ABSTRACT

Using a constant infusion of two indicators, T-1824 bound to albumin and tritiated water, flow and transit time were measured in the left coronary system of intact man. Indicators were infused for 6 minutes into the left coronary artery with sampling from the coronary sinus in a region that drained exclusively the inflow of the left coronary artery and from the brachial artery for recirculation. The degree of heterogeneity of myocardial perfusion could be defined by the time required for the curve to reach a plateau. A correlation coefficient of 0.966 was found between the two indicator-measured blood flows. The average myocardial hematocrit was calculated and found to be similar to the arterial. In the presence of myocardial disease, total flow of the left coronary artery was increased. When this was divided by tissue volume, the blood flow per unit volume of tissue was decreased in the presence of the idiopathic cardiomyopathy.

ADDITIONAL KEY WORDS: left coronary blood flow, cardiomyopathy, myocardial transit time, volume, myocardial hematocrit, T-1824, coronary artery disease, tracer dilution, tritiated water.
(1) was limited by the accuracy of our analytical methods to measure the occurrence of a plateau, and whether the longest transit had been included. To test our analytic accuracy, two indicators were used, Evans blue dye (T-1824) on albumin, and tritiated water (H2O) to measure flow. The agreement of the two flow measurement was an indication that a plateau was probably present. The disadvantage of the constant infusion method of measuring flow is that spontaneous flow changes during the time of infusion can distort the curve leading to errors in interpretation of what is a plateau.

We have applied the constant infusion technique to the left coronary system in a group of patients with both coronary artery and myocardial disease. The results are from those patients in whom a plateau occurred.

Methods

PROCEDURE

Patients undergoing diagnostic cardiac catheterization, in whom coronary angiography was indicated, were included in the study. Informed consent was obtained for this part of the procedure. Patients were divided into five groups following catheterization: normal, familial cardiomyopathy, cardiomyopathy, coronary artery disease, and a miscellaneous group. Patients were placed in the normal group when cardiac catheterization and coronary angiography results were within normal limits. Cardiomyopathy was diagnosed when the coronary arteries were found to be normal, and no other etiology could be detected to explain the abnormal hemodynamics. All patients were studied in the fasting state in the morning. Previous medication given was 50 mg of meperidine. Heparin was used to maintain catheter patency. A number 7 Roderguiez-Alvarez Cordis catheter was then passed into the aortic sinus. This was confirmed angiographically. Either catheter was advanced into the coronary sinus so that its tip was in the region of the left coronary artery. This position of the catheter in the left coronary artery was again determined angiographically. Studies were rejected if the following technical errors occurred:

1. There was leakage of radiopaque dye into the aorta from the catheter in the left coronary artery during coronary angiography;
2. The catheter in the left coronary artery changed position during this study;
3. The venous phase of the left coronary angiogram did not opacify the region of the coronary sinus catheter;
4. The venous phase of the right coronary angiogram revealed opacification in the region of the coronary sinus catheter;
5. Following injection of an indicator (cardio green) into right coronary artery, the indicator was recovered from the coronary sinus catheter.

All angiograms were recorded on cinefilm at a speed of 40 frames/sec. The total duration of time required for the study was from 6 to 12 minutes. In two instances repeat studies were performed.

INDICATORS

Two indicators were used, T-1824, and H2O. Both indicators were not used in every study. The

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2The Radiochemical Centre, Amersham, England.

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total quantity of 4H2O infused was less than 5cc. Trace amounts of albumin were added to the infusate to prevent loss of dye by binding to catheters.

