Intermittent Reversal of Flow in a Case of Patent Ductus Arteriosus

A Physiologic Study with Autopsy Findings

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The direction of blood shunts between abnormally communicating ventricles or large vessels is dependent upon blood pressure differences in the adjacent structures, and upon the respective vascular resistance in both circulating systems distal to the communication. In a case of patent ductus arteriosus, physiologic measurements suggested that the direction of blood flow through the ductus was reversed intermittently during the systolic phase of the cardiac cycle. Pathologic studies confirmed the hypothesis by demonstrating the presence of "impingement" plaques on the aortic as well as on the pulmonary artery walls opposite the lumen of the ductus. They also gave information concerning the lesions in the pulmonary vascular bed which might be held responsible for the considerable increase in resistance, the pulmonary systolic hypertension and, attendant to it, the cyclic reversal of blood flow.

In patent ductus arteriosus the direction of blood flow is ordinarily from aorta to pulmonary artery during the entire cardiac cycle. This direction of flow is determined by the higher pressure prevailing in the aorta during systole as well as diastole.

Under certain circumstances, as a late complication, this pressure relationship may be reversed, resulting in the flow of some mixed venous blood into the aorta and causing cyanosis. French clinicians have called this condition "cyanose tardive."

The following case is an example of partial reversal of flow in a patient with patent ductus arteriosus where physiologic measurements supported this diagnosis during life and were confirmed by autopsy findings.

Case Report

Clinical Data. The patient was a 42 year old woman whose heart disease was discovered following a hemoptysis at the age of 6 years. Exertional dyspnea had been present since childhood and had become severe and persistent following a pregnancy at the age of 31. She had received digitalis and mercurial diuretics for many years. Seven months before admission to the hospital, she developed ankle edema and entered another institution, where an attempt was made to ligate a patent ductus arteriosus; the operation was abandoned because of technical difficulties.

On admission to Bellevue Hospital, the physical examination revealed a small but well developed white woman who became dyspneic and faintly cyanotic on the slightest exertion. The blood pressure was 110/70. The pertinent findings were confined to the chest. The heart was enlarged both to right and left, with increased upper retrosternal dullness. A diastolic thrill was present over the entire precordium but was most intense in the third and fourth left intercostal spaces. The rhythm was regular with a ventricular rate of 90. The second pulmonic sound was impure, but louder than the second aortic sound. There was a soft apical systolic murmur (Grade II) and a harsh diastolic murmur (Grade IV) loudest in the third and fourth left intercostal spaces but heard over the entire precordium and in the interscapular region. Examination of the lungs revealed no abnormalities. The liver and spleen were enlarged. No ankle edema was present. There was no clubbing of fingers or toes.

Laboratory examinations showed a hemoglobin of 16.6 Gm. and a hematocrit of 54 per cent. A Decholin circulation time was 27 seconds, ether time 17 seconds. Venous pressure measured 120 mm. of saline. An electrocardiogram (fig. 1) revealed normal sinus rhythm with right axis deviation, diminished amplitude of T waves in Lead I, depression of the S-T segments and diphasic T waves in Leads II and III. The unipolar precordial leads were suggestive of right ventricular hypertrophy. A stethocardiogram (fig. 1) recorded simultaneously with Lead II and taken over the pulmonic area, showed abnormal vibrations during early systole.
and throughout the latter two-thirds of diastole. Chest x-ray films (fig. 2) showed marked enlargement of the pulmonary artery and its branches, enlargement of the right ventricle and either displacement posteriorly or enlargement of the left ventricle. By fluoroscopy, a “hilar dance” was demonstrated. Chest x-ray films (fig. 2) showed marked enlargement of the pulmonary artery and its branches, enlargement of the right ventricle and either displacement posteriorly or enlargement of the left ventricle. By fluoroscopy, a “hilar dance” was demonstrated.

The clinical diagnosis was congenital heart disease, patent ductus arteriosus, enlarged heart, normal sinus rhythm, II B.

Physiologic Data. Table 1 summarizes the results of cardiac catheterization. Blood samples drawn from the superior vena cava, right auricle, and tricuspid area of the right ventricle were almost identical in oxygen content, indicating no intracardiac shunts in these areas. In the main pulmonary artery, however, the oxygen content was very much higher than in the right ventricle, which suggests that oxygenated blood was being added to mixed venous blood at the level of the pulmonary artery, i.e., through a patent ductus arteriosus. Since the oxygen content of the pulmonary artery blood was only 0.8 volumes per cent less than in the brachial artery, it is obvious that the catheter tip was located very near the mouth of the ductus; hence this sample represented almost entirely left ventricular blood. Unfortunately, as was first pointed out by Eppinger and associates,1 this incompletely mixed sample precludes any accurate flow calculations through the ductus by means of the Fick equation. The finding of a higher oxygen content in the sample from the right ventricular outflow tract than in the sample from the tricuspid area was interpreted as evidence

![Fig. 1. The electrocardiogram (top) and stethogram (bottom) of an adult with patent ductus arteriosus and intermittent reversal of flow. For discussion see text.](http://circ.ahajournals.org/cover.jpg)
of incompetence of the pulmonary valve. The other possibility, that of a high interventricular septal defect, was ruled out because there was no harsh systolic murmur heard over the base of the heart.

