Cardiorespiratory Responses to Incremental Exercise in Patients With Asbestos-related Pleural Thickening and Normal or Slightly Abnormal Lung Function*  

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An increasing number of patients with asbestos exposure are being identified with pleural thickening (PT) alone, with little or no impairment in standard tests of lung function despite their frequent complaint of dyspnea. We have employed incremental cardiorespiratory exercise testing to evaluate the types and mechanisms of impairment in 23 such patients. All had normal lung fields on radiographic examinations and normal (group 1, n = 12) or minimally reduced (group 2A, slight restriction, n = 5, group 2B, slight obstruction, n = 6), lung function. Excessive ventilation was common in all groups, but especially in group 2B. Abnormal dead space ventilation (VD/VT) was more frequent in groups 2A (4/5) and 2B (4/6) than in group 1 (3/12). It was associated with O2 desaturation in three patients in groups 2A and B. Cardiovascular abnormalities were rare (1/23). Excessive ventilation and dead space provide a basis for the symptom of dyspnea in these patients. (Chest 1993; 103:1045-50)

The impact of asbestos-related (AR) pleural thickening (PT) on pulmonary function has become increasingly apparent in the last decade. It is by now well recognized that diffuse PT may result in restrictive ventilatory impairment1-3 and death2 from respiratory failure even when AR interstitial pulmonary fibrosis (asbestosis) is minimal or absent. In addition, statistically significant decrements in vital capacity have been ascribed to circumscribed PT (pleural plaque) when it is present alone or together with asbestosis.4-6

With the widespread efforts to identify individuals with AR disease, more and more patients are diagnosed as having PT alone, with little or no impairment in results of standard tests of lung function despite frequent complaints of dyspnea. Since dyspnea in the presence of normal resting pulmonary function is a classic indication for incremental exercise testing, we have been interested in applying this approach to evaluate the types and mechanisms of functional impairment in these patients. This article reports our findings in 23 patients, 10 with diffuse and 13 with circumscribed PT. All had normal lung fields on radiographic examination and normal (n = 12) or minimally reduced lung function, five restrictive and six obstructive.

METHODS

All patients were referred to the Mount Sinai Medical Center in New York for evaluation of AR disease. All had PT (of varying extent) and normal pulmonary parenchyma on radiographs read by an expert ("B") reader (A.M.) according to the latest International Labour Office (ILO) Classification of Pneumoconioses.7 Overall extent of PT was quantitated using an integrative index.8 Dyspnea was defined as shortness of breath or difficulty breathing on climbing 2 flights of stairs.

Spirometry and single breath diffusing capacity of the lung for carbon monoxide (Dco) were performed according to American Thoracic Society guidelines.9,10 Predicted values were those published by the authors using similar methods.11,12 The forced vital capacity (FVC) and Dco were considered normal when they were ≥80 percent and minimally decreased when they were between 64 and 79 percent of predicted. The forced expiratory volume in 1 s (FEV1/FVC was considered normal when it was ≥0.70 and minimally decreased when it was between 0.60 and 0.69. Disease was classified as obstructive when the FEV1/FVC was decreased. Those patients with greater decrements in lung function were not included.

Exercise testing was performed on a breath-by-breath-system (model 2000 or CPX Medical Graphics, St. Paul, Minn.) under continuous clinical, electrocardiographic, and oximetric (Ohmeda Bix 3700 pulse oximeter, Boulder, Colo) monitoring. The work load was increased each minute at a rate (generally 15 to 20 W) sufficient to reach maximum VO2 in approximately 8 to 10 min. Testing was terminated when VO2 or heart rate was ≥75 percent of predicted maximum values or the patient indicated intolerable dyspnea, fatigue, or leg pain. Arterial blood gases were sampled at rest and at each 1-min interval, allowing calculation of O2 saturation,
Table 1 — Physiologic Measurements in Incremental Exercise Testing

A. Ventilatory
1. Reserve (NL: FEV1, X 40 – Ve Peak ≥30 L)
2. Response, ΔVe/ΔVO2 (NL: <0.029)
3. Equivalents at Anaerobic Threshold NL: VO2 defined at 34, Ve/VO2 = 31
(Ventilatory Pattern: NL: Frequency <50 with Vr/Vc ≥0.5 and/or Frequency <40. This criterion was not used to classify ventilatory responses)
B. Gas Exchange
1. VO2 peak (NL: ≥75% of predicted VO2max)
2. VO2 pulse, VO2/HR (NL: ≥80% of predicted max O pulse)
C. Cardiovascular
1. VO2, peak (NL: ≥75% of predicted VO2max)
2. Peak heart rate (NL ≥80% of predicted HR max)
3. O2 pulse, Ve/VO2 (NL: ≥80% of predicted max O pulse)
4. Heart rate response
5. Anaerobic threshold (NL: ≥40% of predicted VO2max)
6. ECG, blood pressure, angina

