The Dynamics of Eisenmenger’s Complex
An Integration of the Pathologic, Physiologic and Clinical Features

By H. Goldberg, M.D., E. N. Silber, M.D., A. Gordon, M.D., and I. N. Katz, M.D.

Pulmonary venous blood and pulmonary venous pressure were obtained by catheterization technic in a case of Eisenmenger’s complex with anomalous pulmonary venous drainage into the right auricle. This made possible measurement of the true total pulmonary vascular resistance and evaluation of a pulmonary factor in the cyanosis accompanying this anomaly. No evidence for inadequate oxygenation in the lungs was apparent, and it is concluded that the cyanosis in Eisenmenger’s complex is due solely to venoarterial shunting.

The pathologic anatomy of the heart in Eisenmenger’s complex has been known for more than 50 years and considerable progress has been made in its clinical recognition. Recently, striking morphologic changes in the intrapulmonary vessels have been demonstrated in this anomaly; yet the pathophysiology underlying many of its manifestations, for example, delayed cyanosis, has remained confused. It has been postulated that the cyanosis may result from (a) some congenital abnormality of the pulmonary epithelium or capillaries which interferes with the complete oxygenation of the blood in the lungs or (b) that blood is sucked from the right ventricle directly into the aorta by the vigorous pumping action of the left ventricle.

The application of cardiac catheterization to the investigation of congenital heart disease has provided the means for a physiologic approach to the study of the clinical features of this disease. From such studies it has been learned that pulmonary hypertension and systemic arterial unsaturation are two of the physiologic derangements consistently present in Eisenmenger’s complex.

Recently, we had the opportunity to study an unusual case of Eisenmenger’s complex by cardiac catheterization, in which, in addition to the usual features, anomalous pulmonary venous drainage into the right auricle was demonstrated by the entrance of the catheter into one of these veins during the procedure. This afforded us the unique opportunity to measure directly the vascular resistance to blood flowing through the lungs and to determine whether or not a pulmonary factor for the production of cyanosis actually exists in this condition. The information obtained from this case, when correlated with that of other investigators, makes it possible to present a logical sequence of the natural history of the disease.

Case Report

The patient, a 19 year old white girl, was sent to Michael Reese Hospital for investigation of a “heart condition” known to have existed since birth. Although physical activity was limited, the patient considered herself to be in good health until three years prior to this admission at which time she developed pneumonia. Since that illness the patient had noticed increasing dyspnea and cyanosis; the latter, intermittent at first, was now persistent. There was no history of squatting.

Physical examination revealed a well nourished girl who appeared small for her stated age. There was marked cyanosis of the lips and nail beds. She did not appear dyspneic and clubbing was not present. Examination of the heart revealed that the apex beat was palpable in the left fifth intercostal space at the midclavicular line. The second pulmonic sound was associated with a palpable shock in the second left intercostal space. Except for dullness over the lower sternum, there was no evidence of cardiac enlargement on percussion. The
second pulmonic sound was markedly accentuated and greater than the second aortic sound. A grade II systolic murmur was heard in the pulmonic area and at the fourth intercostal space near the left sternal border. No diastolic murmurs were heard. The blood pressure was 112/80. There were no signs of congestive heart failure.

Using Decholin to determine the circulation time, two end points were obtained: one at 14 seconds and the other at 23 seconds. The hemogram revealed a red blood cell count of 5.3 million per cu. mm. and 16.8 Gm. hemoglobin.

On fluoroscopy the striking feature in all views was the markedly enlarged pulmonary artery and

**FIG. 1.** Anteroposterior roentgenogram of the chest showing the catheter in the right inferior pulmonary vein which drains into the right auricle in this case. Note the markedly enlarged “main” pulmonary artery and its right hilar branch.

**FIG. 2.** Diagram of the roentgenogram in figure 1

**FIG. 3.** Pressure curve (upper) obtained with catheter in the anomalous pulmonary vein. Note the venous character of the pulse. The electrocardiogram, lead II, is below. Time is in 0.04 second, scale for electrocardiogram is 0.1 millivolt. Discussed in text.
its hilar branches. These vessels as well as their intrapulmonary branches were hyperdynamic. The lung fields showed increased vascularity. In the right anterior oblique position enlargement of the outflow tract of the right ventricle was noted. All other chambers were within normal limits. Laminar calcification in the main pulmonary artery was demonstrable by teleroentgenogram in the left anterior oblique view. The electrocardiogram revealed right heart strain.

