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# MUCUS CLEARANCE AT REST AND DURING EXERCISE IN PATIENTS WITH BRONCHIAL HYPERSECRETION

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**ABSTRACT. The purpose of this study was to measure the effects on mucus clearance after physical exercise. We measured mucociliary clearance at rest and during exercise in eleven patients with mild or moderate bronchial hypersecretion. The subjects inhaled an aerosol containing $^{99m}$Tc-labelled albumin millimicrospheres. Four sets of scintigraphic images were obtained with 15 minute intervals. The lung retention of radioactivity was quantified using a gamma camera and the clearance of particles from the lungs were calculated for each 15 min period. The first image was obtained directly after inhalation, the second after a period of 15 min rest, the third after a period of exercise on a bicycle ergometer and the final fourth image after another period of rest. We found no differences in the clearance rate at rest and after exercise.**

*Key words:* aerosols, radionuclide imaging, respiratory function test, bronchial hypersecretion, chronic bronchitis.

Mucus is cleared from the airways by mucociliary transport and by cough. The rate of transport of inhaled particles deposited on ciliated airways can be measured by external monitoring of the clearance of inhaled radiolabelled particles (16).

Mucociliary clearance is affected by autonomic stimuli. Adrenergic (8, 12, 14) as well as cholenergic drugs (7) increases the rate of clearance. Mucociliary clearance is slower during sleep than in wakefulness. In view of this, mucociliary clearance might be expected to increase during exercise. The effects of physical activity on clearance has been studied in normal subjects with conflicting results. Wolff et al. (21) found clearance to be slightly increased, after exercise, whereas no substantial effect was seen in a study by Olséni & Wollmer (19).

Patients with bronchial hypersecretion often have reduced mucociliary clearance, and various forms of chest physiotherapy are used to increase the elimination of secretions. Traditional chest physiotherapy includes breathing exercises, cough, postural drainage, percussion and vibration. The basic mechanism for and efficacy of each component are incompletely known, and the optimal scheme for chest physiotherapy remains controversial (13, 20).

In recent years, increasing emphasis has been placed on techniques for physical therapy which include physical activity and active participation of the patient. Various forms of exercise have thus been introduced in the physical therapy of patients with chronic lung disease and been shown to improve exercise tolerance and gas exchange (3, 9, 10, 15). Physical exercise has therefore been suggested to improve the quality of life in patients with chronic lung diseases. Little is known about the effect of exercise on mucus clearance in patients with bronchial hypersecretion. We are aware of only one study in which mucus clearance was found to be greater during exercise than at rest (18).

The purpose of this study was to measure the effects on mucus clearance of a simple exercise program which could be done by the patient on his own.

## MATERIAL AND METHODS

We studied mucociliary clearance at rest and during exercise in eleven patients (6 men and 5 women) with bronchial hypersecretion. Their daily sputum production was estimated from the history to be about 20–30 ml. Eight patients, four current smokers and four ex-smokers, had chronic bronchitis and three non-smoking patients had bronchiectasis. Their mean age was 51 ± 12 (SD) years. The study was approved by the local research ethics committee and informed consent was obtained from each subject.

Spirometry including vital capacity (VC) and forced expiratory volume in one second ($FEV_1$) was performed with a bellows spirometer. Predicted values were obtained from Berglund et al. (5).

Mucus clearance was assessed with a technique based on measurement of the clearance of inhaled radiolabelled particles. The subject was positioned in front of a gamma camera (Maxicamera 400T, General Electric Company, Milwaukee, Wis., USA). A transmission scintigram of the chest was obtained using a flood source Fig. 1. A large disc containing $^{57}$Co was placed over the anterior aspect of the chest and the gamma rays transmitted through the thorax detected with the

Table I. *Heart rate and ventilatory parameters at rest and during exercise*

| | Heart rate ($min^{-1}$) | Breathing frequency ($min^{-1}$) | Ventilation (l/min) |
|---|---|---|---|
| Rest 1 | 88±15 | 18±4 | 17±4 |
| Exercise | 124±17 | 23±6 | 40±10 |

gamma camera in the posterior view. This scintigram was used in the data analysis to delineate the lungs. The subject then inhaled a radiolabelled aerosol. An air jet nebulizer was used to nebulize a suspension of $^{99m}$Tc-labelled albumin millimicrospheres. The particle size was 4.9 μm mass median diameter with a geometric standard deviation of 1.9 μm (measured with a laser light scattering technique). The subject was instructed to inhale the aerosol by somewhat forced, deep inhalations. The administration of the aerosol was stopped when a count rate of 1 500–2 000 $s^{-1}$ had been reached, corresponding to a delivered dose of approximately 20 MBq of $^{99m}$Tc. Four sets of scintigraphic images were obtained with exactly 15 min intervals. Each set of scintigrams consisted of images in the anterior and posterior view, acquired for 2 min and stored in a 64×64 image matrix in a computer. A total of 150 000–250 000 counts were accumulated over the lungs in each image.

The first set of images was obtained immediately after the inhalation of the aerosol. The subject was allowed to rest in the sitting posture for 15 min before the second set of images was obtained. The subject then exercised on a bicycle ergometer with a work load corresponding to approximately 60% of the predicted normal maximum capacity (17). The third set of images was obtained after 15 min (approximately 13 min exercise). A second period of 15 min of rest in the sitting posture was followed by the final set of images.

