Effect of Breathing Oxygen on Pulmonary Artery Pressure and Pulmonary Vascular Resistance in Patients with Ventricular Septal Defect

By HIRAM W. MARSHALL, M.D., H. J. C. SWAN, M.D., HOWARD B. BURCHELL, M.D., AND EARL H. WOOD, M.D.

In 1946 von Euler and Liljestrand demonstrated that the pulmonary artery pressure in the cat was increased when the animal breathed a gas mixture of low oxygen content. Comparable results have been demonstrated in other species, including man. In spite of a degree of variability in the results of experiments designed to elucidate the mechanism of this response, most studies suggest that hypoxia can cause the pulmonary vessels to constrict. Further studies on the comparative effects of breathing a gas mixture of low oxygen tension in one lung while breathing a gas mixture of normal oxygen tension in the other suggest that constriction takes place in the vessels of the hypoxic lung.

Relatively little attention has been paid to the effect exercised on the pulmonary vascular bed by high oxygen tension in the inspired air, although a fall in pulmonary artery pressure has been demonstrated in man, both with normal pulmonary circulation and with pulmonary hypertension. Further, the timing and sequence of events in relation to the change in the oxygen concentration in the inspired gas mixture have not been clearly described.

The present study concerns the effect of breathing gas mixtures of high oxygen tension on the pulmonary and systemic arterial pressures and vascular resistances in 31 patients with ventricular septal defect and varying degrees of elevation of pulmonary artery pressure. Particular attention has been given to the timing of the effects on the pulmonary vascular bed and the changes in the systemic arterial oxygen saturation and heart rate also produced by the change from breathing air to breathing oxygen, and to the interrelation of these events.

The data indicate that in patients with a ventricular septal defect a significant decrease in pulmonary vascular resistance is associated with breathing of high-oxygen mixtures. The decrease in pulmonary artery pressure and heart rate followed by a few seconds the increase in oxygen saturation of systemic arterial blood.

Material and Methods

The diagnosis of ventricular septal defect was considered clearly established on the basis of findings from clinical examination and cardiac catheterization. In 11 of the 31 cases, the diagnosis was verified at operation for correction of the defect. The average age of these 31 patients was 16 years, with a range of 7 months to 43 years.

Measurements

The cardiac catheterization was performed with the technics and instrumentation described previously. The procedure was carried out under rectal thiobromoethanol (Avertin) anesthesia in 13 of the younger patients, the remaining 18 having been studied while awake, but after administration of ½ grain codeine and ½ grain secobarbital (Seconal). Arterial oxygen saturation was recorded by ear oximeters. Intraaortic pressures were recorded and the presence of arterialization in the right ventricle was established. A pulmonary artery wedge pressure was obtained, and then the catheter was positioned in the pulmonary artery. A needle was inserted into the radial or femoral artery. Expired air was collected for 5 to 10 minutes in a large-volume, low-resistance plastic balloon. The volume of the gas was measured and its composition analyzed immediately by the Haldane method for the calculation of oxygen consumption. Midway during the determination of oxygen uptake, blood samples were drawn simultaneously from a systemic

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artery and the pulmonary artery for measurement of oxygen content and capacity. Pulmonary and systemic arterial pressures and other variables were recorded midway during the withdrawal of these blood samples.

Continuous simultaneous recordings of the pulmonary and systemic arterial pressures, arterial oxygen saturation, and other variables were obtained as the gas mixture being breathed by the patient was changed suddenly from room air to a high (95 to 99.5 per cent) oxygen mixture. In 14 of the 31 cases the oxygen was delivered via a low-resistance, small dead-space system, incorporating a carbon dioxide absorber and containing approximately 35 liters of a mixture of 95 per cent oxygen and 5 per cent nitrogen after equilibration with the subject's respiratory gases. The oxygen consumption while breathing oxygen, measured over a 3-minute period after an interval averaging 7½ minutes of oxygen breathing, was found to be increased over the values obtained while breathing air by an average of 11 ml. per sq. meter of body surface (p = 0.05). The remaining 17 patients breathed oxygen via a modified BLB face mask which had a small dead space, and the flow of oxygen was set at a rate high enough to prevent appreciable rebreathing of the expired air. In these 17 cases the oxygen consumption while breathing air and while breathing oxygen was assumed not to differ significantly for the purpose of calculation. During the determination of oxygen consumption from the closed-circuit spirometer or during the period of oxygen breathing from the mask, blood samples again were withdrawn from the pulmonary and systemic arteries for determination of the oxygen capacity and content, and pressures were recorded from these sites.

