Measurement of Pulmonary Blood Flow Using the Indicator-Dilution Technic in Patients with a Central Arteriovenous Shunt

By ALFREDO A. RAMIREZ DE ARELLANO, M.D., PETER S. HETZEL, M.D., AND EARL H. WOOD, M.D., PH.D.

The possibility of measuring pulmonary blood flow in patients with central arteriovenous shunts utilizing the initial portion of indicator-dilution curves was explored in 16 patients by comparing these values for pulmonary blood flow with determinations by the direct Fick method. A good correlation between Fick and indicator-dilution values was obtained, and no systematic differences were demonstrated. The standard deviation of the differences between Fick and dye values was in the order of 20 to 25 per cent.

It has been observed by Nicholson and associates,1 and confirmed by Broadbent and Wood,2 that indicator-dilution curves obtained following intravenous injections of dye into patients with a central arteriovenous shunt present the same general configuration. In its typical form this pattern is characterized by: (1) an appearance time and build-up time of normal duration, (2) a maximal concentration lower than would be anticipated in a normal person for the amount of dye injected, (3) a prolongation of the disappearance time, and (4) an absence of the normal secondary peak of dye concentration due to systemic recirculation of dyed blood. Broadbent and Wood2 have conclusively demonstrated that these distinctive alterations of the dilution pattern are produced by the changes in circulatory dynamics as a result of the existence of such a shunt.

These observations suggested that analysis of the indicator-dilution curve would permit quantitation of the pulmonary blood flow in patients with a central arteriovenous shunt. The major problem in accomplishing this has been the distortion of the disappearance slope produced by the early appearance of dyed blood which has recirculated through the lungs via the abnormal circulatory pathway. This has prevented the use of the semilogarithmic extrapolation method of Hamilton. Theoretically, this difficulty would be obviated if the curve describing the first passage of the indicator through the lungs could be predicted from measurements of the initial, undistorted section of the recorded curve.

Two recently described modifications for estimating cardiac output by the indicator-dilution technic in subjects with a normal circulatory pathway seem to offer some hope in this direction. One, the forward triangle method of Hetzel and associates,3, 4 requires measurement of the build-up time and the maximal concentration. The other, developed by Dow,5 depends on the peak concentration time, appearance time and maximal concentration. It has been stated that the variability of these two indicator-dilution methods is of the same order as that of the Hamilton method.4, 5 Since only the initial portion of the curve is required, it is suggested that these two methods of analysis can be applied to estimate the pulmonary blood flow in patients with a central arteriovenous shunt. In the present study, the validity of such application is demonstrated by comparing values for pulmonary blood flow determined by each of these two methods with values obtained by the
TABLE 1.—Values for Pulmonary Blood Flow in Patients With Central Arteriovenous Shunt as Determined by the Fick Method and by the Dilution Technic Using the Forward Triangle and Dow Methods

