Resting Energy Expenditure*
Evolution During Antibiotic Treatment for Pulmonary Exacerbation in Cystic Fibrosis

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Study objectives: To compare the changes in resting energy expenditure (REE) to concomitant changes in clinical status and pulmonary function in cystic fibrosis (CF) patients during treatment for acute pulmonary exacerbation. To determine if weight loss during exacerbation in CF is related to decreased calorie intake or increased energy needs.

Design: Measurements of REE, pulmonary function tests, oxygen saturation, respiratory rate, maximal inspiratory pressure (MIP), white blood cell count, chest x-ray films and attribution of clinical score (ACS) on admission, mid-hospitalization, and discharge. Anthropometric measurements on admission, assessment of dietary intake and nitrogen balance upon admission and prior to discharge.

Subjects: Thirteen CF patients admitted for treatment of acute pulmonary exacerbation with a mean age of 11.0 ± 7.9 (SD) years.

Results: From admission to discharge, REE decreased from 44.5 ± 9.0 to 33.8 ± 8.5 kilocalorie (kcal)/kg/d (p<0.003). Similarly, the ACS improved from 7.5 ± 2.0 to 4.0 ± 3.2 (p<0.0001); the absolute neutrophil count decreased from 10,685 ± 6,226 /µl to 6,363 ± 3,168 /µl (p<0.005); respiratory rate decreased from 32.6 ± 6.2 to 25.0 ± 3.7 breaths per minute (p<0.01); and MIP increased from 77.5 ± 20.0 to 90.0 ± 20.4 cm H₂O (p<0.01). In parallel, less significant improvements occurred in pulmonary function tests, oxygen saturation and chest x-ray film scores. Calorie intake was 1,893 ± 635 and 2,054 ± 707 kcal/d on admission and discharge, respectively (p = NS); during hospitalization, weight increased from 23.6 ± 10.1 to 25.7 ± 10.1 kg (p<0.005).

While carbohydrate and fat content of the diet remained essentially unchanged, a significant increase in protein intake (3.15 ± 0.92 to 3.5 ± 0.81 g/kg/d [p<0.05]) and in nitrogen balance (1.8 ± 2.5 to 5.6 ± 2.9 g of nitrogen per day [p<0.05]) were observed.

Conclusions: In acute CF, pulmonary exacerbation, changes in REE parallel those of clinical improvements and are more sensitive than pulmonary function tests and chest x-ray films as an objective clinical correlate. Increased metabolic requirements but not decreased dietary intake are the cause of weight loss in CF patients.

(CHEST 1993; 103:1819-25)

Resting energy expenditure (REE) has been shown to be elevated in patients with cystic fibrosis (CF).1-7 It has been postulated that this increase is due not only to the higher energy cost of breathing seen in patients with chronic airflow limitation, but also secondary to wasted ventilation caused by increased dead space. The increased heat dissipation from the patients' poorly insulated body also may play a role. Malnourished patients with COPD have higher REE and diet-induced thermogenesis, especially when fed a carbohydrate-rich diet.1 The higher respiratory quotient (RQ) observed in stable CF patients may well be due in part to the fact that most have steatorrhea and consequently their dietary energy is derived primarily from carbohydrate sources.1 Recently, elevated REE has been shown to be associated with deteriorating pulmonary function rather than with the ΔF508 gene CF mutation.8 The use of inhaled bronchodilators, such as albuterol, has been postulated as another contributory factor to the increased REE observed in CF.9

Weight loss, anorexia, and worsened pulmonary function with increased work of breathing are all observed during pulmonary exacerbations in CF patients. The relative contribution of these factors to the already elevated REE in these patients is unknown. Moreover, the evolution of REE during treatment for an acute pulmonary exacerbation has not been documented.

We hypothesized that in CF patients, REE is affected not only by pulmonary factors, but rather

ACS = acute clinical score; ANC = absolute neutrophil count; CF = cystic fibrosis; MIP = maximal inspiratory pressure; REE = resting energy expenditure; RR = respiratory rate; RV = residual volume; RQ = respiratory quotient

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Manuscript received July 7; revision accepted October 12.
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CHEST / 103 / 6 / JUNE, 1993 1819
reflects a more generalized measure of metabolic efficiency. Furthermore, the serial determination of REE could be a potentially helpful tool in the evaluation and follow-up of these patients.