ANALYTICAL METHODS

All samples were placed in ice upon withdrawal and centrifuged in the cold. Hematocrit was determined on both arterial samples and those from the coronary sinus. A correction of 6% was made for trapped plasma. T-1824 was measured spectrophotometrically in plasma (5). A modified Somogyi filtrate (6) was prepared (0.5 ml plasma, 1 ml 4.7% barium hydroxide, 1 ml of 38 zinc sulfate). 0.5 ml of this filtrate was added to 15 ml of scintillation solution containing 7 g/liter PPO (2, 5-diphenyloxazole), 0.3 g/liter dimethyl POPOP (1, 4-bis-2-[5-phenyloxazolyl]benzene) and 100 g/liter naphthalene in dioxane and counted using a Triarb liquid scintillation spectrophotometer (Model 3375). Efficiency was 34% for tritium. Quenching was monitored using an external standard and was constant in all samples. Sufficient counts were collected to assure a standard deviation of less than 1% of the mean.

CALCULATIONS

The time-corrected concentrations of coronary-sinus indicator minus recirculation were plotted on graph paper for both indicators. An equilibrium state for the indicator was recognized when the curve became asymptotic (plateaued). Curves which failed to reach a plateau were rejected. The average concentration of the indicator during the plateau was used to calculate the plasma or blood flow depending on the indicator. There were usually from six to eight measurements of each indicator concentration for T-1824, and these to five for 4H2O during equilibrium. Indicators were made comparable by dividing their plasma concentration by the injectate concentration, and then correcting this value to a common volume of distribution. A smooth curve was constructed from the individual plasma concentrations.

The mean transit time (t) was calculated by integrating the area subtended by the washin curve and the asymptote of the plateau extrapolated to zero time. This area was divided by the concentration of indicator during equilibrium (c_e) as suggested by Zierler (7).

Plasma flow in the left coronary artery (Q_LCA) was measured using the following formula:

\[
Q_{LCA} = \frac{I}{t} \int_0^\infty c(t) \, dt
\]

Plasma flow (Q_LCA) in the left coronary artery was calculated using the following formula:

\[
Q_{LCA} = \frac{I}{t} \int_0^\infty c(t) \, dt
\]

The optical density (OD) refers to the concentration of T-1824 in the injectate (Inj.), coronary sinus (CS), and brachial artery (BA) as measured analytically.

When tritiated water is the indicator used, the same formula yields blood flow (Q_BCA). Blood flow can also be calculated from the plasma flow using T-1824-measured plasma flow, and the arterial hematocrit as follows:

\[
Q_{BCA} = \frac{Q_{LCA}}{1 - H(t)}
\]

The volume of distribution of the indicator can be calculated from the formula suggested by Zierler (7):

\[
V = Q \times t
\]

As two indicators were used to measure flow, T-1824 which measures plasma flow and 4H2O which measures blood flow, a true myocardial hematocrit can be calculated using the following formula:

\[
Hct_{myo} = \frac{Q_{LCA} - Q_{BCA}}{Q_{LCA}}
\]

Results

In the first 30 patients investigated, a successful flow determination was made on 14 occasions. Of the last 32 patients investigated, the criteria for a successful flow study was present in 24. The most common cause of failure of a study was the catheter in the left coronary artery slipping out of the origin of the vessel during infusion. The results reported in this study are from 22 patients recently studied. No complications of the procedure were encountered. The maximum volume of blood removed during a study was 150 ml. When repeat studies were performed, the sample size and number were reduced.
### TABLE 1