Table 1 summarizes the many physiologic parameters analyzed, along with the normal values for our laboratory. The latter generally follow Hansen et al. and Wasserman et al.,17 including the resting value for VO2 at rest (≥0.42), which is 1.65 SD above the mean value of their reference subjects.18 Following the suggestion of Cotes et al.19 to evaluate exercise parameters at a "standard submaximal work load" equivalent to 1.0 L VO2, we have adopted the normal value at this workload of ≥0.25 of Jones et al. To confirm these values for VO2/VRT, we measured estimated VO2/VRT in 21 normal adults (age range, 23 to 53 years), all of whom achieved a peak VO2 ≥75 percent of predicted. Of the 21, 19 were nonsmokers while 2 had discontinued smoking 1.5 and 4 years earlier; 15 were male. The mean value for VO2 at rest was 0.337 ± 0.071 and at 1.0 L VO2 was 0.300 ± 0.039. Only one subject exceeded 0.25 at 1 L VO2 (estimated VO2/VRT = 0.26). The mean value for ventilatory response (ΔVe/ΔVO2), using the method of Reebuck et al.20 (linear regression up to the anaerobic threshold [AT]) was 0.212 ± 0.051 in our normal subjects.

Statistical significance was assessed by the two-tailed Student’s t test (for mean values) and by Fisher’s exact test (for frequencies).

RESULTS

Of the 23 patients studied, 21 were male subjects who had been occupationally exposed to asbestos as insulators or in shipyards beginning 18 or more years earlier, when workplaces were less controlled. Durations of exposure were variable (from less than 1 year to more than 30 years). Two patients were wives of such workers (“household exposure”). Mean age of all patients was 61 years (range, 37 to 74 years). Five were lifetime nonsmokers and the remaining 18 were former smokers, a distribution of smoking histories similar to large cohorts of these trades.1 Durations of smoking ranged from 10 to 38 years. Of the 18 former smokers, 17 had discontinued 5 or more years (range, 5 to 30 years).

The profusion score for small parenchymal opacities was 0/1 or 0/0 for all patients. Ten had diffuse PT defined by obliteration of an ipsilateral costophrenic angle, and 13 had circumscribed PT. The extent of PT ranged from minimal (unilateral B,2 or face on 1 or bilateral A,1, face on) to severe (bilateral ≥B,2 plus face on), with integrative indices ranging from 2 to 26.

Table 2 shows mean values for pulmonary function and exercise parameters in groups 1 and 2. The 12 patients in group 1 had normal values for spirometry (mean FVC, 92 percent of predicted; FEV1/FVC, 0.79) and Dcoab (mean, 116 percent of predicted) while the 5 patients in group 2A had slight restriction (mean FVC for these 5, 75 percent of predicted) and the 6 in group 2B had slight obstruction (mean FEV1/FVC for these 6, 0.63). Of the 11 patients in group 2, Dco was slightly decreased in 6 (mean value for these 6, 72 percent of predicted).

There was no difference in extent or type of PT between those with normal pulmonary function (group 1) and those with minimal impairment (group 2), 5 of the 12 patients in group 1 and 5 of the 11 in group 2 had diffuse PT. The FVC was lower in the patients with diffuse (mean, 77.2 percent of predicted) as compared with circumscribed PT (mean, 88.2 percent of predicted) whether they were in group 1 or group 2. Values for FEV1/FVC were similar in both types of PT.

Mean values for ventilatory responses (VE/VO2 at AT and ΔVe/ΔVO2) were somewhat more impaired in group 2B, although the differences were not statistically significant. Ventilatory reserve was significantly less in groups 2A and 2B, reflecting in part their lower ventilatory capacity. There was no difference in Vd/Vr at exercise, in peak VO2, or in AT.