<table>
<thead>
<tr>
<th>Subject</th>
<th>Diagnosis*</th>
<th>Age, years</th>
<th>Surface area, M²</th>
<th>Pressures, mm Hg</th>
<th>Systemic index, L/min/M²</th>
<th>Injection site</th>
<th>Pulmonary flow, L/min/M²</th>
<th>Per cent difference: (Fick-dye) X 100</th>
<th>Forward triangle method</th>
<th>Method of Dow</th>
<th>Fick method</th>
<th>Forward triangle</th>
<th>Dow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ASD†</td>
<td>42</td>
<td>1.76</td>
<td>25/12</td>
<td>113/68</td>
<td>S.V.C.</td>
<td>6.4</td>
<td>6.7</td>
<td>4.1</td>
<td>-56.1</td>
<td>-63.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>ASD</td>
<td>23</td>
<td>0.80</td>
<td>130/68</td>
<td>2.7</td>
<td>I.V.C.</td>
<td>6.9</td>
<td>7.1</td>
<td>8.0</td>
<td>13.8</td>
<td>11.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>ASD†</td>
<td>44</td>
<td>2.2</td>
<td>23/10</td>
<td>126/67</td>
<td>S.V.C.</td>
<td>6.6</td>
<td>7.9</td>
<td>8.0</td>
<td>17.5</td>
<td>16.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>ASD‡</td>
<td>44</td>
<td>1.66</td>
<td>32/14</td>
<td>91/51</td>
<td>S.V.C.</td>
<td>9.0</td>
<td>9.2</td>
<td>1.4</td>
<td>-40.6</td>
<td>-39.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>ASD‡</td>
<td>32</td>
<td>1.78</td>
<td>25/12</td>
<td>173/56</td>
<td>S.V.C.</td>
<td>5.6</td>
<td>5.4</td>
<td>5.3</td>
<td>-5.7</td>
<td>-1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>ASD‡</td>
<td>20</td>
<td>1.51</td>
<td>23/12</td>
<td>122/67</td>
<td>—</td>
<td>11.6</td>
<td>12.6</td>
<td>13.3</td>
<td>12.8</td>
<td>5.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>ASD‡</td>
<td>37</td>
<td>1.58</td>
<td>82/13</td>
<td>138/79</td>
<td>S.V.C.</td>
<td>3.4</td>
<td>3.3</td>
<td>2.3</td>
<td>-47.8</td>
<td>-47.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>ASD‡</td>
<td>48</td>
<td>1.59</td>
<td>106/29</td>
<td>121/75</td>
<td>S.V.C.</td>
<td>9.8</td>
<td>9.6</td>
<td>10.4</td>
<td>5.8</td>
<td>7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>ASD</td>
<td>45</td>
<td>1.50</td>
<td>40/12</td>
<td>122/74</td>
<td>S.V.C.</td>
<td>12.7</td>
<td>13.1</td>
<td>12.4</td>
<td>-2.4</td>
<td>-5.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>VSD</td>
<td>15</td>
<td>1.91</td>
<td>21/7</td>
<td>151/68</td>
<td>S.V.C.</td>
<td>2.9</td>
<td>2.6</td>
<td>1.1</td>
<td>29.3</td>
<td>36.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>VSD</td>
<td>10</td>
<td>1.36</td>
<td>25/10</td>
<td>127/65</td>
<td>S.V.C.</td>
<td>5.7</td>
<td>5.8</td>
<td>8.5</td>
<td>32.9</td>
<td>31.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>VSD</td>
<td>14</td>
<td>1.37</td>
<td>35/14</td>
<td>114/65</td>
<td>S.V.C.</td>
<td>5.7</td>
<td>5.8</td>
<td>1.7</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>VSD†</td>
<td>0</td>
<td>0.68</td>
<td>80/52</td>
<td>100/10</td>
<td>S.V.C.</td>
<td>11.5</td>
<td>11.8</td>
<td>11.6</td>
<td>-0.9</td>
<td>-1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>VSD</td>
<td>9</td>
<td>0.35</td>
<td>63/35</td>
<td>105/50</td>
<td>S.V.C.</td>
<td>10.5</td>
<td>10.8</td>
<td>12.5</td>
<td>-2.4</td>
<td>-4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>PDA‡</td>
<td>42</td>
<td>1.60</td>
<td>51/25</td>
<td>247/97</td>
<td>—</td>
<td>6.8</td>
<td>6.8</td>
<td>6.8</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>PDA‡</td>
<td>14</td>
<td>1.18</td>
<td>95/63</td>
<td>125/60</td>
<td>S.V.C.</td>
<td>10.2</td>
<td>10.2</td>
<td>10.6</td>
<td>3.8</td>
<td>3.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ASD = atrial septal defect; VSD = ventricular septal defect; PDA = patent ductus arteriosus.

† Brach. v. = brachial vein; I.V.C. = inferior vena cava; S.V.C. = superior vena cava; P.A. = pulmonary artery.

‡ Diagnosis subsequently verified at operation.
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direct Fick method during cardiac catheterization in a group of patients with a central arteriovenous shunt.