We performed the present study in order to establish the change in REE occurring during the treatment of a pulmonary exacerbation in CF patients and compare the changes of concomitant clinical, radiologic, and laboratory criteria with measured REE. We were also interested in assessing changes in dietary and caloric intake in these patients during the same time. The aim was to determine whether the usually observed weight gain associated with treatment of a pulmonary exacerbation was due to increased caloric intake, to decreased metabolic requirements, or to both.

**Methods**

**Patients**

Patients with CF admitted to Children's Hospital Los Angeles with the diagnosis of pulmonary exacerbation were considered eligible for the study. Patients were excluded if they were oxygen-dependent, had associated conditions such as pneumonia, diabetes, and hemoptysis, or were receiving corticosteroids or oral bronchodilators. After the ethics institutional committee approval, informed consent from the patient or from the legal guardian, if the subject was not of legal age, was obtained.

**Clinical Data**

The diagnosis of CF was based on characteristic clinical features and two positive pilocarpine iontophoresis sweat tests. A pulmonary exacerbation was defined as an increase in cough, sputum production, shortness of breath, and weight loss that was unresponsive to standard outpatient therapy including oral or aerosolized antibiotics, or both, increased frequency of chest physical, and aerosolized bronchodilator therapy. All CF inpatients were treated with a combination of intravenous antibiotics according to previous sputum cultures. Antibiotic treatment was modified if necessary, after results of sputum culture done at the time of admission became available. Intensive chest physiotherapy, inhaled bronchodilator treatment, oral pancreatic enzyme, and vitamin supplements were administered routinely. Patients ate ad libitum, an unrestricted diet, and no nutritional support, such as total parenteral nutrition or nasogastric enteral feeds, was instituted. Although the results of all tests performed were readily available, decisions regarding a patient's discharge or clinical management were made by the primary attending physician based on clinical, radiologic, and laboratory criteria and without interference from the investigators.

Evaluation upon admission included history, physical examination, chest x-ray films, sputum culture, and assessment of the severity of the patient's condition using the acute clinical score (ACS) of Jewett et al. In brief, scores from 0 to 3 points were assigned to the degree of cough, intercostal retractions, oxygen saturation, respiratory rate (RR), hemoptysis, fever, and abnormal lung sounds so that the maximal, and therefore, the most severe score would be 21 points. The ACS was always assessed by the same investigator (D. G.). In addition, clinical scoring of patients' baseline disease severity was performed using the NIH scoring system as noted by Taussig et al. Leukocyte count and differential serum concentrations of albumin and total protein also were measured.

**Radiologic Score**

Scoring of weekly chest x-ray films were performed by one of us (R. C. G.) using the scoring system put forth by Brasfield et al. This investigator was blinded to the clinical status and other laboratory data of the patients.

**Pulmonary Function Tests**

Pulmonary function tests (PFT) were performed by patients who were able to accomplish maximal expiratory maneuvers. These tests were carried out upon admission, and every week thereafter until discharge.

Tests were performed in the pulmonary function laboratory of Children's Hospital Los Angeles, located at sea level (mean atmospheric pressure, 751 mm Hg). The vital capacity and its subdivisions were measured from a slow exhalation with a wedge spirometer (model 3000, Medscience, St. Louis). Forced vital capacity, FEV₁, mean forced expiratory flow during the middle half of forced vital capacity and maximal expiratory flow volume curves were obtained from forced expiration into the wedge spirometer. Functional residual capacity was measured with a body pressure plethysmograph (SensorMedics 2900 Autobox, Yorba Linda, Calif) by the method of Dubois et al. Individual test results were analyzed and considered abnormal if they were greater than ± 2 SD from available reference values appropriate for age, height, and gender.

Maximal inspiratory pressure (MIP) as a measure of ventilatory muscle strength was measured weekly, using a modified version of the technique described by Black and Hyatt and Nickerson and Keens. In brief, all measurements were done with the subject seated, wearing nose clips. A rubber stopper was used with both a 6-mm hole and a 14-gauge needle through it, placed in the inspiratory port of a two-way Hans-Budolph valve. The subject inspired to total lung capacity and performed a slow exhalation to residual volume (RV). Maximal inspiration was then achieved while the 6-mm hole was occluded. The MIP was measured at least 20 times, and the three highest values had to be within 5 percent of each other to ensure a true maximal value.

