Effects of Isoproterenol on the Pulmonary Circulation in Patients with Chronic Obstructive Lung Disease

By M. Irené Ferrer, M.D., Yale Enson, M.D., Margaret M. Kilcoyne, M.D., and Réjane M. Harvey, M.D.

SUMMARY
Isoproterenol produced an increase in pulmonary blood volume and pulmonary blood flow without a significant change in pulmonary vascular pressures in 14 patients with obstructive lung disease, six of whom had cor pulmonale. These findings are consistent with a vasodilating effect on the pulmonary vasculature. Evidence is presented that muscular pulmonary arteries constricted by hypoxia were affected by the drug. There is little to suggest that the compliance of the elastic arteries was altered by isoproterenol.

Additional Indexing Words:
Cor pulmonale Pulmonary arterial compliance Pulmonary blood volume
Pulmonary vasodilatation

Isoproterenol, a powerful inotropic and chronotropic agent, is also reported to be a dilator of the pulmonary vasculature.1-7 Studies in patients with valvular heart disease and primary myocardial disease have shown that this drug will produce a slight fall in pulmonary arterial and pulmonary wedge pressures and an increase in pulmonary blood volume, findings compatible with vasodilatation.3, 6 Similar definitive studies have not been made in patients with chronic obstructive lung disease or cor pulmonale, although there is evidence that the drug may produce a fall in pulmonary arterial blood pressures.4, 5 The present study was undertaken to define more completely the effect of this drug on patients with chronic obstructive lung disease and, in particular, to assess its effects on pulmonary blood volume, the abnormal pulmonary diastolic pressure gradient across the lungs which these patients display,8 and the compliance characteristics of the elastic pulmonary arteries.

Methods

Fourteen patients with chronic obstructive pulmonary disease and normal sinus rhythm were examined (tables 1 and 2). Six of the 14 patients had evidence of cor pulmonale. Only one (1644a) was in right ventricular failure at the time of study; he was studied again after right ventricular failure had subsided (1644b). The remaining five patients with cor pulmonale were studied after recovery from right ventricular failure. Six patients had no heart disease. Two patients had left ventricular disease as well as chronic obstructive lung disease: one had right and left ventricular enlargement and failure at the time of study. The origin of his left ventricular disease was not identified. The other patient with an enlarged left ventricle had a history of systemic hypertension and a previous myocardial
infarction, but no evidence of right or left ventricular failure.

To define the types of chronic obstructive lung disease, we utilized the classification of Nash, Briscoe, and Cournand. They have described two major categories: type A—patients who display cough, occasional scanty sputum, fixed dyspnea, thin habitus, large translucent lungs with low diaphragm and small cardiothoracic ratio, absence of cor pulmonale, and a normal hematocrit; type B—patients who manifest much cough and sputum, fluctuating dyspnea, normal or stout habitus, normal appearing lung fields and normal position of the diaphragm on X-ray, normal or increased cardiothoracic ratio, congestive failure due to cor pulmonale, and a high hematocrit. A third, or intermediate type, displays features of both A and B. Of the six patients with cor pulmonale (tables 1 and 2), three were classified as type B (1653, 1613, and 1610) and three were of the intermediate type. Three of the six patients without heart disease were of type A, (1611, 1620, and 1612) and three displayed features of both A and B. The patients with left ventricular disease were of the intermediate type.

Each patient had the protocol explained to him in detail, and his written permission was secured for all procedures. The day before the study, the patients were familiarized with the respiratory equipment. They were studied in the nonsedated, postabsorbive basal state.

Two double-lumen catheters were placed: one in the pulmonary artery for measurement of the pulmonary wedge and pulmonary arterial blood pressures and blood gases; the other in the right atrium with the tip adjacent to the tricuspid valve. The distal lumen of this second catheter was used to inject radioiodinated human serum albumin (Risa-131) for the measurement of cardiac output and pulmonary blood volume by the radiocardiographic technique. The proximal lumen was utilized for the infusion of the drug and measurement of right atrial mean pressure. A brachial artery was cannulated for measurement of systemic blood pressure, blood gases, and blood pH.

