The effects of postural drainage and positive expiratory pressure physiotherapy on tracheobronchial clearance in cystic fibrosis

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The Effects of Postural Drainage and Positive Expiratory Pressure Physiotherapy on Tracheobronchial Clearance in Cystic Fibrosis*

Jann Mortensen, M.D.; Merete Falk; Steffen Groth, M.D., DMSc.; and Christian Jensen

We studied the effects of two chest physiotherapy regimens on whole lung and regional tracheobronchial clearance (TBC) in ten patients with cystic fibrosis. The regimens were given on two separate days and consisted of 20 min of (1) postural drainage and the forced expiration technique (PD + FET), and (2) positive expiratory pressure (PEP-mask) and FET (PEP + FET). A third day served as control. The study days were randomized. Each day, the clearance of lung radioactivity was measured for 3 h by gamma camera. The number of spontaneous coughs was recorded and the sputum expectorated was sampled. We found that both PD + FET and PEP + FET improved whole lung TBC at 30 minutes and 1 h four or fivefold (p<0.01) compared with control, whereas at 2 h and 3 h only the improvement following PEP + FET (approximately 1.4 times) was significant (p<0.05). There was no significant difference in whole lung or regional TBC between the PD + FET and PEP + FET treatments. The correlations between TBC and the radioactivity content in sputum expectorated (r = 0.76) and between TBC and numbers of coughs (r = 0.65) were better than between TBC and the weight of sputum expectorated (r = 0.39). We conclude that PD or PEP when combined with FET have similar effects on short-term whole lung and regional TBC in patients with cystic fibrosis. Evaluation of TBC during chest physiotherapy when only based on the weight of sputum expectorated seems inadequate.

Chest physiotherapy is considered important for enhancement of mucus clearance in patients with cystic fibrosis.1-5 Postural drainage (PD) or positive expiratory pressure (PEP) by a PEP-mask combined with the forced expiration technique (FET) have been introduced as efficient methods of increasing sputum yield5-4 and in many centers they have now replaced conventional PD, including percussion and cough. PEP-mask treatment appears to be useful in the prophylactic pulmonary treatment of postoperative patients,6 patients with chronic bronchitis, and patients with cystic fibrosis.6-9

In patients with cystic fibrosis, PD + FET have been suggested to be more effective than PEP + FET in improving the clearance of secretions in terms of the weight of sputum expectorated.10

The noninvasive radioaerosol technique involving inhalation of radioaerosol and subsequent external detection of the removal of the radioactivity, when embedded in mucus, may provide a more reliable evaluation of the effect of chest physiotherapy on mucus clearance.11

The aim of this study was to evaluate the short-term effects of PD + FET and PEP + FET on whole lung and regional tracheobronchial clearance of radioaerosol and on sputum production in patients with cystic fibrosis. In addition, we wanted to examine the usefulness of sputum weight as an index of tracheobronchial clearance.

**Patients and Methods**

Ten patients with cystic fibrosis, who had been chronically infected with *Pseudomonas aeruginosa* for 3 to 21 years, entered the study in the last of two weeks of regular hospital admission for intravenous antipseudomonas treatment. There was no significant change in the semiquantitative bacterial sputum content during the week of examination. The patient characteristics, daily medication, and lung function are given in Table 1. The medication, which usually was taken 2 to 3 h before the study was begun, remained unaltered during the study. In none of the patients did the FEV₁ increase by >15 percent after inhalation of a β₂-agonist. All patients were nonsmokers.

**Study Design**

The study was a randomized, single-blind crossover trial. In each patient tracheobronchial clearance was measured every 30 minutes for 3 h on three occasions separated by 48 hours. Each study run included a 20-minute session of PD + FET, PEP + FET, or control. The sessions started immediately after the radioaerosol inhalation and acquisition of the initial distribution of radioactivity in the lung.