The RR rate and oxygen saturation by pulse oximetry (Nellcor 100, Nellcor Inc, Hayward, Calif) were assessed on each occasion prior to REE measurements while patients were breathing room air.

**Resting Energy Expenditure**

Resting energy expenditure was measured within 24 h of admission and weekly thereafter, until discharge. Measurements were always performed between 7:00 and 8:00 a.m., before breakfast, and prior to administration of any medications or bronchodilator inhalations. Measurements were performed with patients awake at least 30 min prior to testing. Subjects were lying comfortably in bed and watching television through a clear Plexiglas hood. Patients were not allowed to fall asleep during the study.

Oxygen consumption was measured using indirect calorimetry by a flow-through system similar to that described by Lister and colleagues. The circuit consists of an open Plexiglas hood connected by ventilator tubing to a mixing chamber in the 2900 Horizon System Metabolic Measurement Cart (SensorMedics Corporation, Yorba Linda, Calif). Room air is gently suctioned through the hood by a vacuum pump via a dry-gas flowmeter, and samples of mixed expired air are analyzed for O₂ and CO₂ analyzers. Oxygen consumption, carbon dioxide production, and RQ are calculated, and resting metabolic expenditure is then derived using the equations described by Weir and expressed as kilocalories per day, kilocalories per kilogram per day, and kilocalories per kilogram of lean body mass.

In general, at least 30 min of continuous steady state sampling were performed and results averaged. The quality and consistency of recording were assessed by means of a graphic display. Only values within 5 percent of the calculated average were retained for final analysis.
**Table 1—Mean Results of Pulmonary Function Tests, Maximal Inspiratory Pressure, and Chest X-ray Film Scores in 13 Cystic Fibrosis Patients on Admission, Mid-hospitalization and Discharge**

<table>
<thead>
<tr>
<th>Parameter†</th>
<th>Admission</th>
<th>Mid-hospitalization</th>
<th>Discharge</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>32.6 ± 6.2</td>
<td>28.5 ± 4.6</td>
<td>25.0 ± 3.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>89.5 ± 3.7</td>
<td>93.1 ± 2.7</td>
<td>94.4 ± 3.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total lung capacity, % predicted</td>
<td>125.4 ± 26.1</td>
<td>116.4 ± 26.4</td>
<td>114.6 ± 23.2</td>
<td>NS</td>
</tr>
<tr>
<td>RV, % predicted</td>
<td>341.6 ± 97.6</td>
<td>323.9 ± 119.8</td>
<td>290.1 ± 116.8</td>
<td>NS</td>
</tr>
<tr>
<td>Vital capacity, % predicted</td>
<td>55.3 ± 15.6</td>
<td>55.7 ± 10.1</td>
<td>56.8 ± 12.7</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>38.9 ± 12.7</td>
<td>39.9 ± 10.9</td>
<td>40.4 ± 12.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean forced expiratory flow during middle half of forced vital capacity, % predicted</td>
<td>18.9 ± 7.4</td>
<td>18.4 ± 12.5</td>
<td>18.8 ± 13.7</td>
<td>NS</td>
</tr>
<tr>
<td>MIP, cm H₂O</td>
<td>77.5 ± 20.0</td>
<td>84.9 ± 33.3</td>
<td>90.0 ± 20.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chest x-ray film score</td>
<td>16.7 ± 3.6</td>
<td>17.2 ± 2.9</td>
<td>16.4 ± 3.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± SD. p value shown for A versus D.
†Pulmonary function test results relate to ten patients only.

**Nutritional Assessment**

A full nutritional assessment consisting of anthropometric measurements and calculation of lean body mass and percentage of body fat was performed on admission. Anthropometry included the triceps, biceps, anterior superior iliac and subcapular skin folds, midarm circumference, height, and weight. Lean body mass and percentage of body fat were derived from standard equations.

