The Presence of Venoarterial Shunts in Patients with Interatrial Communications

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Evidence is presented which indicates that shunting of small amounts of blood from right to left occurs frequently through interatrial communications. Such right-to-left shunts are of small magnitude in the usual case of atrial septal defect, but it appears that of the fractions of blood shunted, a greater proportion has originated from the inferior vena cava than from the superior vena cava.

In the majority of cases of uncomplicated atrial septal defect the major hemodynamic change is an arteriovenous (left-to-right) shunt of considerable magnitude. Because cyanosis or significant desaturation of the systemic arterial blood is uncommon, a shunt in the opposite direction (venoarterial, or right-to-left) is now considered unusual in this condition. In certain reports, which included a number of atypical cases or cases in which the complete diagnosis was not clearly established, significant arterial desaturation has been noted.

The oxygen saturation of the systemic arterial blood determined by manometric methods in normal persons has been found to average 97.6 per cent with a range of analytic values of from 94 to 101 per cent. This variability in normal subjects may preclude the detection of venoarterial shunts of less than 15 per cent of systemic flow on the basis of desaturation of the systemic arterial blood. When significant arterial desaturation due to a venoarterial shunt is found, an additional structural anomaly or pulmonary hypertension or cardiac failure, singly or in combination, is likely to be present. Right-to-left shunts may frequently be associated with pulmonary stenosis with intact ventricular septum and occur through a "valve-competent," patent, foramen ovale or through a coexistent atrial septal defect. The term "interatrial communication" is used to include all direct pathways between the atria, normal and abnormal.

The demonstration of the presence and site of a communication through which a right-to-left shunt is occurring, by dilution curves of T-1824, is now an established technic. In this paper, evidence will be presented which indicates that shunting of small amounts of blood from right to left occurs frequently through interatrial communications. Such right-to-left shunts are of small magnitude in the usual case of atrial septal defect but it appears that of the fractions of blood shunted, a greater proportion has originated from the inferior vena cava than from the superior vena cava.

Methods

Dilution curves of T-1824 were obtained following injection of dye into both the inferior and the superior vena cava in four patients with uncomplicated atrial septal defect, three patients with persistent common atroventricular canal, one patient with atrial septal defect and mitral stenosis, one patient with anomalous pulmonary venous connection of the right lung and a small atrial septal defect, one patient with pulmonary stenosis, intact interventricular septum and valve-competent foramen ovale and one patient with pulmonary stenosis, intact interventricular septum and atrial septal defect. In an additional patient with atrial septal defect, dilution curves were obtained, but the instant of injection of T-1824 was not indicated on the record; hence these curves have not been included in this series, although they did not differ in general appearance from the curves obtained in the majority of other patients.

Each patient was studied as completely as possible by the cardiac catheterization technic to establish the nature of the anomaly present. Dilution curves were recorded photographically, utilizing...
earpiece oximeters attached to both ears and a cuvette oximeter connected to a 20-gage needle in the right radial artery. The dilution curves were obtained while the patients breathed 100 per cent oxygen and, in some instances, while they breathed room air. Injections of dye were made through the cardiac catheter into the inferior vena cava 1 to 3 cm. below the diaphragm and into the superior vena cava a short distance cephalad to its junction with the right atrium. A number 6, or less frequently a number 5 or number 7, Courand bird's eye tip catheter was used and the selected dose of dye (in a volume of 1.5 or 2.0 cc.) was injected as rapidly as possible (one to two seconds). This was followed immediately by a further injection of 5 cc. of isotonic saline solution. In these patients dilution curves were also recorded following injection of T-1824 into right or left pulmonary arteries or into the main pulmonary trunk, or into all of these vessels. The systemic and pulmonary flows were calculated, when possible, both when air and when oxygen was being breathed. For estimations of pulmonary flow (liters per minute) the oxygen consumption (in cubic centimeters per minute) was divided by the difference between the oxygen content of blood in the pulmonary vein (assumed to equal 98 per cent of the oxygen capacity, in cubic centimeters per liter of blood + 3.0 cc.) and the oxygen content of blood in the pulmonary artery (in cubic centimeters per liter of blood), as estimated by the method of Van Slyke and Neill. For estimations of systemic flow (liters per minute) the oxygen consumption (in cubic centimeters per minute) was divided by the difference between the oxygen content of radial-artery blood and the content of mixed venous blood. The latter value \( S_r \) was calculated from the relationship, 

\[
S_r = \frac{S_s + 2S_v}{3} \times O_2 \text{ capacity,}
\]

in which \( S_s \) = per cent saturation of superior vena cava blood and \( S_v \) = per cent saturation of inferior vena cava blood, in each instance determined by cuvette oximeter, and in which \( S_r \) and \( O_2 \) capacity are expressed as cubic centimeters of oxygen per liter of blood.

