Dye Dilution Curves in Cyanotic Congenital Heart Disease

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Use of cuvette and earpiece oximeters facilitates the recording of the immediate dilution pattern of the dye T-1824 (Evans blue) in the arterial blood. In patients with venoarterial shunts the pattern of the dilution curves differs from normal. Quantitative analysis of such curves from patients with cyanotic congenital heart disease has been undertaken to establish the proportion of blood which bypassed the pulmonary circulation. The results obtained have been compared with estimates of the volume of the shunt from cardiac catheterization data and related to the arterial oxygen saturation.

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IDENTIFIABLE substance injected almost instantaneously into the blood vessels is diluted in a specific manner by the blood stream. Nicholson, Burchell and Wood\(^1\) used cuvette and earpiece oximeters\(^2\) to record continuously the dilution curve of Evans blue dye in arterial blood flowing from the radial artery and through the heat-flushed ears of normal subjects and of patients with heart disease. Beard and associates\(^3\) have shown that dye dilution curves, obtained when radial or femoral arterial blood is drawn continuously through a whole-blood cuvette oximeter, are similar in contour to curves simultaneously recorded by an earpiece oximeter. Dye curves recorded by an earpiece oximeter are, therefore, an adequate qualitative guide to the dilution pattern of dye in the arterial blood.

Dye dilution curves have been obtained for patients suffering from both congenital and acquired heart disease.\(^1\) \(^5\) \(^6\) In congenital defects with a venoarterial or arteriovenous shunt the basic pattern of the dye dilution curve is altered. In such conditions the morphology of the curve may indicate the presence, direction and magnitude of the shunt. The method has been extended by the technic of injection of dye by way of the cardiac catheter into the cardiac chambers and great vessels. In several cases this has permitted more accurate localization of the defect than would otherwise have been possible\(^7\) (fig. 1). Quantitation of the volume of the shunt from dye curves of peripheral blood would be of considerable value, and Broadbent and associates\(^8\) have reported a method of analysis of the dye curves obtained from patients with arteriovenous (left-to-right) shunts. Prinzmetal\(^9\) reported four cases of venoarterial shunt in which he attempted to estimate the volume of the shunt from the ether and saccharine circulation times. It is the purpose of this paper to outline a method of analysis whereby the proportion of aortic flow which has bypassed the lungs via the defect can be estimated from the dye curve of patients suffering from cyanotic congenital heart disease.

METHODS

Dilution curves of Evans blue dye in arterial blood were obtained from patients with cyanotic congenital heart disease. Twenty of the 25 patients whose dye curves were analyzed for this study underwent cardiac catheterization either on the same occasion or within three days of the time that the dye was recorded.

The dye curves were usually obtained according to the technic of Nicholson, Burchell and Wood\(^1\) but, at times, the dye was injected through a cardiac catheter, the tip of which lay in the superior vena cava. The dye curves were recorded while the patient breathed 100 per cent oxygen because the

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oximeters are sensitive to changes either in oxygen saturation of blood or in concentration of dye, and changes in oxygen saturation are usually less likely when the patient is breathing 100 per cent oxygen. Continuous photographic records were obtained at a camera speed of 5 mm. per second with a photokymographic recording assembly described elsewhere.9 Measurements of the time and concentration components of the dye curve were made directly from the photographic record.

The time components of a normal dye curve are presented in figure 2. This figure is similar to one published in an earlier report, except that the term, "passage time" (PT) now replaces "clearance time," and "maximal concentration time" (MCT) has been substituted for the term "peak time." The components were defined and the average and range of values obtained in normal subjects were reported in the previous publications.1,8

In this study dye curves recorded by an earpiece oximeter have been used, but the dye curves obtained by cuvette oximeter from blood flowing from a radial or other systemic artery could have been used equally well. If the latter are used, correction must be made in appearance and peak times for the interval needed for the dye to pass from the artery to the recording instrument. For some of the patients in the series to be reported dye curves had been obtained by earpiece oximeters only.