METHODS

The subjects were 16 patients with congenital heart disease associated with a central arteriovenous shunt. Nine of the patients had an atrial septal defect, 5 a ventricular septal defect and 2 a patent ductus arteriosus.

All subjects were studied by cardiac catheterization, using the technic and recording system previously described. In each instance the nature of the lesion was established by this procedure. In many instances the diagnosis was subsequently verified during operation.

The direct Fick procedure for determination of the pulmonary blood flow was carried out during cardiac catheterization. Determination of the oxygen consumption was done by the closed-circuit technic. Simultaneous blood samples were collected from the pulmonary artery through the cardiac catheter and from the radial artery for analysis of their oxygen content according to the method of Van Slyke and Neill.

Following the Fick procedure, indicator-dilution curves were recorded according to the method described by Nicholson and associates and, more recently, by Swan and Wood. Doses of 2.5 to 32 mg. of Evans blue dye (average 0.2, range 0.1-0.6 mg./Kg.) in volumes of 1 to 2 ml., were injected from a calibrated syringe through the cardiac catheter into one or more of the following sites: inferior vena cava, superior vena cava, and pulmonary artery. In two instances the injection was made into the brachial vein. The dilution curves were recorded photographically, using a cuvette oximeter through which blood was caused to flow at a constant rate from the radial artery. Calibration of the oximeter cuvette for Evans blue dye was carried out according to the procedure of Nicholson and Wood.

Twenty-three studies were conducted while the patients were breathing 100 per cent oxygen. Six additional studies were carried out while the patients were breathing room air.

Values for pulmonary blood flow were calculated by the direct Fick principle, and from the indicator-dilution curves using the forward triangle and Dow methods.

The forward triangle method was applied using the formula: $PF = \frac{60\ I}{C_p T_B} \times k$ where $PF$ = pulmonary blood flow in L./min.; $I = quantity of dye injected in mg.; C_p = maximal concentration in mg./L.; T_B = buildup time in sec.; $k = 0.37$ for curves obtained following injection of the indicator into the chambers of the heart and great vessels, and 0.32 for curves obtained following peripheral injections.

The calculations by the Dow method were done according to the formula:

$$PF = \frac{60\ I}{C_p T_B (0.3 - 0.9) T_A} \times 1.26$$

where, in addition to the other values, $T_P = peak concentration time in sec.; T_A = appearance time in sec.$

The correction factor 1.26 was used to correct for the systematic difference which has been found between cardiac output values determined by the Hamilton replot method and the Dow method in a series of normal subjects.

RESULTS

Vital statistics and physiologic data obtained during cardiac catheterization in the 16 patients are summarized in the table. All patients were shown to have a unidirectional shunt from left to right.

The results of pulmonary blood flow determinations, expressed in L./min./M.², are presented in the table. The values for pulmonary blood flow as determined by the direct Fick method averaged 8.5 L./min./M.², and ranged from 2.3 to 17.3 L./min./M.².

Figure 1 shows a comparison of values for...
Comparison of values for pulmonary blood flow determined by the direct Fick method (abscissa), and from indicator-dilution curves, using the Dow method (ordinate), in 16 patients with central arteriovenous shunt. The letters and numerals identify the individual patients listed in table 1.

In figure 2 the values for pulmonary flow obtained by the Dow method are plotted against the values determined by the direct Fick method. A good correlation was also obtained between these two methods (r = 0.93). No systematic difference was evident. The standard deviation of the differences between the paired values was 22.9 per cent.

DISCUSSION

It has been previously demonstrated that the forward triangle method gives a valid measurement of the cardiac output in subjects with a normal circulatory pathway. Comparable results have also been obtained using the Dow method. The calculation in both methods is simple to carry out and measurements can readily be made from the photographic record. The forward triangle method has the practical advantage that it involves the measurement of only three parameters while the Dow method requires four. Also, since the appearance time and the peak concentration time are not required in the forward triangle method, the laborious necessity of correcting these two components for the interval taken for blood to flow from the sampling site to the photosensitive portion of the cuvette is avoided.