The oxygen saturation of radial-artery blood was determined while the patient breathed room air according to the formula,

\[
O_2 \text{ saturation (air)} = \frac{O_2 \text{ content} - 0.3}{O_2 \text{ capacity}} \times 100
\]

in which saturation is expressed as a percentage, and content and capacity in cubic centimeters per 100 cc. of blood.

When the patient breathed 100 per cent oxygen the saturation of the radial-artery blood was considered to be 100 per cent if the oxygen content exceeded the capacity by more than 1 volume per cent. The oxygen tension required to produce this concentration of dissolved oxygen is equivalent to or exceeds the oxygen tension of 400 mm., expressed in terms of mercury, required to produce practically complete saturation of hemoglobin with oxygen. When the physically dissolved oxygen was less than 1 volume per cent of the oxygen, saturation was estimated from the oxygen tension (calculated on the basis of the quantity of oxygen in physical solution) \(^*\) by reference to the oxygen dissociation curve established at high levels of oxygen pressure \((\text{pO}_2)\) by Nahas and colleagues. \(^{16}\)

**Results**

In the table the major hemodynamic findings in each case are given, together with certain data from dilution curves of T-1824 following its injection into the superior and the inferior vena cava and into the right ventricle or right, left or main pulmonary artery.

The two patients with pulmonary stenosis (cases 2 and 3) both showed considerable elevation of the right ventricular pressure while in one case of atrial septal defect (case 7) the pressure in the right ventricle exceeded that in the pulmonary artery by more than 20 mm. Hg. In neither of the former patients was it possible to demonstrate significant left-to-right shunting of blood on the basis of repeated sampling of blood from the right side of the heart; however, in case 3 following injection of dye into the pulmonary trunk the contour of the dye-dilution curve indicated that indeed a left-to-right shunt of small magnitude was present. It has been found in this laboratory that dye-dilution curves recorded following injections of dye directly into the central circulation may permit the recognition of left-to-right shunts when the relations of the oxygen saturation of blood drawn from different locations in the right atrium and both venae cavae are within normal limits. In regard to the moderate difference between the systolic pressures in the pulmonary artery (case 7) and those in the right ventricle, it is

\* Approximate \(O_2\) tension

\[
= \frac{(B - 47) \cdot (O_2 \text{ content} - O_2 \text{ capacity})}{100 - 38^*}
\]

in which \( B = \) barometric pressure (mm. of Hg), and \( \alpha 38^* = \) solubility coefficient for oxygen at 38 C. = 0.0209 + 0.000108 (volume per cent oxygen capacity).
not possible to be certain whether or not this patient has a congenital pulmonary stenosis of mild degree in addition to an atrial septal defect, since significant differences between these pressures occur frequently in patients with atrial septal defect.\(^9\)

In three of the nine patients without pulmonary stenosis a diagnosis of persistent common atrioventricular canal was made after cardiac catheterization. This condition must always be considered in the differential diagnosis of atrial septal defect. In these three patients the oxygen-saturation data indicated a source of moderate arterialization in the right ventricle in addition to the arterialization in the atrium. In each patient the catheter was passed from the right atrium to the left ventricle and the position of its shaft lay in the axis of the coronary sinus, giving rise to an unusual but, for this condition, typical radiologic appearance.

The dilution curves recorded following injection of T-1824 into the superior and the inferior vena cava while the patients breathed 100 per cent oxygen are reproduced for patients 1 to 8 in figure 1. In each instance there is evidence of a right-to-left shunt when the injection of dye is made into the inferior vena cava, although in case 8 this consists only of an abnormal rounding of the initial part of the dilution curve. The appearance time of these curves is less than the appearance time of dye injected at a more central site (table),

