infectious disease. *Jpn J Thorac Dis* 1983;21:564–573.
3. Amitani R, Tanaka E, Suzuki Y, et al. A study on ultrastructure and motility of tracheo-bronchial cilia in patients with diffuse panbronchiolitis. *Jpn J Chest Dis* 1988;47:483–490.
4. Isawa T, Teshima T, Hirano T, et al. Radioaerosol inhalation lung cinescintigraphy: a preliminary report. *Tohoku J Exp Med* 1981;134:245–255.
5. Isawa T, Teshima T, Hirano T, et al. Mucociliary clearance mechanism in smoking and nonsmoking normal subjects. *J Nucl Med* 1984;25:352–359.
6. Ito S, Mikami R, Ryujin Y, et al. Application of aerosol inhalation cinescintigraphy: clinical investigation of mucociliary transport. *Jpn J Thorac Dis* 1984;22:961–969.
7. Kudou S, Hagiwara K, Uetake K, et al. Clinical effect of low-dose long-term erythromycin chemotherapy on diffuse panbronchiolitis. *Jpn J Thorac Dis* 1987;25:632–642.
8. Sawaki M, Mikami R, Mikasa K, et al. The long-term chemotherapy with erythromycin in chronic lower respiratory tract infections: second report; including cases with *Pseudomonas* infections. *Kansenshogaku Zasshi* 1986; 60:45–50.
9. Chijimatsu Y, Tamura N, Maeno H, et al. A study of erythromycin therapy for the patients of diffuse panbronchiolitis. *Jpn J Chest Dis* 1986;45:299–305.
10. Yamamoto M, Kondo A, Tamura M, et al. Long-term therapeutic effects of erythromycin and newquinolone antibacterial agents on diffuse panbronchiolitis. *Jpn J Thorac Dis* 1990;28:1305–1313.
11. Mikami M. Clinical and pathological significance of neutrophil elastase in sputum and the effect of erythromycin in chronic respiratory disease. *Jpn J Thorac Dis* 1991;29:72–83.
12. Sade J. The role of mucus in transport by cilia. *Am Rev Respir Dis* 1970; 48–52.
13. Sackner MA, Rosen MJ, Wanner A. Estimation of tracheal mucus velocity by bronchofiberscopy. *J Appl Physiol* 1973;34:495–499.
14. Friedman M, Scott FD, Poole DO, et al. A new roentgenographic method for estimating mucus velocity in airways. *Am Rev Respir Dis* 1977;115:67–74.
15. Yeates DB, Aspin N, Levison H, Jones MT, et al. Mucociliary tracheal transport rates in man. *J Appl Physiol* 1975;39:487–495.
16. Morrow PE, Gibb FR, Gazioglu KM. A study of particulate clearance from the human lungs. *Am Rev Respir Dis* 1967;96:1209–1221.
17. Wanner A. Clinical aspects of mucociliary transport. *Am Rev Respir Dis* 1977;116:73–125.
18. Ninomiya H, Ichikawa Y, Koga H, et al. Elastase activity in bronchoalveolar lavage fluid from patients with diffuse panbronchiolitis. *Kansenshogaku Zasshi* 1991;65:672–680.
19. Tegner H, Ohlsson K, Toremalm NG, et al. Effect of human leukocyte enzyme on tracheal mucosa and its mucociliary activity. *Rhinology* 1979; 17:199–206.
20. Smallmann LA, Hill SL, Stockley RA, et al. Reduction of ciliary beat frequency in vitro by sputum from patients with bronchiectasis: a serine proteinase effect. *Thorax* 1984;39:663–667.
21. Kita E, Sawaki M, Oku D, et al. Suppression of virulence factors of *Pseudomonas aeruginosa* by erythromycin. *J Antimicrob Chemother* 1991; 27:273–284.
22. Mikasa K, Kita E, Sawaki M, et al. The anti-inflammatory effect of erythromycin in zymosa-induced peritonitis of mice. *J Antimicrob Chemother* 1992;30:339–348.
23. Tanakadate A, Sasaki K, Nemoto H, et al. Effect of long-term, low doses of erythromycin on diffuse pan-bronchiolitis (DPB). *J Med Soc Toho Jpn* 1991;38:211–220.
24. Imai T, Ohishi H, Katada H, et al. Bronchoscopic findings and aerosol inhalation cine-scintigraphy in cases with diffuse panbronchiolitis treated effectively by erythromycin. *J Jpn Soc Bronchology* 1990;12:382–390.
25. Ohnuki M, Ito S, Imai T, et al. The immediate effect of terubutaline sulphate, a β-adrenoreceptor stimulating agent, on the mucociliary transport system. *Jpn J Chest Dis* 1990;49:536–541.

Scatter

(Continued from page 5A)

Happily, Thomas' foreboding evoked by Mahler's Ninth Symphony has not been sustained by events since the publication of that essay. In seeking inspiration in music, I prefer the message of Beethoven's Ninth Symphony in which the promise of the first movement, darkened by the brooding of the second, is ultimately fulfilled in the fourth. The exhilaration and optimism are explicitly expressed in the words of Schiller which become the text for the final movement. This renaissance of hope occupies my thoughts as I recall the dark days of 50 years ago and the progress since then in using atomic energy.

Stanley J. Goldsmith, MD, Editor-in-Chief
The Journal of Nuclear Medicine
August 1995