Hemodynamic Effect of Hydralazine in Advanced, Stable Chronic Obstructive Pulmonary Disease with Cor Pulmonale*  
Immediate and Short-Term Evaluation at Rest and During Exercise  
Eulo Lupi-Herrera, M.D.; Mario Seoane, M.D.; and Juan Verdejo, M.D.

Hydralazine was administered to eight patients (mean age, 69 ± 2 years) who had stable, advanced chronic obstructive pulmonary disease (COPD), pulmonary arterial hypertension (mean pulmonary arterial pressure, 31 ± 3 mm Hg), and cor pulmonale. All of the patients were studied at rest and during exercise. After intravenous administration of hydralazine at rest, there were statistically significant increases in pulmonary arterial pressure (p < 0.05), cardiac index (p < 0.005), arterial oxygen saturation (p < 0.01), and mixed venous saturation (SVO₂) (p < 0.005). Pulmonary vascular resistance did not change, and systemic resistance decreased (p < 0.005). During exercise, pulmonary arterial pressure increased in all patients, and this increase was not blunted by hydralazine; however, cardiac index (p < 0.005), arterial oxygen pressure (p < 0.005), and SVO₂ (p < 0.001) increased further during exercise. The increase in pulmonary vascular resistance was significantly blunted by hydralazine (p < 0.005). Therapy with the drug was continued orally in seven patients because one patient showed a deleterious response in pulmonary hemodynamics. After seven days of oral hydralazine, pulmonary arterial pressure and pulmonary vascular resistance were not statistically different from control. There were statistically significant increases in cardiac index (p < 0.005) and SVO₂ (p < 0.05), systemic resistance decreased (p < 0.01). The same condition was found during exercise; however, only two patients showed pulmonary gas exchange and pulmonary hemodynamic benefit at rest and during exercise with hydralazine therapy. Our results suggest that it is unlikely that vasodilator therapy with hydralazine will be useful in patients with advanced stable COPD and cor pulmonale who seem to have fixed pulmonary vascular disease.

Vasodilators have been used recently for the treatment of primary pulmonary arterial hypertension. From the studies reported, it can be concluded that vasodilator therapy is effective for selected patients, namely, those with lower mean pulmonary arterial pressure and pulmonary arteriolar resistance. In these patients, vasodilator drugs might counteract the vasoconstriction of the pulmonary circulation that is considered a major factor responsible for the hypertensive state. Pulmonary hypertension can complicate various forms of acute and chronic pulmonary disease. Recently, hydralazine has been used in patients with chronic obstructive pulmonary disease (COPD), and the study has shown that this drug can produce a decrease in mean pulmonary arterial pressure when cardiac output was increased markedly, with little change in pulmonary arterial wedge pressure, suggesting that hydralazine was capable of dilating the pulmonary vascular bed in patients with COPD. The experience of other investigators' contrasts with the previously mentioned work. As a rule, no hemodynamic or clinical improvement and serious adverse reactions were observed; however, this study did not include patients with COPD.

In the present study, we attempted to better define the effect of hydralazine on patients with COPD and, in particular, in those with cor pulmonale. We evaluated the hemodynamic effects of short-term intravenous therapy with hydralazine in eight patients at rest and with exercise. In addition, in seven patients the changes in hemodynamics and blood gas exchange after seven days of oral therapy with hydralazine were recorded, both at rest and during exercise. Only two patients who had improvement in hemodynamics and blood gas exchange without adverse reactions were continued on oral therapy with hydralazine.

Materials and Methods

Patients

Eight patients with stable COPD due to chronic bronchitis, emphysema, or both were evaluated between January 1981 and January 1982. All were born and raised at an altitude of 2,240 meters and were permanent residents of Mexico City. Their diagnosis was based on clinical history, physical examination, and tests of pulmonary function (Table 1). The patients were relatively uniform with respect to ventilatory characteristics. Based on pulmonary function tests, six patients had very severe COPD, and two had severe pulmonary function impairment.