Diagnostic cardiac catheterization was carried out by utilizing strain gauge manometers, cuvette and earpiece oximeters and a photokymographic recording system.9 The calculations of the volume

![Diagram](image-url)

**Fig. 1.** Dye dilution curves recorded simultaneously from both ears and the right radial and right femoral arteries in a patient with Eisenmenger's complex. The dilution curves were recorded following injection into the pulmonary artery (left panel) and brachial vein (right panel). The contours of the dilution curves recorded from the four sites in each panel were similar. The delay in appearance of the dye at the cuvette oximeters is due to the time required for the blood to pass from the intraarterial needle to the recording portion of the instrument. The differences in the magnitude of the recorded deflections are due to unequal sensitivities of the four oximeters. (Note oxygen calibration scales upper left corner.) The random variations in the oximeter curves before and after the injections of dye are caused by spontaneous variations in oxygen saturation resulting from changes in the venoarterial shunt associated with the respiratory cycle. Note in both panels the rise in arterial saturation at A' resulting from the increased respiratory effort at A. Such spontaneous variations, when they occur, are the chief difficulty in the analysis of dilution curves in cases of cyanotic congenital heart disease. Note also the presence of the shunt pattern when the injection was made into a systemic vein and the absence of the shunt pattern when the injection was made into the pulmonary artery proving that the defect was proximal to the pulmonary artery.

![Diagram](image-url)

**Fig. 2.** Method of measurement of the circulation times and time components of a dilution curve of Evans blue dye in the arterial blood of a normal subject.

of shunted blood were made by the method of Burchell and Wood.10
INTERPRETATION OF DYE CURVES OF PATIENTS WITH CYANOTIC CONGENITAL HEART DISEASE

Among patients with cyanotic congenital heart disease without cardiac failure the dye dilution curve differs from normal in that the appearance time is usually short, although the maximal concentration time is frequently normal. In addition there is a secondary hump on the build-up slope of the dilution curve and the peak deflection is reduced. In figure 3 a dye curve obtained from a normal adult is contrasted with a curve from a 23 year old woman suffering from pulmonary hypertension and atrial septal defect who had an oxygen saturation of 82 per cent in peripheral arterial blood while at rest. This abnormal curve, which is typical of moderately severe cyanotic heart disease, can be explained by the passage of a portion of the dyed blood directly from the right atrium into the systemic circulation. As the passage of this portion of the dyed blood to the periphery is not delayed by traversing the pulmonary circuit, it arrives at the periphery earlier than the remainder of the dyed blood which passes by the more circuitous route through the lungs. This results in an appearance time which is less than normal, an initial hump in concentration due to the shunted blood, followed by, and partially fused with, the hump in concentration caused by the dyed blood which has traversed the normal circulatory pathway through the lungs.

In the following paragraphs the normal curve (the second hump, fig. 3 lower panel) representing dyed blood which has passed by way of the lungs will be referred to as the primary curve, while the “shunt” curve (the initial abnormal hump, fig. 3 lower panel) will be referred to as the secondary curve. These two curves represent the division of the dose of dye into two fractions which go by different routes to the periphery.

After the rapid injection of dye into a peripheral vein it is assumed that adequate mixing of dye and blood occurs before the intracardiac defect is reached; that is, a preferential flow of dye either toward or away from the defect is considered unlikely although such a situation could arise in the rare condition of a persistent left superior vena cava draining into the left atrium. The primary clearance of dye from the heart will result in the passage of a fraction of the total amount of dye through the defect in the same proportion as blood is passing through the defect and passage of a fraction of the total amount of dye into the lungs in the proportion that blood is passing into the lungs. In other words the relative quantities of dye passing through the shunt and through the lungs are directly proportional to the relative volumes of blood flowing by these two routes.