*FET = Forced expiration technique; PD = postural drainage; PEP = positive expiratory pressure; r = Spearman rank correlation coefficient (r); RV = residual volume; TBC = tracheobronchial clearance; TBR = tracheobronchial retention; \( ^{m}Tc = \) technetium
Abbreviations: F = female; M = male; inhaled -agonist; COL = inhaled colistine; T = theophylline; MUCOL = mucolytic drug; VC = vital capacity; FEV1 = forced expiratory volume in 1 s; PEF = peak expiratory flow rate; MEFe = maximal expiratory flow at 50 percent of forced vital capacity.

**Chest Physiotherapy Treatments**

Instruction and practice with the PD + FET treatment were given to each patient before the study. The patients were accustomed to PEP + FET treatment.

**Control:** The patients rested in the upright position. Spontaneous coughing was allowed.

**Postural Drainage and the Forced Expiration Technique:** Two positions for PD were maintained for 10 minutes each. They were the left and right lateral decubitus with 20° head-down tilt. In each position, 1-min periods of deep breaths with relaxed expirations (thoracic expansion exercises), relaxation, and gentle breathing (breathing control) were followed by the FET. FET consisted of one or two forced expirations “huffs” from mid lung volume to low lung volume, a short period of breathing control, and cough.

**Positive Expiratory Pressure and the Forced Expiration Technique:** The system used for PEP consisted of a face mask and a one-way valve to which an expiratory resistor had been attached. During treatment, a manometer determining the exact PEP level was inserted between the valve and the resistor. The diameter of the resistor had been determined for each patient to give a steady PEP of 10 to 20 cm H2O. This pressure should be maintained in the middle part of expiration during tidal volume breathing with only slightly active expirations through the system. The diameter of appropriate resistors ranged from 3.0 to 1.5 mm. Treatment was carried out in the sitting position. One-minute periods of tidal volume breathing with PEP were followed by FET and coughing.

The physiotherapy treatments were administered by the patients themselves and supervised by a physiotherapist. The number of FET periods as well as the number of directed huff and cough maneuvers performed during the two physiotherapy sessions were standardized for each patient. Recordings of the exact number of directed huffs and coughs included in the first active treatment session (PEP + FET or PD + FET) were used to ensure that the patient performed the same number of huffs and coughs during the subsequent active treatment session.

Spontaneous cough was allowed in the posttreatment periods. The exact numbers of productive coughs (ie, resulting in sputum expectorated) and nonproductive coughs were recorded separately during each 30-minute period during the 3 h of examination. After 20 minutes of treatment or control sessions, the patients rested in the upright position for the rest of the study periods.

**Radioaerosol Procedure**

The patients inhaled an ultrasonically nebulized 99mTc-human albumin colloid. Less than 1 000 of 99mTc leached from 99mTc-albumin in vitro during 24 hours as measured chromatographically. Inhalation, limited to a volume of 750 ml, commenced at residual volume (RV). The radioaerosol was administered as a bolus in the last 250 ml of the inhalation volume. The inhaled flow rate was monitored by a pneumotachograph and kept about 1 L/A. The expiration to RV was slow. This radioaerosol inhalation technique was used to obtain a predominantly central airways deposition by particle impaction during inspiration and to avoid airway compression during expiration, thus trying to prevent subsequent coughing. The subjects made a mean of 45 inhalations until a count rate of about 700 counts/s (range, 400 to 800) was obtained by a gamma camera. This corresponded to a retained dose of 7 to 10 MBq 99mTc in the thorax. Usually, 90 percent of radioactivity came from the lung region and 10 percent came from the pharynx, stomach, and two 99mCo-markers placed onto the skin above the cervical and lumbar spine.

Immediately following the radioaerosol inhalation, the subjects rinsed their mouth three times and swallowed some water to remove any particles from the mouth, pharynx, and esophagus. Within 1 minute, detection of the distribution of radioactivity in the lungs was begun by placing the subjects against a posteriorly positioned gamma camera. The posterior position was chosen because of more comfort for the patients and because this made it easier to place the 99mCo-markers precisely and similarly in every patient without having them interfering with the lung radioactivity readings. The design of the chair, which limited subjects’ moving during the data acquisition, and the 99mCo-markers helped to reposition the subjects at each data acquisition. The data acquisition was obtained as a 1 * 5 min static gamma camera exposure due to the relatively low count rates. The gamma camera readings were repeated each 30 minutes for three hours and stored in a dedicated computer system. Some water was swallowed before each data acquisition.