A control period, during which only isotonic saline was infused, lasted 20 to 30 min. Isoproterenol, as a solution of 0.8 mg in 500 ml of 5% dextrose in water, was then infused for 10 to 26 min at a rate of 3.3 to 5.0 μg/min.

Systemic and pulmonary arterial blood pressures, the pulmonary wedge and right atrial pressures, and heart rate were recorded every 5 to 10 min during the control period and every 3 to 5 min during the infusion of the drug. The electrocardiogram was constantly monitored. Total blood volume was measured at the end of the control period and, in four instances, at the end of the drug infusion period. Cardiac output, pulmonary blood volume, ventilation, blood gases, and pH were measured at least once toward the end of each period. For brevity, only representative values are given in tables 1 and 2.

Cardiac output was measured by the direct Fick and/or the radiocardiographic technique. Pulmonary mean transit time (PMTT) was calculated by the radiographic technique of Guininti and associates. PMTT, which is the average time required for blood to travel between the pulmonary artery and the left atrium, is expressed in heart cycles or number of stroke outputs needed to traverse the lung circulation. The volume of blood in the lungs, of course, would determine this transit time. Hence, pulmonary blood volume was calculated by multiplying PMTT in heart cycles by the stroke output or stroke volume. The latter was derived from the Fick technique, except once when radiocardiography was employed. The estimate of total blood volume was made from the plasma concentration of T 1824 (Evans blue dye) or of Risa-131 10 min after their injection and from the hematocrit reading according to the considerations of Noble and Gregersen. The hematocrit was corrected for trapped plasma and adjusted to body hematocrit. Blood pH was determined by a microanalyzer (Instrumentation Laboratory, Inc., model 113-S2). Blood gases were analyzed by the technique of Van Slyke and Neill and by the microanalyzer.

The pulse pressures recorded in the elastic pulmonary arteries reflect their compliance characteristics plus the effect of the stroke volume imposed upon them. Since measurement of the compliance of this segment of the arterial tree is not presently feasible in intact man, we have assessed compliance indirectly by examining the relationship between pulmonary arterial systolic (or mean) pressure, stroke volume, and diastolic pressure. Previous consideration of this relationship in normal man, both at rest and during exercise, has indicated that systolic pressure is accurately expressed in the following manner:

\[
P_A = 1.41 + 1.61 P_A + 0.09 SV \quad (1)
\]

and the mean pressure by the following equation:

\[
P_m = -1.33 + 1.34 P_A + 0.05 SV \quad (2)
\]

where \( P_A \), \( P_m \), \( P_m \), and \( SV \) = pulmonary arterial systolic, diastolic, and mean pressures, respectively, and \( SV \) = stroke volume.

We have also found that these relationships as expressed by equations 1 and 2 hold equally well in subjects with chronic obstructive lung disease, and interpret these findings as suggesting that the compliance characteristics of the elastic vessels in

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Table 1
Effects of an Infusion of Isoproterenol on Blood Flow, Blood Volume, Blood Pressures, and Heart Rate in 14 Patients with Chronic Obstructive Lung Disease