**Plasma Flow, Mean Transit Time (t), and Calculated Indicator Volumes of the Left Coronary Artery System**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Plasma Flow (ml/min)</th>
<th>t (sec)</th>
<th>Blood Flow (ml/min)</th>
<th>t (sec)</th>
<th>1-18 24</th>
<th>VO2 (ml)</th>
<th>1-18 24</th>
<th>VO2 (ml)</th>
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<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>M</td>
<td>Normal</td>
<td>140</td>
<td>24.8</td>
<td>193</td>
<td>72.7</td>
<td>57.8</td>
<td>294.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>M</td>
<td>Normal</td>
<td>99</td>
<td>13.1</td>
<td>142</td>
<td>54.3</td>
<td>23.4</td>
<td>128.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>M</td>
<td>Normal</td>
<td>87</td>
<td>29.4</td>
<td>158</td>
<td>57.3</td>
<td>24.8</td>
<td>151.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>M</td>
<td>Normal</td>
<td>81</td>
<td>15.3</td>
<td>158</td>
<td>57.3</td>
<td>24.8</td>
<td>151.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>M</td>
<td>Familial cardiomyopathy</td>
<td>689*</td>
<td>22.7</td>
<td>1,167*</td>
<td>40.2</td>
<td>260.1</td>
<td>940.5</td>
<td></td>
<td></td>
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<tr>
<td>6</td>
<td>45</td>
<td>M</td>
<td>Dystrophic myotonia</td>
<td>117</td>
<td>19.4</td>
<td>183</td>
<td>64.3</td>
<td>30.0</td>
<td>106.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>M</td>
<td>Friedreich's ataxia</td>
<td>156</td>
<td>12.5</td>
<td>309</td>
<td>48.4</td>
<td>54.6</td>
<td>246.8</td>
<td></td>
<td></td>
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<tr>
<td>8</td>
<td>42</td>
<td>F</td>
<td>Familial cardiomyopathy</td>
<td>175</td>
<td>19.9</td>
<td>255</td>
<td>42.2</td>
<td>58.2</td>
<td>179.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>39</td>
<td>M</td>
<td>Cardiomyopathy</td>
<td>63</td>
<td>24.2</td>
<td></td>
<td></td>
<td>32.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>41</td>
<td>M</td>
<td>Cardiomyopathy</td>
<td>141</td>
<td>14.6</td>
<td>221</td>
<td>64.1</td>
<td>34.3</td>
<td>235.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>59</td>
<td>M</td>
<td>Cardiomyopathy</td>
<td>85</td>
<td>26.3</td>
<td>171</td>
<td>104.8</td>
<td>39.6</td>
<td>250.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>59</td>
<td>M</td>
<td>Cardiomyopathy</td>
<td>127</td>
<td>13.6</td>
<td>222</td>
<td>73.6</td>
<td>28.7</td>
<td>206.0</td>
<td></td>
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</tr>
<tr>
<td>13</td>
<td>36</td>
<td>M</td>
<td>Alcoholism</td>
<td>296</td>
<td>10.6</td>
<td>475</td>
<td>70.9</td>
<td>52.1</td>
<td>206.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>32</td>
<td>M</td>
<td>Alcoholism</td>
<td>277</td>
<td>12.0</td>
<td></td>
<td></td>
<td>55.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>F</td>
<td>Coronary artery disease</td>
<td>286</td>
<td>30.6</td>
<td>319</td>
<td>77.0</td>
<td>144.4</td>
<td>484.7</td>
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<tr>
<td>16</td>
<td>50</td>
<td>M</td>
<td>Coronary artery disease</td>
<td>199</td>
<td>27.2</td>
<td>320</td>
<td>74.4</td>
<td>90.1</td>
<td>415.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>49</td>
<td>F</td>
<td>Coronary artery disease</td>
<td>162</td>
<td>14.0</td>
<td>237</td>
<td>52.6</td>
<td>37.8</td>
<td>208.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>49</td>
<td>M</td>
<td>Coronary artery disease (1)</td>
<td>128</td>
<td>13.5</td>
<td>190</td>
<td>46.8</td>
<td>26.7</td>
<td>147.9</td>
<td></td>
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</tr>
<tr>
<td>19</td>
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<td>30.1</td>
<td>195.4</td>
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<td></td>
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<tr>
<td>20</td>
<td>54</td>
<td>M</td>
<td>Coronary artery disease</td>
<td>147</td>
<td>20.3</td>
<td>256</td>
<td>37.2</td>
<td>43.6</td>
<td>158.5</td>
<td></td>
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</tr>
<tr>
<td>21</td>
<td>49</td>
<td>F</td>
<td>Schizophrenia</td>
<td>228</td>
<td>17.5</td>
<td>358</td>
<td>52.6</td>
<td>65.9</td>
<td>194.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>55</td>
<td>F</td>
<td>Diabetes mellitus</td>
<td>120</td>
<td>24.3</td>
<td>108</td>
<td>73.4</td>
<td>88.4</td>
<td>241.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Patient with a single coronary artery.