Clearance of mucus from the lung was assessed by the radioactivity retention in percentage of the initial activity after correction for background and physical decay. An additional 24-hour reading of the retention of 99mTc-albumin was taken as an estimate of radioaerosol on nonciliated airways, ie, alveolar deposition. The 24-hour retention was subtracted from all readings of the whole lung retention curve to give a tracheobronchial retention (TBR) curve—describing clearance of radioaerosol deposited only on airways mucus. A 99mKr-ventilation scintigram was used to measure the lung volume in different regions of the lung and to define the outline of the lung (Fig 1). Regional TBR was assessed in a similar way as explained for the whole lung TBR curve. The initial aerosol deposition was characterized by calculating the penetration index as the ratio of peripheral to central zone radioactivity for 99mTc divided by the same ratio for 99mKr (Fig 1).

**Table 1—Patient Characteristics, Daily Medication, and Lung Function (in Percentage Predicted)**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Sex</th>
<th>Medicine</th>
<th>VC</th>
<th>FEV1</th>
<th>FEV1/VC</th>
<th>PEF</th>
<th>MEFe</th>
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<tr>
<td>1</td>
<td>20</td>
<td>162</td>
<td>F</td>
<td>β1+COL</td>
<td>67</td>
<td>35</td>
<td>56</td>
<td>85</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>167</td>
<td>M</td>
<td>β1+COL</td>
<td>112</td>
<td>101</td>
<td>92</td>
<td>119</td>
<td>121</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>155</td>
<td>M</td>
<td>β1+COL</td>
<td>48</td>
<td>28</td>
<td>71</td>
<td>49</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
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<td>168</td>
<td>M</td>
<td>COL</td>
<td>66</td>
<td>37</td>
<td>68</td>
<td>54</td>
<td>17</td>
</tr>
<tr>
<td>5</td>
<td>22</td>
<td>164</td>
<td>F</td>
<td>β1+COL</td>
<td>63</td>
<td>26</td>
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<td>6</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>180</td>
<td>M</td>
<td>MUCOL</td>
<td>90</td>
<td>76</td>
<td>85</td>
<td>91</td>
<td>49</td>
</tr>
<tr>
<td>7</td>
<td>17</td>
<td>185</td>
<td>M</td>
<td>β1+COL</td>
<td>74</td>
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<td>154</td>
<td>F</td>
<td>β1+COL</td>
<td>53</td>
<td>40</td>
<td>107</td>
<td>56</td>
<td>49</td>
</tr>
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<td>9</td>
<td>22</td>
<td>184</td>
<td>M</td>
<td>β4+T+COL</td>
<td>60</td>
<td>27</td>
<td>50</td>
<td>53</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>18</td>
<td>157</td>
<td>F</td>
<td>COL</td>
<td>61</td>
<td>49</td>
<td>75</td>
<td>90</td>
<td>23</td>
</tr>
<tr>
<td>Median</td>
<td>20</td>
<td>165.5</td>
<td>6 M, 4 F</td>
<td></td>
<td>65</td>
<td>38.5</td>
<td>72</td>
<td>65.5</td>
<td>20</td>
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<td>Range</td>
<td>15-26</td>
<td>154-185</td>
<td>6 M, 4 F</td>
<td></td>
<td>48-112</td>
<td>26-101</td>
<td>50-107</td>
<td>49-119</td>
<td>6-121</td>
</tr>
</tbody>
</table>

*Abbreviations: F = female; M = male; β1 = inhaled β1-agonist; COL = inhaled colistine; T = theophylline; MUCOL = mucolytic drug; VC = vital capacity; FEV1 = forced expiratory volume in 1 s; PEF = peak expiratory flow rate; MEFe = maximal expiratory flow at 50 percent of forced vital capacity.
The lung zones were created after visual inspection of the central airways from Tc-albumin scintigrams. The central zone (17 percent of total pixel area) mainly covered the trachea and the main bronchi. The mid zones (24 percent of pixels) covered mainly the lobar, segmental, and subsegmental bronchi. The peripheral zones (59 percent of pixels) covered the subsequent bronchial generations. Each zone also included alveolar regions. As indicated from Krypton ventilation scintigrams, the proportions of alveolar volume in the central, mid, and peripheral zones were in median (range) 13 percent (11 to 16), 36 percent (29 to 44), and 50 percent (41 to 59), respectively.