![Fig. 1. Dilution curves of T-1824 recorded by earpiece oximeters following injection of indicator into superior vena cava (left panel) and inferior vena cava (right panel) in patients 1 to 8 with interatrial communications, recorded while 100 per cent oxygen was being breathed. For each dilution curve the instant of injection is represented by the vertical arrow below which the amount of dye injected is indicated. The oxygen saturation scale to the left of each panel is a measure of the relative sensitivity of the recording instrument for each subject, and the peak concentration of dye is indicated to the right of each panel. In the curves for patients 1 to 3 in the left panel the initial break in the dilution curve indicates the shunting of a portion of superior caval blood in the right-to-left direction. In the right panel an initial break is present in all curves indicating that a right-to-left shunt of inferior caval blood was present in all these patients. Note that only in case 3 does the magnitude of the shunt of superior caval blood exceed that of inferior caval blood.](http://circ.ahajournals.org/doi/fig/1)
<table>
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<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>Age, sex</th>
<th>Surface area, meters</th>
<th>Patient breathing</th>
<th>Pressure, mm. of Hg</th>
<th>Flow L/min./M²</th>
<th>Radial artery blood oxygen</th>
<th>Dye-dilution data††</th>
<th>More proximal site</th>
<th>Superior vena cava</th>
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<td>Air</td>
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<td>1.7</td>
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<td>-</td>
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<td>Pulm. stenosis, probe-patent foramen ovale*</td>
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<td>1.6</td>
<td>Air</td>
<td>12/6</td>
<td>7/3</td>
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<td>1.4</td>
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<td>-</td>
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<td>7/3</td>
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<td>1.4</td>
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<td>1.68</td>
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<td>3.2</td>
<td>1.4</td>
<td>-</td>
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</table>

* Catheterization diagnosis confirmed during surgical correction of the anomaly (Dr. John W. Kirklin).
† Recorded by ear oximeter.
†† Abbreviations: AT, appearance time; PCT, peak concentration time; RPA, right pulmonary artery; LPA, left pulmonary artery; PT, pulmonary trunk; RV, right ventricle.
indicating that the shunt in question occurs at atrial level.

In 7 of the total of 11 patients the dilution curves following injection of dye into the superior vena cava did not indicate the presence of a right-to-left shunt and in two patients there was no evidence of a right-to-left shunt from either cava. In the remaining patients the initial hump of the curve following injection into the superior vena cava was greater than the initial hump following injection into the inferior vena cava in one case, equal to it in one case, and smaller in two cases. Thus in 9 of the 11 patients a right-to-left shunt could be demonstrated, and further in seven of these patients the proportion of inferior vena-caval blood shunted right to left through the atrial defect was larger than that from the superior vena cava.

A method of analysis of dilution curves whereby the magnitude of right-to-left shunts may be estimated has recently been described. An assumption basic to this method is that complete mixing of indicator with the blood has occurred before the mixture of blood and indicator reaches the site of the defect. The evidence presented in this paper indicates that this condition is not fulfilled in the case of right-to-left shunt through an interatrial communication, for in all but one instance the proportion of indicator shunted right to left differed obviously between the caval injection sites (fig. 1). However, in the absence of a more acceptable method of analysis the volume of right-to-left shunt has been calculated according to the method of Swan and associates, recognizing the possibility of appreciable error in certain values. Nevertheless

![Diagram](image-url)

Fig. 2. Relation of the magnitude of right-to-left shunt determined from dye-dilution curves to systemic arterial saturation (left panel, 11 patients breathing room air) and to volume of oxygen in physical solution in arterial blood (right panel, 10 patients breathing 100 per cent oxygen). The average of the shunts ($S$) from the superior and the inferior cava was calculated thus: $S = S_{sa} + 2S_{si}$, in which $S_{sa}$ is the shunt from superior vena cava and $S_{si}$ the shunt from the inferior vena cava (table 1). The solid squares represent the average values for normal subjects, and the range is indicated. The diagonal lines represent the calculated relation of the systemic arterial saturation to the volume of right-to-left shunt. These lines were estimated on the basis of the average oxygen capacity (16.7 volumes per 100 cc. of blood) and the arteriovenous difference (4.9 volumes per 100 cc. of blood) found in the group studied. In each panel the solid line represents the relationship which would pertain if the oxygen saturation of the shunted blood were the same as that of mixed venous blood (71 per cent for room-air data and 83 per cent when the patients breathed 100 per cent oxygen), and the dashed line the relationship if the saturation of the shunted blood were the same as that of pulmonary-artery blood (78 per cent and 92 per cent respectively when the patients breathed air and 100 per cent oxygen).
it is thought that the values probably indicate the approximate magnitude of the right-to-left shunt in most instances.