Calculations

Systemic (Qs) and pulmonary (Qp) blood flows while breathing air and oxygen were calculated by means of the standard Fick equations. The oxygen content of the mixed venous blood was determined by averaging the contents of superior and inferior caval blood in all cases while breathing air and in 30 of the 31 cases while breathing oxygen. If the oxygen saturation of the arterial blood was less than 95 per cent while the subject breathed air, and the right-to-left shunt calculated by the oxygen saturation data was similar to the right-to-left shunt determined by the indicator-dilution technics,16 the total oxygen content of the pulmonary vein blood was taken to be 98 per cent of the oxygen capacity plus 0.3 ml. per 100 ml. of blood.

In two of the children catheterized under anesthesia, the degree of desaturation of arterial blood was greater than could be accounted for on the basis of right-to-left shunts determined from dilution curves and was considered to be due in part to desaturation of pulmonary vein blood associated with deficient pulmonary ventilation. In these two cases the oxygen saturation of the pulmonary vein blood was calculated from the magnitude of the right-to-left shunt determined by the dye-dilution technic16 and the oxygen-saturation values of the mixed venous and arterial bloods. Always when the patients breathed oxygen, the pulmonary vein blood was assumed to contain 1.8 ml. of oxygen per 100 ml. of blood in dissolved form.16

Systemic and pulmonary resistances (pressure/flow ratios) were calculated by the usual equation.

Findings

Original photographic recordings showing the immediate response of pulmonary and systemic arterial pressures and the change in arterial oxygen saturation and heart rate during the change from breathing air to breathing oxygen are given in figure 1. In this patient (who was 8 months old), the arterial oxygen saturation began to increase within 3 seconds after the change to breathing oxygen, and the pulmonary artery pressure commenced its decline within 10 seconds after the change to oxygen. Systemic arterial pressure was not demonstrably changed; the heart rate decreased slightly.

The average values and the variability of the immediate effects of the change from breathing air to breathing oxygen in 28 of the patients are shown in figure 2. The increase in systemic arterial oxygen saturation began 5 (2 to 9) seconds after the start of breathing oxygen. As shown in figure 3, the decrease in pulmonary artery pressure followed the change in systemic arterial oxygen saturation in every instance, the interval averaging 8 (1 to 20) seconds. Of the decrease in pulmonary artery pressure during the first 3 minutes, 60 per cent occurred in the first 30 seconds; and only a slight further decrease in pulmonary artery pressure and in heart rate was recorded in the period from 3 minutes to 10 minutes after the change from breathing air to breathing oxygen.

The averages and ranges of the oxygen consumption and heart rates and of the pulmonary and systemic arterial pressures, blood
Effects of change from breathing air to breathing 99.5 per cent oxygen on systemic and pulmonary arterial pressures, heart rate, and arterial oxygen saturation in an 8-month-old boy with ventricular septal defect (diagnosis confirmed at operation). Upper panel shows continuous recording (paper speed: 5 mm. per second) from this patient during change (marked by vertical arrow) from air to oxygen. Note that arterial oxygen saturation began to increase within 3 seconds and pulmonary artery pressure to decrease within 10 seconds after change from air to oxygen. Arterial pulse and mean pressures were recorded simultaneously by double galvanometer assemblies.11 (Reproduced with permission from: Savard, M., Swan, H. J. C., Kirklin, J. W., and Wood, E. H.: Hemodynamic alterations associated with ventricular septal defects. Symposium on congenital heart disease, p. 141.) The lower panel shows recordings taken at a paper speed of 25 mm. per second 2 minutes before and 3 minutes after the change from air to oxygen. Note the decrease in pulmonary artery pressure and heart rate with relatively little change in systemic artery pressure.
flows, and resistances obtained from all patients while breathing air and after an average of 7½ (5 to 17) minutes of breathing oxygen are given in table 1. The directional changes were independent of the severity of the pulmonary hypertension and of the use of anesthesia. For the group there was a significant fall in pulmonary artery systolic, mean, and diastolic pressures, although the pulmonary artery pressure increased slightly in two patients. The mean pulmonary artery wedge pressure was not changed significantly. The pulmonary blood flow was increased by an average of 32 per cent (fig. 4). However, four of the six adult patients without pulmonary hypertension showed a small decrease in pulmonary blood flow.