The dynamics affecting the dilution curves of dye in the shunted and unshunted blood differ according to the circuit taken. While the dye passing through the defect will be influenced by a number of complex dilution factors in the heart and arterial system, the dye passing through the lungs will be affected by pulmonary factors in addition. The length and capacity of different pulmonary vessels, and the rate of flow through them will determine the rate at which the dye makes the circuit and reaches the left atrium. Therefore, the primary curve (normal circulation pathway) will show a longer passage time (PT) than might be found for the secondary curve (abnormal pathway) in which the dye is cleared directly from the right side of the heart into the arterial system. For this reason comparison of maximal concentrations may not indicate
the true relative magnitude of the quantities of dye passing through the two circuits. Nevertheless, the primary and secondary curves still represent the division of the dye into separate fractions at the intracardiac defect. They possess components in time and concentration which together are a measure of the amount of dye which passed by each route.

Inspection of the contour of the dye curve suggested that each component could be expressed as a right-angled triangle\(^3\) two sides of which are the build-up time and maximal concentration (fig. 4). The area of such a triangle, to be called the "build-up triangle," is equal to half the product of the build-up time and the maximal deflection. In the primary curve the maximal deflection is proportional to the maximal concentration (MC\(^t\)) and may be measured in centimeters from the base line to the peak of the primary curve. In the secondary curve the maximal concentration is the distance in centimeters from the base line to the maximal deflection in the secondary curve (MC\(^s\)). The peak deflection of the secondary curve may be indefinite in cases in which the shunt is small and in such cases this peak concentration is taken to be at the indentation on the main build-up slope, as shown in figure 4 (lower panel). Since absolute quantitation is not attempted, it is possible to use the measurement of concentration in centimeters, and conversion into units of concentration of dye is unnecessary. The build-up time of the secondary curve is the interval between the first appearance of the dye and the time of maximal concentration of the secondary curve (BT\(^s\)). Therefore, three of the required measurements may be obtained directly from the record. However, it is necessary to estimate what the build-up time of the primary curve would have been if no shunt of dye had taken place. Because of the symmetry of dye curves it appeared possible to determine the build-up time by its relation to another variable which could be measured on the abnormal dye curve. In 42 dye curves obtained from individuals with varying cardiac outputs but no intracardiac defect a positive correlation \((r = 0.95)\) was found between appearance time (AT) and maximal concentration time (MCT). The ratio AT: MCT averaged \(0.56 \pm 0.007\).* In the abnormal dye curves the maximal concentration time was measured and from this figure the theoretic appearance time for the primary component was calculated (AT' = 0.56 MCT). The build-up time of the primary curve was then obtained (BT' = MCT - AT', or BT' = 0.44 MCT).

It is important to know the relationship between the build-up triangle and the whole curve which it is taken to represent, for the object of

\* The figure following the ± sign is the standard error of the mean; \(N = 42\).
time and build-up time. The ratio BT:PT was 0.38 ± 0.006.* As the area of the whole triangle is given by the product of passage time and one half of the maximal concentration, and the concentration factor is common also to the build-up triangle, it is clear that the build-up triangle is in fact representative of the total dilution curve. Also the build-up triangle would be unlikely to reflect changes in the primary dilution curve due to concomitant pulmonary recirculation (left-to-right shunt) which not infrequently occurs in association with a venoarterial shunt.

Calculation of the Shunt. If the build-up triangles of the primary (Δ′) and secondary (Δ″) dye curves are representative of the division of dye into two components with subsequent dilution in the blood stream, then the sum of both triangles indicates the total systemic blood flow. The proportion of dye passing through the shunt is obtained by the ratio of the secondary build-up triangle to the sum of both triangles or

\[
\text{percent shunt} = \frac{\Delta''}{\Delta' + \Delta''} \times 100.
\]

The dye curves of 25 patients were selected for study. Those of six other patients were excluded from the series as follows: those of two who had Ebstein's disease, those of two who had tricuspid atresia in which the appearance times were abnormally short but no primary curve could be identified, and those of two who had ventricular septal defects in association with a patent ductus arteriosus with reversal of flow in which variations in arterial oxygen saturation coincident with respiration nearly obliterated the oximetric recording of the contour of the dye curve so that analysis was impossible.