An additional definition of regions of interest was used to compare the effect of the gravity-assisted treatment (PD + FET) to the non-gravity-assisted (PEP + FET) treatment and control on mucus clearance of the dependent lung region (Fig 1, right). The bottom zone was created to mainly cover the lower lobe bronchus and lobe.

Half of the patients were asked to collect their 24-hour urine production for measurement of the Tc excretion in urine on the control day.

**Effect Parameters**

1. Whole lung and regional tracheobronchial clearance every 30 minutes for 3 h.
2. Sputum weight—sputum produced during treatment and in the follow-up period were collected separately. A precision balance was used to get the exact weight of sputum.
3. Tc-sputum—The technetium content in each sputum sample was measured in a scintillation counter (Well-Type).

**Lung Function**

All recordings of flow-volume curves were made on computerized lung function equipment (Jaeger) before the tracheobronchial clearance measurement. The largest of three acceptable flow-volume curves was used to ensure that the intrapatient FEV₁ differed less than 15 percent before each of the three examinations.

**Ethics**

The study was approved by the local ethical committee of Copenhagen and was in accordance with the Helsinki Declaration II. Informed consent was given by the patients, and if they were younger than 18 years, by their parents too.

**Statistical Methods**

Statistical significance (p<0.05) was assessed by nonparametric methods. The tests used were the Friedman analysis of variance by ranks and the Page test for trends. If significant differences were found, the Wilcoxon rank sum test for paired data was used to compare the study days two by two. The Spearman rank correlation coefficient (r,') was used for correlation analysis.

**RESULTS**

There was no significant difference in initial FEV₁.

**Table 2—Penetration Index (Tc Peripheral/Central Zones), Total Lung Retention at 24 Hours, and FEV₁ in Percent Predicted on the Days of Control, Positive Expiratory Pressure + Forced Expirations (PEP + FET), and Postural Drainage and Forced Expirations (PD + FET), Values in Median (and Ranges)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PEP + FET</th>
<th>PD + FET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penetration</td>
<td>0.54</td>
<td>0.61</td>
<td>0.58</td>
</tr>
<tr>
<td>index:</td>
<td>(0.28-0.91)</td>
<td>(0.31-1.00)</td>
<td>(0.27-0.92)</td>
</tr>
<tr>
<td>Retention</td>
<td>51.32</td>
<td>51.04</td>
<td>47.54</td>
</tr>
<tr>
<td>at 24 h</td>
<td>(24.43-67.50)</td>
<td>(12.41-71.72)</td>
<td>(26.61-69.01)</td>
</tr>
<tr>
<td>FEV₁, % pred</td>
<td>42.75</td>
<td>37.30</td>
<td>42.75</td>
</tr>
<tr>
<td></td>
<td>(26.40-108.00)</td>
<td>(27.06-101.00)</td>
<td>(23.40-109.00)</td>
</tr>
</tbody>
</table>
penetration index, or total lung retention at 24 hours on the three days of study (Table 2). The penetration index correlated positively with the whole lung retention at 24 hours ($r_s = 0.407$), and negatively with the whole lung clearance ($r_s = -0.406$) ($p<0.05$), after pooling the total number of examinations ($n = 30$). The correlation between penetration index and clearance was strongest ($r_s = -0.866$, $p<0.05$) in the subjects with the relatively "best" lung function, e.g., for those subjects with FEV$_1$ > 50 percent predicted.

Tracheobronchial Clearance

Whole lung TBR at 30 minutes (TBR$_{30}$) and TBR$_i$ were significantly smaller ($p<0.01$) after PEP + FET and PD + FET treatments than after control (Fig 2 and Table 3), i.e., mucus clearance was greater after treatments than after control. Whole lung TBR$_i$ and TBR$_{30}$ after PEP + FET was significantly smaller than after control. Retention curves after PEP + FET and PD + FET were not significantly different.