The frequency of abnormal responses to incremental exercise is summarized in Table 3. Two-thirds of all patients (15/23), including half of those with normal lung function, had at least one abnormal test of ventilation. Of the 15 such patients, 11 or three

### Table 2 — Pulmonary Function and Incremental Exercise Parameters in 23 Patients With AR PT

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Pulmonary Function</td>
<td>A. Slight Restriction</td>
<td>B. Slight Obstruction</td>
</tr>
<tr>
<td>Age, yr</td>
<td>58.0 ± 10.3</td>
<td>63.6 ± 7.2</td>
<td>64.0 ± 5.1</td>
</tr>
<tr>
<td>FVC, % pred</td>
<td>91.5 ± 12.3</td>
<td>75.1 ± 1.0*</td>
<td>77.5 ± 8.8*</td>
</tr>
<tr>
<td>FEV1/FVC x 100</td>
<td>79.3 ± 6.8</td>
<td>77.2 ± 4.5</td>
<td>63.2 ± 3.3*</td>
</tr>
<tr>
<td>Dco, % pred</td>
<td>116 ± 23</td>
<td>100 ± 34</td>
<td>84 ± 20*</td>
</tr>
<tr>
<td>Vent reserve, L</td>
<td>65.4 ± 23.3</td>
<td>32.0 ± 24.0*</td>
<td>23.3 ± 13.5*</td>
</tr>
<tr>
<td>Ve/VO2 at AT</td>
<td>30.4 ± 6.1</td>
<td>30.8 ± 3.7</td>
<td>35.8 ± 3.8</td>
</tr>
<tr>
<td>ΔVe/ΔVO2</td>
<td>0.285 ± 0.09</td>
<td>0.270 ± 0.06</td>
<td>0.345 ± 0.06</td>
</tr>
<tr>
<td>Vd/Vr, rest</td>
<td>0.328 ± 0.06</td>
<td>0.370 ± 0.03</td>
<td>0.355 ± 0.06</td>
</tr>
<tr>
<td>Vd/Vr, VO2 1 L</td>
<td>0.249 ± 0.09</td>
<td>0.282 ± 0.07</td>
<td>0.253 ± 0.04</td>
</tr>
<tr>
<td>V02 peak, % pred</td>
<td>80.3 ± 26.7</td>
<td>89.2 ± 14.9</td>
<td>76.2 ± 13.2</td>
</tr>
<tr>
<td>AT, % VO2max</td>
<td>60.0 ± 17</td>
<td>67.4 ± 9.3</td>
<td>60.5 ± 11.2</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with group 1.
quarters showed two or more abnormal responses. Respiratory rate was somewhat increased (>40) in one third; all seven patients with increased respiratory rate had at least one abnormal test of ventilation. An abnormal pattern was seen in three patients, all in group 1.

The Vd/Vt was increased in one quarter of patients in group 1 (3/12), but three quarters (8/11) of those in group 2, with similar frequency in those with slight restriction (4/5) and slight obstruction (4/6). All 11 patients with elevated Vd/Vt on exercise had at least one abnormal ventilatory parameter. Using the more rigorous standard of ≈0.42 as the normal value at rest, only two patients manifested an abnormal value at rest (and were abnormal at VO₂ = 1 L as well). Using a normal value of ≈0.35, an additional nine patients would be classified as abnormal at rest; but all but one was abnormal at VO₂ = 1 L. Stated another way, a high normal or “intermediate” resting value for Vd/Vt of 0.36 to 0.42 was observed in nine patients, eight of whom had an abnormal exercise Vd/Vt and all of whom had one or more ventilatory abnormalities.

Desaturation was seen in three patients in group 2; all three had a decreased Dco₃. Desaturation was not seen in group 1.

More than half the patients in group 1 (7/12) and all but one of the five in group 2A reached a peak VO₂ ≥75 percent of predicted, a level achieved by only two of six in group 2B. No patient had an excessive heart rate response, and only 1 of the 23 had a decreased AT.

Since many of the patients came to medical attention or were referred for further evaluation because of dyspnea, it was expected that most of the subjects in this study (16 of the 23) would complain of this symptom. Of interest is that 10 of the 16 (63 percent) patients who complained of dyspnea had abnormal Vd/Vt compared with only 2 of the 7 (29 percent) who did not complain of dyspnea.

**DISCUSSION**

Our purpose was to assess standard pulmonary function tests and cardiorespiratory responses to incremental exercise in patients with a wide range of AR PT and no clinical evidence of pulmonary asbestosis. The latter was ruled out by ILO readings ≤0/1, absence of rales or clubbing, and normal or increased Dco₃/alveolar volume. Readings of plain radiographs were confirmed by standard or high-resolution computed tomographic scans in half the patients.

