Effects of Infusion of Acetylcholine on Pulmonary Vascular Resistance in Patients with Pulmonary Hypertension and Congenital Heart Disease

By John T. Shepherd, M.D., Herbert J. Semler, M.D., H. Frederic Helmholz, Jr., M.D., and Earl H. Wood, M.D.

Survival following surgical correction of congenital cardiovascular defects is unlikely if pulmonary hypertension cannot be decreased significantly. Infusions of acetylcholine decreased pulmonary vascular resistance in 6 of 11 patients having pulmonary hypertension associated with atrial or ventricular septal defects. When the acetylcholine was combined with the breathing of oxygen, resistance decreased further. These findings are consistent with the theory that, at some stage, the pulmonary hypertension in cases of congenital heart disease is maintained at least in part by vasoconstriction and therefore is potentially reversible.

Many patients with pulmonary hypertension associated with intracardiac or great vessel defects have increased resistance to blood flow through the pulmonary vascular bed. It is important to know how much, if any, of this increased resistance is due to active vasoconstriction. If vasoconstriction can play an important role, then its assessment may be helpful in evaluating the condition of patients with pulmonary hypertension before surgical correction of the defects, and in understanding the way in which the constriction is induced and maintained.

Acetylcholine, which causes local vasodilation when injected intra-arterially into systemic vessels has been used recently in the study of the pulmonary circulation. Rapid inactivation of this substance in the circulating blood makes possible its injection into the pulmonary artery in sufficient concentration to affect the pulmonary vessels without altering the hemodynamics of the systemic circulation. Harris found that sudden single injections of acetylcholine into the pulmonary artery of patients with pulmonary hypertension, some of whom had congenital heart disease, could produce a transient fall in the pulmonary artery pressure. He suggested that this fall resulted from a decrease in pulmonary vascular resistance.

We have extended the technic by the use of constant-rate infusions of acetylcholine in an attempt to obtain the data necessary to calculate the changes in pulmonary vascular resistance. These observations were made first with the patients breathing air and repeated with the patients breathing oxygen; the latter was done because oxygen breathing alone can lower pulmonary resistance.

The results show that the elevated pulmonary vascular resistance may be decreased during administration of acetylcholine, whether the patient is breathing air or oxygen.

Methods

Eleven patients, aged 8 to 51 years, with pulmonary hypertension were studied. Six had an atrial septal defect, 4 a ventricular septal defect, and 1 an atrial and a ventricular septal defect (table 1). The usual technic was as follows: A 7-F. catheter of the Lehman type with a bird's-eye tip

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### Table 1.—Results of Continuous Infusions into Main Pulmonary Arteries

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr.) &amp; sex</th>
<th>Diagnosis*</th>
<th>When measurements were made†</th>
<th>Acetylcholine (mg./min.)‡</th>
<th>Pulmonary artery Mean pressure (mm. Hg)</th>
<th>Flow (L/min.)</th>
<th>Total pulmonary resistance (dynes cm.⁻²)</th>
<th>Systemic arterial O₂ saturation (%)</th>
<th>Systemic arterial O₂ saturation (%)* (breathing air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29M ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>39</td>
<td>38</td>
<td>7.0</td>
<td>9.2</td>
<td>445</td>
<td>330</td>
</tr>
<tr>
<td>2</td>
<td>31F ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>60</td>
<td>60</td>
<td>4.0</td>
<td>5.3</td>
<td>1200</td>
<td>905</td>
</tr>
<tr>
<td>3</td>
<td>35F ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>60</td>
<td>58</td>
<td>4.1</td>
<td>6.0</td>
<td>1170</td>
<td>775</td>
</tr>
<tr>
<td>4</td>
<td>35F ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>35</td>
<td>27</td>
<td>8.0</td>
<td>10.4</td>
<td>350</td>
<td>210</td>
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<tr>
<td>5</td>
<td>40M ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>66</td>
<td>68</td>
<td>3.2</td>
<td>4.1</td>
<td>1650</td>
<td>1325</td>
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<td>51F ASD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
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<td>45</td>
<td>4.8</td>
<td>—</td>
<td>750</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>8M VSD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>69</td>
<td>67</td>
<td>3.4</td>
<td>4.3</td>
<td>1620</td>
<td>1250</td>
</tr>
<tr>
<td>8</td>
<td>15F VSD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>72</td>
<td>75</td>
<td>3.6</td>
<td>3.4</td>
<td>1565</td>
<td>1765</td>
</tr>
<tr>
<td>9</td>
<td>43F VSD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>93</td>
<td>88</td>
<td>4.0</td>
<td>7.5</td>
<td>1860</td>
<td>940</td>
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<tr>
<td>10</td>
<td>49M VSD</td>
<td>Before</td>
<td>Air 12.0 Oxygen§</td>
<td>86</td>
<td>86</td>
<td>3.6</td>
<td>4.9</td>
<td>1910</td>
<td>1400</td>
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<tr>
<td>11</td>
<td>25M ASD &amp; VSD</td>
<td>During</td>
<td>Air 12.0 Oxygen§</td>
<td>77</td>
<td>75</td>
<td>5.3</td>
<td>5.5</td>
<td>1160</td>
<td>1090</td>
</tr>
</tbody>
</table>