The daily food intakes were recorded and the average nutrient intake of the three days immediately following admission and prior to discharge was assessed. Protein, carbohydrate, and fat intakes were derived from the dietary records using a nutritional software package (Nutripractor 6000, Practorcare Inc, San Diego, Cal). Nitrogen balance was determined from analysis of a 24-h urine collection for urine urea nitrogen on the days of admission and discharge.

**Data Analysis**

Data were expressed as mean ± SD. For each measured parameter, changes occurring during the course of treatment were compared by the paired Student’s t test. Separate one-way (group) × two-way (ACS corresponding to mid-hospitalization and at discharge) analyses of variance with repeated measures were applied to the data. Dependent variables entered included all studied parameters. An alpha level of 0.05 was employed to determine the significance of F ratios. Tukey’s post hoc procedure was used to test significant mean differences.

Data were also expressed as percentage change between each two measurements, in order to compare changes occurring between different parameters. The mean percentage changes thus obtained were compared by the Wilcoxon signed rank sum test. A probability value of less than 0.05 was considered to reach statistical significance.

**Results**

Thirteen CF inpatients admitted for pulmonary exacerbation completed the study. Their mean age was 11.0 ± 7.9 (SD) years, ranging from 2 to 26 years. Ten were females, and their mean NIH score was 55.0 ± 17.3 (n = 10). Hospital stay averaged 14.7 ± 2.1 days. The mean ACS upon admission was 7.5 ± 2.0, which decreased by mid-hospitalization to 5.7 ± 2.1 (p < 0.0001), and further improved by discharge (4.0 ± 2.2 [p < 0.0001]).

**Figure 1.** Admission (A) to discharge (D) percent changes in ACS, REE, ANC, RR, oxygen saturation (SaO₂), MIP values, and pulmonary function tests in 13 CF patients treated for acute pulmonary exacerbation.
Table 2—Changes in Weight and Resting Energy Expenditure in 13 Cystic Fibrosis Patients Undergoing Treatment for Pulmonary Exacerbation on Admission, Mid-hospitalization, and Discharge*

<table>
<thead>
<tr>
<th>Clinical Data</th>
<th>Admission</th>
<th>Mid-hospitalization</th>
<th>Discharge</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>23.6 ± 10.1</td>
<td>24.0 ± 10.1</td>
<td>25.7 ± 10.0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>REE, kcal/d</td>
<td>994 ± 311</td>
<td>895 ± 272</td>
<td>801 ± 244</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>REE/kg body weight, kcal/kg/d</td>
<td>44.5 ± 9.0</td>
<td>40.1 ± 10.8</td>
<td>33.8 ± 8.5</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>REE/kg lean body mass, kcal/kg/d</td>
<td>51.8 ± 10.1</td>
<td>47.2 ± 12.2</td>
<td>41.0 ± 9.6</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± SD; p value shown for admission versus discharge.

The absolute neutrophil count (ANC) decreased from 10,685 ± 6,226 /μl on admission to 6,363 ± 3,168 /μl (p<0.01), and decreased further to 5,487 ± 2,730 /μl from admission to discharge (p<0.005). No significant changes in serum protein and albumin concentrations were observed.

Chest x-ray film scores (Brasfield et al9) did not change significantly throughout the hospitalization in all patients (Table 1). Serial PFT measurements in ten of our patients showed significant improvements in some of the measured parameters (Table 1). The MIP percent changes from admission to discharge were significantly greater than for any other PFT (Fig 1). Correction of MIP values for hyperinflation was calculated by normalizing MIP for both RV and the ratio of RV to total lung capacity. The corrected mean MIP values showed no significant change from admission to discharge.

The evolution of measured REE throughout the hospitalization showed a significant decrease from 44.5 ± 9.0 kilocalories (kcal)/kg/d on admission to 33.8 ± 8.5 kcal/kg/d on discharge (Fig 1 and Table 2 [p<0.003]). Total REE and REE/per kilogram of lean body mass per day evolved similarly (Table 2). Mean RQ was 0.98 ± 0.04 and no significant changes in RQ were observed throughout hospitalization. A significant coefficient of correlation was found between the percentage change of REE from admission to discharge and percentage of body fat calculated from anthropometric measurements (r = -0.65; p<0.05).