The major criterion for inclusion in this study was the demonstration of a cardiac index at rest below 5.5 L/min sq m (ie, absence of hyperdynamic hemodynamic profile) (normal values for Mexico City, 2.5 to 5.4 L/min/sq m). No patient was included if known to have had cardiac failure or a respiratory infection within ten weeks.
Table 1—Pulmonary Function in Eight Patients with COPD and Cor Pulmonale*

<table>
<thead>
<tr>
<th>Case, Sex, Age (yr)†</th>
<th>VC, L</th>
<th>RV, L</th>
<th>TLC, L</th>
<th>FEV1, L</th>
<th>FEF25-75%, L/min</th>
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</thead>
<tbody>
<tr>
<td>1, M, 70</td>
<td>1,600 (49)</td>
<td>2,200 (147)</td>
<td>3,800 (76)</td>
<td>0.55 (22)</td>
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<td>2,870 (152)</td>
<td>4,120 (76)</td>
<td>0.35 (15)</td>
<td>9 (6)</td>
</tr>
<tr>
<td>3, M, 74</td>
<td>2,850 (80)</td>
<td>3,180 (167)</td>
<td>6,000 (100)</td>
<td>0.75 (27)</td>
<td>12 (5)</td>
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<td>4, M, 74</td>
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<td>1,600 (122)</td>
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<td>60 (45)</td>
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<tr>
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<td>3,900 (160)</td>
<td>4,700 (100)</td>
<td>0.35 (14)</td>
<td>19 (13)</td>
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<td>6, M, 77</td>
<td>2,350 (70)</td>
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<td>5,480 (90)</td>
<td>0.90 (20)</td>
<td>15 (10)</td>
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<tr>
<td>7, M, 57</td>
<td>2,100 (52)</td>
<td>1,650 (144)</td>
<td>3,500 (75)</td>
<td>0.81 (22)</td>
<td>42 (17)</td>
</tr>
<tr>
<td>8, M, 60</td>
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<td>4,800 (100)</td>
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</tr>
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<td>2,553 (143)</td>
<td>4,475 (85)</td>
<td>0.77 (27)</td>
<td>26 (16)</td>
</tr>
<tr>
<td>± SE</td>
<td>± 196 (6)</td>
<td>± 296 (6)</td>
<td>± 332 (4)</td>
<td>± 0.12 (5)</td>
<td>± 6 (5)</td>
</tr>
</tbody>
</table>

*VC, Vital capacity; RV, residual volume. Numbers within parentheses are percentage values representing percent of predicted normal for each value, based on age, sex, and height.†††Mean age, 69 ± 2 years.

...prior to the study, although all of them had a respiratory infection and recovered between four and eight months before the study. All patients had dyspnea and fatigue on minimal to moderate exertion. None of the patients had clinical or electrocardiographic evidence of systemic hypertension, valvular heart disease, coronary arterial disease, or primary myocardial disease. All had cor pulmonale, with the diagnosis made on the basis of either radiographic or electrocardiographic evidence of right ventricular enlargement.†††

In order to exclude pulmonary vasodilatation due to bronchodilators, this therapy was suspended 12 hours prior to each of the hemodynamic studies. None of the patients had evidence of reversible bronchoconstriction (200 μg of albuterol salbutamol; Ventolin); however, all of the patients were treated with conventional therapy for at least two years before the study. This therapy included bronchodilators, antibiotic agents, diuretic drugs, and supplemental oxygen as each patient's clinical status indicated. Supplemental oxygen therapy was discontinued six hours before and throughout each cardiac catheterization. None of the patients had been hemodynamically studied before. Our protocol was approved by the local committee for clinical investigation. All of the procedures were explained to the patients, and their consent was obtained.

Hemodynamic and Pulmonary Measurements

Our procedure for cardiac catheterization at rest and at exercise has been described elsewhere. In brief, cardiac output was measured by the thermodilution method, and pressures were obtained by a Swan-Ganz catheter. Standard formulas were used to calculate cardiac index, right ventricular work index, pulmonary arterial resistance, systemic resistance, and the left ventricular work index. Systolic, diastolic, and mean pressures were measured by averaging over at least three respiratory cycles. The stated results represent the average of three clustered measurements with less than 10-percent variation. Samples of blood were obtained from the pulmonary and brachial arteries over a one-minute period and were immediately analyzed using a gas analyzer (Instrumentation Laboratory; 127 bath, 213 electrometer) (normal values for Mexico City: arterial oxygen pressure [PaO2], 67±3 mm Hg; arterial carbon dioxide tension [PaCO2], 33±3 mm Hg; and arterial pH, 7.35 to 7.45).