Calculated pulmonary pressure/flow ratios (resistances) decreased by an average of 36 per cent (fig. 5). The decrease was least among adult patients without pulmonary hypertension, and in one of the six there was a slight increase. The magnitude of the change in resistance in eight patients without pulmonary hypertension was similar to that in 18 normal subjects studied in this laboratory (fig. 6). Although the pulmonary artery wedge pressure was not measured in all patients, among the 14 from whom values during the breathing of air and of oxygen were available the average decline in pulmonary "arteriolar" resistance was from 750 to 455 dynes sec. cm.².

The changes in resistance were not directly correlative with the age of the patients. All the patients aged 10 years and younger showed large decreases in pulmonary resistance while breathing oxygen. Several of the patients in the older groups, including some in middle

**Figure 2**

*Interrelation of cardiovascular effects produced by change from breathing air to breathing oxygen in 28 patients with ventricular septal defect. Pulmonary and systemic arterial pressures and heart rate are expressed as percentages (scale at left) of control values (indicated at right) which were obtained while breathing air. The wide lines representing the variables measured indicate the mean plus and minus one standard error. Note that the increase in arterial oxygen saturation which occurs within 5 seconds from the change from breathing air to oxygen (marked by vertical line) is followed within 10 seconds by a decrease in pulmonary artery pressure and heart rate.*
PULMONARY ARTERY PRESSURE

age, also showed changes of the same order of magnitude as the changes in the children. Among the older patients were several in whom the changes in pulmonary resistance were insignificant. The majority of these patients, however, were those without severe pulmonary hypertension.

Among the whole series, the average systemic blood flow decreased by 15 per cent (p = 0.02), though in seven patients the systemic flow increased slightly. The average systemic resistance was increased by 25 per cent. This change was due to a substantial increase in systemic resistance among the younger patients. In patients aged 12 years and more, the average systemic resistance did not change significantly during the breathing of oxygen. The absolute magnitude of the decrease in pulmonary vascular resistance was greater in patients with fairly severe degrees of pulmonary hypertension than for those with mild or no pulmonary hypertension (figs. 7 and 8). The percentage of decrease in pulmonary vascular resistance, however, tended to be greatest where pulmonary hypertension was moderately severe and to be somewhat less in the cases of very severe pulmonary hypertension, where the pulmonary vascular resistance equaled or exceeded systemic vascular resistance.

Discussion

Considerations on Measurement

Because the pulmonary vascular resistance normally is low, only relatively large changes in this resistance produce changes in pulmonary artery pressure of an absolute magnitude sufficient for measurement with reasonable accuracy in the intact organism. Accurate interpretation of the cause of such changes in pressure is even more difficult in the light of changes that may occur concomitantly in blood flow, heart rate, respiration, and other variables. The lack of agreement among the results from the numerous studies of factors affecting the pulmonary circulation probably is due in great measure to the large errors of observation and interpretation inherent in most of these investigations.

In the presence of pulmonary hypertension, however, the percentage of error in such observations is reduced; for if blood flow is unchanged, the absolute magnitude of the change in pressure caused by a given percentage change in pulmonary vascular resistance is directly related to the level of the pulmonary artery pressure. A large share of patients with ventricular septal defect have pulmonary hypertension and thus constitute a suitable group for a study of the response of the pulmonary circulation to changes in the oxygen tension of the inspired gas mixture. Since in normal subjects also the breathing of oxygen causes a small decrease in pulmonary artery

Figure 3

Relation of time from onset of breathing oxygen to onset of increase in oxygen saturation of arterial blood and onset of decrease in pulmonary artery systolic pressure in 23 patients with ventricular septal defect. Patients were excluded whose change in pulmonary artery pressure was too small or gradual to be accurately timed. Patients have been distinguished on the basis of severity of pulmonary hypertension (pulmonary artery systolic pressure greater or less than 70 per cent systemic artery pressure). Diagonal line of identity. Note that decrease in pulmonary artery systolic pressure uniformly followed increase in oxygen saturation of systemic arterial blood.
Table 1

