Effects of Inhalation of 100 Per Cent Oxygen on the Pulmonary Blood Volume in Patients with Organic Heart Disease

By Gerald Glick, M.D., Bernard F. Schreiner, Jr., M.D., Gerald W. Murphy, M.D., and Paul N. Yu, M.D.

Many workers have demonstrated that breathing 100 per cent oxygen (hyperoxia) or infusion of acetylcholine into the pulmonary artery may lower an increased pulmonary arterial pressure and an elevated pulmonary vascular resistance. Other investigators have observed similar falls even when these parameters were normal. It has generally been assumed that both these agents most likely act by abolishing pulmonary vasoconstriction and are, consequently, active vasodilators of the pulmonary vascular bed.

That acetylcholine does indeed cause active vasodilation has been substantiated by recent work from this laboratory. In seven of eight patients studied, a fall in pulmonary vascular distending pressure occurred, despite a concomitant increase in pulmonary blood volume. This discordant change in the distending pressure and the pulmonary blood volume strongly suggests active vasomotion in the pulmonary vascular bed.

The effect of hyperoxia in the pulmonary vascular bed is not nearly so well understood. That it works by a mode of action different from acetylcholine is suggested by the studies of Shepherd and co-workers. They showed an almost additive effect of hyperoxia and acetylcholine in lowering the pulmonary vascular resistance in patients with congenital heart disease associated with pulmonary hypertension. Furthermore, these workers found no correlation between the initial pulmonary vascular resistance and the magnitude of the subsequent decline following hyperoxia.

Harris, on the other hand, using acetylcholine, found a response that was definitely related to the initial level of pulmonary arterial pressure, the fall being greatest in patients with moderately elevated pressures. Bateman and associates also observed the synergistic action of hyperoxia and acetylcholine on lowering pulmonary arterial pressure. These results suggest to us that these agents act at different sites.

Gaddum and Holtz and Alcock et al., working on the isolated cat and dog lungs, demonstrated a fall in pulmonary arterial pressure following small doses of acetylcholine, but Nisell and Duke, also using an isolated cat-lung preparation, did not find any response to hyperoxia.

The present study was undertaken in an attempt to clarify the mode of action of 100 per cent oxygen on the pulmonary vascular bed of unanesthetized man.

Material and Methods

Eight patients, ranging in age from 26 to 62, were studied by right and transseptal left heart catheterization. Six of the patients were men and two were women. Three patients had aortic stenosis, two aortic insufficiency, two mitral stenosis, and one a myxoma of the left atrium.

The method used in this laboratory for right and left heart catheterization and the determination of pulmonary blood volume has been described in detail in two companion and previous papers. Briefly, catheters are placed in the main pulmonary artery and in the left atrium, and a Courand needle is inserted into a systemic artery. Indicator-dilution curves are recorded from the arterial sampling site after rapidly sequential injections of indocyanine green (Cardiogreen) into
the pulmonary artery and into the left atrium. The cardiac output and the mean transit time from the pulmonary artery to the left atrium are calculated from these curves by the Stewart-Hamilton method. While constituting at present the only direct approach to the measurement of the pulmonary blood volume, it must be recognized that this method has unavoidable limitations imposed upon it by the intrinsic shortcomings of indicator-dilution technic. These factors have been enumerated and discussed in two accompanying articles.13, 19

The average of pulmonary arterial and left atrial mean pressures was considered as the pulmonary vascular distending pressure.20 A change of pulmonary blood volume in the amount of 50 ml./M.2 or greater is significant.12, 18

Studies were carried out with the patient (a) breathing room air, (b) while breathing 100 per cent oxygen for 15 to 20 minutes, and (c) in five instances, after 15 minutes of breathing room air. In a ninth patient, case 9, data were obtained only during hyperoxia and following recovery. Each study consists of a determination of the pulmonary blood volume and recording of pressures from pulmonary artery, left atrium, and a systemic artery. Systemic arterial oxygen saturation is determined by the method of Van Slyke and Neill.21

Results

The results of this study are tabulated in table 1.

During acute hyperoxia pulmonary blood volume fell significantly in four of the eight patients. It fell insignificantly in one and remained unchanged in two. In the last patient a rise of 42 ml./M.2 was observed. Of the six studies carried out following recovery from hyperoxia, pulmonary blood volume was unchanged in four patients and rose in two.

Pulmonary vascular resistance fell or remained unchanged in all cases. Those patients with the highest initial values showed the greatest decreases.

The left atrial mean pressure fell in two, remained unchanged in four, and rose significantly (> 4 mm. Hg) in two patients. In one of the patients who showed an increase in left atrial mean pressure, the left ventricular end-diastolic pressure was also measured and rose an equal amount. The left atrial mean pressure in this case increased from 22 to 27 mm. Hg, while the left ventricular end-dias-

tolic pressure rose from 24 to 30 mm. Hg. One of the two patients with increased left atrial mean pressure manifested a coincident increase in pulmonary blood volume, and the other patients showed no change in pulmonary blood volume during oxygen breathing.

The pulmonary arterial mean pressure fell in four of six patients in whom it was originally elevated. The other two patients with high initial pressures showed no change and were the two patients described above who had significant elevations in left atrial mean pressure while on oxygen. The remaining two patients, who had normal pulmonary arterial mean pressures, displayed no changes while breathing oxygen.

Pulmonary vascular distending pressure fell significantly (> 3 mm.) in four, rose significantly in one, and showed no significant change in three.