Measurements of pulmonary volume were made with the patients seated in a volume-displacement plethysmograph (J.H. Emerson). Total lung capacity (TLC) was measured by the method of Dubois et al. Recordings were made on an oscillographic photographic recorder (Electronics for Medicine VR-6). Pulmonary function results were compared to normal values reported by Comroe et al., Baldwin et al., and Morris et al. and were expressed as a percentage of the predicted normal values. The mean forced expiratory flow during the middle half of the forced vital capacity (FEF25-75%) and the ratio of the forced expiratory volume in one second over the forced vital capacity (FEV/FVC) were not adjusted for the decreased air density at altitude. A person who at high altitude has expiratory flow below the predicted normal range at sea level clearly has airway obstruction.†††

Exercise Testing

Patients were familiarized with the exercise technique. After control measurements, supine exercise tests were performed. All pressures were recorded continuously except during collection of blood samples. Samples of blood and air were collected simultaneously, and cardiac output was measured during the final minute of exercise.

Hydralazine Therapy

After obtaining baseline hemodynamic measurements at rest and during exercise, intravenous hydralazine (0.33 mg/kg of body weight) was infused into the pulmonary artery over three minutes. Pulmonary arterial and mean systemic arterial pressures were recorded continuously, except during the collection of samples of blood. Cardiac output was measured every five minutes. The exercise test was performed in eight patients after a significant increase in cardiac output was observed. Only those patients who showed a beneficial effect on pulmonary and systemic hemodynamics and gas exchange in the intravenous trial were placed on oral therapy with hydralazine. During the intravenous trial of hydralazine, pulmonary hemodynamics worsened in patient 7 during rest and exercise (pulmonary arterial pressure increased from 50 to 43 mm Hg and pulmonary arteriolar resistance from 9 to 12 units/ sq m at rest; with exercise, pulmonary arterial pressure rose from 48 to 53 mm Hg), and it was decided not to continue with orally administered hydralazine.

After six hours of intravenous therapy with hydralazine, the drug was administered orally (50 mg every six hours) in seven out of the eight patients, and the hemodynamic measurements at rest and during exercise were repeated seven days later. Before each dose of hydralazine, pulse rates in the supine and standing positions and blood pressures were monitored. The last dose of hydralazine was always given one to two hours before cardiac catheterization.

Statistical analysis and the significance of results were calculated using standard methods for standard and paired t-tests. All of the results were expressed as the mean ± SE.†††

Results

Hemodynamic Data at Rest

All eight patients had elevated pulmonary arterial pressure and pulmonary arteriolar resistance...
Table 2—Hemodynamic Data Obtained at Rest (Eight Patients)*

<table>
<thead>
<tr>
<th>Case</th>
<th>Drug</th>
<th>Heart Rate, beats per min</th>
<th>VO2, ml/min</th>
<th>PAF, mm Hg</th>
<th>PWP, mm Hg</th>
<th>Cardiac Index, L/min/sq m</th>
<th>Resistance, units/sq m</th>
<th>RVWI, kg/m/min/sq m</th>
<th>LVWI, kg/m/min/sq m</th>
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*C, Control; H, hydralazine; PAF, mean pulmonary arterial pressure; PWP, pulmonary wedge pressure; Rp, pulmonary arteriolar resistance; Rs, systemic resistance; RVWI, right ventricular work index; LVWI, left ventricular work index; NS, not significant.
†Not continued with oral hydralazine.

(31.7 ± 3.1 mm Hg and 7.38 ± 0.89 units/sq m) (Table 2). Pulmonary wedge pressure at rest was normal in all patients. After the infusion of hydralazine into the pulmonary artery, there were statistically significant increases in heart rate (p < 0.001), pulmonary arterial pressure (p < 0.05), cardiac index (p < 0.005), and right ventricular work index (p < 0.05). Total-body oxygen consumption (VO2), pulmonary wedge pressure, and pulmonary arteriolar resistance did not change, and systemic resistance decreased (p < 0.005) without any adverse effects.

Gas Exchange at Rest

All eight patients had hypoxemia, and only patients 1

Table 3—Effects of Hydralazine at Rest on Gas Exchange (n = 8)

<table>
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<tr>
<th>Case</th>
<th>Drug*</th>
<th>PaO2, mm Hg</th>
<th>PaCO2, mm Hg</th>
<th>FiO2, mm Hg</th>
<th>SaO2, percent</th>
<th>SvO2, percent</th>
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*C, Control; and H, hydralazine.
Table 4—Data on Hemodynamics and Blood Gas Exchange Obtained during Exercise*  