Pressure tracings were of particular interest. The systolic values of the pulmonary artery exceeded those in the systemic (brachial) artery, suggesting that, during at least part of systole, blood flow through the ductus was reversed; i.e., blood passed from the pulmonary artery into the aorta. The diastolic and mean pressures in pulmonary and brachial arteries, however, favored the usual aortic-pulmonary flow.

A 91 per cent arterial saturation in the brachial artery also suggested a partial and intermittent right-to-left shunt and this was substantiated several days later with the method proposed by Burchell. Oxygen saturation was determined on blood samples drawn simultaneously from the right brachial and femoral arteries and was found to be 6 per cent lower in the latter than in the former. The cause for this difference in saturation becomes apparent when one considers that, as a rule, the junction of the

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\begin{array}{|c|c|c|c|}
\hline
\text{Pressure (mm. Hg)} & \text{Syst.} & \text{Diast.} \\
\hline
\text{Superior vena cava} & 122 & \\
\text{Right auricle} & 120 & \\
\text{Right ventricle (tricuspid area)} & 123 & \\
\text{Right ventricle (outflow tract)} & 142 & 135 & 1 \\
\text{Pulmonary artery} & 187 & 132 & 51 & 83 \\
\text{Brachial artery} & 195 & 109 & 74 & 86 \\
\text{Femoral artery} & 180 & \\
\hline
\end{array}
\]

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Fig. 4.—Gross specimen showing the aorta above and the heart below. The aorta has been opened to demonstrate the aortic opening of the ductus arteriosus, through which a black paper marker has been passed. The "impingement plaques" may be seen to the right of the opening.

Fig. 5.—Gross specimen with a clamp attached along the right border of the main pulmonary artery. Note the numerous thick atheromatous plaques in the wall of the pulmonary artery.
ductus arteriosus and the aorta is distal to the arterial supply of the upper extremities (fig. 3). Therefore, of the mixed venous blood which is "reversed" into the aorta, a greater proportion will enter the descending aorta than will enter the vessels to the upper extremities. Hence, the arterial oxygen saturation of blood from the femoral artery will be lower than that from the brachial.

impossible to section the ductus. Closure was attempted by tightening two ligatures of umbilical tape around the ductus, following which the thrill could no longer be felt. However, postoperatively, the murmurs previously heard were still present. On the fifth postoperative day, death occurred shortly after a blood transfusion.

Pathologic Report. Pertinent autopsy findings were

Fig. 6.—Photomicrograph of a section of a medium sized branch of the pulmonary artery. Note the eccentric narrowing of the lumen by the accumulation of large numbers of lipid-laden macrophages in the intima, an early atheromatous change.

It was suspected clinically that the extreme hypertension of the pulmonary artery might have been due in part to pulmonary arteriolar sclerosis.

The patient underwent surgery for the second time a few weeks after the physiologic studies. A very wide patent ductus arteriosus of the "window type" was found. Considerable difficulty was encountered in isolating and freeing the ductus because of the surrounding scar tissue from the previous operation. Due to technical difficulties, it was confined to the heart and lungs. The right auricle was not enlarged. There was marked hypertrophy and dilatation of the right ventricle, the wall of which measured 7–11 mm. in thickness. Microscopically, the right ventricle showed focal fibrosis and hypertrophy. The left ventricle was not grossly enlarged and its wall measured 12–15 mm. in thickness. A very large ductus arteriosus was present which had no measurable length, as it existed almost as a side-to-side anastomosis between the aorta and the
Pulmonary artery. The ductus was patent with an internal diameter of 5 mm., although the ligatures were still in place. Following removal of the ligatures the internal diameter measured 10 mm. The aorta measured 7.5 cm. in circumference and showed minimal atherosclerosis except for three large discrete plaques which were located just opposite the aortic opening of the ductus. These have been called "impingement plaques" (see fig. 4), and are presumably due to the high velocity of the jet of blood from the patent ductus striking the wall of the vessel. The pulmonary artery was greatly enlarged, its circumference measuring 10.0 cm. There was marked atherosclerosis of the walls of the pulmonary artery and all of its branches which could be examined grossly (see fig. 5). On the wall of the main pulmonary artery, opposite the pulmonic opening of the ductus, there were lesions which resembled the "impingement plaques" described above.