Our particular interest was to study patients with AR PT and normal or only slightly impaired pulmonary function since we encounter many such patients and many have instituted claims for compensation. We have found it difficult to explain their frequent complaint of dyspnea.

Certain observations on the results of incremental exercise testing in our 23 patients can be made:

1. Excessive ventilation was common in AR PT whether diffuse or circumscribed. Increased ventilation was noted in half the patients when results of standard pulmonary function tests were normal (6 of 12) or (slightly) restrictive (3/5) but was more frequent when (slight) obstruction was present (6/6).

2. Abnormal Vd/Vt on exercise was far more frequent when results of pulmonary function tests were (only slightly) abnormal, whether restrictive or obstructive (8/11 vs. 3/12 when function was normal) and may be accompanied by desaturation or increased F(A-a)O₂ (3 of 11).

3. Excessive ventilation was usually manifested by more than one parameter (of the 15 with one abnormal measurement of ventilation, 11 [73 percent] had at least one additional ventilatory abnormality).

4. Elevated Vd/Vt during exercise was always associated with abnormal ventilatory parameters.

5. Cardiovascular abnormalities were extremely rare in the patients we studied (1 of 23) despite their age and their many risk factors for cardiovascular disease. However, this was not a study of the prevalence of such disease in patients with AR PT since those with clinically apparent heart disease were deliberately excluded.

6. High-normal or intermediate values for Vd/Vt at rest appeared to predict elevated values on exercise. However, this probably reflected patient

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**Table 3—Frequency of Abnormal Exercise Responses in AR PT**

<table>
<thead>
<tr>
<th>Dco</th>
<th>Group 1</th>
<th>Group 2A</th>
<th>Group 2B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>2/5</td>
<td>4/6</td>
</tr>
<tr>
<td>Abnormal ventilation, one or more responses</td>
<td>6/12</td>
<td>3/5</td>
<td>6/6*</td>
</tr>
<tr>
<td>(2 or more abnormal responses)</td>
<td>(4/12)</td>
<td>(2/5)</td>
<td>(5/5)*†</td>
</tr>
<tr>
<td>Abnormal pattern</td>
<td>3/12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal Vd/Vt (exercise)</td>
<td>3/12</td>
<td>4/5*</td>
<td>4/6</td>
</tr>
<tr>
<td>Desaturation and/or ↑ in F(A-a)O₂</td>
<td>0</td>
<td>1/5</td>
<td>2/6</td>
</tr>
<tr>
<td>≥75% of pred VO₂max</td>
<td>7/12</td>
<td>4/5</td>
<td>2/6</td>
</tr>
<tr>
<td>Abnormal AT</td>
<td>1/12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>↑ HR</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*p<0.06. †Data only on one response (ventilatory reserve) in one patient.
selection, since we did not observe this in our normal subjects with intermediate resting values.

The impact of AR PT on lung function has been confirmed in recent studies. The FVC was lower (by 3.7 percent of predicted) in sheet metal workers and by 0.4 L in insulators. Even when the study was confined to those with circumscribed PT without asbestosis, FVC was 6.9 percent of predicted lower in shipyard workers and 4.3 percent of predicted lower in railroad car repairers. In a study of 1,211 sheet metal workers, Schwartz et al noted the FVC to be approximately 4 percent of predicted lower with circumscribed PT and 10 percent lower with diffuse PT whether or not asbestosis was detectable. Many investigators have demonstrated a greater decrement in FVC for the same profusion score when PT was present. A recent study by our group of 2,611 long-term insulators demonstrated the FVC to be lower (by 6.5 percent of predicted) in the presence of circumscribed PT and (by 19.9 percent of predicted) in the presence of diffuse PT. At a profusion score of 1/1, the FVC was lower by 7.3 percent of predicted in those with circumscribed PT and by 20.0 percent of predicted in those with diffuse PT. Because the patients in the present report were selected on the basis of normal or only slightly impaired pulmonary function, they cannot be compared with these large studies. Nevertheless, they demonstrate the greater impact on resting pulmonary function of diffuse (mean FVC 77.2 percent of predicted) contrasted with circumscribed PT (mean FVC 88.2 percent of predicted).

