

Mucociliary clearance in patients with chronic autonomic failure

PAUL JENKINS, DEMETRI PAVIA, J R M BATEMAN, S W CLARKE, K M CITRON, AND ROGER BANNISTER

From the Department of Thoracic Medicine, Royal Free Hospital, the Brompton Hospital, and the National Hospital for Nervous Diseases, Queen Square, London

ABSTRACT Mucociliary clearance was measured in four patients with chronic autonomic failure and normal ventilatory function using a method of scanning the clearance of inhaled polystyrene particles tagged with ^{99m}Tc . Previous surgical and experimental evidence has suggested that autonomic denervation might be expected to impair clearance. However, the four patients in this study showed no significant difference in clearance rate compared to groups of sex-matched control subjects. A fifth patient was found to have impaired mucociliary clearance. However she had the symptoms and ventilatory function of smoking-related chronic obstructive bronchitis, a condition which has previously been shown to impair mucociliary clearance.

Surgical division of the autonomic nerve supply to the lungs has been tried in the past to treat intractable airways obstruction in man.^{1,2} The complications of this procedure included mucus retention and recurrent respiratory tract infections.³ In animals there is experimental evidence to confirm that interruption of both sympathetic and parasympathetic nerve supply to the lungs slows mucus clearance⁴; conversely, adrenergic agents have been shown to increase mucociliary clearance.^{5,6} Patients with autonomic denervation might therefore be expected to have abnormalities of mucociliary clearance, and this has not previously been studied in man. We have studied the rate of mucociliary clearance in four patients with autonomic failure and normal ventilatory function, and have compared their rate of mucociliary clearance to sex-matched control groups of healthy volunteers.

Methods

Five patients with chronic autonomic failure gave informed consent to be studied. The clinical criteria for this diagnosis were postural hypotension and associated defects of cardiovascular reflexes. These include lack of systolic overshoot

with impaired rate changes in phases II and IV of the Valsalva response, lack of sinus arrhythmia, lack of pressor and pulse rate response to stress (mental arithmetic), and drug-induced hypertension.^{7,8} The disease may occur alone or in association with multiple system atrophy⁹ or Parkinsonism.¹⁰ The clinical details of the five patients are given in table 1.

Before the study each patient completed a simple questionnaire relating to any previously diagnosed respiratory illness and symptoms of cough, sputum expectoration, and shortness of breath together with smoking history (table 2).

Simple tests of ventilatory function were performed, FEV₁ and FVC with dry spirometer and PEF_R with Wright peak flow meter (table 3).

Patient 1 gave a history of cough with sputum expectoration and had an obstructive defect sufficient to fulfil Medical Research Council criteria for chronic obstructive bronchitis.¹² This patient was excluded from the study.

The remaining four patients had no respiratory symptoms and normal ventilatory function (table 3). Seventeen healthy volunteers (10 male) were studied as control subjects.

Whole lung clearance was determined by the method of Thomson and Pavia.¹³ In brief, patients inhaled a radioaerosol comprising uniform 5 μm polystyrene particles firmly tagged with emitting radioisotope ^{99m}Tc (half-life six hours)

Table 1 Clinical features of patients studied

Patient	Sex	Age (yr)	Duration of symptoms (yr)	Postural hypotension	Parkinsonism	Pyramidal signs	Defective sweating	Impotence	Urinary symptoms	Clinical diagnosis
1	F	64	4	+	0	0	+	-	0	AF
2	F	22	10	+	0	0	+	-	+	SAF
3	M	39	4	+	+	+	+	+	+	AF+MSA
4	F	51	4	+	+	0	+	-	+	AF+MSA
5	F	73	2	+	0	0	+	-	+	AF

+ = present, 0 = absent, - = not applicable. AF = pure autonomic failure, AF+MSA = autonomic failure with multisystem atrophy, SAF = autonomic failure of subacute onset in childhood now chronic.¹¹

