

# Composition of bronchopulmonary secretions from patients with bronchiectasis

T D BROGAN, B H DAVIES, H C RYLEY, P J ROSS, AND L NEALE

*From the Asthma Research Unit, Sully Hospital, Sully, and Department of Microbiology, Welsh National School of Medicine, Cardiff, South Glamorgan*

**ABSTRACT** Pulmonary function tests were carried out on 17 patients with bronchiectasis and six indices were selected to grade severity. Average concentrations of nine plasma proteins were determined by quantitative immunoelectrophoresis in specimens of sputum and serum from each patient. Wide patient-to-patient variation in concentration was encountered which appeared to follow a continuous progression unrelated to clinical severity. Patients at the upper end of the scale appeared to be responding by exudation and a pulmonary hypersensitivity reaction may be occurring in their lungs. There was evidence of selective concentration in sputum of  $\alpha$ 1-antichymotrypsin and IgA although IgA concentrations were lower than would be expected in patients with chronic bronchitis. It is suggested that sputum IgA levels could be explored as a diagnostic criterion in those patients who could equally be suffering from chronic bronchitis.

Bronchiectasis is a histopathological description of an alteration in the architecture of the bronchi and the development of symptoms is related to the onset of infection.<sup>1</sup> Before the advent of antibiotic therapy, patients with bronchiectasis tended to produce copious quantities of foul and foetid sputum. However, improvements in oral hygiene and the ready availability of antimicrobial drugs has changed this picture. Symptoms of dyspnoea and wheeze are frequent in bronchiectasis and have been related to the development of chronic bronchitis.

The composition of the ground substance of the sputum has been found by us to be related to the diagnosis in some chest diseases.<sup>2,3</sup> In the present investigation we examined the soluble proteins of sputum specimens from a series of patients with clinically proven bronchiectasis to see whether the composition of the sol or continuous phase of sputum can be a guide to the existence of bronchiectasis or the development of chronic bronchitis, or if it can be related to the severity of the disease.

## Methods

Seventeen patients (nine women and eight men, average age  $45 \pm 12$  years) with a clinical diagnosis of bronchiectasis were admitted to Sully

Hospital for investigation.

A clinical questionnaire was completed on all patients noting age of onset of symptoms, cough frequency and nature of sputum, haemoptysis, dyspnoea, and systemic symptoms such as weight loss and malaise. A past history of severe respiratory infection in early childhood was noted specifically and the patient's smoking habits were documented. Clinical examination by a single observer evaluated the presence or absence of clubbing, cyanosis, anaemia, pulmonary crackles, and right ventricular hypertrophy. Bronchograms had been carried out on 14 of the patients; the remaining three had radiographic changes compatible with bronchiectasis. Radiographic classification was performed by the method of Simon,<sup>4</sup> and the severity assessed on the basis of the number of lobes involved; all films were assessed by one observer.

The forced expiratory volume in one second (FEV<sub>1</sub>) and forced vital capacity (FVC) were measured with an eight litre McDermott spirometer. All values were compared to the predicted normal values of Cotes.<sup>5</sup>

A 24-hour collection of sputum was carried out on each of the patients. All specimens were processed immediately after collection and weighed aliquots of sputum were centrifuged at 120 000 g (average rotor radius = 8.5 cm) using the SW50 rotor in a model L2 spinco ultracentrifuge (Beckman Instruments, California, USA) for

Address for reprint requests: Dr BH Davies, Asthma Research Unit, Sully Hospital, Sully, Penarth, South Glamorgan.

three and a half hours at 4°C. Quantitative immunoelectrophoresis of the soluble proteins in the sputum sol phase was carried out substantially by the same methods as those described in detail elsewhere.<sup>6</sup> The concentration of the plasma proteins in the specimens of serum from each patient was measured by the techniques employed for determining the concentration of the corresponding proteins in the sol phase of sputum.

