We examined the effect of physical training on cardiopulmonary function in 21 patients with chronic obstructive pulmonary disease and compared the results with similar observations in eight untrained patients. The training consisted of daily walking on a treadmill at increasing speeds and grades and other graded physical exercises. Evaluation of pulmonary function, including spirometric studies, lung volumes, and arterial blood gas levels, showed no significant change after training. Hemodynamic functions, including heart rate, cardiac index, stroke index, pulmonary vascular resistance, and arteriovenous oxygen content difference, were similarly unchanged at comparable submaximal loads. Pulmonary arterial wedge pressure increased after training in the treated group at rest and during exercise, but this may be related to changes in respiratory mechanics. Consumption of oxygen and minute ventilation decreased in the treated group during treadmill exercise, suggesting improved neuromuscular coordination and efficiency of walking on the treadmill. Total work performed on the treadmill increased significantly in the trained group. This increase was unexplained by physiologic observations but was thought to be due in part to increased efficiency of walking and increased motivation. We conclude that improvement in the capacity for exercise following physical training for four weeks is not associated with improvement in cardiopulmonary function at submaximal exercise.

Physical conditioning improves the capacity for work in normal people. Improvement in physical performance in general is related not only to increased output of energy by aerobic and anaerobic processes but also to increased motivation and neuromuscular coordination.\(^\text{15-16}\) Studies in normal people who have undergone physical training have shown an increased maximal cardiac output and arteriovenous oxygen content difference to account for the increased maximal aerobic capacity. At submaximal levels of exercise, training decreases the heart rate, corresponding to a higher stroke volume or to a lower cardiac output for the same consumption of oxygen.\(^\text{17}^{18}\) While physical conditioning improves the capacity for work in patients with chronic obstructive pulmonary disease (COPD).\(^\text{6-14}\) hemodynamic data in such patients after conditioning are scarce, and no clear-cut pattern for hemodynamic function after training has been observed.

This study was designed to examine the multiple facets that influence the results of a program of rehabilitation and exercise for patients with COPD. The results dealing with the pulmonary physiologic data and the psychologic status following the program have been reported previously.\(^\text{15,16}\) Some patients showed an improvement in work performance which was not related to pulmonary function but rather to the psychologic factors of depression and anxiety.\(^\text{15}\) This report deals mainly with the hemodynamic function of these patients before and after a four-week program of physical training. In addition, we compared the results to that of a control group of patients with COPD of comparable severity.

**Materials and Methods**

Twenty-one male patients with COPD who were partially or completely disabled due to shortness of breath were selected for this study. A control group of eight, untrained patients was also selected. They were matched for age, sex, level of disability, and duration of the disease.

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studied. The following criteria were applied in the selection of the patients: (1) the patient was disabled from dyspnea due to COPD as defined by the criteria of the American Thoracic Society;17 (2) the patients were 60 years of age or younger; (3) there were no other seriously disabling diseases, either physical or psychologic; and (4) the patients were able to exercise on a treadmill at zero grade at 2 mph for six minutes. The respective candidates were screened by an investigator, and the objectives of the program were explained to the patient and his family. A careful history and the findings from physical examination were then recorded. Routine laboratory tests, an electrocardiogram, and chest x-ray films were obtained.

Pulmonary and cardiac physiologic studies were then performed. The patients were studied by means of a 13.5-L spirometer (Collins). The forced expiratory volume in one second (FEV₁), the mean forced expiratory flow during the middle half of the forced vital capacity (maximal midexpiratory flow; FEF25-75%) the mean forced expiratory flow between 200 ml and 1,200 ml of the forced vital capacity (maximal expiratory flow rate; FEF200-1,200), and the ratio, FEV₁/FVC, were measured. The normal values for the subjects were calculated from the values of the Veterans Administration-Army cooperative study.18 Intrapulmonary gas distribution was studied by means of the single-breath oxygen test.19 The lung volumes were measured by means of the method of helium closed-circuit equilibration, and the normal values were obtained from the Veterans Administration-Army cooperative study.20 The functional residual capacity was also studied as the volume of thoracic gas in the body plethysmograph.21

The body plethysmograph was also utilized to determine the airway resistance (Raw) in the patients.22 The product of the volume of thoracic gas times the resistance was utilized for the specific resistance (SRaw).23,24 The steady-state diffusing capacity for carbon monoxide (Dss) was obtained by an end-tidal sampling method.25 Measurements of blood gas levels were obtained using the standard oxygen and carbon dioxide electrodes of a blood gas analyzer (Instrumentation Laboratory model 113).26 Expired gas was collected, and the alveolar-arterial oxygen pressure difference (P[A-a] O₂) was obtained with the patient breathing room air and 100 percent oxygen. The physiologic dead space was assessed using the Bohr equation. Blood and expired gases were collected simultaneously during the fifth and sixth minute of treadmill exercise at zero grade at 2 mph. From this the consumption of oxygen (measured in liters per minute per square meter) and the minute ventilation were calculated. In addition the ventilatory equivalent in terms of liters per minute of ventilation per liter of oxygen uptake was calculated during exercise on the treadmill.