Retention in the central region was significantly smaller ($p<0.01$), i.e., clearance was greater than that in the peripheral region after the treatments (PEP + FET and PD + FET) at 30 minutes, 1 h, 2 h, and 3 h (Fig 2). After control retention was only significantly smaller ($p<0.05$) smaller in the central region than in the peripheral region at 2 h and 3 h (Fig 2).

The TBR of the peripheral region was significantly smaller at 1 h, 2 h, and 3 h after PEP + FET compared with control ($p<0.05$). After PD + FET treatment, TBR was only significantly smaller than control at one hour. The retention in the peripheral zone after PEP + FET and PD + FET did not differ significantly from each other. In seven of the patients, the control day TBR$_i$ was less than TBR$_{30}$, whereas TBR$_i$ was slightly higher compared with TBR$_{30}$ in one patient and much higher in two patients. By inspection of the scintigrams there was no obvious indication of mucus back-flow from the central airways to more peripheral airways in these three "abnormal" patients. The reason for the increase in retention values at 1 h in the peripheral region (and in whole lung TBR$_{30}$ of patient No. 5 seen in Table 3) most likely is a combination of measurement uncertainty, inexact repositioning of the lung at the 30-minute and 1 h readings, a possible difference in the gamma camera reading of radioactivity swallowed and localized in the stomach, and movement of radioactivity into a region where there is less tissue between the radioactivity and the chest surface. 

The central region TBR was significantly smaller after the two treatments (PEP + FET, PD + FET) compared with control at 30 minutes and 1 h ($p<0.01$) and at 2 h ($p<0.05$), whereas at 3 h the difference was nonsignificant. There was no significant difference between the effects of the two treatments (PEP + FET vs PD + FET).

The initial deposition of radioactivity and the 24-hour retention in the bottom zone of the right lung (Fig 1, right) was not significantly different on the three study days (Table 4). At 30 minutes and at 1 h after PD + FET and at 30 minutes after PEP + FET treatment, the TBR in the bottom zone was significantly smaller than at control (Fig 3). The retention after PEP + FET and PD + FET did not differ significantly from each other.

Table 3—Tracheobronchial Retention at 30 Minutes and Three Hours on the Days of Control, Positive Expiratory Pressure and Forced Expirations (PEP + FET), and Postural Drainage and Forced Expirations (PD + FET)

<table>
<thead>
<tr>
<th>No.</th>
<th>Control</th>
<th>PEP + FET</th>
<th>PD + FET</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 min</td>
<td>3 h</td>
<td>30 min</td>
</tr>
<tr>
<td>1</td>
<td>84.26</td>
<td>40.91</td>
<td>63.55</td>
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<td>2</td>
<td>98.65</td>
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<td>50.53</td>
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<td>5</td>
<td>109.10</td>
<td>57.07</td>
<td>72.16</td>
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<td>6</td>
<td>75.86</td>
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<tr>
<td>10</td>
<td>92.82</td>
<td>54.87</td>
<td>60.46</td>
</tr>
<tr>
<td>Median</td>
<td>92.70</td>
<td>58.71</td>
<td>65.77</td>
</tr>
<tr>
<td>Range</td>
<td>50.53-109.10</td>
<td>23.96-83.29</td>
<td>44.53-91.13</td>
</tr>
</tbody>
</table>

*p<0.01 compared with control.  
†p<0.05 compared with control.

Table 4—Initial Deposition of Radioactivity and Retention at 24 Hours in the Bottom Zone of the Right Lung, Values in Median (and Ranges)*

<table>
<thead>
<tr>
<th></th>
<th>Control, %</th>
<th>PEP + FET, %</th>
<th>PD + FET, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retention</td>
<td>54.00</td>
<td>55.19</td>
<td>54.01</td>
</tr>
<tr>
<td>at 24 h</td>
<td>(21.58-79.04)</td>
<td>(14.94-82.66)</td>
<td>(25.20-78.35)</td>
</tr>
<tr>
<td>Initial</td>
<td>73.00</td>
<td>75.57</td>
<td>72.63</td>
</tr>
<tr>
<td>deposition</td>
<td>(64.42-85.26)</td>
<td>(64.57-86.55)</td>
<td>(62.05-85.96)</td>
</tr>
</tbody>
</table>