Cardiac catheterization was performed without anesthesia according to the technic of Courand and Ranges. During the procedure the catheter was passed from the right auricle directly into the right lung field (figs. 1 & 2), suggesting entrance into an anomalous pulmonary vein. The pressure curve at this site was a venous pulse (fig. 3) and blood obtained was 91.4 per cent saturated, confirming our fluoroscopic impression. The catheter was then withdrawn into the right auricle and advanced into the right ventricle and right pulmonary artery. Pressures were recorded in the right pulmonary artery, main pulmonary artery and the right ventricle (fig. 4), right auricle and pulmonary vein, and blood samples were withdrawn from these sites as well as from the superior and inferior venae cavae and from the brachial artery. Blood oxygen content was determined by the method of Van Slyke and Neill. Oxygen consumption was calculated from expired air collected in a Tissot spirometer and gaseous oxygen determined by the Pauling gas analyzer. The data obtained during catheterization are summarized in table 1.

Blood obtained from the anomalous pulmonary vein had an oxygen content of 20.3 volumes per cent which is 91.4 per cent saturated. This blood may be considered to be fully saturated (95 per cent), since the latter would correspond to 20.9 volume per cent and the difference between this figure and the one obtained falls within the range of error of the method of blood gas analysis. The maximum difference in oxygen content of blood samples from various chambers is within the accepted normal

### Table 1.—Summary of Data in Case R. P.

<table>
<thead>
<tr>
<th>Site of Catheter</th>
<th>Oxygen Content Vol. %</th>
<th>Intracardiac Pressures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Systolic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mm.Hg</td>
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<tr>
<td>Right Pulmonary</td>
<td></td>
<td>14.7</td>
</tr>
<tr>
<td>Artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main Pulmonary</td>
<td></td>
<td>15.0</td>
</tr>
<tr>
<td>Artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Ventricle:</td>
<td>a) near pulmonic valve</td>
<td>14.9</td>
</tr>
<tr>
<td></td>
<td>b) midventricle valve</td>
<td>14.7</td>
</tr>
<tr>
<td></td>
<td>c) near tricuspid valve</td>
<td>14.8</td>
</tr>
<tr>
<td>Right Auricle:</td>
<td>a) near tricuspid valve</td>
<td>13.5</td>
</tr>
<tr>
<td></td>
<td>b) midauricle valve</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>c) near superior vena cava</td>
<td>14.7</td>
</tr>
<tr>
<td>Superior Vena Cava</td>
<td></td>
<td>13.9</td>
</tr>
<tr>
<td>Inferior Vena Cava</td>
<td></td>
<td>15.4</td>
</tr>
<tr>
<td>Pulmonary Vein</td>
<td></td>
<td>20.3</td>
</tr>
<tr>
<td></td>
<td>Brachial Artery</td>
<td></td>
</tr>
<tr>
<td>Oxygen content</td>
<td></td>
<td>17.1</td>
</tr>
<tr>
<td>of 22.2 vol. per cent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>77 per cent</td>
<td></td>
</tr>
<tr>
<td>Oxygen pressure</td>
<td>112/80 mm. Hg</td>
<td></td>
</tr>
<tr>
<td>Resting Oxygen Consumption</td>
<td>206 cc. per minute</td>
<td></td>
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<tr>
<td>Cardiac Output:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic Blood Flow</td>
<td>9.23 L. per min.</td>
<td></td>
</tr>
<tr>
<td>Pulmonic Blood Flow</td>
<td>3.76 L. per min.</td>
<td></td>
</tr>
<tr>
<td>Effective Pulmonic Blood Flow</td>
<td>3.76 L. per min.</td>
<td></td>
</tr>
<tr>
<td>Intracardiac Shunt:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right to left through overriding aorta—5.47 L. per min.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Vascular Resistance—1731 dynes second cm.$^{-1}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic Vascular Resistance—813 dynes second cm.$^{-1}$</td>
<td></td>
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</table>
range of variation. Hence there is no demonstrable significant left-to-right shunt despite the presence of an anomalous pulmonary vein entering the right auricle. The peripheral unsaturation (77 per cent) in the presence of fully saturated blood returning from the lungs indicates a right-to-left shunt. The findings of identical systolic pressures in the right ventricle, pulmonary artery, and brachial artery indicates that the aorta and pulmonary artery are in communication with the right ventricle. The absence of a systolic pressure gradient between the pulmonary artery and the right ventricle rules out the presence of pulmonic stenosis. Hence the combination of an over-riding aorta, high interventricular septal defect, right ventricular hypertension without pulmonic stenosis establishes the diagnosis of Eisenmenger’s complex.