## Results

### CLINICAL ASSESSMENT

Patients were graded on a simple score on the basis of six indices chosen because they appeared to provide the best basis of discrimination between the individual patients studied. The indices were: the onset of symptoms before the age of 5 years; the presence or absence of dyspnoea when walking quietly on level ground; the presence of pulmonary crackles; the radiological involvement of four or more lobes (for this purpose the lingula was considered as a separate lobe); the presence of airways obstruction, (FEV<sub>1</sub>/FEV ratio less than 60%) and a history of cigarette smoking. The results of the clinical grading are summarised in table 1. It can be seen that 10 of the patients had relatively mild bronchiectasis (grades 0, 1, or 2) and the remainder had moderately severe or severe bronchiectasis (grades 3, 4, or 5).

### IMMUNOCHEMISTRY

Wide variation was encountered when the concentrations of plasma proteins in the sol phase of sputum were measured (table 2). Patient-to-

patient variation in sputum sol phase albumin concentrations appeared to follow a progressive type of pattern that was unrelated to clinical grading (fig 1). All other plasma protein concentrations, with the exception of IgA ( $r=0.46$ ,  $0.05 < p < 0.1$ ) showed significant correlation with the sputum sol phase albumin concentrations. The concentration ratios of albumin in matched specimens of serum and sputum were inversely related to the sputum sol phase albumin concentrations ( $r=0.95$ ,  $p < 0.0001$ ), and all other protein concentration ratios correlated significantly with the albumin concentration ratio except IgA ( $r=0.29$ ),  $\alpha_1$ -antichymotrypsin ( $r=0.24$ ), and C3 ( $r=0.25$ ); the probabilities in each case were  $0.2 < p < 0.5$ . The mean concentrations of IgA relative to transferin matched pairs of sputum and serum were  $9.51 \pm 6.03$  and  $1.49 \pm 0.63$  ( $t=5.29$ ,  $< 0.0001$ ) and those of  $\alpha_1$ -antichymotrypsin in sputum and serum were  $4.45 \pm 3.19$  and  $1.73 \pm 1.42$  ( $t=3.11$ ;  $0.0001 < p < 0.0005$ ) thus suggesting selective concentration in sputum of these two plasma proteins. In contrast, the corresponding relative concentrations of C3 in sputum and serum were  $3.52 \pm 1.43$  and  $2.37 \pm 0.78$  and these differences only just achieved significance ( $0.025 < p < 0.05$ ).

## Discussion

The patient-to-patient variation in the concentrations of the plasma proteins in the sol phase of the sputum specimens seemed to follow a continuous progression. Although some patients appear to produce sputum resembling that of patients with chronic bronchitis, others at the

Table 1 Clinical grading of patients with bronchiectasis

Patient number	Indices						Score
	Onset of symptoms at age 5 years	Dyspnoea	Pulmonary crackles	Radiographic evidence of involvement of four lobes	Ratio FEV <sub>1</sub> /FVC > 60%	Cigarette smoking	
1	—	—	—	—	—	—	0
2	+	+	+	+	—	—	5
3	—	—	—	+	NT	+	2
4	+	+	+	+	+	—	5
5	+	—	+	—	+	—	3
6	—	—	—	—	—	—	0
7	—	—	+	—	—	+	2
8	—	—	—	—	NT	—	0
9	—	—	—	—	—	+	1
10	+	+	+	+	+	—	5
11	—	—	—	—	—	+	1
12	—	—	—	—	—	+	1
13	+	—	—	—	—	—	1
14	+	+	+	+	+	—	5
15	—	+	+	—	—	+	3
16	—	—	—	—	—	—	0
17	+	—	+	+	+	—	4

NT—not tested

Table 2 Average concentrations of nine plasma proteins in the sol phase of sputum and in matched serum specimens from 17 patients with bronchiectasis