*No significant differences compared with control.
The patients were stratified according to their lung function in percent predicted (FEV\textsubscript{1}, maximal expiratory flow at 50 percent of vital capacity [MEF\textsubscript{50}], or FEV\textsubscript{1}/VC) for analyses of the effect of the treatments on tracheobronchial clearance at 30 minutes (TBC\textsubscript{0.5}) in the patients (subgroup 1) with the most pronounced airway obstruction (eg, subjects with FEV\textsubscript{1}<50 percent predicted) in comparison with the patients (subgroup 2) with the least airway obstruction (eg, FEV\textsubscript{1}>50 percent predicted). There was no significant correlation between any of the lung function parameters and normalized TBC\textsubscript{0.5} (mean TBC\textsubscript{0.5} after PEP+FET and PD+FET minus TBC\textsubscript{0.5} during control: [PEP+FET TBC\textsubscript{0.5} + PD+FET TBC\textsubscript{0.5}] / 2 – control TBC\textsubscript{0.5}). Furthermore, normalized TBC\textsubscript{0.5}, in any of the pairs of subgroups analyzed, did not significantly differ from each other (eg, the median difference in TBC\textsubscript{0.5} among patients with FEV\textsubscript{1}<50 percent predicted and patients with FEV\textsubscript{1}>50 percent predicted was 12 percent, 95 percent confidence limits: –14 percent to +34 percent). This indicates that the effects of PEP+FET and PD+FET on mucus clearance was not related to the degree of airway obstruction.

Additional analyses in the seven patients who used β\textsubscript{2}-agonists and the three patients who did not use β\textsubscript{2}-agonists daily revealed no significant differences in normalized TBC\textsubscript{0.5} (median difference 4 percent, 95 percent confidence limits: –24 percent to +23 percent) or in control TBC\textsubscript{0.5} (median difference 0 percent) between the two groups of subjects.

**Huff, Cough, and Sputum**

The total number of huffs performed during the active treatment sessions were in median (and range): PEP+FET 18 (10 to 36) and PD+FET 18 (10 to 35). The intrapatient difference in numbers of huffs during PEP+FET and PD+FET sessions was 0 (0 to 2).

In the period zero to 30 minutes, the total number of cough maneuvers was as follows: control 1 (0 to 7), PEP+FET 16.5 (8 to 23), and PD+FET 18 (10 to 23). The intrapatient difference in the number of coughs during PEP+FET and PD+FET was 1 (0 to 13). The number of productive coughs during this period was significantly larger (p<0.05) during PEP+FET 13.5 (5 to 23) and PD+FET 11.5 (8 to 21).
than during control 0 (0 to 5). The number of coughs during PD + FET and PEP + FET sessions did not differ significantly from each other. The number of nonproductive coughs was not significantly different during PEP + FET 0.5 (0 to 5), PD + FET 2 (0 to 9), and control 0.5 (0 to 3) sessions (0 to 30 minutes).

In the period 31 to 180 minutes, the number of productive coughs was not significantly different after PEP + FET 2 (0 to 7), PD + FET 2 (0 to 7), and control 4.5 (0 to 27), nor was the number of nonproductive coughs significantly different after PEP + FET 4.5 (0 to 34), PD + FET 4 (0 to 41) and controls 3.5 (0 to 19).

Weight of sputum expectorated (in gram) during the period 0 to 30 minutes was significantly larger (p<0.01) with PEP + FET 8.6 (3.5 to 19.9) and PD + FET 8.0 (2.3 to 13.9) compared with control 0 (0 to 2.1). Similarly, sputum content of $^{99m}$Tc (in MBq) was significantly larger (p<0.01) with PEP + FET 1.2 (0.1 to 5.6) and PD + FET 1.0 (0.6 to 3.7) compared with control 0.0 (0.0 to 2.1). In neither of these indices was any difference between PEP + FET and PD + FET treatments observed.