By use of these calculations it may be shown (fig. 2) that the magnitude of the right-to-left shunt is inversely related to the volume of oxygen in physical solution in arterial blood when the patient is breathing 100 per cent oxygen and to the systemic arterial saturation when the patient breathes air. Small shunts (less than 10 per cent) are associated with a normal complement of physically dissolved oxygen (1.4 to 2.2 volumes per 100 cc. of blood)\(^4\) when the patient is breathing oxygen and with normal arterial saturations (94 to 101 per cent)\(^5\) when he is breathing air. When the volume of dissolved oxygen is less than 1.5 volumes per cent during the breathing of oxygen and the arterial saturation is less than 94 per cent during the breathing of air, right-to-left shunts of greater magnitude are found.

**COMMENT**

It is of interest that in 9 of the 11 cases studied the dilution curves recorded following injections of dye into the inferior and the superior vena cava indicated the presence of a right-to-left shunt through the defect in the atrial septum. In five of the nine cases the shunt was demonstrable only from the inferior vena cava, and in these instances the total venoarterial shunt was small.

In cases 4 to 11 the clinical features were considered to indicate a diagnosis of atrial septal defect, with the addition that a coincidental pericarditis was present in case 8. Use of currently available cardiac catheterization technics\(^12, 13\) permitted a more nearly complete diagnosis in several instances.

The findings reported above indicate that, although a right-to-left shunt is frequently present, it is of small magnitude in the usual case of atrial septal defect, which is in keeping with the more generally accepted view concerning this condition. In two of the four cases with moderate shunts, pulmonary stenosis was present, while in the remaining two cases the anomalies were not simple.

Two important facts may be noted. First, these developments of the dye-dilution technic offer a highly sensitive method for the demonstration of right-to-left shunts. In its more general application the method permits the certain identification of an interatrial communication in the absence of a significant left-to-right shunt. Second, for relatively small right-to-left shunts (3 to 15 per cent of systemic flow) these methods allow for approximate quantitation of their magnitude when even demonstration on the basis of oxygen-saturation data may be impossible. It must be pointed out, however, that the arterial dilution curves are produced by complex dilution and mixing processes which cannot be accurately quantitated at present. Hence attempts at more precise quantitation of the magnitude of shunts demonstrated by the technic are of questionable value at this time.

In the majority of cases a greater shunt was demonstrated to occur from the inferior than from the superior vena cava. In case 3 the shunt occurring from the superior vena cava was of considerably greater magnitude than that from the inferior vena cava. This finding was at variance with the results in the other cases and cannot be adequately explained. On the basis of past experience,\(^20, 21\) it was thought to indicate a defect lying in the cephalic part of the atrial septum, but in fact at operation the defect was found in the region of the foramen ovale.

Using angiocardiographic technics, Lind and Wegelius\(^23\) observed in patients with atrial septal defect and in normal newborn infants that some of the contrast medium injected into the inferior vena cava passed into the left atrium but returned from this chamber to the right atrium. As a possible explanation for their findings these workers suggested that the sudden injection of contrast medium increased the volume and pressure in the right side of the heart, and hence a transient right-to-left shunt occurred. It is unlikely that such an explanation pertains to the present findings, for the volume injected was small (1 to 2.0 cc. of dye, followed by 5 cc. of saline solution) in relation to the volume of blood returning to the heart.

The usual direction of flow across an atrial septal defect has been ascribed to the differ-
ences in pressure between the atria first demonstrated in man by Cournand. Calazel and co-workers found that a pressure gradient existed between right and left atria in patients with moderate to large venaarterial shunts. An arteriovenous shunt was present in patients with a gradient from left atrium to right atrium. In the latter group a transient reversal of this pressure gradient at the beginning of atrial filling was demonstrated, which was thought to cause a small venaarterial shunt. Little and associates measured simultaneously the left and the right atrial pressure in dogs before and after the creation of atrial septal defects. They found that a pressure gradient existed from left atrium to right atrium even when relatively large (5 to 8 mm.) defects were created. This difference was abolished and a reverse gradient was created for certain phases of the cardiac cycle when the pulmonary artery was acutely constricted.

In the usual case of atrial septal defect (valve incompetent foramen ovale) in man it may not be possible to demonstrate a significant difference between the pressure levels in the right and left atria. In such cases the pattern and direction of inflow and outflow streams through the atria may be related at least in part to the shunts which occur. It has been demonstrated that mixing of blood from the left and right lungs in the left atrium is incomplete in the great majority of patients with atrial septal defect, for a greater proportion of blood from the right lung is shunted to the right atrium while a greater proportion of blood from the left lung passes to the systemic circulation. When the blood flow through the right atrium is large, the atrium may function during diastole more as a channel than as a storage chamber. Blood streams from the superior and the inferior vena cava and from each lung may traverse this channel to the respective ventricles while still retaining a certain degree of identity.