The percentage changes from admission to discharge are shown for most measured parameters in Figure 1. Similar changes occurred in ACS and in ANC, RR, MIP, and REE, which were all significantly greater than those measured for other PFT, chest x-ray film scores, and SaO₂ oxygen saturation (p<0.01).

Nutritional Assessment

On admission, body weight and percentage of ideal body weight were 23.6 ± 10.1 kg and 87.6 ± 9.9 percent, respectively. Percentage of body fat was 14.4 ± 4.8 percent. Body weight increased to 25.7 ± 10.1 kg upon discharge (Table 2; p<0.005). Percentage of body fat and ideal body weight remained essentially unchanged for the duration of the hospital stay.

Caloric intake on admission was 1,893 ± 635 kcal/d and on discharge, 2,054 ± 707 kcal/d (Table 3 [p = NS]). These represent 85.2 ± 21.6 kcal/kg/d and 89.6 ± 15.6 kcal/kg/d on admission and discharge, respectively (p = NS). The daily energy intake-REE ratio increased, however, from 1.83 ± 0.21 on admission to 2.53 ± 0.37 (p<0.02), indicating a significant increase in net energy intake. The relative composition of the mean dietary intakes is shown in Table 3. Fat constituted 30.4 ± 5.9 and 30.9 ± 6.1 percent of total calorie intake on admission and prior to discharge (p = NS). Similarly, carbohydrates accounted for 55.7 ± 6.4 and 54.9 ± 7.9 percent of total calorie intake, respectively (p = NS). In contrast, protein intake increased from 14.8 ± 2.3 percent on admission to 15.7 ± 1.9 percent at the time of discharge (Table 3 [p<0.05]). In parallel, nitrogen balance increased from 1.8 ± 2.5 g of nitrogen per day on admission to 5.6 ± 2.9 g of nitrogen per day at the time of discharge (Table 3 [p<0.05]).

Discussion

In the present study, significant changes in REE were observed in CF patients during hospital treatment of an acute pulmonary exacerbation. These changes coincided with clinical improvement assessed by a clinical score, demonstrating that pulmonary infection is associated with a significant elevation in metabolic requirements in CF.

In our working hypothesis, we assumed that the evolution of REE during treatment reflected changes occurring in the degree of infection as well as in respiratory mechanics. Buchdahl et al² showed that REE was elevated in CF patients and found a weak correlation between energy expenditure and total white blood cell count. These investigators suggested that some degree of subclinical infection may play a role in the elevation of REE in CF. In the present study, infection was gradually controlled by appropriate intravenous antibiotic therapy, and therefore, the parallel changes in ANC and REE observed in our

Table 3—Mean Dietary Intake in 13 Cystic Fibrosis Patients on Admission and at Discharge

<table>
<thead>
<tr>
<th>Dietary Intake</th>
<th>Admission</th>
<th>Discharge</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Kcal/d</td>
<td>1,893 ± 635</td>
<td>2,054 ± 707</td>
<td>NS</td>
</tr>
<tr>
<td>Protein, g/kg/d</td>
<td>3.15 ± 0.92</td>
<td>3.5 ± 0.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Carbohydrate, g/kg/d</td>
<td>11.85 ± 3.21</td>
<td>12.20 ± 2.17</td>
<td>NS</td>
</tr>
<tr>
<td>Fat, g/kg/d</td>
<td>2.9 ± 0.95</td>
<td>3.11 ± 0.90</td>
<td>NS</td>
</tr>
<tr>
<td>Nitrogen balance, g/d</td>
<td>1.8 ± 2.5</td>
<td>5.6 ± 2.9</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
study suggest that the correlation between these two measurements may be more than coincidental. Of note, none of our patients was febrile at the time of the study, since pyrexia, which has been shown to increase REE, could have a confounding effect.\textsuperscript{23,24}