*ASD, atrial septal defect; VSD, ventricular septal defect.
†Before and during refer to measurements made just before and during infusion of acetylcholine.
‡Dose of acetylcholine that produced maximal response while patient was breathing air or oxygen.
§Measurements made when the patient was breathing air and 99.6 percent oxygen respectively.

was used. This catheter, which has an internal diameter of 1.4 mm., was attached by a special adapter to a 3-way stopcock which allowed interchangeable connection of the catheter to a strain-gage manometer for recording pressure and to a cuvette oximeter for continuous recording of the oxygen saturation. The special adapter which was interposed between the catheter and the stopcock had a side arm through which a plastic catheter tubing of small size (outside diameter 0.6 mm., inside diameter, 0.3 mm.) was inserted via a packing nut and a close-fitting gasket. This inner tubing was advanced so that its distal tip lay just within the intracardiac end of the catheter to be inserted into the right heart. An airtight seal between the shaft of this small plastic tube and the side arm of the adapter was accomplished by tightening the packing nut onto the side arm of the adapter. This airtight seal made possible the recording of pressure or withdrawal of blood samples via the lumen remaining between the inner plastic tubing and the internal surface of the lumen of the conventional right heart catheter.

The 7-F. catheter containing the long plastic tube was introduced, usually via a percutaneous puncture of an antecubital vein with a special thin-walled, 12-gage needle. After the tip of the catheter had been manipulated into the right heart and positioned in the pulmonary artery, the packing nut securing the inner plastic tube was loosened and the tube was advanced so that its tip was 2 to 3 cm. distal to the tip of the right heart catheter. The packing nut was again tightened securing the inner tubing in this position. It was now possible to inject acetylcholine via the inner plastic tubing while simultaneously recording pressure or oxygen saturation of the blood via the outer catheter. Acetylcholine in
PULMONARY VASCULAR RESISTANCE

graded doses was infused through the plastic tubing with a pneumatic stainless steel syringe described previously. Acetylcholine was injected at a constant rate for 1 to 2 minutes. The Lehman catheter was used to monitor alternately the pulmonary artery pressure by a strain-gage manometer and the oxygen saturation by a cuvette oximeter before, during, and after the infusion. The aim was to infuse the acetylcholine into both pulmonary arteries, hence the tip of the Lehman catheter was positioned just beyond the pulmonary valve.

Radial artery pressure was measured continuously by a needle in the artery connected to a strain-gage manometer, and an absolute-recording ear oximeter was used to monitor the systemic arterial oxygen saturation. Tidal volume and oxygen consumption before, during, and after the infusion were monitored by a closed circuit spirometer. An electrocardiogram of standard lead I was recorded throughout.

In 3 cases in which the 7-F. catheter was too large for the vein, 2 5-F. catheters of Lehman type were used and inserted into the pulmonary artery. One was used for the injection and the other was connected via a 2-way stopcock to a strain-gage manometer and cuvette oximeter for monitoring pressure and oxygen saturation. In some patients the oxygen saturation of radial arterial blood was determined continuously during the infusion by a cuvette oximeter.