During the period 31 to 180 minutes, no significant differences were found in sputum weight after PEP + FET 2.2 (0.0 to 9.4), PD + FET 1.8 (0.0 to 7.4), and control 2.1 (0.0 to 7.3), or in sputum content of $^{99m}$Tc after PEP + FET 0.1 (0.0 to 1.2), PD + FET 0.1 (0.0 to 0.3), and control 0.3 (0.0 to 7.3).

All correlation coefficients seen in Table 5 among sputum measurements, cough, and whole lung tracheobronchial clearance, after pooling all 0- to 30-minute periods (n = 30), were significant (Spearman rank correlation test between two variables). The $^{99m}$Tc content of sputum ($r = 0.757, p<0.0001$) correlated better to tracheobronchial clearance than did the sputum weight ($r = 0.387, p<0.05$).

**Urine content**

The $^{99m}$Tc content in the 24-hour urine sample in five of the subjects (No. 2, 4 to 6, and 9) was on the control day in median 0.82 MBq (0.38 to 1.93). The value corresponds to approximately 7.0 percent (5.6 to 15.4) of the initial deposited radioactivity. In two healthy control subjects, the corresponding values were similar, namely 0.52 MBq and 7.0 percent.

**DISCUSSION**

This study shows that mucus from the airways of patients with cystic fibrosis is cleared significantly faster with 20 minutes of PD + FET and PEP + FET than without treatment. No statistical differences between the effects of PEP + FET and PD + FET regimens were observed.

The most pronounced effect of the physiotherapy was seen immediately after the treatment. At 30 minutes, approximately four to five times more radioactivity was cleared from the whole lung after PD + FET and PEP + FET than after control. However, only PEP + FET increased clearance over control at 3 h, and at the end of the examination pulmonary retention was only slightly smaller (approximately 1.4 times) after PEP + FET than at the control study. This indicates that the physiotherapy regimens, which included cough maneuvers, in our patients were effective, but that the patients themselves were able to catch up by spontaneous mucociliary clearance and coughing when no treatment was applied. Unfortunately, previous studies demonstrating increased radioaerosol clearance by chest physiotherapy have included shorter posttreatment periods than the present study, if any at all.

**Regional Clearance**

Both treatments resulted in a substantial immediate improvement in central region mucus clearance (eg, at 30 minutes, 10 to 20 times more mucus was cleared than after control). Mucus clearance in the peripheral regions was also accelerated by the treatments. This improvement, however, was smaller and not significant until 1 h after the start of treatments.

The principle of PD is gravity-assisted drainage of secretions from different lung areas. It has been shown that PD with allowed additional coughing may increase tracheal mucus transport rates in patients with cystic fibrosis but not in healthy subjects. In addition, it has been suggested to include so-called thoracic expansion exercises to further enhance the removal of secretions. We found that thoracic expansion exercises and PD resulted in a mucus clearance from the lower lobe that was similar to the mucus clearance caused by tidal breathing with PEP in the upright position when both regimens were supplements to FET. In other radioaerosol studies, an additional effect of PD11,15,17,18 on radio labeled mucus clearance has not been conspicuous compared with directed huffing and coughing alone.

Application of PEP improves airways' patency and promotes airflow to obstructed airways and may thus...
enhance clearance of mucus from such regions. Beneficial effects of PEP on peripheral airway obstruction in cystic fibrosis has been inferred from the demonstration of improvements in $O_2$-tension, and intrapulmonary ventilation and reduction of volume of trapped gas. Yet, no difference between the effects of PEP + FET and PD + FET on mucus clearance from peripheral lung zones could be observed in the present study. A number of factors, however, hamper a straightforward comparison of mucus clearance from different regions of interest. The lung is three dimensional, but acquisition with a gamma camera is two dimensional and is inherently heavily influenced by tissue attenuation of the gamma rays. Moreover, mucus retention in the central region depends on the mucus clearance away from this region and the mucus supply from more peripheral regions. Peripheral regions of interest as seen by the gamma camera not only contain peripheral airways and alveoli (approximately 50 percent of alveoli) but also a considerable number of relatively large subsegmental bronchi, whereas central regions of interest not only include large central airways but also bronchioli and alveolar regions (approximately 13 percent of alveoli). Therefore, to contend that central airway and peripheral airway clearance can be measured by defining central and peripheral regions of interest must remain an arbitrary approximation.