Barclay, Franklin and Prichard found that the greater part of a contrast medium injected into the “posterior caval channel” (inferior vena cava) of lambs in the late fetal period passed into the left atrium, while all of the contrast medium reaching the heart by way of the “anterior caval channel” (superior vena cava) passed to the right ventricle. If the inferior vena cava is cut across and viewed from below in the heart of a patient who has died from a cardiac or noncardiac cause, the limbus of the fossa ovalis can be seen to straddle the atrial orifice of the inferior vena cava so that a portion of the inflow from the inferior cava impinges directly on the floor of the fossa ovalis (fig. 3). Thus when the valve of the foramen (septum primum) is not fused to the septum secundum or when a true defect in this location exists, the blood from the inferior vena cava could pass equally well into either the right or the left atrium. The small left-to-right pressure gradient which usually exists between the atria results in a left-to-right shunt and apparently prevents the flow of all but a small part of the inferior caval blood into the left atrium in most patients. In contrast to that of the inferior vena cava the atrial orifice of the superior vena cava is usually directed toward the tricuspid valve. The direct stream of flow from the superior cava therefore would not appear to pass in as close a relation to the fossa ovalis and defects thereof as would blood from the inferior vena cava.

The relative proportions of blood shunted from each caval site should depend on the proximity of the stream under consideration to the defect and hence should permit the site of the defect to be predicted. This has been conclusively demonstrated by Silver and co-workers who created defects in the atrial septum of dogs which were subsequently studied by the dye-dilution technic. The pattern of the dilution curves recorded following injection of dye into the lobar branches of the right pulmonary artery, the left pulmonary artery and the inferior and the superior vena cava was found to indicate correctly the approximate location of the defect in the atrial septum. This has also been found to be true in human patients. In case 1 the dilution curves indicated that the atrial defect lay in the same relationship to the flow from both the inferior and the superior vena cava. In cases 2, 5 and 6 the defect was thought to lie more closely in relation to the inferior than to the superior vena cava. When surgical correction was
undertaken in these patients (Dr. J. W. Kirklin) the locations of the defects were found to be as predicted. In case 11 no right-to-left shunt was demonstrated, but a small atrial septal defect was found in association with anomalous venous connection of the right lung. In case 3 the dilution curves suggested that the defect was located in close relation to the superior vena cava but an atrial septal defect of moderate size was found in the region of the fossa ovalis.

**SUMMARY**

Dilution curves of T-1824 have been recorded by the oximeter technic in 11 patients with interatrial communications, following injection of the dye into both the inferior and the superior vena cava. In 9 of 11 cases a right-to-left shunt could be demonstrated when dye was injected into the inferior vena cava. In the seven cases in whom no shunt occurred from the superior vena cava, the oxygen saturation of systemic arterial blood was normal, and the amount of oxygen in physical solution in the blood when the patient was breathing 100 per cent oxygen exceeded 1.5 volumes per cent. In the remaining patients the shunt was found to occur also from the superior vena cava, and the physically dissolved oxygen was less than 1.5 volumes per cent. The existence of such right-to-left shunts is probably associated with the relation of the septal defect to the stream of blood passing from either vena cava to the right ventricle. In four of the five cases in which successful surgical correction was carried out, the approximate site of the defect was correctly predicted.

**SUMARIO ESPAÑOL**

Curvas de dilución de T-1824 han sido registradas por la técnica del oxímetro en 11 pacientes con comunicaciones interatriales, luego de la inyección del tinte en la vena cava superior e inferior. En 9 de 11 casos un "shunt" de derecha a izquierda se pudo demostrar cuando el tinte fue inyectado en la vena cava inferior. En los siete casos en los cuales un "shunt" no ocurrió de la vena cava superior, la saturación de oxígeno de la sangre arterial sistémica fue normal y la cantidad de oxígeno en solución física en la sangre cuando el paciente estaba respirando oxígeno al 100 por ciento excedió 1.5 volumenes por ciento. En el restante de los pacientes el "shunt" se encontró ocurrir también de la vena cava superior y el oxígeno en solución física fue menos de 1.5 volumenes por ciento. La existencia de tal "shunt" de derecha a izquierda está probablemente asociada a la
relación del defecto septal al chorro de sangre pasando de una de las vena cava al ventrículo derecho. En cuatro de los cinco casos en que se efectuó corrección quirúrgica con éxito, el lugar aproximado del defecto se pudo predecir.

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