Investigations of exercise responses in patients with AR diseases have been few and have varied in the intensity of exercise, the parameters measured, the definitions of normal responses, and the types of AR disease studied. Most studies have included large numbers of smokers who were not analyzed separately. A useful study to compare with the present one is that of Howard et al involving 90 shipyard workers with pleural plaques, 17 of whom had "mildly increased interstitial markings." There were 46 patients with normal pulmonary function, including 7 with "increased markings." Elevated Vd/VT (not specified whether at rest or exercise) was present in 13 of these 46 (28 percent). Those with elevated Vd/VT included all patients with "increased markings." Smoking histories were not taken into consideration. The frequency of increased Vd/VT was greater (27/44 or 61 percent) when resting pulmonary function was abnormal. The Vt/Vo2 was increased in all groups. Only 11 patients of the total of 90 had a "mild increase" in P(A-a)O2 during exercise; all of these 11 had abnormal pulmonary function. The high frequency of abnormal Vd/VT, the far lesser frequency of increased P(A-a)O2, the limitation of the latter finding to those with abnormal pulmonary function, and the frequent increase in one parameter of ventilatory response (Vt/Vo2) are all similar to our findings.

Picado and coworkers studied six patients with pure AR PT, rigorously defined by normal CT and gallium scans; five of the six were smokers. They noted increased ventilatory response (Vt/Vo2), respiratory rate, and estimated Vd/VT. Cardiac responses to exercise, judged by heart rate and cardiac output (measured in four patients), were normal. Again, these findings parallel ours.

Agostoni et al studied 120 shipyard workers, of whom 73 (61 percent) had parenchymal disease ± PT and 42 (35 percent) had PT alone. Smokers comprised 82 percent of the study population; 63 percent were current smokers. Of the entire group, 64 percent had abnormal pulmonary function. Their criteria for assessing responses to exercise differed in many ways from those of Howard et al and Picado et al (cited above) and from ours. Dead space was considered abnormal only if it failed to decrease on exercise, a much more stringent criterion. Evaluation of ventilatory responses was limited to ventilatory reserve, again, a very limited test. Cardiac limitation was noted in 38 percent of patients. Meaningful comparisons cannot be made with the present study or those of Howard or Picado.

The study of Sue and coworkers has been frequently cited. Their group has been in the forefront in developing the concepts, methods, and normal values for cardiorespiratory exercise testing. Smoking and nonsmoking subjects (73 of each) were matched for age and asbestos exposure. While 24 subjects (17 percent) had parenchymal disease, no classification of pleural abnormalities was given. Analysis of pulmonary function and exercise results was by smoking category. These differences in study design render comparisons difficult. Despite the inclusion of subjects with parenchymal asbestosis and with greater pulmonary function impairment than in the present study, only 20 percent (23 of 114) demonstrated at maximal exercise a P(A-a)O2 > 30 mm Hg. A similar 22 percent (25 of 114) manifested a high Vd/VT on exercise, but the definition of this abnormality (> 0.30 at maximal exercise) is different from, and more exclusionary than, our definition (≥ 0.26 at a Vo2 of 1 L). Using their definition, 16 percent (9 of 57) nonsmokers had a high Vd/VT on exercise.

A study limited to assessment of dyspnea and ear oximetry in 25 patients noted greater dyspnea and fall in saturation in small numbers of patients with diffuse AR PT compared to those with asbestos exposure and a normal chest radiograph. Findings in those with diffuse PT resembled findings in subjects with parenchymal asbestosis. Smoking was not considered.

Finally, in an early study, Becklake and coworkers evaluated changes in resting pulmonary function and
in VE at rest and at two levels of exercise as a function of increasing profusion of small opacities. Minor increases in exercise VE were noted when profusions reached 1/0 or greater. Effects of PT were not assessed. Smoking was not considered.

An important question in the present investigation (and in most of those cited above) is whether (some of) the findings can be attributed to the effects of smoking. Workers who are occupationally exposed to asbestos are likely to smoke; most series report 80 to 90 percent with a positive smoking history. Furthermore, the effects of the inhalation of asbestos and of cigarette smoke are synergistic on pulmonary function, adding another dimension to the problem of attribution.1

The clearest way to separate the effect is to look at asbestos-exposed nonsmokers. Unfortunately, we could not recruit a sufficient number who met the other criteria: PT, absence of interstitial fibrosis, normal or near normal pulmonary function, and ability to do a maximal exercise test; 5 of the 23 (22 percent) were not cigarette smokers, 4 in group 1 and 1 in group 2B. Two of the five had abnormal ventilatory responses and two had increased Vd/Vt. We then took the next best approach, by using former smokers in addition to lifetime nonsmokers. Of the remaining 18 subjects, 17 had discontinued smoking for 5 to 30 years.