Results

The results are given in table 1. In the 17 adult patients the appearance time was short with a mean value of 8.6 seconds (range: 5.2 to 14.0), the maximal concentration time was normal, 23.7 seconds (range: 14.3 to 34.8). In a series of dye curves from normal subjects, the appearance time was 14 seconds (range: 10 to 19) and the maximal concentration time, 23.9 seconds (range: 16 to 35).

The volume of the venoarterial shunt as calculated from the catheterization data in 20 of our 25 cases has been plotted against the values determined by the dye method in the same 20 cases (fig. 5). The results obtained by the two methods correlated well (r = 0.89); however, the volume of shunt calculated from cardiac catheterization data averaged 35 (7 to 60) per cent of systemic blood flow as compared to 26 (6 to 42) per cent calculated by the dye method. This systematic difference of 9 ± 1.5* per cent between the two methods was statistically significant (p < 0.001). The standard deviation of the differences between the paired determinations from the catheterization data and from the dye curve was 7 per cent of systemic blood flow or 21 per cent of the absolute shunted blood flow.

The most likely explanation for the systematic difference between the methods was that the declining concentration slope of the initially-occurring secondary curve influenced the maximal concentration of the following primary curve. This is also an important criticism of the method just outlined. If this were the case the area of the primary triangle (Δ′) would be overestimated due to the inclusion of a falsely high value for maximal concentration. Therefore, final calculation would tend to underestimate the magnitude of the shunt because of a high value for the denominator in the fraction given. The figure used for the maximal concentration of the primary curve was reduced by a third as an arbitrary correction factor, thereby eliminating the systematic difference between the methods.

Although rapid sampling of blood from the various cardiac chambers by means of a whole blood cuvette oximeter increases the accuracy of calculation of shunts from catheterization data, this method of calculation still serves only to give an approximate value. In a number of the cases of ventricular septal defect with pulmonary stenosis studied, evidence of pulmonary recirculation has been found both

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* The figure following the ± sign is the standard error of the mean; N = 20.
Table 1.—Relationship of Appearance and Maximal Concentration Times of Evans Blue Dye, the Magnitude of the Venous Arterial Shunt Calculated from Data Obtained from Cardiac Catheterization and Dye Dilution Curves, to the Levels of Arterial Oxygen Saturation in Patients With Cyanotic Congenital Heart Disease