<table>
<thead>
<tr>
<th>Case Age, sex</th>
<th>Cardiac output (liters/min/m²)</th>
<th>Heart rate (beats/min)</th>
<th>PBV (ml)</th>
<th>PBV/TV (mm Hg)</th>
<th>Pulmonary artery s/d, m (mm Hg)</th>
<th>PAw (mm Hg)</th>
<th>RA (mm Hg)</th>
<th>Brachial artery s/d, m (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td>1644a 62 M</td>
<td>C 2.67 115</td>
<td></td>
<td></td>
<td></td>
<td>67/34,47</td>
<td>15</td>
<td>18</td>
<td>118/70,89</td>
</tr>
<tr>
<td>1644b 62 M</td>
<td>C 2.55 90 406 11.1</td>
<td></td>
<td></td>
<td></td>
<td>33/18,23</td>
<td>5</td>
<td>1</td>
<td>127/70,90</td>
</tr>
<tr>
<td>1653 54 M</td>
<td>C 3.30 101 400 8.7</td>
<td></td>
<td></td>
<td></td>
<td>56/29,35</td>
<td>3</td>
<td>2</td>
<td>147/89,110</td>
</tr>
<tr>
<td>1647 50 M</td>
<td>C 3.27 107 528 8.9</td>
<td></td>
<td></td>
<td></td>
<td>50/31,37</td>
<td>2</td>
<td>-1</td>
<td>111/77,90</td>
</tr>
<tr>
<td>1613 55 M</td>
<td>C 3.35 81 587 12.6</td>
<td></td>
<td></td>
<td></td>
<td>41/19,27</td>
<td>9</td>
<td>2</td>
<td>133/71,99</td>
</tr>
<tr>
<td>1.89 I12 68 M</td>
<td>C 4.93 (47%) 115 859 18.5</td>
<td></td>
<td></td>
<td></td>
<td>44/18,26</td>
<td>6</td>
<td>3</td>
<td>113/61,75</td>
</tr>
<tr>
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<td>C 2.45 86</td>
<td></td>
<td></td>
<td></td>
<td>37/18,24</td>
<td>3</td>
<td>3</td>
<td>152/77,102</td>
</tr>
<tr>
<td>1610 61 M</td>
<td>C 4.67 (91%) 114</td>
<td></td>
<td></td>
<td></td>
<td>40/22,26</td>
<td>5</td>
<td>2</td>
<td>156/75,97</td>
</tr>
<tr>
<td>1611 61 M</td>
<td>I11 2.96 88</td>
<td></td>
<td></td>
<td></td>
<td>47/21,29</td>
<td>6</td>
<td>-</td>
<td>148/79,103</td>
</tr>
<tr>
<td>1619 59 M</td>
<td>C 3.07 96 465 8.5</td>
<td></td>
<td></td>
<td></td>
<td>41/17,23</td>
<td>9</td>
<td>5</td>
<td>131/79,98</td>
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<tr>
<td>1.93 I11</td>
<td>C 5.29 (72%) 119</td>
<td></td>
<td></td>
<td></td>
<td>43/19,27</td>
<td>8</td>
<td>6</td>
<td>153/80,113</td>
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</table>

Cor pulmonale

No heart disease
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<tr>
<th>Time</th>
<th>C</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>Mean ± sd</th>
<th>Mean difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1621</td>
<td>59 M</td>
<td>C</td>
<td>3.80</td>
<td>86</td>
<td>488</td>
<td>12.1</td>
<td>33/11,20</td>
<td>0</td>
</tr>
<tr>
<td>1.50</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>5.09</td>
<td>120</td>
<td>693</td>
<td>17.2</td>
<td>36/11,18</td>
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</tr>
<tr>
<td>1618</td>
<td>51 M</td>
<td>C</td>
<td>2.48</td>
<td>101</td>
<td>361</td>
<td>8.6</td>
<td>30/15,18</td>
<td>7</td>
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<tr>
<td>1.73</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>4.09</td>
<td>122</td>
<td>522</td>
<td>12.5</td>
<td>31/12,18</td>
<td>8</td>
</tr>
<tr>
<td>1611</td>
<td>67 M</td>
<td>C</td>
<td>2.94</td>
<td>100</td>
<td>—</td>
<td>—</td>
<td>30/11,18</td>
<td>3</td>
</tr>
<tr>
<td>1.52</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>4.53</td>
<td>118</td>
<td>—</td>
<td>—</td>
<td>33/13,20</td>
<td>2</td>
</tr>
<tr>
<td>1620</td>
<td>66 M</td>
<td>C</td>
<td>2.28</td>
<td>74</td>
<td>498</td>
<td>10.5</td>
<td>28/10,17</td>
<td>4</td>
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<tr>
<td>1.94</td>
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<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>3.42</td>
<td>97</td>
<td>496</td>
<td>10.5</td>
<td>34/10,17</td>
<td>2</td>
</tr>
<tr>
<td>1612</td>
<td>71 M</td>
<td>C</td>
<td>3.20</td>
<td>75</td>
<td>531</td>
<td>15.5</td>
<td>25/8,14</td>
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<tr>
<td>1.44</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>3.85</td>
<td>113</td>
<td>490</td>
<td>14.3</td>
<td>28/9,15</td>
<td>5</td>
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*Left ventricular disease*