**Discussion**

Ever since the classic work of Lundsgaard and Van Slyke the venoarterial shunt has been considered the chief cause of cyanosis in congenital heart disease. In favor of this is the fact that fully saturated blood from the pulmonary vein has been obtained in cyanotic patients with various forms of congenital heart disease, such as auricular septal defect and tetralogy of Fallot. Friedlich and associates also concluded that blood leaving the lungs is fully saturated on the basis of pulmonary venous blood obtained in 24 cases of congenital heart disease. It might be reasonable to assume that in Eisenmenger’s complex a similar situation prevails. However, Burwell and Taussig and Blalock have suggested that in Eisenmenger’s complex a pulmonary factor is operative in addition to the right-to-left shunt responsible for the systemic arterial unsaturation. This was based on the fact that arterial saturation could be raised when the patient was breathing pure oxygen. They claimed that there is an alteration in the pulmonary alveolar lining or capillaries which prevents complete oxygenation of the blood passing through the lung. The finding in our case of marked peripheral unsaturation in the presence of fully saturated blood obtained directly from the pulmonary vein indicates that the unsaturation in the systemic arterial blood is due solely to venoarterial shunting of blood. This eliminates a pulmonary factor as a contributing cause for cyanosis in Eisenmenger’s complex.

For the first time in Eisenmenger’s complex, a measure of the total pulmonary vascular resistance was made possible by directly obtaining the true pulmonary venous pressure. Previously calculations were made either by assuming the pulmonary venous pressure to be zero or by utilizing pulmonary “capillary” pressure as an index of pulmonary venous pressure. The pulmonary vascular resistance was of the order of 1730 dynes second cm. which is approximately 25 times the normal. In a second case studied by us the pulmonary vascular resistance index was over 5000 dynes second cm. calculated by the method of Bing. In both cases the resistance of the pulmonary circuit appeared to be twice that of the systemic circuit.

A constant finding in Eisenmenger’s complex is pulmonary hypertension. Our 2 cases were no exceptions. Blood pressure is determined by two factors—blood flow in the arteries and peripheral resistance. The pulmonary pressure increase may therefore result from an increase in the amount of blood flowing through the pulmonary artery and/or an increase in the peripheral resistance in the pulmonary vascular bed. The latter may be due to an increased pulmonary venous pressure, an increased viscosity and/or a narrowing of the peripheral pulmonary vascular bed. In Eisenmenger’s complex the pulmonary blood flow is either low or normal, and the pulmonary venous pressure is also normal. Increased blood viscosity resulting from polycythemia is an unlikely etiologic factor. In the tetralogy of Fallot we have observed, as has Dexter, hematoctits as high or higher than those found in Eisenmenger’s complex, yet the pulmonary arterial resistance does not approach the order of magnitude obtained in the latter condition. Moreover, in chronic cor pulmonale, it has been noted that elevated hematoctits occur with pulmonary hypertension of a degree considerably less than that found in Eisenmenger’s complex. By exclusion therefore, it may be concluded that the cause for the elevated pulmonary arterial pressure in Eisenmenger’s complex is a narrowing of the peripheral pulmonary vascular bed.

In normal individuals the systemic circuit offers a considerable resistance to the blood flowing through it, in contrast to the relatively
small resistance offered by the pulmonary circuit. If a similar relationship existed in Eisenmenger's complex in the presence of a physiologic common ventricle, all the blood ejected by the heart would be shunted through the pulmonary artery to the lung with little or none going through the aorta to the systemic circuit. Under these circumstances, the pulmonary capillaries could be subjected to abnormally high pressures resulting in pulmonary edema and death of the individual. The existence of the high pulmonary arteriolar resistance serves to readjust such potentially dangerous disturbances in circulatory dynamics, thereby "protecting" the capillary bed from such untoward effects.

Since there is little evidence to support the existence of an active vasomotor control over the pulmonary vascular tree, it would appear that the major cause for the resistance to flow through the pulmonary arterial tree in the established Eisenmenger's complex is organic change in the pulmonary arterioles. Such structural changes have recently been found in 3 cases of Eisenmenger's complex by Edwards. The changes observed were primarily in the muscular arteries. In the 2 older patients these changes consisted of medial hypertrophy, narrowing of the lumen and nonatheromatous intimal thickening with fibrous tissue. In the youngest case, aged 11 months, the medial hypertrophy and luminal narrowing were present but there was no intimal thickening. The findings in this third case are similar to the histologic appearance of the muscular arteries in the normal human fetus. Edwards concludes that the medial changes in these arteries are primary and a carry-over from fetal life. It would appear that this is so because of cessation of the normal involution in the presence of the Eisenmenger's complex. The intimal fibrous changes appear to be secondary and occur later.