<table>
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<tr>
<th>Case</th>
<th>Drug</th>
<th>Heart Rate, beats per min</th>
<th>VO_2, ml/min</th>
<th>PAP, mm Hg</th>
<th>Cardiac Index, L/min/sq m</th>
<th>Resistance, units/sq m</th>
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p     |     | <0.05                     | <0.05        | <0.005       | <0.001                   | <0.005        | <0.005        | <0.001         | <0.001         | <0.001           |

*C, Control; H, hydralazine; PAP, mean pulmonary arterial pressure; Rp, pulmonary arteriolar resistance; Rs, systemic resistance; and NS, not significant.
†Not continued with oral hydralazine.

and 5 had increased PaCO_2 (>35 mm Hg)† (Table 3). After intravenous therapy with hydralazine, there were statistically significant increases in PaO_2 (p<0.05), mixed venous partial pressure of oxygen PVO_2 (p<0.005), arterial oxygen saturation (SaO_2) (p<0.01), mixed venous oxygen saturation (SVO_2) (p<0.005), and arterial pH (p<0.05). The PaCO_2 decreased (p<0.05).

Table 5—Data on Hemodynamics and Blood Gas Exchange Obtained at Rest after Seven Days of Oral Hydralazine (Seven Patients)*

<table>
<thead>
<tr>
<th>Case</th>
<th>Drug</th>
<th>Heart Rate, beats per min</th>
<th>PAP, mm Hg</th>
<th>Cardiac Index, L/min/sq m</th>
<th>Resistance, units/sq m</th>
<th>PaO_2, mm Hg</th>
<th>PaCO_2, mm Hg</th>
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<th>SVO_2, percent</th>
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p    |     | <0.005                    | <0.005      | <0.01                    | NS            | NS            | NS            | NS             | <0.05           |

*C, Control; H, hydralazine; PAP, mean pulmonary arterial pressure; Rp, pulmonary arteriolar resistance; Rs, systemic resistance; and NS, not significant.
†After drug was discontinued.
Hemodynamics and Gas Exchange during Exercise

Although cardiac index increased with exercise relative to control values (rest, 3.51±0.22 L/min/sq m; exercise 4.26±0.24 L/min/sq m [p<0.005]), after hydralazine a further increase was noted (p<0.005) (Table 4). The same response was shown for heart rate (p<0.05), PaO₂ (p<0.005), SaO₂ (p<0.001), SvO₂ (p<0.001), arterial pH (p<0.001), and VO₂ (p<0.05). Mean pulmonary arterial pressure increased in all patients, relative to resting values, and this increase was not blunted by hydralazine at exercise. The increase in pulmonary arteriolar resistance during exercise was significantly blunted by hydralazine (p<0.05). During exercise, all patients had exertional dyspnea and severe fatigue.

Data at Rest after Seven Days of Oral Therapy

Mean pulmonary arterial pressure and pulmonary arteriolar resistance were not statistically different from the basal values (Table 5). The same response was shown for PaCO₂ and SaO₂.

There were statistically significant increases in heart rate (p<0.005), cardiac index (p<0.005), and SvO₂ (p<0.05). Pulmonary arteriolar resistance (p<0.01) decreased.

Patient 4 showed a favorable hemodynamic response and a worsening in blood gas exchange that was reversed after therapy with the drug was discontinued. This situation was not observed before with intravenous therapy with hydralazine.

Data at Exercise

Cardiac index was significantly increased during exercise after seven days of oral treatment (p<0.05) (Table 6). The same condition was found for SvO₂ (p<0.05) and arterial pH (p<0.001). The increase in pulmonary arterial pressure and in pulmonary arteriolar resistance was not blunted by hydralazine. Systemic resistance decreased significantly (p<0.005). Heart rate, VO₂, PaO₂, SaO₂, and PaCO₂ were not different from controls.

Clinical Responses

The deleterious response to intravenous therapy with hydralazine in patient 7 precluded the continuation of oral therapy. In the rest of the patients, no severe systemic hypotension was observed, although four of the seven patients had nausea and headache which disappeared with continued therapy. Only one of the seven patients (patient 5) had clinical improvement after four days of treatment (relief of dyspnea on mild exertion). One patient (case 4) did not complain of symptoms, although a significant decrease in PaO₂ was noted (from 55 to 45 mm Hg).