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<tr>
<th>Time</th>
<th>C</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>I&lt;sub&gt;n&lt;/sub&gt;</th>
<th>Mean ± sd</th>
<th>Mean difference</th>
<th>P</th>
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<tbody>
<tr>
<td>1646</td>
<td>55 M</td>
<td>C</td>
<td>2.15</td>
<td>120</td>
<td>265</td>
<td>6.4</td>
<td>79/44,57</td>
<td>29</td>
</tr>
<tr>
<td>1.53</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>3.73</td>
<td>130</td>
<td>422</td>
<td>10.2</td>
<td>75/36,49</td>
<td>24</td>
</tr>
<tr>
<td>1639</td>
<td>65 M</td>
<td>C</td>
<td>3.83</td>
<td>82</td>
<td>518</td>
<td>10.3</td>
<td>20/7,13</td>
<td>5</td>
</tr>
<tr>
<td>1.59</td>
<td></td>
<td>I&lt;sub&gt;n&lt;/sub&gt;</td>
<td>4.69</td>
<td>100</td>
<td>473</td>
<td>10.3</td>
<td>19/7,12</td>
<td>6</td>
</tr>
</tbody>
</table>

Abbreviations: BSA = body surface area; s/d, m = systolic, diastolic, mean pressures; C = control state; I = isoproterenol infusion (subscript indicates duration in minutes); PA<sub>lw</sub> = mean pulmonary arterial wedge pressure; RA = mean right atrial pressure; PBV = pulmonary blood volume; TBV = total blood volume; sd = one standard deviation; P = significance of difference between means of paired observations; N.S. = not significant.

Except for patient 1639, values for cardiac output were estimated by the Fick technique.
such patients do not differ significantly from normal. In the present study, systolic and mean pressures were calculated according to equations 1 and 2 during the control and infusion periods. Calculated and observed pressures during each period were then compared by standard techniques of regression analysis\textsuperscript{15} to assess any alteration in compliance which may have attended the administration of isoproterenol.

### Results

The response to isoproterenol was fairly uniform despite the heterogeneity of the patients (fig. 1).

The onset of the drug effect was always signalled by a rise in sinus rate and change in the contour of the brachial arterial pressure curve,\textsuperscript{16} and was usually noted 5 to 7 min after the beginning of the drug infusion.

The cardiac output (table 1) during the control period varied from low to slightly elevated, and rose strikingly during the administration of the drug in all subjects. There was a significant relationship between the initial level of blood flow and the percentage increase in cardiac output ($r = -0.581, P < 0.025$); thus, those with the lowest levels sustained the greatest increase. Although the initial level of cardiac output bore no relationship to the initial level of right atrial mean pressure ($P < 0.20$), the change in cardiac output was found to be closely related to the initial level of right atrial mean pressure ($r = 0.834, P < 0.001$). Thus, the higher the initial level of right atrial mean pressure, the greater the increase in cardiac output (fig. 2). No relationship could be demonstrated between the initial level of mean pulmonary wedge pressure and either the initial level of blood flow ($P < 0.10$) or its change ($P < 0.20$). The change in cardiac output showed no relationship to change in heart rate ($P < 0.50$).

Heart rate and stroke volume increased significantly. However, in five subjects the
latter did not change, and in the one patient (1612, table 1) whose heart rate rose the most, stroke volume actually declined 12 ml (−20%).

After isoproterenol infusion, pulmonary blood volume and the ratio of pulmonary blood volume to total blood volume rose in all but three patients. The pulmonary mean transit time did not change (P < 0.20). Although there was no significant relationship between the control level of systemic arterial oxyhemoglobin saturation and pulmonary blood volume (P < 0.10), those with the lowest initial oxygen saturations sustained the greatest percentage increase in pulmonary blood volume after the drug (r = −0.677, P < 0.02), as shown in figure 3. The relationship between the change in oxygen saturation and the change in pulmonary blood volume was of borderline significance (P < 0.05). The initial level of pulmonary blood volume bore no relationship to the initial level of blood hydrogen ion concentration (P < 0.60) or to ventilation (P < 0.20); nor did change in hydrogen ion concentration or ventilation bear any relationship to the change in pulmonary blood volume (P < 0.30 and P < 0.25, respectively).