Hemodynamic studies were performed on the patient while he was in the postabsorptive state, without premedication; administration of drugs and respiratory therapy were discontinued 12 hours earlier. Right cardiac catheterization was performed in the conventional manner, using either the right or left antecubital vein. A Cournand needle was inserted into the brachial artery. Pressures were measured using a strain-gauge pressure transducer (Statham PE23Db) and a recorder (Electronics for Medicine). Cardiac output was measured by the indicator-dilution method using indocyanine green, and the area under the curve was determined by the method of Williams et al.27 The volume of expired gas collected over a three-minute period was measured in a Tissot spirometer and was analyzed for oxygen by the Haldane method. Determinations of blood gas levels were performed as indicated previously. Arteriovenous oxygen content difference (C(a-v)O₂) was calculated by dividing the oxygen consumption by the cardiac output. The pulmonary arterial wedge pressure and the pulmonary arterial pressure, cardiac output, C(a-v)O₂, and oxygen consumption were obtained with the patient at rest. Pulmonary vascular resistance (expressed in units) was calculated as the mean pulmonary arterial pressure minus the mean pulmonary arterial wedge pressure divided by cardiac output. Supine exercise on the bicycle ergometer was then performed against external workloads of either 150 kg-m/min or 300 kg-m/min for six minutes.28 Data during exercise were obtained during the last three minutes of exercise.

After the initial assessment the control patients were discharged and readmitted four weeks later for retesting. During this time, they received no special treatment. The treated group was hospitalized throughout the period of study. Training was initiated by daily exercise on the treadmill, which was then increased in speed, grade, and duration during four weeks. During this exercise the heart rate was monitored electrocardiographically; the mean heart rate during the training on the treadmill was 125 ± 18 beats per minute. The total amount of work performed on the treadmill was quantified by means of the formula: work (in kilograms) = weight of the patient (in kilograms) × distance walked (in meters) × sin θ (θ = angle of inclination). In addition the patients also exercised with a rowing machine, a bicycle ergometer, and wall-mounted pulley weights to tolerance. This group also received daily chest physiotherapy, breathing exercises, postural drainage, and therapy with intermittent positive-pressure breathing four times daily (with administration of isoproterenol). In addition, there was an active program of psychologic and vocational rehabilitation, which has been described elsewhere.15 This program was continued for four weeks, at the end of which all of the physiologic tests done previously were repeated. Changes in measurements were analyzed by Student’s t-test for paired values. A P value of less than 0.01 was considered significant.

RESULTS

Data obtained with the patient at rest and during exercise were compared to similar data obtained after training. The results of tests of pulmonary function are available from 21 patients who underwent physical training and eight control patients. Hemodynamic data are available from 17 patients at rest and 13 during exercise, on 6 control patients at rest and four during exercise. Missing hemodynamic data are due to the fact that some patients were unable to complete six minutes of exercise during cardiac catheterization. One patient had a history compatible with coronary arterial disease. This was proved angiographically, and at this time, abnormal left ventricular function was noted; data from his catheterization are excluded from the analysis. The average age of the physically trained patients was 51 ± 6 years. The weights and levels of hemoglobin were comparable at the different stages of testing. No subjects had evidence of heart failure, and none was receiving digitalis. All subjects were cigarette smokers, although six of the 21 trained
subjects and three of the eight control subjects had stopped prior to the study.

Figures 1 and 2 illustrate the baseline ventilatory characteristics of the two groups at rest. The reduction in rates of flow is similar in both groups and is consistent with a severe obstructive ventilatory defect and hyperinflation. Patients of both groups exhibited moderate hypoxemia at rest, with normocapnia. The P(A–a)O₂ with the patient breathing air was abnormally increased.