Oral therapy with hydralazine was discontinued in patients 1 to 4 and 6 because patient 1 showed an increase in pulmonary arterial pressure without modifications in pulmonary arteriolar resistance and no hemodynamic benefit at exercise. Although patient 2 showed hemodynamic benefit at rest, during exercise the mean pulmonary arterial pressure and pulmonary

Table 6—Data on Hemodynamics and Blood Gas Exchange Obtained at Exercise after Seven Days of Oral Hydralazine (Seven Patients)*

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<tr>
<th>Case</th>
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<th>Resistance, units/sq m</th>
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*C, Control exercise; H, hydralazine; PAP, mean pulmonary arterial pressure; Rp, pulmonary arteriolar resistance; Rs, systemic resistance; and NS, not significant.
arteriolar resistance increased. Patient 3 had an unfavorable hemodynamic response both at rest and at exercise. In patient 4, a favorable hemodynamic response at rest and at exercise occurred; however, a worsening in blood gas exchange was noticed. Patient 6 showed a worsening in pulmonary hemodynamics at rest. Only patients 5 and 8 were discharged on hydralazine (50 mg every six hours) and have been followed for nine months. Only patient 5 had continued improvement of the dyspnea. No major complications like deterioration of renal function, severe hypertension, or any clinical manifestation of a lupus-like syndrome have been observed.

**Discussion**

In patients with COPD and cor pulmonale, there is evidence that isoproterenol, a well-known pulmonary vasodilator, may produce an increase in pulmonary blood flow without an increase in pulmonary vascular pressure. A recent report by Rubin and Peter showed that short-term administration of hydralazine improves hemodynamics during rest and exercise in patients with pulmonary arterial hypertension secondary to COPD. More recently, Simonneau and coworkers showed that nifedipine acutely dilates pulmonary vessels constricted by hypoxia without deleterious effects on arterial oxygenation in patients with COPD. These reported beneficial effects of vasodilators suggest that pharmacologically reversible pulmonary vasoconstriction is important in patients with pulmonary arterial hypertension and COPD.

In the present study, analyzing the group as a whole, intravenous and short-term administration of hydralazine did not improve pulmonary hemodynamics during rest. An increase in cardiac output after hydralazine was accompanied by an increase in the resting level of pulmonary arterial pressure and a constant pulmonary arteriolar resistance. After intravenous hydralazine at rest, a favorable effect was found in blood gas exchange.

This effect could be the result of the increase in systemic cardiac output, with a secondary increase in mixed venous oxygen content, a major determinant of systemic oxygen saturation in COPD.

During exercise, after intravenous therapy with hydralazine, a transitory pulmonary hemodynamic benefit was observed. This could be attributed to the improvement in blood gas exchange noticed at rest prior to the exercise. After intravenous therapy with hydralazine, SVO₂ at rest increased significantly, and after exercise, it remained significantly higher than that observed during exercise without hydralazine. Hyman and co-workers have presented data that suggest that the PVO₂ may exert an important regulatory role in controlling pulmonary arterial pressure and pulmonary vascular resistance in the cat. Therefore, their finding and our data might suggest that the increased SVO₂ could explain why the increase in pulmonary arteriolar resistance during exercise was significantly blunted by hydralazine.

On the other hand, it is not obvious to us why hydralazine failed to produce a hemodynamic benefit in the pulmonary circulation at rest, if SVO₂ was markedly increased after intravenous therapy with hydralazine. A possible explanation for this observation could be related to the level of the cardiac output achieved (at rest after intravenous hydralazine increased by 14 percent, and 35 percent at exercise). It has been stated that when states of low cardiac output are associated with low PVO₂, these could be important factors in maintaining increased pulmonary arterial pressure. On the other hand, states of high cardiac output with higher PVO₂ may lead to reduced pulmonary vascular resistance. Therefore, along with the increase in PVO₂, it seems necessary to achieve a significant increase in cardiac output to elicit a favorable pulmonary hemodynamic response after hydralazine. In our series, although a significant increase in PVO₂ was maintained, the relative increase in cardiac output could be insufficient to produce a reduction in pulmonary arteriolar resistance.

After the short-term oral administration of hydralazine, for the group as a whole, no significant reduction in pulmonary arteriolar resistance was found. On the other hand, the decline in resistance in the systemic circulation exceeded in most instances that mild decrease observed in the pulmonary circuit. The reduction in pulmonary arteriolar resistance and the increase in heart rate, cardiac output, and SVO₂ occurred in spite of the absence of a reduction in the right ventricular impedance.