**Cough**

It has been reported that PEP + FET administered four times a day may result in less sputum expectorated than PD + FET treatment in patients with cystic fibrosis, but that the effect on oxygen saturation or lung function tests is the same. In a radioaerosol study, 30 minutes of PD + FET was found to be superior to 20 minutes of PEP + FET treatment in patients with chronic bronchitis. Unfortunately, in neither of these two studies was the number of cough maneuvers reported. It is therefore unknown whether some of the difference in the effects of the regimens reported in these studies could be attributed to differences in numbers of coughs included in the regimens. It has been demonstrated earlier that cough improves the clearance of radioaerosol and sputum yield in patients with mucus hypersecretion. It was not the objective of this study to selectively look at the effect of cough, but still a standardized number of coughs was part of both physiotherapy regimens. In the present study, we found similar effects of PD and PEP on mucus clearance when accompanied by similar numbers of huff and cough maneuvers. The relationship observed between the number of coughs and tracheobronchial clearance or sputum weight was also the same. In fact, coughing accounted for 42 percent (the determination coefficient = $r^2 = 0.649$) of the variation in tracheobronchial clearance, and for 57 percent ($r^2 = 0.756$) of the variation observed in sputum weight. Moreover, a similar improvement in mucus clearance was observed after 20 minutes of either treatment in the patients with chronic bronchitis.

**Sputum Measurements**

The measurement of expectorated sputum weight accounted for only 15 percent ($r^2 = 0.387$) of the variation in externally detected radioactivity clearance from the lung, whereas the radioactivity content in the same sputum samples accounted for 57 percent ($r^2 = 0.757$) of the variation in tracheobronchial clearance. A similar weak correlation between sputum weight and lung radioaerosol clearance has previously been found in patients with chronic bronchitis. Other studies have been unable to find any correlation between these indices. In fact, discrepancy between results of sputum measurements and radioaerosol clearance has been the common finding in chest physiotherapy studies.

Drying of sputum to measure the dry macromolecular weight does not seem to improve the information obtained by assessing the wet weight of sputum, which might be influenced by the mixing of saliva. Mucus is transported from the bronchial airways by mucociliary clearance, spontaneous coughs, directed huffs, and coughs. Subsequently, it is either expectorated or swallowed.

Our results therefore substantiate the general view that measurements of sputum collected during and following treatments is no reliable index of the mucus clearing effects of treatments. Radioaerosol techniques should be preferred. The 24-hour urine content of $^{99m}$Tc was small. This indicates that the blood uptake of $^{99m}$Tc from the lung and/or from the gastrointestinal tract after the $^{99m}$Tc-albumin had been transported by mucociliary clearance was small. In an earlier study, the relative contributions to total blood uptake were found to be 3 percent of initial pulmonary retention absorbed from the lung and 14 percent of initial extrapolunary retention absorbed from the gastro- intestinal tract. Thus, externally detected transport of $^{99m}$Tc-albumin from the lung is an index of tracheobronchial clearance of the patients with cystic fibrosis and not of pulmonary absorption of $^{99m}$Tc-albumin. Pulmonary absorption of $^{99m}$Tc-albumin, which at most accounted for 7 percent of lung radioactivity clearance during 24 hours, may be caused by transepithelial $^{99m}$Tc-albumin transport, but enzymatic breakdown of $^{99m}$Tc-albumin can not be excluded.

We conclude that PEP or PD measured under similar circumstances in this study were equally effective. The total or overall benefits of these physiotherapy techniques on lung clearance, however, can-
not solely be answered. This is partially because of a statistically significant increase in numbers of productive coughs during and after PEP and PD for the first 30 minutes compared with the control experiment. This was the observation period where the most significant changes occurred.

To study the short-term effects of chest physiotherapy on airway clearance, radioaerosol techniques are preferable to simple indices such as weight of sputum expectorated.

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