The mean transit time between pulmonary artery and left atrium fell in all the patients except the two in whom left atrial mean pressure rose significantly.

In general, there was a slight decrease in cardiac index.

All the patients had systemic arterial oxygen saturation below the normal mean value, which, for this laboratory, is 94 per cent. Their saturations ranged from 81.9 to 93.9 per cent (average 89.9 per cent). With hyperoxia, all except one patient increased their saturation to above 100 per cent.

Discussion

The pulmonary blood volume during the inhalation of 100 per cent oxygen showed a significant decrease in four of the eight patients studied. The magnitude of the fall bore no relation to the initial arterial oxygen saturation. Scrutiny of the data from the four patients who did not apparently display a significant fall in pulmonary blood volume raises some interesting speculations. In one of the patients (case 5) it declined, but not to a significant extent. This subject, however, had the smallest pulmonary blood volume at rest, and the change noted amounted to 12 per cent of the original value. It is possible,
### Table 1

**Hemodynamic Data During Inhalation of 100 Per Cent Oxygen**

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<th>Case no.</th>
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**Legend:**

- BSA = Body surface area (M²)
- AI = Aortic insufficiency
- AS = Aortic stenosis
- MI = Mitral insufficiency
- MS = Mitral stenosis
- AF = Atrial fibrillation
- NSR = Normal sinus rhythm
- H.R. = Heart rate (beats per minute)
- SaO₂ = Arterial blood oxygen saturation (%)

- PA = Pulmonary artery
- LA = Left atrium
- P₁₀₂ = Pulmonary distending pressure
- BA = Systemic artery
- PVR = Pulmonary vascular resistance (dynes.sec/cm²)
- CI = Cardiac index (L/min./M²)
- MTT = Mean transit time from the pulmonary artery to the left atrium (seconds)
- PBV = Pulmonary blood volume (ml./M²)
therefore, that her ability to react fully was impaired by an already shrunken pulmonary blood volume.

One patient (case 7) who increased his pulmonary blood volume to an almost significant degree, 42 ml./M.², also manifested a significant rise in left atrial mean pressure. It is conceivable that the oxygen effect, which tends to decrease pulmonary blood volume, was counteracted by the augmented back pressure effects from the left atrium, which would tend to distend passively the pulmonary vascular tree. The increase in left atrial mean pressure was undoubtedly the result of the observed rise in left ventricular end-diastolic pressure.

One of the two patients who showed no change in pulmonary blood volume (case 8) also developed a significant rise in left atrial mean pressure during oxygen breathing. Such an acute rise, in itself, would tend to increase pulmonary blood volume passively by the increased back pressure effect mentioned above. The fact that no change was noted, however, supports the supposition that hyperoxia had a counterbalancing effect. This argument gains added support from the fact that when oxygen was discontinued the left atrial mean pressure remained acutely elevated, and the pulmonary blood volume rose by 109 ml./M.². Thus, the rise in pulmonary blood volume during recovery may be attributed to a passive effect of back pressure with the braking effect of oxygen no longer present to counteract it. By inference, then, oxygen breathing did have an effect on pulmonary blood volume, but this action was masked by the back pressure effect transmitted from the left atrium. We cannot account for the remaining patient’s (case 6) lack of change in pulmonary blood volume.

These results help to explain some of the disparities between the effects of hyperoxia and the infusion of acetylcholine on the pulmonary vascular bed. Whereas acetylcholine increases the pulmonary blood volume by actively dilating regions within the pulmonary circulation, 100 per cent oxygen has a different action—it decreases the pulmonary blood volume. Since, at the same time as the volume decreases, the pulmonary artery and left atrial mean pressures and, hence, the pulmonary vascular distending pressure tend to fall, a passive mechanism of action for 100 per cent oxygen must be invoked. A possible explanation is that 100 per cent oxygen reflexly produces systemic venodilation with a consequent redistribution of blood from the pulmonary to the systemic compartment. Such an explanation would account for the inability to show effects of high oxygen on pulmonary arterial pressure in isolated lung preparations. Moreover, it would also account for the additive effects of the two agents that have been noted in patients since acetylcholine would abolish heightened pulmonary vascular tone, while hyperoxia would decrease the pulmonary blood volume.

From a clinical standpoint, our data suggest that inhalation of 100 per cent oxygen may improve the status of patients with pulmonary edema, not only by increasing arterial oxygen content, but also by decreasing the amount of blood in the lungs, thereby relieving pulmonary congestion. Its effects on normal subjects, however, while possibly similar to those described, must await further investigation before they are clarified.

Summary

The effect of breathing 100 per cent oxygen on the pulmonary blood volume, pulmonary arterial pressure, left atrial pressure, and pulmonary vascular distending pressure was studied during cardiac catheterization in eight patients with organic heart disease. In half of the patients, a significant decrease in pulmonary blood volume was observed. This decline in pulmonary blood volume in the face of a decrease or no change in the pulmonary distending pressure is interpreted as evidence for a passive mechanism of action for 100 per cent oxygen.

The effects of hyperoxia are compared to those of acetylcholine, which works by actively dilating the pulmonary vascular bed.
Acknowledgment

We would like to thank Miss Mary Ellen Lindsay, Miss Ann Gratiot, and Mr. Waddell Johnson for their technical assistance and Mrs. Paula Robbins and Mrs. Bonnie Sollie for their secretarial aid.

References

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