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, yr.</th>
<th>Diagnosis</th>
<th>AT,* sec.</th>
<th>MCT,* sec.</th>
<th>Per cent systemic flow</th>
<th>Arterial O2 per cent*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>By cardiac catheterization</td>
<td>By dye method before correction</td>
<td>By dye method after correction</td>
<td></td>
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<tr>
<td>1†</td>
<td>5</td>
<td>Pulmonary stenosis; atrial septal defect</td>
<td>4.2</td>
<td>16.1</td>
<td>60</td>
<td>42</td>
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<tr>
<td>2</td>
<td>23</td>
<td>Tetralogy of Fallot</td>
<td>7.0</td>
<td>24.7</td>
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<td>3</td>
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<td>Tetralogy of Fallot</td>
<td>11.8</td>
<td>24.4</td>
<td>42</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>Pulmonary hypertension; ventricular septal defect</td>
<td>10.1</td>
<td>34.8</td>
<td>41</td>
<td>27</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
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<td>24.7</td>
<td>33</td>
<td>32</td>
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<tr>
<td>6</td>
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<td>Pulmonary hypertension; atrial septal defect; ventricular septal defect</td>
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<td>19.3</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>7†</td>
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<tr>
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<td>10.0</td>
<td>28.1</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>Tetralogy of Fallot</td>
<td>12.3</td>
<td>31.0</td>
<td>42</td>
<td>26</td>
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<tr>
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<tr>
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<td>14</td>
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<tr>
<td>13‡</td>
<td>3½</td>
<td>Pulmonary stenosis; ventricular septal defect</td>
<td>4.6</td>
<td>12.8</td>
<td>33</td>
<td>32</td>
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<tr>
<td>14</td>
<td>28</td>
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<td>27.4</td>
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<td>19</td>
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<tr>
<td>15</td>
<td>20</td>
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<td>6.8</td>
<td>14.3</td>
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<tr>
<td>16</td>
<td>16</td>
<td>Pulmonary stenosis; ventricular septal defect</td>
<td>9.3</td>
<td>23.0</td>
<td>25</td>
<td>20</td>
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<tr>
<td>17†</td>
<td>4½</td>
<td>Pulmonary stenosis; ventricular septal defect</td>
<td>4.9</td>
<td>13.3</td>
<td>25</td>
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<tr>
<td>18</td>
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<td>4.3</td>
<td>15.1</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>19†</td>
<td>4½</td>
<td>Tetralogy of Fallot</td>
<td>3.5</td>
<td>11.1</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>20†</td>
<td>3½</td>
<td>Pulmonary stenosis; ventricular septal defect</td>
<td>4.0</td>
<td>10.0</td>
<td>7</td>
<td>6</td>
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<tr>
<td>21§</td>
<td>25</td>
<td>Tetralogy of Fallot</td>
<td>5.2</td>
<td>23.2</td>
<td>45</td>
<td>56</td>
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<tr>
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<td>49</td>
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<td>32.0</td>
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<td>23§</td>
<td>37</td>
<td>Atrial septal defect; ventricular septal defect</td>
<td>9.0</td>
<td>31.0</td>
<td>42</td>
<td>52</td>
</tr>
<tr>
<td>24§</td>
<td>41</td>
<td>Eisenmenger's syndrome (?)</td>
<td>7.4</td>
<td>25.6</td>
<td>33</td>
<td>42</td>
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<tr>
<td>25§</td>
<td>52</td>
<td>Eisenmenger's syndrome (?)</td>
<td>6.4</td>
<td>19.8</td>
<td>19</td>
<td>25</td>
</tr>
</tbody>
</table>

* AT = Appearance time; MCT = Maximal concentration time; arterial O2% = Oxygen saturation in arterial blood.
† Dye values corrected to agree with cardiac catheterization estimate by reducing the area of the primary triangle by one third.
‡ Under light Avertin anesthesia.
§ Patients 21 to 25 were not studied by cardiac catheterization.
¶ Necropsy on this patient revealed bronchiectasis, emphysema with pulmonary vascular sclerosis, grade 3, but no fistulous communication could be demonstrated. It is probable that the abnormal dye curve is caused by the passage of some blood through the bronchiectatic region (AT = 14 seconds) followed by a slower rate of flow by way of the normal channels in the emphysematous lung.

In the contour of the dye curves obtained and in the cardiac catheterization data, it may be difficult to obtain adequate samples to establish the true value for oxygen saturation.
of mixed venous blood and it is likely that a good proportion of the variability between the methods was due to error in the determination from the catheterization data. In spite of such difficulties a relatively good agreement has been found between the estimates of the shunt by the dye method (corrected) and from data collected by cardiac catheterization.

In figure 6, left, the oxygen saturation of arterial blood of the patients at rest is plotted against the per cent of the shunt as estimated by the dye method (corrected). If the volume of the shunt is less than 30 per cent of the systemic blood flow, then the degree of oxygen desaturation is not severe. If the volume of the shunt exceeds 40 per cent of systemic blood flow, then a marked fall in oxygen saturation occurs. It might be expected that in the larger shunts the low oxygen content of the arterial blood passing to the periphery results in the return to the heart of grossly desaturated blood, part of which again passes to the arterial system by way of the defect. It is probable that such a cycle underlies the marked fall in oxygen saturation of arterial blood in the presence of shunts of more than 35 per cent of systemic flow.