Figure 3 shows the hemodynamic data. The cardiac index and the stroke index were within normal limits. The mean pulmonary arterial pressure and the pulmonary vascular resistance were at the upper limits of normal. These data show the two groups to be comparable with respect to the severity of the cardiopulmonary dysfunction. The results of tests of pulmonary function for the groups before and after training are summarized in Table 1. None of the measurements changed significantly in either group. In Table 2 the results of the arterial blood gas analyses, including the P(A–a)O₂ with the patients breathing air and 100 percent oxygen, are noted. These values also showed no significant change in both the physically trained and untrained

**Figure 1.** Baseline data on pulmonary function in physically trained (solid circles) and control (open circles) subjects with COPD. Shaded areas represent predicted normal values. MVV, Maximal voluntary ventilation; and RV/TLC%, ratio of residual volume to total lung capacity, expressed as percent.

**Figure 2.** Baseline data on blood gas levels for physically trained (solid circles) and control (open circles) subjects with COPD. Shaded areas represent predicted normal values. PaCO₂, Partial pressure of carbon dioxide in arterial blood.

**Figure 3.** Baseline hemodynamic data for physically trained (solid circles) and control (open circles) subjects with COPD. Shaded areas represent predicted normal values. SI, Stroke index; CI, cardiac index; PVR, pulmonary vascular resistance; PAW, mean pulmonary arterial wedge pressure; and PA, mean pulmonary arterial pressure.
Table 1—Pulmonary Function before and after Physical Training in 21 Patients with COPD and in Eight Untrained Control Subjects with COPD*

<table>
<thead>
<tr>
<th>Data</th>
<th>Physical Training</th>
<th>Untrained Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>FEV1, L/sec</td>
<td>1.31 ± 0.57</td>
<td>1.24 ± 0.64</td>
</tr>
<tr>
<td>FEF25-75%, L/sec</td>
<td>1.74 ± 1.27</td>
<td>1.59 ± 1.26</td>
</tr>
<tr>
<td>Maximal voluntary ventilation, L/min</td>
<td>58 ± 24</td>
<td>56 ± 25</td>
</tr>
<tr>
<td>Residual volume, L</td>
<td>4.37 ± 1.20</td>
<td>4.57 ± 1.92</td>
</tr>
<tr>
<td>DS, ml/min/mm Hg</td>
<td>13.6 ± 3.6**</td>
<td>12.7 ± 3.4**</td>
</tr>
<tr>
<td>Raw, cm H2O/L/sec</td>
<td>3.70 ± 1.05</td>
<td>3.96 ± 0.98</td>
</tr>
<tr>
<td>Volume of thoracic gas, L</td>
<td>5.75 ± 1.75</td>
<td>5.84 ± 1.70</td>
</tr>
<tr>
<td>SRaw, sec cm H2O</td>
<td>21.6 ± 10.4</td>
<td>23.5 ± 11.2</td>
</tr>
<tr>
<td>Ratio of dead space to tidal volume</td>
<td>0.41 ± 0.07†</td>
<td>0.42 ± 0.08‡</td>
</tr>
</tbody>
</table>

*Table values are means ± SD. **n = 19. †n = 6.

Figure 5 summarizes the oxygen consumption and minute ventilation for the physically trained group during exercise on the bicycle and on the treadmill. While there was no significant change in oxygen consumption and minute ventilation during exercise on the bicycle, it can be seen that the consumption of oxygen decreased from 447 ± 72 ml/min/sq m to 401 ± 56 ml/min/sq m (P<0.01) and that the minute ventilation during exercise on the treadmill decreased from 29.8 ± 6 L/min to 26.1 ± 5 L/min (P<0.01). In contrast, the oxygen consumption and minute ventilation of the control group did not change significantly during exercise on the bicycle or treadmill. The ventilatory equivalent was unchanged in both groups with both methods of exercise.

The quantity of treadmill work performed by the physically trained group was measured at the beginning and end of the program. The total work

Table 2—Arterial Blood Gas Levels before and after Physical Training in Patients with COPD and in Control Subjects with COPD*