Microscopically, the pulmonary arteries showed marked atherosclerosis with large numbers of cholesterol-laden macrophages in the intima (fig. 6). Van Gieson stain on these vessels revealed a fraying out and rupture of the elastic tissue of the media at focal points along the vessel wall with aneurysmal-like bulging of the intima at such points (fig. 7). Throughout the lungs the small arteries and arterioles showed moderate to marked thickening of their walls, due to intimal proliferation and medial hypertrophy (fig. 8).

**Discussion**

From the physiologic data and pathologic findings, notably the presence of "impingement
plaque's on the aortic wall opposite the ductus, it can be concluded that this patient, probably late in her disease, had an intermittent, partial reversal of flow through the ductus arteriosus. It is most likely that the marked pulmonary hypertension was the major factor responsible for this reversal. It has been emphasized that under resting conditions the pulmonary artery pressures in patent ductus arteriosus may remain normal. However, many investigators have described pulmonary hypertension in patients with this defect. The cause for the hypertension is not definitely known. It is unlikely that the increased blood flow alone is responsible unless it reaches at least three times the normal pulmonary flow. However, if this value is exceeded, pulmonary hypertension may occur. It has not yet been proved, however, whether a very large and sustained pulmonary blood flow will produce pulmonary vascular sclerosis. The latter possibility is not supported by the data of Welch and Kinney, who did not find any increase in pulmonary vascular sclerosis in any of the 25 patients with a large patent ductus arteriosus. However, these authors assumed the presence of a large pulmonary blood flow solely on the basis of the large size of the aorticopulmonary connection. They stress the presence of sclerosis of the pulmonary vascular tree in all patients over the age of 40.

Fig. 8.—Photomicrograph of a section through the lung. Note the intimal and medial thickening of the walls of small arteries and arterioles. This change was present throughout both lungs.
In the patient here reported it may well be that the prolonged increase in pulmonary blood flow eventually resulted in pulmonary hypertension. As she grew older, marked sclerotic changes may have occurred in the pulmonary arterioles, largely as a result of the aging process, and pulmonary vascular resistance was thus further increased, leading to an increase in pulmonary hypertension. It has been recently stressed\(^9\) that, in patients having a communication between the pulmonary and systemic circulations, the proportion of blood shunted through one or the other circulation is dependent upon the resistance of the peripheral arteriolar bed on one side, the local resistance at the site of the anomalous communication and the resistance of the pulmonary vascular bed distal to it on the other. As the pulmonary hypertension increased over the years, the aortopulmonary shunt through the ductus may well have decreased gradually and hence, the final blood flow may not represent the maximal flow present in earlier years. The findings in this case serve to expand Hamilton’s concept\(^9\) by indicating the relationship of increased pulmonary vascular resistance to temporary reversal of flow through the ductus. Pulmonary hypertension in this patient probably not only resulted in decreasing the left-to-right shunt but served to initiate the intermittent right-to-left shunt.

The question may be raised as to whether the ductus arteriosus should be ligated in the presence of a partial reversal of flow associated with atherosclerotic changes in the pulmonary vessels. Since the increased pulmonary blood flow doubtless plays a role in the production of pulmonary hypertension, ligation of the ductus which would result in a marked reduction of both the pulmonary blood flow and pulmonary hypertension, would appear to be beneficial, even under these circumstances.

The finding of a reduction of blood oxygen saturation in the femoral artery as compared to that in the brachial artery is not pathognomonic of intermittent reversal of flow in a patent ductus arteriosus. Similar findings have been postulated by Taussig\(^10\) in cases of coarctation of the aorta of the infantile type with hypoplasia of the ascending aorta, overriding of the interventricular septum by a pulmonary artery communicating with the descending aorta through a patent ductus arteriosus. It should be mentioned that in the presence of such a syndrome, the total systemic flow cannot be calculated with the Fick principle. Even though venous blood samples might be obtained separately in the superior and inferior vena cava, the unknown quantity of oxygen consumption in each separate system makes even an approximative value for total systemic flow unreliable.

**SUMMARY**

1. A case of patent ductus arteriosus, with intermittent reversal of flow through the ductus, is reported in an adult woman.

2. The intermittent reversal of flow was demonstrated during life by pressure measurements in the pulmonary and the systemic circulations, and by blood oxygen values in blood samples drawn simultaneously from right brachial and femoral arteries.

3. Pathologic findings following postoperative death supported the diagnosis by demonstrating “impingement plaques” on the aortic wall around the mouth of the patent ductus arteriosus.

4. The physiologic mechanisms leading to reversal of blood flow are discussed.

**REFERENCES**


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