We cannot ascribe \textit{a priori} all the changes in REE to infection alone, since a similarly weak correlation coefficient between REE and the ratio of FEV\textsubscript{1} to forced vital capacity was found by Buchdahl and colleagues\textsuperscript{10} in stable CF patients. The existence of this correlation on stable CF patients also has been reported by other investigators, suggesting that decreased pulmonary function and the resulting increase in work of breathing may play a significant role in the elevated REE found in clinically stable CF patients.\textsuperscript{3,5} Although significant improvement in spirometric measurements was seen with treatment, the magnitude of changes occurring in pulmonary mechanics was significantly lower than that observed in REE, as well as that of ACS and ANC. The changes in PFT in our patients were similar, however, to those reported in 17 hospitalized CF patients serially measured while undergoing treatment.\textsuperscript{8} Thus, if lung function was the major determinant of REE changes, we would expect to observe changes in REE similar to those measured in PFT. This was not the case. Therefore, the contribution of lung function to REE changes and clinical improvement during an acute pulmonary exacerbation does not appear to be of major significance. In another study of serial PFT measurements in CF patients during an acute exacerbation, we have shown that changes occurring in distribution of ventilation rather than those in lung volumes or flows are most sensitive to clinical improvement.\textsuperscript{56} In addition, the changes observed in RR in this study were similar to those occurring in REE and were significantly greater than the changes in PFT, suggesting that the degree of dead space ventilation may have been reduced with clinical improvement and may have resulted from both decreased metabolic requirements and improved homogeneity of ventilation. In summary, the role of pulmonary mechanics in REE deserves further investigation.

In this study, less marked changes in REE were observed in those patients with more severe malnutrition expressed as percentage of body fat, indicating that impaired nutritional state is associated with smaller metabolic increments during infection. The eventuality of an adaptive mechanism has been proposed, whereby with increasing malnutrition, energy-sparing processes could become operative or reflect lower metabolic and immune responses to infection.\textsuperscript{27}

Respiratory muscle strength may be decreased, normal, or even increased in CF patients with malnutrition or severe lung disease or both.\textsuperscript{30-31} However, Lands and colleagues\textsuperscript{30} showed that MIP values were within normal range, even in severely affected patients when measured MIP were corrected for volume. These investigators also demonstrated that while nutritional status affected MIP, it was not to a clinically significant degree. In some contradiction to these findings, long-term nutritional rehabilitation improved MIP without significantly affecting pulmonary function.\textsuperscript{22} At the time of discharge, the MIP measurements in our patients were similar to those obtained by other investigators.\textsuperscript{23-32} Since the percentage of change in MIP was comparable to ACS and significantly greater than that occurring in PFT in general, it would appear that factors other than respiratory mechanics affect MIP during an acute exacerbation.

However, when we corrected MIP values for the degree of hyperinflation, no significant change in MIP was present from admission to discharge. Therefore, while no significant changes in intrinsic respiratory muscle strength (MIP corrected for RV) are to be expected during management of acute pulmonary exacerbation, the uncorrected MIP offers the potential of being a more accurate clinical correlate than any other measured PFT.

It is currently believed that weight loss observed during acute pulmonary exacerbations is due to decreased oral feedings associated with poor appetite, so that the overall intake may be reduced to 80 to 90 percent of the recommended energy intake.\textsuperscript{24} In the present study, a decrease in metabolic requirements and not an increase in nutritional intake seemed to be the source of weight loss during treatment for CF exacerbations. Our results concur with those found in adult patients with emphysema, in whom weight loss was related to heightened energy demands.\textsuperscript{26} In spite of increased energy needs associated with acute infection, no significant changes in total daily calorie intake were found between admission and discharge in our patients, suggesting that they were unable to respond adequately with increased intake to the higher metabolic requirements induced by the acute pulmonary exacerbation. Similar findings recently have been reported in adult patients with COPD in whom the combination of inadequate dietary intake for energy expenditure and failure of an adaptive response to undernutrition were found as contributing factors for weight loss.\textsuperscript{36} Therefore, CF patients appear to have already maximized their compensatory capacity to increase dietary intake voluntarily. The decrease in REE observed with the improvement in clinical status induced a significant change in intake-REE ratios and in parallel reversal of the catabolic state. The reasons, however, for such significant increase in weight from admission to discharge, as found in our patients, are unclear. The decrease in REE alone could have accounted for an average weight gain of 0.5 kg in the two-week period, since calorie intake was essentially
unchanged during this time interval. We postulate that improved tissue oxygenation may have had a beneficial effect on nutrient utilization. Furthermore, clinical improvement with decreased infective load may have resulted in a decrease in severity of the malabsorptive state. In support of this assumption, although fecal fat losses were not measured, patients verbally reported fewer gastrointestinal symptoms. Further studies are required, however, to substantiate this hypothesis. Fluid shifts or increased fluid intake also could have played a significant role in weight accretion. Weight gain in our patients was particularly prominent during the second week of hospitalization. The contribution of changes in net water balance to weight gain was not addressed in the present study and remains to be determined. Finally, a decrease in patient daily activity during the hospitalization cannot be overlooked.