<table>
<thead>
<tr>
<th>Group and Time</th>
<th>PaO2 mm Hg</th>
<th>PaCO2 mm Hg</th>
<th>Arterial pH</th>
<th>SaO2 percent</th>
<th>P(A-a)O2 (FIO2=1.0), mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical training</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest (n=21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before training</td>
<td>66 ± 7</td>
<td>588 ± 26</td>
<td>38 ± 4</td>
<td>7.44 ± 0.03</td>
<td>92.6 ± 1.7</td>
</tr>
<tr>
<td>After training</td>
<td>67 ± 7</td>
<td>590 ± 21</td>
<td>37 ± 5</td>
<td>7.45 ± 0.03</td>
<td>92.8 ± 2.6</td>
</tr>
<tr>
<td>Exercise (n=19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before training</td>
<td>69 ± 12</td>
<td>...</td>
<td>39 ± 5</td>
<td>7.40 ± 0.03</td>
<td>91.7 ± 4.8</td>
</tr>
<tr>
<td>After training</td>
<td>68 ± 10</td>
<td>...</td>
<td>39 ± 6</td>
<td>7.40 ± 0.04</td>
<td>91.6 ± 4.4</td>
</tr>
<tr>
<td>Control group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest (n=8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>67 ± 14</td>
<td>589 ± 30</td>
<td>40 ± 5</td>
<td>7.43 ± 0.03</td>
<td>91.0 ± 4.5</td>
</tr>
<tr>
<td>After</td>
<td>64 ± 10</td>
<td>587 ± 35</td>
<td>40 ± 3</td>
<td>7.42 ± 0.02</td>
<td>91.3 ± 4.1</td>
</tr>
<tr>
<td>Exercise (n=6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>72 ± 13</td>
<td>...</td>
<td>41 ± 5</td>
<td>7.40 ± 0.02</td>
<td>92.3 ± 4.3</td>
</tr>
<tr>
<td>After</td>
<td>66 ± 10</td>
<td>...</td>
<td>42 ± 5</td>
<td>7.39 ± 0.03</td>
<td>91.2 ± 3.5</td>
</tr>
</tbody>
</table>

*Table values are means ± SD. FIO2, Fractional concentration of oxygen in inspired gas; PaCO2, partial pressure of carbon dioxide in arterial blood; and SaO2, arterial oxygen saturation.

**n = 20.
performed increased from 864 ± 805 kg-m to 4,253 ± 3,010 kg-m (P < 0.01), while the rate of work increased from 79 ± 37 kg-m/min to 192 ± 118 kg-m/min (P < 0.01). In addition the maximal heart rate that was achieved increased from 120 ± 12 to 131 ± 18 beats per minute (P < 0.01).

DISCUSSION

A program of physical conditioning in normal people improves cardiopulmonary performance. The utilization of such programs has been proposed for the rehabilitation of dyspneic patients with COPD. While the lack of improvement in standard spirometric values, lung volumes, and diffusing capacity has been well documented, only three previous studies measured hemodynamic factors and only one utilized a control group. We were unable to confirm the observation of Degre et al that physical training results in an improvement in resting oxygen tensions. We measured blood gas levels with patients at rest on two occasions in our study. On both of these occasions, no increases in arterial oxygen tension (PaO₂) were noted, which is in agreement with other authors who examined this measurement. In the absence of a true right-to-left shunt of blood, the P(A-a)O₂ is a measure of the efficiency of the transport of gases across the lung. Since this value was unchanged after training, we conclude that training has no impact on gas transport.

Woolf and Suero suggested improved matching of ventilation and perfusion as a mechanism of improved tolerance for exercise in patients with COPD; however, his group under study was small, and the results presented were not statistically significant. A decrease in the ventilatory equivalent (that is, a decrease in minute ventilation per liter of oxygen uptake) could be a result of improved matching of ventilation and perfusion. In our study, this measurement was unchanged with exercise on both bicycle and treadmill, and this is in agreement with other authors. In Lefcoe and Paterson's extensive review article on adjunctive therapy for COPD, an improvement in the ventilatory equivalent of Christie is discussed. In Christie's study the conclusion of an improved ventilatory equivalent is based on the observation that at a comparable
workload, there was a decreased minute ventilation, while the oxygen consumption remained similar. These authors did not directly examine the ratio of minute ventilation over oxygen consumption by statistical means. On reanalyzing their data, we believe that their conclusion is unfounded, since the ventilatory equivalent by a paired t-test is unchanged. Despite the general increase of work capacity, we did not see an improvement in hemodynamic variables in our patients.

A decreased heart rate and increased stroke volume for the same level of work is the hallmark of a conditioning effect following physical training. The response to a training program is determined by the frequency, duration, and intensity of effort relative to the individual's initial aerobic power. Although increases are greatest when training is done at 90 to 100 percent of the maximal heart rate, significant improvements have been noted at 50 to 70 percent of the maximal heart rate. Our treated group trained at a mean heart rate of 125 ± 18 beats per minute, which was approximately 70 percent of their maximal heart rate. The mean duration of the training on the treadmill was 15 min/day. In addition, other graded physical exercises were done so that the daily program of exercise lasted from one to two hours. Thus, a program of suboptimal training is an unlikely cause of the absent response of the heart rate. In fact, several of the previous studies of physical conditioning in patients with COPD have failed to show a decrease in heart rate after training at comparable submaximal levels of exercise. Where a change has been noted, the level of exercise after training was associated with a decreased consumption of oxygen, and, as such, the results are not comparable.