Averages (and Ranges) of Circulatory Variables in Thirty-one Patients* with Ventricular Septal Defect While Breathing Air and after Seven and a half (Five to Seventeen) Minutes of Breathing 95 to 99.5 Per Cent Oxygen

<table>
<thead>
<tr>
<th></th>
<th>Breathing air</th>
<th>Breathing oxygen</th>
<th>Difference</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen consumption, ml./min./M.²</td>
<td>211 (153-279)</td>
<td>222 (159-303)</td>
<td>+11</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart rate, beats/min.</td>
<td>104 (64-141)</td>
<td>96 (62-143)</td>
<td>-8</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean pulmonary artery wedge pressure, mm. Hg</td>
<td>10.1 (5-18)</td>
<td>11.1 (7-20)</td>
<td>+1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Pulmonary artery pressure, mm. Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>75 (18-124)</td>
<td>66 (15-124)</td>
<td>-9</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>37 (7-72)</td>
<td>32 (7-68)</td>
<td>-5</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean</td>
<td>53 (11-86)</td>
<td>46 (11-81)</td>
<td>-7</td>
<td>0.001</td>
</tr>
<tr>
<td>Systemic artery pressure, mm. Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>108 (62-166)</td>
<td>107 (60-161)</td>
<td>-1</td>
<td>0.6</td>
</tr>
<tr>
<td>Diastolic</td>
<td>61 (30-98)</td>
<td>65 (32-89)</td>
<td>+4</td>
<td>0.3</td>
</tr>
<tr>
<td>Mean</td>
<td>78 (41-119)</td>
<td>79 (42-114)</td>
<td>+1</td>
<td>0.5</td>
</tr>
<tr>
<td>Pulmonary blood flow, L./min./M.²</td>
<td>6.3 (1.8-19.4)</td>
<td>8.3 (2.0-24.9)</td>
<td>+2.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Systemic blood flow, L./min./M.²</td>
<td>4.1 (1.6-8.2)</td>
<td>3.5 (2.0-7.0)</td>
<td>-0.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Pulmonary vascular resistance, dynes sec. cm⁻⁵</td>
<td>970 (120-2520)</td>
<td>616 (110-1930)</td>
<td>-354</td>
<td>0.001</td>
</tr>
<tr>
<td>Systemic vascular resistance, dynes sec. cm⁻⁵</td>
<td>1635 (790-3530)</td>
<td>2040 (930-4550)</td>
<td>+405</td>
<td>0.01</td>
</tr>
<tr>
<td>Rp/Rs</td>
<td></td>
<td></td>
<td>0.57 (0.10-1.36)</td>
<td>0.33 (0.09-1.00)</td>
</tr>
</tbody>
</table>

*Except for measurements of oxygen consumption while breathing oxygen and measurements of wedge pressures, values for all parameters were obtained from each of the 31 patients both when breathing air and when breathing oxygen.

†Oxygen consumption while breathing oxygen was measured in 14 patients.

‡Mean pulmonary wedge pressures were obtained from 14 patients while breathing air and while breathing oxygen.

§In these values for vascular resistance, no correction was made for pulmonary or systemic venous pressure.

||Ratio of pulmonary to systemic vascular resistance.
pressure and a significant decrease in heart rate, it is likely that the normal pulmonary circulation responds in a similar manner—although this is by no means certain.

**Decrease of Pulmonary Resistance**

The patients studied had a wide range of pulmonary vascular resistances that included those encountered in normal subjects. As would be expected, the smallest absolute changes with breathing of oxygen were observed in the patients with low pulmonary resistance values and without pulmonary hypertension when they breathed air. Even in those patients with severely elevated pulmonary vascular resistances, a decrease of considerable magnitude was evident.