The procedure was usually carried out first with the patient breathing air and then repeated with the patient breathing 99.6 per cent oxygen. No measurements were made until the patient had been breathing oxygen for at least 5 minutes. As a safety measure and in order to be certain that an effective concentration of acetylcholine reached the small pulmonary vessels, a dose-response curve was made for each patient. In patients who showed a significant fall in pulmonary artery pressure, or a rise in pulmonary artery oxygen content, or both, without systemic or respiratory effects, no attempt was made to increase the dose to a point where changes in heart rate, systemic blood pressure, tidal volume, or respiratory rate were produced. If no effect was observed on the pulmonary circulation, the dose was increased until slight systemic effects were noted. The usual dose of acetylcholine chloride was 2 to 4 mg. per minute dissolved in isotonic saline solution, but in 1 patient 24 mg. was given per minute. The volume infused did not exceed 24 ml. per minute.

The total pulmonary resistance, expressed in dynes second cm.\(^{-5}\), was calculated from the ratio: (pulmonary artery mean pressure [mm. Hg] × 1332) divided by (pulmonary flow [ml. per second]). For calculation of pulmonary blood flow the oxygen content of blood in the pulmonary artery was obtained from the oxygen capacity estimated by the method of Sendroy as modified by Roughton, Darling, and Root and the percentage saturation of blood in the pulmonary artery was determined by the cuvette oximeter.

All except 1 patient (case 7, table 1) had a veno-arterial shunt, the magnitude of which was estimated from the indicator-dilution curve recorded just before the infusion of acetylcholine by a method described elsewhere. The magnitude of the shunt ranged from 5 to 32 per cent. For this reason the arterial oxygen content could not be used to indicate oxygen content of the blood in the pulmonary vein. As our patients except patient 6 (table 1) had no evidence of pulmonary disease, the oxygen content of pulmonary vein blood was assumed to equal 98 per cent of the oxygen capacity plus 0.3 vol. per cent to allow for physically dissolved oxygen when the patient was breathing air, and to equal the oxygen capacity plus 1.9 vol. per cent when the patient was breathing 99.6 per cent oxygen.

For patient 6 (table 1), who had pulmonary disease, the oxygen content of pulmonary vein blood was estimated as follows. The magnitude of the veno-arterial shunt was estimated from an indicator-dilution curve and since the oxygen saturation of mixed venous blood and the oxygen saturation of blood in the radial artery were known, it was possible to calculate the oxygen content of blood in the pulmonary vein.

RESULTS

Pulmonary Hypertension Associated with Atrial Septal Defect. During administration of acetylcholine to a 35-year-old woman (case 4, table 1) who had an atrial septal defect and pulmonary hypertension, the pulmonary artery pressure fell promptly from 66/18 to 52/12 mm. Hg and a small but concomitant rise occurred in the oxygen saturation of the right ventricular blood (fig. 1). The heart rate increased from 78 to 84 beats per minute, the systemic pressure fell by 5 to 7 mm. Hg, and the respiration slowed from 15 to 12 per minute. After the infusion was stopped, the pulmonary artery pressure returned slowly to the control level, a finding previously reported by Harris. The total pulmonary resistance dropped from 330 to 220 dynes sec. cm.\(^{-5}\) The resistance when the patient was breathing oxygen was 210
and this fell to 140 when acetycholine was administered.

The response observed in a 29-year-old man (case 1, table 1) with an atrial septal defect and pulmonary artery pressure of 65/26 mm. Hg is shown in figure 2. During the infusion of 8 mg. of acetycholine per minute into the pulmonary artery with the patient breathing air, the oxygen saturation in the pulmonary artery blood rose from 79.5 to 82 per cent. This was accompanied by a change in oxygen saturation of radial artery blood from 96 to 95 per cent. Only a slight fall in pulmonary artery pressure, a decrease of about 10 mm. Hg in radial artery pressure, and little change in heart rate occurred. The total pulmonary resistance on infusion of acetycholine fell from 445 to 350 dynes sec. cm.\(^{-5}\) while the patient was breathing air and from 330 to 240 while he was breathing oxygen.