Two patients (18, 19) with coronary artery disease had repeat studies. Patient 9 had two studies, 18 months apart. Number in parentheses is number of studies.
FLOW AND VOLUME IN LEFT CORONARY SYSTEM

Plasma flow (formula 2) and mean transit time (formula 1) of T-1824 are listed in Table 1 for all patients. One patient, 9, was studied on two occasions, 18 months apart. The second study was done after the onset of congestive failure. Two patients (18 and 19) with coronary artery disease were studied twice. Both had an increase in heart rate during the second study. In the second patient this was induced by pacing. Patient 5 was found to have only a left coronary artery, so flow is for the entire heart. This patient is a member of the family reported by Paré et al. (8). The four normal patients had a mean ± 1 sx, left coronary artery plasma flow of 102 ± 13 ml/min, and a mean transit time of 19.2 ± 2.4 seconds.

A typical T-1824 dilution curve is shown in Figure 1. Recirculation as measured in the brachial artery is also plotted. The percent standard deviation for the eight plateau values is less than ± 1, and did not exceed ± 10 in all acceptable curves.

![Image 1](http://circres.ahajournals.org/)

A representative washin curve for T-1824 in one patient. The X symbols are coronary sinus concentrations of indicator corrected for recirculation. The measured values for recirculation (brachial artery) are shown as solid dots. The asymptote to the plateau is shown as a dotted line. Q_{pl}LCA = plasma flow in left coronary artery.

![Image 2](http://circres.ahajournals.org/)

The washin curve and plateau for two indicators T-1824 (a) and HgO (c) as measured simultaneously in a normal patient. Both indicators are expressed as percent of injectate and their spaces of distribution have been normalized by multiplying the T-1824 concentration by the hemocrit. Q_{pl}LCA = plasma flow in left coronary artery; Q_{bl}LCA = blood flow in left coronary artery.

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Blood flow measured using tritiated water and formula 1 has been plotted on the ordinate and blood flow calculated from plasma flow measured from T-1824 and formula 2 is plotted on the abscissa. The solid line is $y = x$. The single high flow point is from the subject with a single coronary artery. Definitions same as for Figures 1 and 2.

The myocardial hematocrit calculated from formula 5 was $0.380 \pm 0.014$. There is no significant difference between these values.

**EFFECT OF DISEASE**

Diagnostic categories were assigned as follows: 1 to 5 normal, 5 to 8 familial cardiomyopathy, 9 to 14 cardiomyopathy, 15 to 20 coronary artery disease, and 21, 22 miscellaneous. Patients with coronary artery disease had predominantly right vessel disease, as the presence of stenotic lesions of the left coronary artery was associated with collateral flow from the right coronary artery to the coronary sinus sampling site. This invalidated these studies.

Blood flow (formula 2) and mean transit time (formula 3) for $^{3}$H$_2$O are also listed in Table 1. For the three normal patients in whom the measurement was made, mean blood flow was $164 \pm 15$ ml/min and mean transit time $61.4 \pm 5.7$ seconds in the left coronary system. The indicator curve of $^{3}$H$_2$O for patient 3 is shown in Figure 2, as well as the T-1824 indicator curve. Although fewer plateau values were recorded for $^{3}$H$_2$O, their variation was similar to that for T-1824.

The reproducibility of measurement was assessed by calculating blood flow for the two indicators, using formula 4 for $^{3}$H$_2$O, and formula 5 for T-1824. Results are plotted in Figure 3. Correlation coefficient is 0.966. The regression equation of pairs, holding $^{3}$H$_2$O blood flow as the dependent variable is $y = 0.99x + 30.3 \pm 19.0$. Our reproducibility is therefore excellent.