Whether cigarette smoking by itself can cause the type of abnormalities we report has been insufficiently studied. Hirsch and colleagues38 studied nine healthy young male smokers with normal lung function. Values for Vd/Vt at rest (0.40±0.07), at 50 W (equivalent to a VO2 of 1.0 L/min; 0.25±0.06), and at 200 W (equivalent to VO2 max; 0.23±0.06) are higher than would be expected, although the authors did not comment on this. Values for P(A-a)O2, and for VE/VO2 and VE/VCO2 at their nadir were within the expected range. Frans and coworkers28 compared healthy smokers (n = 14) with nonsmokers (n = 16) at rest and at 100 W. The P(A-a)O2 was larger in the smokers (although within the normal range) while Vd/Vt was not different. More recently, Malmberg et al39 reported reference values for gas exchange during exercise in healthy male smokers (n = 25) and nonsmokers (n = 25) with normal pulmonary function, evenly distributed in age between 20 to 65 years. Opposite to the findings of Frans et al, smoking was not associated with an increase in P(A-a)O2 at maximal exercise while both Vd/Vt and VE were increased.

If data on the effects of smoking on healthy subjects with normal pulmonary function are sparse and inconsistent, it is even more difficult to separate the effects on exercise responses of disease attributable to smoking from those attributable to other disease. It is a truism in exercise testing that it can detect and quantify impairment and characterize abnormal circulatory, ventilatory, and gas exchange processes but cannot diagnose the underlying respiratory disorder. We therefore limited our study of the effects of AR PT to subjects with normal or near-normal pulmonary function, who are thus less likely to show the pathophysiologic effects of either exposure. Indeed, we report those with fully normal pulmonary function (group 1) separately from patients with slight restriction (group 2A, who are likely to show an asbestos but not a smoking effect) and patients with slight obstruction (group 2B, who are most likely to show a smoking effect). Those with slight obstruction had an even greater frequency of abnormal ventilatory responses, even though more than half the other patients had excessive ventilation, and were less likely to reach predicted VO2 max. Patients with either slight restriction or slight obstruction had a greater frequency of increased Vd/Vt on exercise compared with those with normal pulmonary function.

Our experience with other patient populations offers limited insights. Our 21 normal subjects, cited in the "Methods" section, included two former smokers, whose ventilatory and gas exchange responses were within the expected ranges. We have presented data on 23 patients with metabolic storage diseases in whom the predominant abnormality was circulatory (low ventilatory AT)31,32. Five had a positive smoking history (a strikingly different frequency of smoking from asbestos workers). They ranged in age from 28 to 41 years, the FEV1/FVC was <0.70 in two of the five. The Vd/Vt was normal throughout exercise in all five.

Excessive ventilation on exercise, present in two thirds of the patients with AR PT in this study, may be attributed to decreased chest wall and/or lung compliance caused by the PT alone or to decreased lung compliance caused by parenchymal fibrosis, or to a combination of these processes. Abnormal gas exchange on exercise, manifest especially by elevated Vd/Vt, is better attributed to parenchymal involvement. It is of interest that elevated Vd/Vt was more frequent when results of standard pulmonary function tests were only slightly abnormal (whether restrictive or obstructive) and that the three patients with widened P(A-a)O2 had abnormal results of pulmonary function tests. In a recent review of the physiologic effects of AR PT, Schwartz32 offered several reasons to incriminate parenchymal inflammation and fibrosis when these are not detectable clinically or radiographically. Reasons included the well-known failure of standard radiographs to detect interstitial fibrosis in 10 to 20 percent of cases in which it is manifest on histologic examination34,35 and the demonstration of greater lymphocytic alveolitis in patients with AR PT and normal lung fields compared with similarly exposed persons with fully normal radiographs.36,37
The level of ventilation is an important determinant of dyspnea, and elevated dead space or "wasted" ventilation (ventilation to zones where it is not matched by perfusion and cannot contribute to gas exchange) is a major cause of increased ventilation. Demonstration of both of these mechanisms during progressive exercise in asbestos-exposed patients with pleural disease "alone" provides valuable insight into the symptom of dyspnea in such patients.

REFERENCES