The results for all the patients are summarized in table 1 and in figure 4. All 6 of the patients with atrial septal defects showed
decreases in pulmonary resistance on administration of acetylcholine. If the pulmonary resistance when the patient is breathing air is taken as 100 per cent, the pulmonary resistance in the 5 patients for whom a complete set of data was obtained decreased 23 per cent with infusion of acetylcholine alone, 29 per cent on breathing oxygen, and 43 per cent on breathing oxygen and receiving acetylcholine.

**Pulmonary Hypertension Associated with Ventricular Septal Defect.** The most dramatic response to acetylcholine that was obtained in any of the patients studied is illustrated by figure 3. The patient, an 8-year-old boy (case 7), had a ventricular septal defect. The pressures in the pulmonary artery and femoral artery of this patient were similar at the start of the procedure. On infusion of acetylcholine while the patient was breathing air, the pulmonary artery pressure fell to less than half its previous value and the oxygen saturation in the pulmonary artery blood rose from 75 to 83. The calculated pulmonary resistance fell from 1620 to 510 dynes sec. cm.\(^{-5}\) Breathing oxygen had only a minimal effect with a change in resistance from 1620 to 1250 dynes sec. cm.\(^{-5}\) The high resistance to flow through the pulmonary vessels in this boy permitted the equalization of pressures in the 2 ventricles. When this resistance had been markedly decreased by the acetylcholine, a large pressure gradient developed between the ventricles, and the defect itself now constituted a major part of the resistance limiting the arteriovenous shunt. This patient also (fig. 3) showed a slight but definite decrease in systemic arterial oxygen saturation similar to that shown in figure 2.

Acetylcholine had little effect in reducing the pulmonary resistance in a 43-year-old woman (case 9, table 1) with a ventricular septal defect and pulmonary artery pressure of 139 mm. Hg systolic and 70 mm. Hg diastolic. Pulmonary resistance decreased from 1860 to 1600 dynes sec. cm.\(^{-5}\) while the patient was breathing air and receiving acetylcholine, a change of questionable significance; yet when she was breathing oxygen without acetylcholine, the resistance decreased to 940, a change of nearly 50 per cent. When she received acetylcholine during oxygen breathing, a small further decrease in resistance occurred (940 to 705). In this patient, therefore, oxygen and not acetylcholine had the greater effect on the pulmonary vessels.

Of the 4 patients in the series with ventricular septal defects only 1 (case 8) did not respond to either oxygen or acetylcholine. For the remainder the average percentage decrease in resistance with acetylcholine while breathing air was 31 per cent, while breathing oxygen, 33 per cent, and while breathing oxygen and receiving acetylcholine, 57 per cent. Pulmonary resistance while breathing air is taken as 100 per cent.

**Discussion**

Various assumptions have been made in the calculation of the pulmonary vascular resistance. First, there was no direct measurement of the oxygen content of the blood in the pulmonary veins. On 4 occasions the oxygen saturation of the systemic arterial blood decreased slightly during infusion of acetylcholine when the patients were breathing air (table 1); this occurred at a time when the oxygen saturation of pulmonary artery blood was rising (figs. 2 and 3). This decrease in oxygen saturation, though small, may be significant, but we cannot say with certainty whether it was due to an increase in veno-arterial shunt or a decrease in oxygen content of pulmonary vein blood. Paul Wood has noted that acetylcholine sharply lowered the arterial oxygen saturation in a case of cor pulmonale, and we have seen a similar decrease in a patient who had persistent pulmonary hypertension following apparently complete closure of a ventricular septal defect. Whatever the correct explanation, the assumptions made for the oxygen content of pulmonary vein blood in the present study would not overestimate the pulmonary blood flow during infusion with acetylcholine.
The pulmonary artery wedge pressure which presumably reflects mean left atrial pressure with acceptable accuracy was measured in all patients before administration of acetylcholine and was within normal limits. In 2 patients with atrial septal defects (cases 1 and 11, table 1) the right atrial pressure was monitored continuously and did not change; hence it is unlikely that the left atrial pressure fell. If one accepts then that the left atrial pressure did not fall during infusion, one can conclude that the changes in total pulmonary resistance as determined by the method employed reflect actual changes in pulmonary vascular resistance.