Striking changes in the muscular arteries of the lung occur postnatally in normal man. The muscular element in these vessels practically disappears by the sixth month. The media becomes thin and the vessel lumen wide. This is the anatomic expression of the existing low resistance found in the normal pulmonary circulation. In Eisenmenger's complex, these postnatal changes do not occur. Instead, the muscular arteries have a thick media and narrowed lumen, and resemble those of the systemic circuit. It is suggested, therefore, that pulmonary hypertension present after birth in the infant with Eisenmenger's complex provides the stimulus for the maintenance of the good muscular development found in the fetal pulmonary arteries. Then as the infant and child becomes older the persistent hypertension leads to intimal changes with further narrowing of the lumen and augmentation of the pulmonary vascular resistance to keep pace with the rising arterial pressure. It would seem that the postnatal pulmonary hypertension at first would be accounted for on the basis of increased flow through the lung, abetted by some humoral or neurogenic pulmonary vasoconstriction.

Is the pulmonary vascular resistance in Eisenmenger's complex fixed as has been postulated? That this may not be so is suggested by the work of von Euler and Liljestrand already referred to, in which they demonstrated a decrease in the pulmonary vascular resistance and pressure in animals breathing pure oxygen. This was attributed to vasodilation of the pulmonary arterioles. When patients with Eisenmenger's complex breathe pure oxygen, their peripheral arterial saturation increases almost to normal. This speaks for a reduction in the venoarterial shunt due to a decrease in the pulmonary vascular resistance following vasodilation of the pulmonary arterioles. If the pulmonary vascular resistance is variable, it follows that the pulmonary hypertension is reversible in part. Support for such a view is found in the work of Cournand who demonstrated that the pulmonary hypertension in chronic cor pulmonale is also reversible.

The outstanding clinical feature of Eisenmenger's complex is the late onset of cyanosis. In the light of the foregoing discussion this is readily understandable. Early in the disease the vascular resistance in the pulmonary bed is of the same order of magnitude as in the systemic circuit. Hence, there is minimal right-to-left shunting of blood. As the patient becomes older there is progression of the intimal changes in the lung vessels leading to further elevation
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of the pulmonary vascular resistance, an increase in the veno-arterial shunt and eventually the appearance of cyanosis. This is demonstrated in our cases in which the pulmonary vascular resistance was found to be in excess of the systemic. With advancing age, the cyanosis may be intermittent at first owing to the interplay of the pulmonary and systemic resistance which determines the magnitude of the veno-arterial shunting of blood. Later, it may become persistent. Hamilton26 studied a case of tetralogy of Fallot which was clinically characterized by episodes of intermittent cyanosis and found evidence which supports the foregoing concept. He observed that the veno-arterial shunt from the right ventricle to the aorta varied from minimal to 100 per cent, depending upon the level of the systemic blood pressure. When the blood pressure in the systemic circuit was low, the shunt was great, and conversely, when the systemic pressure was high, the shunt was minimal.

At the present time there is no available treatment for Eisenmenger’s complex. In order that a surgical approach be successful, it must accomplish three objectives: (1) a reduction of the pulmonary artery pressure, thereby lessening or eliminating the progressive changes in the muscular arteries in the pulmonary bed; (2) alleviation of the strain upon the right ventricle; (3) return of the peripheral arterial saturation towards normal. Recently, Civin and Edwards27 have suggested the merit of creating a stenosis in the outflow tract of the right ventricle or in the pulmonary artery trunk. Although this procedure may lower the pulmonary arterial pressure, and thus “protect” the pulmonary arterioles, the strain upon the right ventricle would still be present. This chamber would continue to pump against an enormous systemic peripheral resistance. The dynamics in this situation would be analogous to those in tetralogy of Fallot, the prognosis of which is no better than that of Eisenmenger’s complex, the chief cause of death in both conditions being right ventricular failure. Hence, creation of a pulmonary stenosis would neither rectify nor favorably influence the altered hemodynamics in this condition. A more rational approach would be to attempt to correct the overriding of the aorta and at the same time to obliterate the ventricular septal defect. Such corrections would eliminate the source of the pulmonary hypertension and result in a rise of the peripheral saturation to normal, which would also tend to decrease the pulmonary vascular resistance. If this were done early enough, the secondary detrimental structural changes in the pulmonary vessels might be averted, the strain upon the right ventricle would be reduced, and the circulatory dynamics would tend to return to normal. Although such a procedure is not feasible at this time, amelioration of this condition will be possible if efforts are directed along such lines.

Summary

1. Catheterization data in a case of Eisenmenger’s complex with anomalous pulmonary venous drainage into the right auricle are presented. Pulmonary venous blood and pulmonary venous pressure were obtained directly making possible measurement of the true total pulmonary vascular resistance and evaluation of the pulmonary factor in the cyanosis associated with this cardiac anomaly.

2. It is concluded that peripheral hypoxemia in Eisenmenger’s complex is due solely to the veno-arterial shunt from the right ventricle to the overriding aorta. The view that cyanosis is due to inadequate oxygenation in the lungs could not be supported.

3. The principles of surgical correction of this disease are discussed.

Acknowledgments

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