FIG. 6. The relation of arterial oxygen saturation to the magnitude of the venaarterial shunt. In the left panel two theoretically derived curves have been drawn relating oxygen saturation to volume of shunt when constant systemic flow and arteriovenous oxygen difference were assumed. The upper curve assumes an arteriovenous difference of 5 cc. of oxygen per 100 cc. of blood; the lower, a difference of 3 cc. of oxygen. It is realized that factors other than volume of shunt affect the arterial saturation but the present data do not permit a precise analysis of this relationship.

In the right panel the degree of oxygen was derived from data obtained at cardiac catheterization.

Fig. 5. Comparison of the magnitude of venaarterial shunts as calculated by the cardiac catheterization and dye methods. The broken line represents identity while the fine line is the regression: \( Y = 3.5 + 0.65X \), where \( X \) is the shunt as estimated from the cardiac catheterization data and \( Y \) the shunt calculated by the dye method. The standard error of the coefficient of regression \( (b = 0.65) \) was 0.07 and the standard deviation of any single determination from the calculated line was 6.6 per cent of systemic flow. The correlation between the methods was 0.89.
blood flow. However, the data available do not permit adequate analysis of the many interrelated factors governing the relationship between oxygen saturation and the magnitude of the shunt. The relationship just proposed was not evident in a comparison of oxygen saturation and per cent shunt calculated from the hemodynamic data (fig. 6, right), but it should be pointed out that several of the patients with severe cyanosis did not undergo catheterization and points of comparison in this important low range of oxygen saturation were not available.

For five patients a second dye curve was obtained 8 days to 23 months after the first. Good agreement was found between the calculation of the volume of the shunt on successive occasions. Details of the findings are given in table 2.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time between studies</th>
<th>First occasion</th>
<th>Second occasion</th>
<th>Remarks</th>
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<td>4 mo.</td>
<td>AT 7.0</td>
<td>MCT 24.7</td>
<td>% shunt 41</td>
</tr>
<tr>
<td>3</td>
<td>24 mo.</td>
<td>AT 11.8</td>
<td>MCT 24.4</td>
<td>% shunt 35</td>
</tr>
<tr>
<td>4</td>
<td>16 days</td>
<td>AT 9.4</td>
<td>MCT 29.0</td>
<td>% shunt 26</td>
</tr>
<tr>
<td>6</td>
<td>8 days</td>
<td>AT 5.2</td>
<td>MCT 19.3</td>
<td>% shunt 40</td>
</tr>
<tr>
<td>8</td>
<td>4 mo.</td>
<td>AT 9.5</td>
<td>MCT 26.1</td>
<td>% shunt 32</td>
</tr>
</tbody>
</table>

* AT = Appearance time; MCT = Maximal concentration time; O₂% = Oxygen saturation of arterial blood.

**COMMENT**

The method described in the earlier paragraphs evolves from the concept of division of the dye into two separate fractions which are proportionate to the volume of blood passing into the arterial system by different routes. The shunt calculated by the dye method correlates well with that obtained from cardiac catheterization data although an empiric correction factor would have to be used to eliminate a systemic difference between the two methods. Indeed the inclusion of such a correction factor would appear necessary from simple inspection of normal and abnormal dye dilution curves because the disappearance slope is always less steep than the build-up slope and some influence of the secondary curve on the primary is to be anticipated. A fixed value of 0.66 for the correction factor for the maximal concentration of the primary curve is not entirely satisfactory and a more theoretically accurate determination could be made. However, the shunt as calculated from the catheterization data, the standard of comparison in this study, is itself open to considerable error and further elaboration of the dye method does not at present seem justified.

Dye curves were recorded simultaneously from more than one site for a number of patients. Suitable curves from both ears or from one ear and radial artery were obtained from nine patients. The percentage of blood passing through the shunt did not differ by more than 5 per cent when determinations from two earpieces were compared or by more than 8 per cent when determinations of earpiece and cuvette were compared. The error of measure-
quentely occur in such patients, then a large dose of dye should be used. This difficulty is illustrated in figure 1; a moderate fluctuation in arterial oxygen saturation coincident with respiration renders identification of the points of maximal concentration uncertain. In other records the fluctuations have been even greater. The average dose of dye used for the 25 patients studied was 0.06 mg. per kilogram of body weight with a range of from 0.17 to 1.06 mg. per kilogram.