Long-term nutritional rehabilitation with enteral or parenteral supplementation has been associated with improved well-being and slower deterioration of lung function. An elevation of REE follows, however, the restoration of body composition with this interventional therapy while no long-term measurable effects on protein turnover are seen. Even though these studies emphasize the rationale for aggressive nutritional intervention, data regarding the effect of early institution of nutritional support on REE and nutrient turnover in management of acutely decompensated CF patients are scanty. Hence, further studies to delineate the relative contribution of changes in REE, degree of malabsorption, pulmonary function, and infection to weight gain and body composition are warranted for the implementation of effective interventional nutrition regimens.

A high carbohydrate-fat ratio diet in patients with chronic lung disease is associated with elevated CO₂ production and ventilatory demand. The percentage of mean carbohydrate content in our patients' diets was high. This is in agreement with previous studies in patients with lung disease showing preferential use of carbohydrates in fuel oxidation as well as studies in CF patients in whom percentage of carbohydrate in diet increased with disease severity. The relative content of fat and carbohydrate in the diet on admission and discharge remained unchanged in our patients, and no change in RQ was observed. Therefore, although different nitrogen retention may result from varying carbohydrate-fat diet ratios, this was not the cause of improved nitrogen balance in the present study. Protein intake increased, however, with concomitant increases in nitrogen balance as well as in energy intake-REE ratios, suggesting that REE decrease could be the source of improved nitrogen utilization by improving calorie-protein ratios. In a previous study of CF patients managed for pulmonary exacerbation, protein net deposition and overall protein turnover were favorably affected by institution of immediate nutritional supplementation upon admission, although no such effect could be measured in patients fed a standard diet only. A beneficial result of energy supplementation on protein metabolism in malnourished CF patients was also reported by Pencharz et al., suggesting that acceleration of the natural course of protein balance restoration during treatment of acute exacerbation can be achieved by early institution of supplemental feedings.

In summary, we have shown that REE decreases in CF patients with pulmonary exacerbation as they improve clinically and that the degree of REE change is commensurate with that of other measurable clinical parameters such as ACS, ANC, RR, and MIP. Moreover, these parameters are more sensitive clinical correlates than PFT measurements. In addition, we have demonstrated that weight gain during management of acute pulmonary exacerbation in CF patients is related to a decrease in metabolic requirements and not associated with increased calorie intake. We speculate that serial REE measurements may provide useful information either alone, or in combination with other parameters, for improved assessment of therapeutic interventions in the short- and long-term management of CF patients. Furthermore, we assume that the observed changes in protein composition of the diet and in net calorie intake reflect compensatory mechanisms during recovery from a hypercatabolic state that is induced by the acute illness.

ACKNOWLEDGMENTS: We thank Thomas G. Keens, M.D., and Frank R. Sinatra, M.D., for their helpful suggestions. We thank Michael W. Stabile, M.S., R.P.T., and the staff of the Pulmonary Physiology Laboratory for their assistance in performing PFT.

REFERENCES
2 Katsardis CV, Desmond KJ, Coates AL. Measuring the oxygen cost of breathing in normal adults and patients with cystic fibrosis. Resp Physiol 1986; 65:257-66

Resting Energy Expenditure in CF (Nalon et al)
10 Gibson LE, Cooke RE. A test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine by iontophoresis. Pediatrics 1959; 23:545-49
23 Du Bois EF. The basal metabolism in fever. JAMA 1921; 77:352-55
28 Arora N, Rochester D. Respiratory muscle strength and maximum voluntary ventilation in undernourished patients. Am Rev Respir Dis 1982; 126:5-8