Heart rate, breathing frequency and minute ventilation (Fleisch pneumotachograph) were measured immediately before and at the end of exercise. The number of coughs was counted during each period of measurement.

Regions of interest were delineated in the transmission scintigram and subsequently projected onto the aerosol scintigrams. Three regions of interest were selected for each lung; total lung, central part and peripheral part. The central part was chosen as one fourth of the whole lung and the peripheral part was the difference between the other two regions. The clearance of inhaled particles was measured as the decrease in count rate between successive sets of scintigrams for each of the three regions. For each measurement, the mean value of the count rates in anterior and posterior views was used. The change in count rate measured in the total lung region reflects the amount of radioactivity leaving the lung by mucus clearance. The change in count rate measured in the peripheral region reflects the clearance of particles from peripheral to central airways in the lung. A correction was made for this transport of particles from the peripheral to the central region when clearance from the central part of the lung was calculated.

The results are presented as mean ± one SD. The Friedman test was used for statistical analysis.

## RESULTS

Vital capacity and $FEV_1$ were slightly to moderately reduced in most patients, mean values being 86±23 and 88±25% of the predicted values, respectively.

The scintigrams obtained immediately after the inhalation of aerosol showed prominent deposition of particles in the central airways. On average, 46% of the aerosol was deposited in the central region and 54% in the peripheral region.

The heart rate during exercise corresponded to 74% of the predicted maximum heart rate (Table I). Minute ventilation increased by a factor 2.4.

All patients but one coughed during the measurement. The number of coughs were from 0 to 27 with a mean of 2.6. There was no significant difference in the number of coughs between the different periods of measurement.

Clearance of radioactive particles from the whole lung field was greater during the first period of rest than during exercise and greater during the second period of rest (Table II), but the differences were not statistically significant. The findings in the peripheral region were similar to those in the whole lung field. Clearance from the central region was slightly faster during exercise than during the periods of rest, but again the differences were not statistically significant.

## DISCUSSION

The technique we used for assessing mucus clearance relies on measurement of the clearance of inhaled radiolabelled particles. We measured clearance during different periods after a single inhalation of tracer rather than on different occasions. This design was selected because of the well-known difficulty to achieve reproducible aerosol deposition (11).

Table II. *Clearance of radioactive particles from the lung regions at rest and during exercise expressed as the amount cleared during each period of measurement relative to the initial activity at the beginning of each period*

| | Clearance (% initial activity) | | |
|---|---|---|---|
| | Total | Central | Peripheral |
| Rest 1 | 11.2±5.1 | 25.1±14.3 | 10.7±4.6 |
| Exercise | 10.6±3.7 | 31.9±16.7 | 9.7±4 |
| Rest 2 | 7.1±3.1 | 29.8±19.5 | 8.0±3.4 |

The patient inhaled the aerosol with somewhat forced breaths so that a high deposition should be obtained on ciliated epithelium. Heavy deposition in central airways was also seen in all subjects. Nevertheless, some deposition can be expected to occur in peripheral airways, possibly beyond the ciliated epithelium. This aerosol would constitute a background activity in the clearance measurement. Allowance for the deposition on non-ciliated epithelium can be made by measuring the 24 h retention of particles or by relating the deposition of particles to regional ventilation (16). Neither approach could, for practical reasons, be used in this study. Instead, we related mucociliary clearance during exercise to two periods of rest, one preceding and the other following exercise.

The use of exercise, as a means of self-administered physical therapy in patients with chronic lung disease, is limited to exercise at moderate work load for a relatively short time. We therefore chose to study the subjects at sub-maximal work load for approximately 15 min.

Cough is considered an important mechanism for mucus clearance in patients with bronchial hypersecretion (2, 6). In this study, we made no attempt to eliminate the effect of cough, since this was felt to create too artificial situation. Instead, we counted the number of coughs during each period of measurement.

We did not find any statistically significant difference in mucus clearance between the periods. Clearance gradually slowed down during the periods in the whole lung field and in the peripheral field. This suggests that the clearance rate decreases with time, which is probably related to particle deposition on non-ciliated epithelium. The effect of such deposition would be expected to be less in the central region than in the peripheral since most of the radioactivity measured in the central region originates from large airways. In the central region in contrast, clearance was slightly, but not significantly higher during exercise than at rest.

We thus found no evidence that moderate exercise increases mucus clearance in patients with bronchial hypersecretion. With the experimental design used in this study, small effects of exercise on mucus clearance may have been overlooked. We feel confident, however, that any clinically relevant beneficial effect of exercise on mucus clearance would be detectable.

Oldenburg et al. (18) measured mucus clearance in subjects with chronic bronchitis during intermittent exercise (5×4 min with 4 min intervals). They found clearance to be slightly, but significantly faster during exercise than at rest. They also found, however, that directed coughing alone improved mucus clearance much more than exercise. The patient material in the study by Oldenburg et al. differs from our material by having greater sputum production and greater lung function impairment. A possible explanation for the differences between our results and the results of Oldenburg and co-workers could be that exercise has a greater effect on mucociliary clearance when the patients produce more secretion.

Exercise appears to have small, if any, effects on mucus clearance in normal subjects and in patients with mild to moderate bronchial hypersecretion. Exercise may have many beneficial effects in patients with chronic bronchitis, but should not be regarded a replacement for chest physiotherapy as a means of promoting sputum mobilization and expectoration in all patients.

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