Brachial arterial diastolic and mean pressures fell slightly after infusion of the drug, while the systolic pressure did not change significantly.

During the control period, the level of pulmonary arterial pressures ranged from normal to markedly elevated in these 14 patients. The diastolic pressure gradient across the lung (pulmonary arterial diastolic pressure minus mean pulmonary wedge pressure) ranged from slight to marked. The pulmonary wedge pressure in all but two patients was within normal limits.

Viewing the patients as a group, there was no difference in the levels of pulmonary arterial systolic or mean pressure before and after drug administration. There were, however, variations noted in both these pressures in individuals within the group, which could be related significantly to changes in diastolic pressure and stroke volume.

The pulmonary arterial systolic and mean pressures prior to and after drug infusion were predicted from equations 1 and 2. The relationship between observed and calculated systolic pressures was highly significant both prior to drug administration (r = 0.971, P < 0.001) and after isoproterenol infusion (r = 0.948, P < 0.001). Further, the two relationships did not differ significantly from each other (P > 0.40). The identity of the regressions of calculated on observed values of

**Figure 2**

*Graphic representation of the relationship between the change in cardiac output induced by isoproterenol and the initial level of right atrial mean pressure.*

**Figure 3**

*Graphic representation of the change in pulmonary blood volume induced by isoproterenol and the initial level of systemic arterial oxygen saturation.*
systolic pressure during the two study periods (fig. 4) is indicated by the fact that neither their slopes nor their intercepts differed significantly \( (P > 0.2 \text{ and } P > 0.4, \text{ respectively}) \). Further, neither intercept differed significantly from zero \( (P > 0.5) \). The relationship between observed and calculated mean pressures was highly significant both during the control period \( (r = 0.985, P < 0.001) \) and the infusion of the drug \( (r = 0.978, P < 0.001) \) (fig. 4). Neither the slopes nor the intercepts of these regressions differed significantly from each other \( (P > 0.50 \text{ for each}) \).

In the group as a whole there was little difference in the level of the diastolic pressure between the control and drug periods. The minor changes that did occur in pulmonary arterial diastolic pressure were related to changes in systemic arterial blood oxyhemoglobin saturation \( (r = -0.602, P < 0.001) \) and to changes in mean pulmonary wedge pressure \( (r = 0.542, P < 0.025) \); thus, as oxygen saturation increased, the diastolic pressure fell and vice versa, and as the mean wedge pressure rose or fell, so did the pulmonary arterial diastolic pressure. Variations in diastolic pressure bore no relationship to changes in blood flow \( (P < 0.25) \).

There was no significant difference in the level of the mean pulmonary arterial wedge pressure before or after drug administration in the group as a whole. The changes that did occur were related to the initial level of the wedge pressure \( (r = -0.585, P < 0.02) \). Thus, the higher the initial wedge pressure, the more likely it was that there would be a fall in wedge pressure during the infusion of isoproterenol.

The slight and variable changes in the diastolic pressure gradient across the lung
after the infusion of the drug could be related to changes in the level of blood flow ($r = 0.533$, $P < 0.025$). Thus, the gradient rose in those patients who sustained a large increase in flow, while it remained unchanged or fell in those with a lesser rise (fig. 5). Changes in the pressure gradient could not be related to changes in heart rate ($P > 0.90$) or to changes in ventilation ($P > 0.90$).

The right atrial mean pressure was within normal limits in 12 of the 14 patients and, if the group is considered as a whole, there was no significant difference following administration of the drug. However, the two patients in whom this pressure was elevated in the control period did sustain a fall of $3 \text{ mm Hg}$ at 11 and 15 min after the drug was started.

During the administration of the drug, minute ventilation increased and was accompanied by a slight rise in blood pH. In the control period, systemic arterial blood carbon dioxide tension ranged from normal to moderately elevated in the 14 patients. During the infusion of isoproterenol, carbon dioxide tension also fell slightly but significantly. For the most part, arterial blood oxyhemoglobin saturation was reduced in the control period. Although changes did occur following drug administration, the levels of the group as a whole were not significantly different from those of the control period. After isoproterenol administration, oxygen consumption rose.