Table 2 Physical characteristics and tobacco consumption of patients

Patient	Sex	Age (yr)	Height (metres)	Weight (kg)	Tobacco consumption (pack/years)
1	F	64	1.54	52	23
2	F	22	1.59	45	0
3	M	39	1.74	67	5.5
4	F	51	1.54	49	21
5	F	73	1.64	70	24

Table 3 Ventilatory function of patients expressed as percentage of predicted values for age, sex, and height

Patient	FEV ₁	FVC	FEV ₁ /FVC (%)	PEFR
1	60	77	65	81
2	104	102	103	87
3	140	131	98	118
4	109	101	117	90
5	107	103	110	98

from functional residual capacity in a series of eight breaths (vol 450 ml). Before exhalation a three second breath hold pause was imposed to allow particle deposition.

The initial distribution of deposited radioaerosol across the right lung was determined by rectilinear scanning. Clearance of radioaerosol from both lungs was followed by means of suitably collimated sodium iodide crystals linked to rate meters. Counts of over 100 seconds were taken every 30 minutes for six hours and a final count taken at 24 hours. Counts were corrected for radioactive decay and background and are expressed as a percentage of the initial count to allow for unavoidable difference in radiation dose.

Results

None of the four patients had a significantly different clearance rate from the mean of the sex-matched control group, either in terms of whole

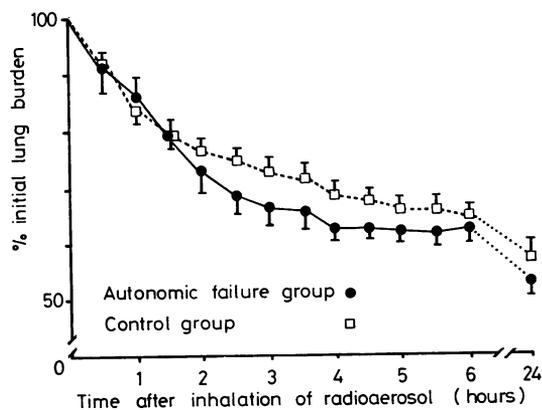


Fig 1 Whole lung clearance curves for the mean of the autonomic failure patients and the mean of the combined control groups (\pm standard error).

lung or tracheobronchial clearance. Further, the mean clearance rate of the autonomic failure patient group was not significantly different from the mean of a combination of the control groups (figs 1, 2). Patient 1, however, had slow whole lung mucociliary clearance when compared to the female control group, becoming significant at the $p < 0.05$ level after three hours and achieving the $p < 0.002$ level by six hours (fig 3). No 24-hour count was performed on this patient so tracheobronchial clearance values are not shown.

Discussion

In autonomic failure, cardiovascular haemostasis is disturbed by lesions at several levels. Patients therefore usually present with symptoms caused by low blood pressure on standing, either dizziness or attacks of loss of consciousness. The autonomic denervation may also produce impotence, disturbance of bladder function, or defective sweating.^{14 15} The effect of autonomic denervation on mucociliary clearance in man has not been studied previously.

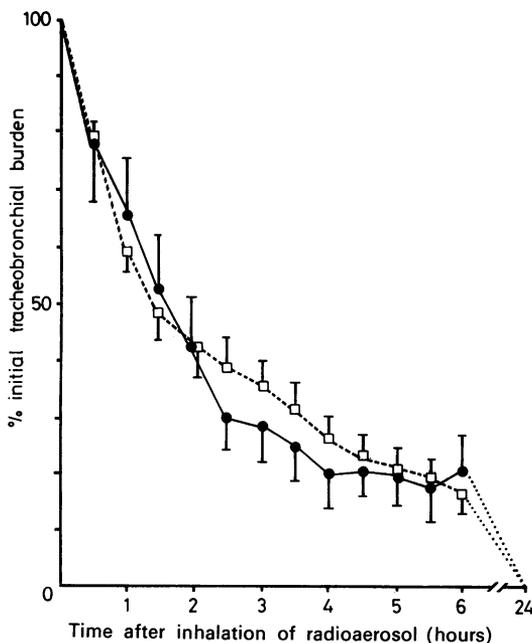


Fig 2 Tracheobronchial clearance curve for the mean of the autonomous failure patients and the mean of the combined control group (\pm standard error).