Another assumption made in these studies is that the rise in oxygen saturation of the pulmonary artery blood indicates an in-
crease in pulmonary blood flow. Such a rise in pulmonary artery saturation with no rise in flow would reduce oxygen absorption by the lungs. Spirometric tracings did not indicate a decrease in oxygen absorption during injection of acetylcholine, but one must remember that an increase in functional residual capacity will simulate oxygen absorption. Inspection of continuous tracings taken before, during and after infusion did not show any evidence of changing functional residual capacity. In 7 patients, there was a fall in pulmonary artery pressure and a rise in oxygen saturation of the pulmonary artery blood during infusion of acetylcholine. If these findings are to be explained as indicating other than a decrease in the resistance of flow in the pulmonary vascular bed, one must assume that the systemic venous return decreased. The relative constancy of arterial pressure and pulse rate makes it unlikely that the infusion affected the left ventricle or systemic arterial bed; hence, such a decrease in systemic venous return if it did occur would have to be due to venous pooling or the combination of an increase in systemic vascular resistance and a decrease in stroke volume. It is concluded that these are unlikely explanations for the findings presented and that, in fact, a decrease in resistance to flow through the pulmonary vascular bed is caused by infusion of acetylcholine.

The assumptions made in concluding that oxygen also causes a decrease in resistance are similar to those described by Marshall and associates.25

Paul Wood26 stated that both acetylcholine and oxygen fail to lower the pulmonary vascular resistance in cases of Eisenmenger’s syndrome in adults and in children more than 5 years old. Any difference between our findings and his can be explained in various ways: 1. It may be that all the patients in Wood’s series resembled the 2 in our series who did not respond (cases 8 and 11). 2. If only the pulmonary artery pressure and the oxygen saturation of systemic arterial blood are measured during a sudden single injection of acetylcholine in a patient with a large ventricular septal defect, the evidence for a drop in resistance may be missed as it would consist chiefly of a change in oxygen content of pulmonary artery blood since systolic pressures in the 2 sides of the heart would be equalized via the large defect. The fact that the oxygen saturation of systemic arterial blood does not change may well be the resultant of a decrease in pulmonary vein oxygen saturation offset by a diminution in a venoarterial shunt. Similarly, in a patient with an atrial septal defect a decrease in pulmonary vascular resistance could be missed if the increased flow through the pulmonary vessels consequent to the infusion of acetylcholine maintained the pressure in the pulmonary artery at its previous level, the principal change being a rise in oxygen content in the pulmonary artery blood.

One additional problem in interpretation merits emphasis. Acetylcholine is a potent bronchoconstrictor, and we have found that doses of acetylcholine which cause bronchoconstriction actually can increase a venoarterial shunt as measured by indicator-dilution curves. It is important, therefore, to monitor the pattern of respiration during infusion. Indeed, such bronchoconstriction might explain the rise in pulmonary artery pressure reported in anesthetized dogs27 and in newborn infants.28

It is difficult to state the magnitude of change in calculated pulmonary resistance that should be accepted as demonstrating an increase in caliber of the pulmonary vessels. If the pulmonary resistance when the patients were breathing air is taken as 100 per cent, a fall in resistance of more than 45 per cent occurred in 4 patients with an atrial and in 2 with a ventricular septal defect when they were receiving acetylcholine, either when they were breathing air or oxygen. We believe that a fall of this magnitude represents a dilatation of vessels in the lung.

In the dosages used, neither inhalation of oxygen nor the infusion of acetylcholine produces a maximal reduction of pulmonary vascular resistance. Indeed, one agent may
be effective and the other ineffective in any given case.

Our results indicate that active vasoconstriction is important in maintaining the increased pulmonary resistance in many patients with congenital heart disease. This constriction is present both in patients with ventricular septal defects in whom the smooth muscle in the pulmonary vessels may have persisted from birth and in patients with atrial septal defect in whom it is likely that the muscle which had regressed since birth has developed again.\(^2\)\(^9\) Vasomotor tone now has been demonstrated in the pulmonary vessels of normal man,\(^1\)\(^6\)\(^,\)\(^2\)\(^9\) in patients with mitral stenosis associated with pulmonary hypertension,\(^9\)\(^,\)\(^3\)\(^1\) and in idiopathic pulmonary hypertension.\(^2\)\(^9\)

**SUMMARY**

Acetylcholine was administered by constant-rate infusion into the pulmonary arteries of 11 patients having pulmonary hypertension associated with atrial or ventricular septal defect.