**INTRAMYOCARDIAL HEMATOCRIT**

Arterial hematocrit for the group was $0.405 \pm 0.013$ and for the coronary sinus $0.406 \pm 0.012$. The myocardial hematocrit calculated from formula 5 was $0.380 \pm 0.014$. There is no significant difference between these values.

**FIGURE 3**

Blood flow measured using tritiated water and formula 1 has been plotted on the ordinate and blood flow calculated from plasma flow measured from T-1824 and formula 2 is plotted on the abscissa. The solid line is $y = x$. The single high flow point is from the subject with a single coronary artery. Definitions same as for Figures 1 and 2.

**FIGURE 4**

Blood flow in the left coronary artery in the four groups: normal (NOR), familial cardiomyopathy (F.C), cardiomyopathy (CARD), and coronary artery disease (CAD). Bars indicate $\pm$ S.E and $P$ values are indicated compared to normal. LCA = left coronary artery.
Blood flow per interstitial and cell water volume in the left coronary system. Calculated by dividing LCA blood flow by the total water volume minus intravascular water volume (T-1824 volume/plasmacrit). Abbreviations as in Figure 4.

Blood flow per interstitial and cell water volume in the left coronary system. Calculated by dividing LCA blood flow by the total water volume minus intravascular water volume (T-1824 volume/plasmacrit). Abbreviations as in Figure 4.

Discussion

Using a constant infusion of indicators, we have been able to make measurements of blood flow, and mean transit time of the left coronary system of intact man. It is pertinent to present arguments on the validity of our method. Zierler has discussed the theoretical basis of the constant infusion to measure flow, transit time, and volume (10).

The first assumption is that mixing occurs in the left coronary artery of man before its bifurcation. Specific studies on the pattern of flow in the left coronary artery are not available in the literature. A consideration of the physical characteristics of this artery and what is known of its blood flow is of importance in the validation of the assumption. The average dimensions of the left coronary artery in man as reported by Baroldi and Scomazzoni (11) are 4 mm in diameter and 13.5 mm in length with a length range from 3 to 23 mm. Bellhouse et al. (12) calculated that the average velocity in the left coronary artery is from 50 to 60 cm/sec. This value approaches that where unstable flow may occur. Andres et al. (10) have shown that mixing can occur in the brachial artery in the absence of turbulence under similar experimental circumstances. Another factor favouring mixing may be orifice effects. At the coronary ostia, flow is unstable (12) and may remain unstable for a number of vessel diameters. The marked velocity changes with systole and diastole observed by Gregg (13) may also be a potent mixing force, through the mechanism of lateral displacement of red cells associated with acceleration, a phenomenon described by Goldsmith (14). It is therefore probable that the origin of the left
coronary artery in man is a potential mixing site. In contrast to man, dog's main left coronary artery is frequently very short, with immediate branching into circumflex and anterior descending branches. This arrangement precludes the use of the proposed technique, as the injectate may be delivered into either of two branches before mixing, resulting in considerable error as shown by Kupic et al. (15).

The second assumption was that the heterogeneity of the system has been recognized. As previously stated, only those studies in which a plateau occurred for the indicator were accepted. In some cases studies may have been rejected, in which a change in coronary flow during the infusion period distorted the plateau.

A third assumption was that there are no functional collateral channels from the right coronary artery draining in the sampling site of the left. This indicator-free blood would tend to cause an overestimate of blood flow, but would not affect \( t \) if the collateral flow was constant. Arterial collateral channels exist in normal hearts (11). The blood flow in these channels has not been quantified in normal or diseased man. The technique of injecting an indicator into the right coronary artery under the same conditions as the injection was given into the left with coronary sinus sampling or by detecting the ECG changes of collateral filling of the left coronary artery from an injection into the right coronary artery (16) are sensitive means of detecting significant collateral flow. The frequency of rejection of studies on this basis was very high in patients with severely stenotic lesions of the left coronary arterial system.