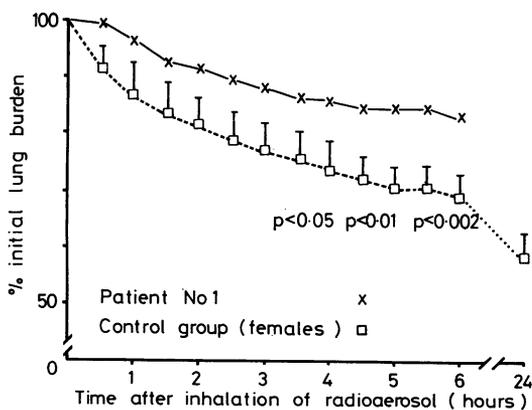


Fig 3 Whole lung clearance curve for patient 1 and the mean of the female control group (\pm standard deviation).

Patient 1 probably had smoking-related chronic bronchitis, so was excluded, as previous workers have shown that patients with chronic bronchitis have slow mucociliary clearance.¹⁶ The diagnosis of chronic bronchitis is made entirely on clinical manifestations of the disease. Before chronic bron-

chitis is diagnosed as the sole cause of expectoration, other conditions which may result in expectoration must be excluded, but it must be remembered that chronic bronchitis may coexist with any of them.¹² It could be said that autonomic failure by impairing normal mucus clearance, resulting in symptoms of cough and sputum expectoration, is one of these conditions. Indeed, the rate of mucociliary clearance in patient 1 was significantly slower than that of the female control group. If, however, her symptoms of cough and sputum expectoration were caused by autonomic failure, some of the other patients would be expected to have similar symptoms, which was not the case. Further, these symptoms have only been recorded in two patients in other studies of autonomic failure,¹⁷ of whom both were in the terminal phase, and one was found to have a lung carcinoma at postmortem.

The present study shows no evidence that autonomic denervation as seen in patients with chronic autonomic failure produces impairment of mucociliary clearance. This is at variance with what might be expected from surgical experience in both animals and humans. There are several factors which may account for this.

1 Cutting the autonomic nerve supply to the lung produces acute denervation as compared to chronic partial denervation as in our patients. It is possible that effects may differ in the long term. Reserve mechanisms or reflexes, perhaps stimulated by pooling of secretions, may correct the slowing of clearance seen in acute studies. Indeed, five of six dogs restudied 120-150 days after surgery in one study showed either complete or significant return to normal mucociliary clearance.⁴

2 In chronic autonomic failure lesions are present in central and peripheral sympathetic and vagal pathways. However, physiological studies show that these defects may be incomplete.^{7,8} Surgical procedures in contrast produce complete interruption of these pathways. It is possible, therefore, that the particular autonomic pathways concerned with the control of mucociliary clearance remain intact in patients with chronic autonomic failure.

3 Disorientation of the ultrastructure and resulting direction of beat of cilia has been thought to account for abnormal secretion clearance in conditions such as Kartagener's syndrome.^{18,19} Transection of the main bronchus, as in the animal experiments,⁴ might produce an area of non-functioning or disorientated cilia around the re-anastomosis line resulting in a "dead zone" past which the mucus could not be cleared.

4 The importance of a particular factor such as autonomic innervation in the control of mucociliary clearance may vary between species.

Autonomic active drugs can only demonstrate the action of the autonomic nervous system. The importance of this system in physiological control of mucociliary clearance can only be determined from denervation or stimulation studies.

The results of the present study suggest that the autonomic nervous system is not a major factor in the physiological control of mucociliary clearance.

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