The oxygen consumption, oxygen saturation in the pulmonary artery and systemic arterial blood, and the pulmonary artery pressure were recorded continuously before, during, and after the infusion. These data were used to determine changes in total pulmonary resistance during infusion of acetylcholine.

All 6 of the patients with atrial septal defects showed some decrease in resistance when receiving acetylcholine. If the pulmonary resistance when the patient was breathing air is taken as 100 per cent, the decrease was 23 (range 15 to 51) per cent with infusion of acetylcholine alone, 29 (range 9 to 33) per cent on breathing oxygen and 43 (range 27 to 60) per cent on breathing oxygen and receiving acetylcholine.

Of the 4 patients with only ventricular septal defect one did not respond to either oxygen or acetylcholine. For the remainder the average percentage decrease in resistance with acetylcholine while breathing air was 31 (range 10 to 69) per cent, while breathing oxygen 33 (range 25 to 66) per cent, and while breathing oxygen and receiving acetylcholine 57 (range 35 to 74) per cent.

One patient with both an atrial and a ventricular septal defect showed no response.

As there was no evidence of a decrease in left atrial pressure with acetylcholine, these changes in total pulmonary resistance demonstrated by the method employed presumably represent an actual reduction in pulmonary vascular resistance.

It is concluded that active constriction of pulmonary vessels can be an important factor in maintaining the high resistance to pulmonary blood flow found in some patients with congenital heart disease.

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**SUMMARIO IN INTERLINGUA**

Acetylcholina esseva administrate a 11 patientes con hypertension pulmonar in association con defectos atrio- o ventriculo-septal. Le administration del droga esseva effectuate per infusion in le arterias pulmonar sub conditiones de fluxo constante.

Ante, durante, e post le infusion, registraiones continue esseva obtenite de (1) le consumption de oxygeno, (2) le saturation oxygenic in le arterias pulmonar e le arterias del circulation systemic, e (3) le tension in le arterias pulmonar. Iste datos esseva utilitate pro determinar alterationes in le total resistentia pulmonar durante le infusion de acetylcholina.

Le 6 patientes con defectos atrio-septal monstrava omnes un certe mesura de reduc-
tion del resistencia durante le infusion de acetylcholina. In comparation con le resistencia pulmonar durante le respiratio de aere in le absencia de acetylcholina, le reduc-tion amontava a un valor medie de 23 pro cento (minimo-maximo: 15 a 51) con le infu-sion de acetylcholina e le respiratio de aere, de 29 pro cento (minimo-maximo: 9 a 33) con le respiratio de oxygeno sin infusion de acetylcholina, e de 43 pro cento (minimo-maximo: 27 a 60) con le infusion de acetylcholina e le respiratio de oxygeno.

Inter le 4 patientes con solmente defectos ventriculo-septal, un respondeva a ni oxygeno ni acetylcholina. Inter le alteres, le percentage medie del reduction del resistencia con infusion de acetylcholina e respiratio de aere eseva 31 (minimo-maximo: 10 a 69), con respiratio de oxygeno e sin infusion de acetylcholina 33 (minimo-maximo: 25 a 66), e con respiratio de oxygeno e infusion de acetylcholina 57 (minimo-maximo: 35 a 74).

Un paciente con defecto atrio-septal e defecto ventriculo-septal mostrava nulle responsa.

Viste que nihil indicava le occurrentia de un reduction del tension sinistro-atrial como effecto del acetylcholina, le alterationes del total resistencia pulmonar demonstrate per le metodo emplaeate representa probablemente un genuin reduction del resistencia pulmono-vascular.

Es concluside que le constriction active del vasos pulmonar pote esser un factor importan-te in manten te alte resistencia al fluxo pulmonar de sanguine que es notate in certe patientes con congenite morbo cardiac.

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