A high degree of repeatability was demonstrated on retesting patients after an interval (table 2). The percentage volume of the right-to-left shunt calculated in three patients differed little after a Blalock operation for tetralogy of Fallot from the preoperative volume although the oxygen saturation of arterial blood was elevated and clinical improvement had occurred. The contour of the dye curves of these patients also indicated the presence of pulmonary recirculation. Two additional patients, data on whom were not included in table 2 also showed no difference in the volume of the arterial shunts are usually unchanged when the patient breathes 100 per cent oxygen. However, in a few patients the magnitude of the shunt was altered or the direction reversed when the patient breathed 100 per cent oxygen. Dye curves obtained for such a patient are shown in figure 7. Also we have demonstrated intracardiac arteriovenous shunts in a few patients when they were breathing 100 per cent oxygen which could not be detected when they were breathing room air. In these patients the oxygen probably lowers the pulmonary resistance and thus permits an increase in the

![Dye Dilution Curves in Heart Disease](http://circ.ahajournals.org/content/5/1/78)

**Fig. 7.** Alteration in the direction of a shunt caused by change in the oxygen content of the inspired air in a 30 year old woman with atrial septal defect, pulmonary hypertension and cardiac failure. The curve in the left panel was obtained while the patient was breathing 100 per cent oxygen, in the right panel while she was breathing room air. All components of the curves are prolonged, associated with the low output of cardiac failure. The disappearance times of the dye curves in the left panel are disproportionately prolonged indicating the presence of a left-to-right shunt. The curves in the right panel, however, show a short appearance time and an abnormal initial hump indicating a shunt in the right-to-left direction which was not present when the patient was breathing 100 per cent oxygen. The scale of sensitivity to dye applies only to the left panel. When the patient was breathing room air the arterial saturation was 84 per cent. Due to this desaturation a second calibration of the cuvette oximeter to dye was not obtained.
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![Diagram](image)

**Fig. 8.** Difference in dye curves from a 44-year-old woman suffering from patent ductus arteriosus and pulmonary hypertension. Dilution curves were recorded from both ears and right radial and right femoral arteries. The appearance and build-up times of the curves obtained from the ears and radial artery were normal but the disappearance time was slightly prolonged consistent with a left-to-right shunt. The curve from the femoral artery, however, showed a short appearance time and an abnormal initial hump, demonstrating the early passage of a portion of dyed blood to the lower part of the body by way of the ductus. The oxygen saturation of the femoral artery blood (83 per cent) was lower than that of a simultaneously withdrawn radial artery sample (94 per cent).

<table>
<thead>
<tr>
<th>No.</th>
<th>Diagnosis</th>
<th>Shunt per cent of systemic flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pulmonary stenosis; atrial septal defect</td>
<td>Air 60</td>
</tr>
<tr>
<td>2</td>
<td>Tetralogy of Fallot</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>Pulmonary hypertension; atrial septal defect</td>
<td>33</td>
</tr>
<tr>
<td>6</td>
<td>Pulmonary hypertension; atrial and ventricular septal defects</td>
<td>45</td>
</tr>
<tr>
<td>8</td>
<td>Tetralogy of Fallot</td>
<td>39</td>
</tr>
<tr>
<td>16</td>
<td>Pulmonary stenosis; ventricular septal defect</td>
<td>25</td>
</tr>
<tr>
<td>18</td>
<td>Pulmonary hypertension; ventricular septal defect</td>
<td>19</td>
</tr>
</tbody>
</table>

Mean change = 1 per cent (change not significant).