The initial benefit observed at rest in blood gas exchange was lost after seven days of oral therapy with hydralazine. This occurred in spite of an increased PVO₂ similar to that observed at rest with intravenous administration of hydralazine. One major concern about vasodilator therapy for patients with primary and secondary pulmonary arterial hypertension is the possibility of causing vasodilation in areas of poor alveolar ventilation, an effect that worsens the hypoxemia in COPD by exaggerating the ventilation-perfusion imbalance already present. This seemed to be the case in patient 4 (Table 5), where systemic hypoxemia occurred after hydralazine. Similar observations have been reported recently by Packer and co-workers in some of their patients with pulmonary arterial hypertension; however, neither a benefit nor a decline in SaO₂ was routinely observed during the short-term administration of hydralazine in our patients with COPD.

The lack of sustained benefit (after intravenous hydralazine) observed after a week of oral treatment
Table 7—Comparison of Data on COPD Reported by Rubin and Petera and by Us

<table>
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<th>Rubin and Peter*</th>
<th>Our Data</th>
<th>p†</th>
</tr>
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<td>27.2±4.9</td>
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<tr>
<td>predicted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEF25-75%, percent</td>
<td>16.1±3.2</td>
<td>16.2±4.5</td>
<td>NS</td>
</tr>
<tr>
<td>predicted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFP, mm Hg‡</td>
<td>46.5±2.5</td>
<td>31.7±3.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>58.2±3.0</td>
<td>43.7±2.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, yr</td>
<td>58±2</td>
<td>69±2</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*Patients 1 to 5 with COPD and patients 8, 10, and 12 with less than 30 percent of FEF25-75%.
†NS, Not significant.
‡PFP, Mean pulmonary arterial pressure.

indicates the need for interpreting with caution the response to a drug evaluated only during a short-term trial. We do not have an explanation for the loss of improved blood gas exchange after seven days of oral treatment; however, bearing in mind that the benefit in blood gas exchange was lost, it is easier to understand why no benefit was obtained in pulmonary hemodynamics or gas exchange at exercise after a week of oral treatment with hydralazine.

The reasons underlying the differences between our study and those reported by Rubin and Petera deserve comment. In their study, hydralazine was capable of dilating the pulmonary vascular bed, since pulmonary arterial pressure was decreased when cardiac output was increased markedly (by 46 percent). When comparing eight patients of Rubin and Petera with our eight patients, a similar degree of bronchial obstruction was found (Table 7). Also, a lower degree of pulmonary arterial hypertension with more hypoxemia in our patients than in those of Rubin and Petera was observed. These data could suggest that the two populations may have differed considerably in the magnitude of pharmacologically responsive pulmonary vasoconstriction. Although this could be an explanation for the different results, we are also aware that our population is older. This could reflect a diminished capacity of the pulmonary vascular bed to dilate, due to fixed vascular disease secondary to structural obliteration of the pulmonary circulation as a major factor responsible for the pulmonary hypertensive state.

Our experience indicates that the administration of hydralazine to patients with pulmonary arterial hypertension and cor pulmonale due to advanced and stable COPD fails to produce consistent hemodynamic and clinical benefits. It is not frequently associated with severe deleterious effects as have been noted in other types of pulmonary arterial hypertension and cor pulmonale that do not include patients with COPD. It has been demonstrated that pulmonary arterial hypertension has a different pathophysiology for each disease. Therefore, the concepts developed for vasodilator therapy in primary pulmonary arterial hypertension or in pulmonary arterial hypertension secondary to vascular disease of the lung (ie, multiple pulmonary emboli) could not be applied entirely to COPD. Furthermore, on the basis of our findings, this idea could also be applied for the same disease at different stages of evolution, as has been demonstrated in primary pulmonary arterial hypertension. It seems unlikely that vasodilator therapy will be useful in the majority of older patients with advanced stable COPD with cor pulmonale who have a poor or a decreased vasoconstrictor tone due to alveolar hypoxia or advanced fixed vascular disease. Our data also emphasize the point that a trial of vasodilators in patients with COPD, when performed, should be done under careful hemodynamic monitoring.

REFERENCES
18 Croxton FE, Cowden DJ. Applied general statistics. New York: Prentice Hall, 1941

Silica, Silicosis, and Cancer

The University of North Carolina will present this international symposium in Chapel Hill, April 1-5, co-sponsored by the Society for Occupational and Environmental Health. For Information, contact: Larry D. Hyde, University of North Carolina, 109 Conner Drive, Suite 1101, Chapel Hill 27514 (919-962-2101).