The fourth assumption was that the coronary sinus site drains only the left coronary arterial system and not the right. Several studies have been performed on the adequacy of the coronary sinus as a sampling site for the outflow of the left coronary artery (17, 18). Klocke et al. (2) have shown that in man, above the lower third of the coronary sinus, contamination with right atrial blood is not found, and Friesinger et al. (18) have shown in dog that the upper half of the sinus drains exclusively the left coronary system. By observing the venous drainage directly by angiography, we could be certain that the sampling site was in the venous drainage region of the system being studied.

**Coronary Blood Flow**

Early attempts to measure coronary blood flow in man, using revived human hearts either as a heart-lung preparation (19) or a Langendorf preparation (20), suggested that the normal flow range was 0.9 to 1.5 ml \( \cdot \) min\(^{-1} \) \( \cdot \) g tissue\(^{-1} \). Values found in diseased hearts ranged from 0.1 ml to 3 ml \( \cdot \) min\(^{-1} \) \( \cdot \) g\(^{-1} \). With the introduction of nitrous oxide as an indicator for coronary blood flow (21), the values reported for coronary flow in intact man were somewhat lower. Ross et al. (22) using xenon 133 injected into the left coronary artery reported a flow per unit volume of from 41 to 84 ml \( \cdot \) 100 ml tissue\(^{-1} \) \( \cdot \) min\(^{-1} \). Using the rubidium technique (23) to measure total coronary nutritional flow, the range for normal subjects was from 92 to 410 ml/min. The inert gas indicator methods and the rubidium method are susceptible to errors from heterogeneity since they do not define its presence; hence, while they may be accurate in normal subjects, they may fail completely in the presence of marked heterogeneity. The basis for this failure is an inability to define the primary curve from recirculation. As both methods do not measure the total flow in the artery and the volume to which the flow is delivered, it is not possible to make a direct comparison with our method.

The inverse of mean transit time (1/1) is equal to flow per unit volume (F/V). This indicator volume relates to the weight of tissue of the left coronary artery through \( \lambda \), Kety's partition coefficient or F/\( \lambda \)W (3). For \(^2\)H\(_2\)O, \( \lambda \) can be calculated as percent water content of the whole tissue divided by water content of blood or 0.88. The average \( t \) for \(^2\)H\(_2\)O in normal subjects was 0.14 seconds or 1.02 minutes. 1/\( t \) = 98 ml \( \cdot \) 100 ml tissue\(^{-1} \) \( \cdot \) min\(^{-1} \). This divided by 0.88 gives 111 ml \( \cdot \) 100 g heart\(^{-1} \) \( \cdot \) min\(^{-3} \). This value for flow per
unit volume is higher than the values reported for normals using inert gas washout methods. It is possible that we have underestimated the unit volume for water. If normal coronary flow were only 80 ml/min, a correction factor for $^3\text{H}_2\text{O}$ I could be calculated as $111/80 = 1.39$ to obtain a correct flow per unit volume. As our total flow measurements were estimated by two indicators, which agreed, it is less likely that flow was overestimated from the plateau concentration than if underestimated. This theoretical factor for $^3\text{H}_2\text{O}$ would increase water volume by 39%, which would be unreasonably large. The range of flow values we have reported per unit volume are similar to those reported by earlier workers using direct measurements.

**Mean Transit Time**

Mean transit time for indicators of the diseased myocardium have not been reported. Klocke et al. (2) have shown that washout curves of $\text{H}_2\text{O}$ may be of considerable duration in the presence of coronary artery disease. As we waited until an equilibrium state existed for the indicator, that is input was equal to output, as shown by the existence of a plateau, we were certain that most of the long transits were included in our analysis of the mean transit time. The T-1824 washin curve was drawn from a restricted number of points. Catheter distortion will have a significant effect upon its shape. While we made corrections for sampling delay, it is possible that the rate of rise of this indicator was more rapid than we recorded and hence our estimates of flow for T-1824 are excessive. A more direct measurement, such as using $^4\text{H}_2\text{O}$ with precordial counting would be of assistance in determining the magnitude of this error.