Although the absolute decrease in pulmonary vascular resistance generally remains large among these patients with pulmonary hypertension, the proportionate decrease in resistance appeared to be less in those patients in whom the pulmonary hypertension was most severe and in whom the pulmonary/systemic resistance ratio approached or exceeded 1.0. This degree of elevation of pulmonary resistance is indicative of the presence of severe organic changes in the pulmonary vessels, and it would be expected that the capacity of such vessels to dilate would be limited. Certain other patients with idiopathic pulmonary hypertension, in whom the pulmonary resistance values were much higher than any obtained in this study, showed no significant decrease in pulmonary vascular resistance while breathing oxygen.

Since no change in pulmonary artery wedge pressure was observed in those patients in whom it was measured, the decline in resistance to pulmonary blood flow is almost certainly due to a fall in the component of this resistance which exists between the large pulmonary arteries and the left atrium—that is, the pulmonary arteriolar or vascular resistance. This decline suggests that the hindrance offered by the smaller pulmonary vessels to flow through them is reduced during breathing of oxygen. Recent publications have stressed the need for extreme care in the in-
Interpretation of such findings. In the conditions under study, however, there is no reason to suspect that intrathoracic pressure changed significantly and, so far as could be determined, there was no significant change in the breathing pattern. The heart rate slowed slightly and the stroke volume increased. Apart from the increase in the stroke volume, none of these factors would be expected to change the calculated vascular resistance. Since the intrathoracic pressure apparently remained virtually unchanged while the intrapulmonary arterial pressure fell, the transmural pressure—that is, the effective distending pressure in these vessels—was significantly reduced. The association of a decrease in transmural pressure with a reduction in vascular resistance strongly suggests a decrease in tone of the pulmonary blood vessels. These results demonstrate that the pulmonary vascular bed remains labile and that vasomotor tone plays a significant part in the pulmonary hypertension which is present in many of these patients.

Timing of Changes

The temporal relation of the change in pulmonary artery pressure to certain other parameters is clearly demonstrated. The initial change in this pressure usually was evident within 15 seconds of the first inspiration of oxygen as compared to the striking increase in alveolar oxygen tension that would occur immediately upon the first inspiration. At a respiratory rate of 20 per minute the alveolar $pO_2$ would have increased to approximately three to four times the control values during this 15-second interval. The beginning of the decrease in pulmonary artery pressure seems more clearly related to the increase in systemic arterial oxygen saturation than to the increase in alveolar $pO_2$, because the time at which the decrease in pulmonary artery pres-
Mechanism of Response

There is no direct information on the mechanism whereby the inspiration of a high-oxygen mixture causes a reduction of pulmonary vascular resistance. However, the effect of the inspiration of gas mixtures of lowered oxygen tension has been extensively studied. Since the change in pulmonary artery pressure and pulmonary vascular resistance appears to be diametrically opposite when gas mixtures of high or low oxygen content are breathed, it is likely that they represent extremes of the same response, and that when ambient air is breathed, the pulmonary blood vessels are maintained in an intermediate state of tone.

The results of the different studies designed to elucidate the mechanism of response to hypoxia are various. In a recent paper, Liljestrand concluded that hypoxia acts on pulmonary vessels by liberation of lactic acid and thereby may effect local regulation of the relation between pulmonary blood flow and ventilation. The previous experimental work was summarized and reviewed in the light of his own most recent findings.

The present studies contribute to an understanding of the mechanism of response in two ways: (1) they define the period that elapses before the response becomes operative and demonstrate it to be of the order of seconds; (2) they indicate that pulmonary artery wedge pressure does not fall during the breathing of oxygen. If the pulmonary artery wedge pressure measures pulmonary capillary pressure, then all of the change in vascular
tone occurred in the precapillary vessels. If, as more probably is true, the pulmonary artery wedge pressure represents the pressure operative in the next pulmonary vascular bed downstream to the wedged catheter in which flow is occurring, then some change of tone in the capillaries and small vessels might not produce detectable changes in the wedge pressure. However, in the presence of pulmonary hypertension with increased vascular resistance, which is almost certain to be precapillary, the relatively large magnitude of the change in vascular resistance in a number of patients indicates that this response must have involved the precapillary vessels.