The mechanism of bradycardia occurring after physical training is obscure, but one possibility may be a decreased sympathetic drive and an increased parasympathetic drive. In addition, the decreased heart rate is related to which limbs are exercised, as shown by the fact that the effect of conditioning of leg exercises is not transferrable to the arms, and vice versa. Dynamic exercise of large groups of muscles is also a requirement for a conditioning effect on aerobic capacity. Although our physically trained subjects were exercising at high heart rates, the level of peripheral activity (that is, movement of muscular groups of the limbs) was low. Presumably, this is related to the high oxygen cost of breathing in these patients. It is conceivable that the relatively low level of peripheral activity was not sufficient to induce a bradycardiac response. If this is the case, then the severely disabled pulmonary patient may not be able, under usual circumstances, to cross the threshold of activity that would induce a conditioning effect on the heart rate.

In view of the lack of a conditioning effect on heart rate, it is not surprising that the response of the stroke volume was also unchanged. The absence of an increase in stroke volume could be partly related to performance of the measurement in the

Figure 5. Upper graphs, Consumption of oxygen (VO2) before and after physical training, as measured on treadmill (top left), vs consumption of oxygen (VO2) on bicycle ergometer before and after training (top right). Consumption of oxygen on treadmill decreased after training. Lower graphs, Minute ventilation (VE) before and after physical training on treadmill (bottom left) vs minute ventilation (VE) on bicycle ergometer before and after training (bottom right). Minute ventilation on treadmill decreased after training.
supine position. Since stroke volume is already greater in the supine position, compared to the upright position, both at rest and during submaximal exercise, a marked effect of physical training would be necessary to yield further significant increases. Since another study using upright testing in subjects with COPD also found no increase in stroke volume after physical training, the possibility that patients with COPD have a limited capacity to augment stroke volume should also be considered.

The mean pulmonary arterial pressure at rest was unchanged after training. Degre et al showed a significant decrease in pulmonary arterial pressure from 18 to 14 mm Hg in their study. We were unable to confirm this, and our results agree with those of Alpert et al. In addition, as noted in Figure 4, the abnormal response of pulmonary arterial pressure to an increase in pulmonary arterial blood flow was unchanged after physical training. Similarly, the control patients showed no improvement in this measurement.

The increased pulmonary arterial wedge pressure after physical training although statistically significant, is probably not indicative of worsening left ventricular function. It has been documented that mean pulmonary arterial wedge pressure can be influenced by extracardiac factors, such as intrathoracic pressure variations, which are dependent upon respiratory mechanics. During hyperventilation or exercise in patients with elevated airway resistance, there is a marked respiratory variation in esophageal and pulmonary arterial wedge pressures. The mean pulmonary arterial wedge pressure may become elevated, and this has been related to the degree of increase in pulmonary arterial pressure during exercise in these patients. Thus, we did not find that physical training resulted in an improvement in hemodynamic measurements or a clear-cut conditioning effect on heart rate and stroke volume. This is in contrast to the readily demonstrable effect of physical training in normal subjects.

In Figure 5, it is noted that while the oxygen consumption and minute ventilation after physical training showed no significant change during exercise on the bicycle ergometer, there was a significant decrease in these two measurements during exercise on the treadmill. Minute ventilation and oxygen consumption were unchanged in the control group during both methods of exercise. While the mechanical efficiency of exercise on the bicycle ergometer varies little, this is not the case with the treadmill. These studies have documented a decreased consumption of oxygen at comparable levels of exercise on the treadmill. This is believed to be associated with increased familiarity with the task in question, improved neuromuscular coordination, and a decreased amount of vertical-lift work, ie, the elevation of the body per step. While most of this improvement may occur early, a continued decrease in consumption of oxygen has been noted to persist for several weeks. Thus, if concurrent measurements of oxygen consumption are not made, an erroneous impression of improvement in physical fitness may be obtained if performance of work on the treadmill and heart rate only are compared.

In contrast to the lack of significant change in cardiopulmonary function is the dramatic improvement in the total work performed on the treadmill by the physically trained group. This improvement may occur secondary to a number of factors, eg, an improved efficiency of walking, as noted previously, and a desensitization to the sensation of dyspnea. From our data, it would seem that improved cardiopulmonary function did not play an important role; however, this does not detract from the potential significance of programs for rehabilitation. Haas and Cardon have demonstrated an improved efficiency and work capacity in specific tasks after training in these tasks. The improvement in work capacity, even in the absence of improvement in cardiopulmonary function, has important implications for vocational and social rehabilitation.

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