Plasma proteins	Serum concentration (mg/100 ml)		Sputum concentration (mg/100 ml sol phase)		Protein concentration ratios : serum/sputum	
	Average	Limits of determined values	Average	Limits of determined values	Average	Limits of calculated values
Albumin	4536	3000-6250	87.5	12-320	122	335-13
Transferin	229	140-410	6.5	1.2-15.6	68	160-15
$\alpha_1$ -acid glycoprotein	179	62-420	2.5	0.3-5.6	121	309-20
Haptoglobin	343	124-690	4.7	0.3-17.5	284	783-23
$\alpha_1$ -antitrypsin	224	110-560	13.5	0.7-48.0	60	188-5.5
$\alpha_1$ -antichymotrypsin	36	10-98	2.5	0.2-10.0	26	150-5.5
B $\beta$ -c globulin (C3)	52	30-75	2.3	0.6-5.6	40	75-8.9
IgA	337	170-840	42.7	6.5-95	13	29-3.6
IgG	1416	470-2277	35.3	5.4-91	78	380-3.4

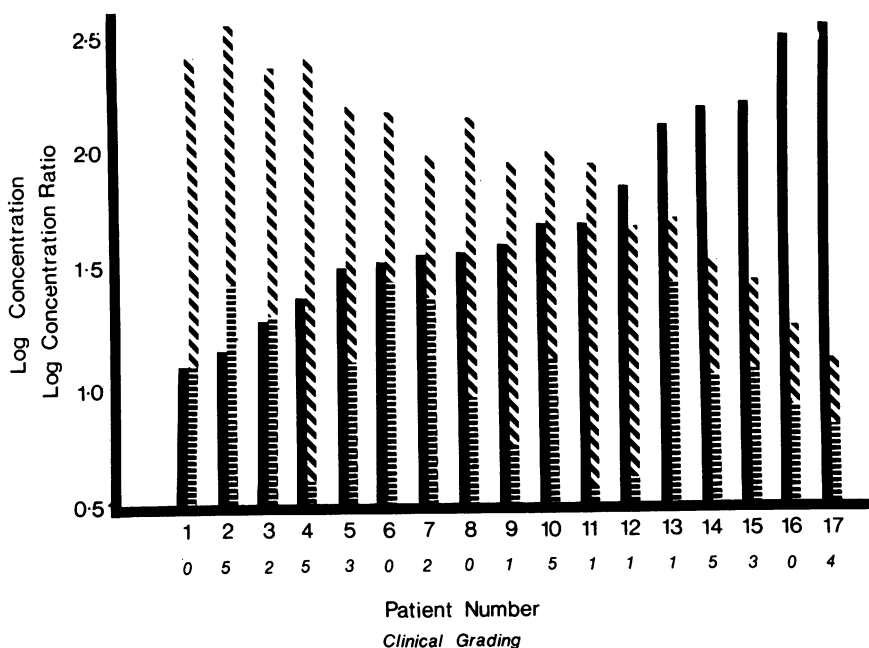


Figure Variation in sputum sol phase albumin concentrations in individual bronchiectasis patients whose clinical grading has been determined, compared with serum:sputum albumin concentration ratios showing inverse correlation of the values. The IgA concentration ratios in matched serum:sputum specimens are also illustrated to show lack of correlation with the corresponding albumin concentration ratios. ■ = Sol phase albumin concentrations, ▨ = serum:sputum albumin concentration ratios, ▤ = serum:sputum IgA concentration ratios.

upper end of the "scale" have high plasma protein concentrations in the sol phase of their sputum, which is similar to that of patients with status asthmaticus.<sup>3</sup> It is thus possible that a pulmonary hypersensitivity reaction, in the broadest sense of the term, may cause the exudative character of the sputum in a proportion of patients with bronchiectasis. It is of interest that our similar findings in patients with cystic

fibrosis<sup>3</sup> could have been caused by the lung damage that characterises this disease and which amounts virtually to bronchiectasis.

Forty per cent of the patients in this study suffered severe bronchiectasis as defined by the indices we describe, but the pulmonary function tests were entirely unrelated to the sputum immunochemistry. There was some evidence suggesting selective concentration of two plasma

proteins ( $\alpha_1$ -antichymotrypsin and IgA) in the sol phase of the patients' sputum and this has been noted by us in other chronic chest diseases. However, the average concentration of IgA in the sputum of patients with bronchiectasis was lower than that of sputum from patients with bronchitis.<sup>3 6</sup> This finding may be worth exploring as a means of providing additional evidence in support of the diagnosis of bronchiectasis in those patients who could equally be suffering from chronic bronchitis.

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