Because of the presence of a left-to-right shunt via the defect in these patients, the pulmonary artery oxygen saturation, unlike that in persons without septal defects, would rise coincidently with the change in systemic arterial oxygen saturation. It is of considerable interest, therefore, that the temporal relation of the increase in arterial oxygen saturation to the subsequent decrease in pulmonary artery pressure is closely similar in this group of patients with left-to-right shunt to the time sequence observed in patients with pulmonary hypertension who respond with a decrease in pressure but do not have a septal defect. This fact is compatible with the interpretation that these effects are not triggered by the increase in oxygen content of pulmonary artery blood. Furthermore, whatever the mechanism, it was not demonstrably affected by the anesthetic agents used to induce general anesthesia in some of the patients included in this study.

Assumptions Used in Calculations

The assumptions concerning the use of the pulmonary artery wedge pressure and the oxygen saturation of pulmonary vein blood have been discussed already, as has the relation of oxygen consumption values when the subject breathes air and breathes oxygen.

Data as to whether samples of blood drawn from the pulmonary artery in the presence of ventricular septal defect are uniformly mixed in regard to oxygen content are not available. It is the practice in this laboratory to obtain multiple samples of blood in rapid succession from the pulmonary artery and its main branches. In 15 of the patients in this series, the average maximal variation in oxygen saturation of multiple (two to six) samples of blood drawn from different locations.
in the pulmonary artery and its main branches during the breathing of either air or oxygen was 1.4 per cent. This small variation permits the conclusion that in the presence of a ventricular septal defect the mixing of blood in the pulmonary artery is, for practical purposes, uniform.

The values for pulmonary and systemic arterial pressures, arterial oxygen saturation, and heart rate approached closely, within 3 minutes after the start of breathing oxygen, the values obtained at the time blood samples were drawn for the calculation of pulmonary and systemic blood flows (5 to 17 minutes after the change to oxygen). Hence it seems reasonable to assume that a steady state in regard to metabolic equilibrium was attained. The average variation between the percentage of oxygen saturation of blood samples drawn from the pulmonary artery through a cuvette oximeter for Van Slyke analysis and that of a second sample drawn within an average of 12 minutes later was only 0.7 per cent, which is strong additional evidence for metabolic stability.

Phasic variations in the oxygen content and flow of blood at the sampling sites probably are of greater magnitude in patients with ventricular septal defect than in persons without intracardiac shunts. However, it appears unlikely that the direction and magnitude of errors these effects could cause in determination of flow by the Fick method would be influenced to a significant degree by the change from breathing air to breathing oxygen. The similarity in the response to breathing oxygen by patients with atrial septal defect and with patent ductus arteriosus lends support to this conclusion.

Summary and Conclusions

During cardiac catheterization, pulmonary and systemic arterial pressure, arterial oxygen saturation, respirations, and heart beats were recorded continuously during the change from breathing air to breathing 95 to 99.5 per cent oxygen in a series of 31 patients with ventricular septal defect. In addition, pulmonary and systemic blood flows were measured under the two circumstances.

Systemic arterial oxygen saturation began to increase about 5 seconds after the change from breathing air to breathing oxygen. Within a few seconds thereafter the pulmonary artery pressure and heart rate began to decrease. After approximately 3 minutes the changes in these parameters appeared essentially complete.

The pulmonary blood flow increased by an average of 32 per cent while systemic flow decreased by 15 per cent during breathing of the high-oxygen mixture. No consistent change in pulmonary artery wedge pressure was observed. The average calculated pulmonary pressure/flow ratio (resistance) was decreased by 36 per cent while the average systemic pressure/flow ratio was increased. The occurrence of these changes was independent of the presence of pulmonary hypertension, of the use of general anesthesia, and of the age of the patient.

It is concluded that in patients having ventricular septal defects, the presence of vasomotor tone in the pulmonary vasculature is usual, and that in those having associated pulmonary hypertension, a significant contributing factor is constriction of the precapillary pulmonary resistance vessels.

References

12. Wood, E. H.: Special instrumentation problems encountered in physiological research concern-

On first thoughts it may seem remarkable that scientific work like this should have been performed by a country parson. In the nineteenth century religion and science became mutually antagonistic, and at the present time it is still uncommon to see them in open association; but in the early years of the eighteenth century the Church looked with success to science for support.—A. E. Clark-Kennedy, M.D., M.R.C.P. Stephen Hales, D.D., F.R.S. Cambridge, University Press, 1929, p. 76.
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