TABLE 3.—The Change in Magnitude of the Venoarterial Shunt Calculated from Cardiac Catheterization Data on Breathing 100 Per Cent Oxygen

Mean change = 1 per cent (change not significant).

proportion of blood entering the pulmonary artery. It should be noted that in cases of patent ductus arteriosus with pulmonary hypertension of a degree to cause reversal of flow through the ductus, the dye dilution curves recorded from the right radial and femoral arteries may differ; the femoral curve indicating a right-to-left shunt and the radial no shunt or a shunt in the left-to-right direction (fig. 8).

In the results just reported data obtained by cardiac catheterization were collected for the most part while the patient was breathing room air, but the majority of dye curves were obtained while the patient was breathing 100 per cent oxygen. When the catheterization data permitted, the volume of shunt when the patient was breathing 100 per cent oxygen was also calculated (table 3), and in the present series did not differ systematically from the shunt obtained during the breathing of air. The differences observed may be within the error of the method. Nevertheless, in a few cases, the possibility does exist that the volume of the shunt may have altered between the time of collection of the catheterization data and the recording of the dye dilution curve.

Evans blue dye dilution curves then can be used to indicate the presence, direction and magnitude of veno-arterial shunts in cyanotic congenital heart disease. In suitable cases it is possible to demonstrate changes in the magnitude and even direction of shunts caused by different procedures. Changes in magnitude of shunts as calculated by the dye method may be more nearly accurate than the absolute volume of the shunt although satisfactory agreement with estimates from the cardiac catheterization data has been obtained in this series. Estimates from the cardiac catheterization data are, however, by no means ideal standards of comparison and calculation from dye dilution curves may be more representative of the volume of shunt at a given moment than the calculations from cardiac catheterization data obtained over a period of several minutes. The degree of correlation obtained between the amount of arterial oxygen desaturation and the relative volume of the shunt as calculated by the dye method lends credence to this concept.

**SUMMARY**

Dilution curves of Evans blue dye in the arterial blood were recorded for 25 patients
with cyanotic congenital heart disease. The first appearance of the injected dye at a recording oximeter attached to the ear was earlier than that for normal persons. An abnormal hump was found on the build-up slope of the curve which was taken to represent dye which had by-passed the pulmonary circuit by way of an intracardiac defect.

Certain features of the dye curve could be measured and it was possible to calculate the proportion of dye which had passed through the intracardiac defect. This indicated the percentage of the total systemic blood flow which had been shunted from the venous system.

For 20 patients data from cardiac catheterization were available which made it possible to compare the volume of the shunt as calculated from the dye curve and from cardiac catheterization data. A systematic difference amounting to 9 per cent of the systemic flow was found between the methods. The standard deviation of the differences between determinations of venoarterial shunts by cardiac catheterization and dye dilution methods was 7 per cent of the systemic flow. For the dye curve method a high degree of repeatability was demonstrated.

The arterial oxygen desaturation was related to the volume of the shunt. When the shunt exceeded 35 per cent of the systemic blood flow, severe oxygen desaturation was present when the patient was at rest.

The method represents a relatively simple and adequate technic for determining the magnitude of the shunt in cases of cyanotic congenital heart disease. From some patients, however, curves have been obtained which do not permit quantitation, either due to spontaneous fluctuation in arterial oxygen saturation sufficient to obscure the dye curve or to dye curves, the components of which were too poorly defined to permit measurements of the type required for the calculation.

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Sumario Español

El uso de un cuvette y un oxímetro de oído facilita el registro del patrón de dilución inmediata del tine T-1824 (azul de Evans) en la sangre arterial. En pacientes con shunts arteriovenosos el patrón de las curvas de dilución difiere de lo normal. Análisis quantitativo de las curvas obtenidas en estos pacientes con enfermedad cianótica congénita del corazón ha sido determinado para establecer la proporción de sangre que circula la circulación pulmonar. Los resultados obtenidos han sido comparados con estimados del volumen del shunt según datos de cationización cardíaca y relacionados a la saturación de oxígeno arterial.

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4. ——-: Estimation of cardiac output by the dye dilution method with an ear oximeter. J. Applied Physiol. 4: 177, 1951.


Dye Dilution Curves in Cyanotic Congenital Heart Disease
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