A second problem may be that we have failed to recognize a long tail in the water curve so that flow for $^3\text{H}_2\text{O}$ was underestimated, that is, the water curve did not reach equilibrium. Against this argument is our finding that blood flow as measured by $^3\text{H}_2\text{O}$ was slightly lower than that measured from the intravascular indicator T-1824. If a true plateau for $^3\text{H}_2\text{O}$ had not been reached, as a systematic error in our technique, the opposite relationship should have been observed with the water flow being higher than T-1824-calculated blood flow. Another potential error in calculating flow for both indicators would be changes in coronary flow during the infusion period.

**Myocardial Hematocrit**

There have been attempts to measure the myocardial hematocrit in animals. Myers and Honig (24) found that the capillary hematocrit in the dog was the same as arterial hematocrit. Our studies suggest that under conditions of disease in man, myocardial hematocrit is similar to arterial hematocrit. Our finding that an average of 21.3% of the water space of the normal heart (T-1824 volume divided by $^3\text{H}_2\text{O}$ volume) is accessible to albumin suggests that the vascular space of the myocardium is quite large. This assumes that albumin is an intravascular indicator. Wearne (25) calculated that up to 19% of the total myocardial weight in man may be occupied by the capillary blood volume, a value which has been questioned by Honig et al. (26) as being much too large. Hirche and Lochner (27) calculated the total blood volume as 15.0 ± 0.5 ml/100 g heart muscle, while Myers and Honig (24) calculated the value to be 6% of heart weight. Hort (28) estimated the capillary volume alone to be about 8% in man with the added arterial and venous volume to be comparable to the value given by Hirche and Lochner for the dog. If erythrocyte mass is added to the T-1824 volume we measured, the low values recorded in patients with myopathy correspond to Hirche and Lochner's value, while our higher values exceed the space described by Wearne. The validity of Hirche and Lochner's measurement is open to question as they measured volume by injecting dye into the branches of the left coronary artery in the dog's heart, and then used assumptions as to distribution of flow to relate this to total flow of the left coronary artery. An explanation for our observed large T-1824 space may be that the albumin space is not a sharply defined space, as the capillary endothelium may leak, with the loss of indicator into lymphatics. It is also possible that the large albumin space was...
related to the prior use of contrast material in the artery. A lack of fixity of tissue spaces in
the myocardium has been commented upon
by Page and Page (29).

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A moderately close agreement was found
between water mass of the left coronary
system and postmortem left ventricular weight
in one patient. The observation of a correla-
tion between geometric mass and the calcu-
lated left coronary system interstitial and cell
water volume indicates that our method is
sensitive to differences in volume. If an
assumption is made that the left coronary
artery supplies
$0.70$
 of a normal heart weighing
$320$ g; $224$ g of tissue, or a water volume of
$(0.8 \times 224)= 179$ ml would be measured. The
mean water volume of the normal patients as
measured by our technique was $171$ ml, which
is quite similar to above calculated value.

This method of investigating blood flow and
volume of the left coronary system of man is
applicable to other indicators as well. From a
knowledge of concentration of metabolites
and electrolytes it should be possible to
calculate the rates of transfer of metabolites
across membranes in the myocardium.

It is apparent from our data that disease of
both the myocardium and coronary arteries
tend to increase the resting total left coronary
blood flow. When marked hypertrophy of
muscle was present, as in cardiomyopathy, we
observed an increase in blood flow, a length-
ening of the mean transit time for $3^2H_2O$, and
a fall in the blood flow per unit volume of
interstitial and cell water volume. This latter
observation is consistent with the observation
made by Wearn (25) and by Dock (20) that
with, hypertrophy the capillary net is relatively
reduced as the cells increase in size.

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FLOW AND VOLUME IN LEFT CORONARY SYSTEM


Blood Flow and Tissue Space of the Left Coronary Artery in Man
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