The present study demonstrates the applicability of these two methods of analysis to the measurement of the pulmonary flow in patients with a central arteriovenous shunt. The variability obtained is of the same order as that obtained between measurements of cardiac output by the Hamilton and Fick methods in subjects without intracardiac shunts.

One limitation in using the indicator-dilution curve for estimating the pulmonary flow in patients with a central arteriovenous shunt is the rapid pulmonary recirculation commonly seen in these patients having a high pulmonary blood flow. When this occurs, the maximal concentration may possibly be increased by recirculated dye, or else it may appear so poorly defined that measurement of the build-up time, peak concentration time and maximal concentration may be inaccurate. It is suggested that this difficulty may be minimized by utilizing the more sharply defined curves which follow injections of the indicator into a central site such as the pulmonary artery. However, the frequent occurrence of preferential shunting of blood draining from the right lung in patients with atrial septal defect renders the pulmonary artery unsuitable as an injection site in such patients, owing to the possibility of the occurrence of a preferential injection of the dye into either the left or the right pulmonary artery. An injection site upstream to the pulmonary valve would avoid this difficulty.

These modifications of the indicator-dilution technic cannot be used to measure pulmonary flow if an appreciable right-to-left shunt is present. Presumably, however, under this circumstance curves recorded following injections downstream to the site of the shunt could be used for calculation of systemic flow.

A standard deviation of the order of 20 per
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It should be remembered, however, that the error in measurement of pulmonary flow by the Fick method in such patients is subject to large errors on the basis of small arteriovenous differences and, in addition, possible errors caused by cyclic variations in blood flow, oxygen content or both.\textsuperscript{11-13}

It is believed that the results obtained indicate that the indicator-dilution technic, using either the forward triangle method or the Dow method, provides a satisfactory means of estimating pulmonary blood flow in patients with a central arteriovenous shunt. It is felt that the accuracy of these two methods of analysis is of an order suitable for use in certain experimental and clinical situations.

**Summary**

The applicability of the indicator-dilution technic, using the forward triangle method or the Dow method, to the measurement of the pulmonary blood flow in patients with a central arteriovenous shunt has been tested by comparing values obtained by each of these two methods of analysis with values obtained by the direct Fick method in 16 patients with congenital heart disease associated with a central arteriovenous shunt.

The results obtained by each of these indicator-dilution methods correlated well with those obtained by the direct Fick method. No systematic error was evident. The standard deviation of the differences between the forward triangle method and the direct Fick method was 22.9 per cent, and that of the differences between the Dow method and the direct Fick method was 24.4 per cent.

It is concluded that these two methods of analysis provide a relatively simple procedure for estimating pulmonary blood flow in patients with a central arteriovenous shunt.

**Acknowledgment**

The authors express their appreciation to Dr. Howard B. Burchell for his assistance in this investigation.

**Summario in Interlingua**

Esseva studiate le applicabilitate del technica a dilution de indicator al mesuration del fluxo de sanguine pulmonar in patientes con un central derivation arteriovenose. Esseva usate le methodo del triangulo anterior e le methodo de Dow. Le valores obtenite per le un e le altere del duo methodos mentionate esseva comparete con valores obtenite per le directe methodo de Fick in 16 patientes con congenite morbo cardiac associate con un central derivation arteriovenose.

Le resultatos obtenite per le duo methodos a dilution de indicator esseva ben correlationate con le resultatos obtenite per le directe methodo de Fick. Nulle error de character systematic esseva evidente. Le deviation standard del differentias inter le methodo a triangulo anterior e le directe methodo de Fick esseva 22,9 pro cento; inter le methodo de Dow e le directe methodo de Fick le differentias monstравa un deviation standard de 24,4 pro cento.

Nos conclude que le duo mentionate methodos a dilution de indicator provide un relativemente simple technica pro estimar le fluxo de sanguine pulmonar in patientes con un central derivation arteriovenose.

**REFERENCES**


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