**Discussion**

The well-known inotropic and chronotropic effects of isoproterenol are once again confirmed by this study. Of particular interest is the finding that the greatest increment in cardiac output was sustained by those patients having the highest initial right atrial pressures. Review of the studies of Schreiner and associates in patients with aortic valvular disease shows that the drug affected the greatest increase in blood flow in those who had the highest initial left atrial mean pressure ($n = 11$, $r = 0.681$, $P < 0.02$). If the level of the initial right (or left) atrial pressure is predominately a consequence of an increase in right (or left) ventricular volume and, hence, in diastolic fiber length, then shortening of these fibers might effect a greater increase in cardiac output than shortening of fibers of more normal length. The fall in wedge pressure with isoproterenol infusion, which was proportional to the initial level of pressure, is probably due to an analogous response to the drug.

The finding of a rise in pulmonary blood volume without a significant variation in the average level of pulmonary arterial or wedge pressures confirms the impressions of others that isoproterenol is a dilator of the pulmonary vasculature in patients with chronic obstructive lung disease. Although the site of action of the drug is not identified, it is noteworthy that those patients with the lowest initial systemic arterial oxyhemoglobin saturations sustained the greatest increment in pulmonary blood volume. This suggests that either the drug affected the greatest response in those vessels constricted by hypoxia or that relaxation of vessels constricted by hypoxia resulted in a greater increase in their luminal diameter than did relaxation of blood vessels under less tension. Silove and Grover found that the vasoconstrictor response of the pulmonary vasculature to acute hypoxia in the neonatal calf could be reversed by isoproterenol. In a study of the effects of isoproterenol on ventilation-perfusion relationships in patients with asthma, Field also came to the conclusion that the pulmonary vasodilating action of the drug occurred predominately in those portions of the lung in which hypoxic vasoconstriction was present. Since several studies have implicated the small muscular arteries as the site of the vasoconstrictor activity of hypoxia, it would appear that these vessels are affected by isoproterenol. The absence of a fall in systemic arterial blood oxyhemoglobin saturation, as might be expected with increased perfusion of poorly ventilated alveoli, is probably a reflection of a concomittant increase in alveolar ventilation as suggested by Lockhart and associates.

The magnitude of increase in pulmonary blood volume is such that it cannot be
ascribed solely to increased volume of the arterial portion of this bed. Since the pulmonary arterial tree contains approximately 25–30% of the pulmonary blood volume, one would have to postulate that the pulmonary arterial volume had doubled if the observed increment in total pulmonary blood volume were limited to this segment of the bed. It is more reasonable to infer that the venous portion of the bed also participated in this volume expansion, particularly since Brody and Stemmler have shown that the drug does cause pulmonary venous dilatation in dogs.

A simple vasodilating effect of isoproterenol on the pulmonary vascular bed may have been complicated by three other effects of the drug. Hyperventilation, in some instances, effected a rise in alveolar oxygen tension, as revealed by an increase in systemic arterial oxyhemoglobin saturation. Relief of hypoxia may well have contributed to pulmonary vasodilatation. Isoproterenol also produced changes in pulmonary wedge pressure, presumably as a consequence of its inotropic action. Variations in wedge pressure may be reflected in pulmonary arterial diastolic pressure in this type of patient and, therefore, may have masked or augmented any fall in pressure induced by the vasodilating action of the drug. Finally, the large increments in blood flow may have, to some extent, masked the vasodilating effects of the drug, at least as reflected by changes in pulmonary arterial diastolic pressure.

While it is possible to implicate an effect of the drug on muscular pulmonary arteries and pulmonary veins, it is not likely that isoproterenol affected the elastic pulmonary arteries. The systolic and mean pressures both before and after drug administration were predicted with equal accuracy from constants derived from normal data. If the compliance characteristics of the elastic arteries had been significantly altered by the drug, the effect of stroke volume on the pulse pressure also would have been altered, and the predicting equations would have failed to give the correct values after drug infusion and, thus, would no longer be applicable. Since the equations were equally applicable before and after drug administration, we can infer that there was no appreciable change in compliance and that isoproterenol affects the muscular pulmonary arteries rather than the elastic vessels.

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