Measurement of Coronary Blood Flow by External Counting with Radioactive Rubidium

Critical Appraisal and Validation of the Method

By L. Donato, M.D., G. Bartolomei, M.D., G. Federighi, M.D., and G. Torreggiani, M.D.

The myocardial clearance of potassium (MCK) can be measured by means of precordial counting after single intravenous injection of $^{42}$KCl or $^{86}$RbCl. It may be considered to measure coronary blood flow per unit mass of myocardium under the assumption that the average extraction of the indicator by the myocardium during the first minutes after injection does not differ significantly from the average total body extraction. Theoretical considerations and experimental evidence suggest that these conditions actually occur in rats, dogs, and humans.

When a precordial counter is used to measure myocardial radioactivity, the obtained value for MCK represents the mean flow per unit mass, and it is conventionally expressed per 100 g of myocardium. Absolute flow cannot be determined with a precordial counter since individual variability in depth and size of the heart prevents an absolute estimate of myocardial uptake of the radioisotope. If the geometric dependence of the measurement could be overcome, coronary blood flow could be estimated as a fraction of cardiac output or in absolute terms. In fact, under conditions of uniform counting efficiency for the entire heart, the fraction of injectate taken up by the myocardium shortly after injection of $^{86}$Rb or $^{42}$K would equal the fraction of the cardiac output perfusing the myocardium.

The present series of experiments has been designed with the following purposes: (1) to verify the validity of the assumptions underlying the method using $^{86}$Rb; (2) to compare the results obtained with the precordial counting method with the values of coronary blood flow simultaneously measured with the nitrous oxide method; and (3) to evaluate a counting apparatus designed to reduce the dependence on geometry of the values obtained by counting.

Methods

Measurement of CBF by $^{86}$Rb Injection

Instruments and Operating Conditions

The instrument used for monitoring intracardiac and myocardial radioactivity is shown in figure 1. It is a twin counter system (TCS*), comprising two NaI scintillation counters (3 by 3 inches), the combined output of which is fed to an amplifier and single-channel pulse-height analyzer. The high voltage supply to the phototubes is adjusted in order to obtain superposable $\gamma$-spectra from the two detectors. Pulses from the analyzer are fed to a scaler and a linear ratemeter, operating in parallel, and the output of the ratemeter is fed to a DC amplifier of an oscillographic recorder.

The scintillation detectors are housed in lead collimators, with cylindrical collimating channels. The crystals are recessed 40 cm in the collimators, and the diameter of the collimating channels can be adjusted from 7.5 to 9 cm. The two collimators are mounted on a movable stand arranged so that the two crystals face each other on the same vertical axis. The lower detector can be positioned under the catheterization table and the distance of the upper detector can be adjusted. This arrangement yields a rather uniform distribution

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*This instrument was developed as part of the work performed under the sponsorship of the U. S. Atomic Energy Commission, Contract AT(30-1)-2648.
Measurement of Coronary Blood Flow

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Figure 1

The twin counter system (TCS) is shown with the Perspex block in position for calibration of the in vivo measurement (see text).

of counting efficiency within a cylinder defined by the collimating channels. A detailed discussion of this point is given in the appendix, and it includes the procedure for calibration.

Experimental Procedure

The procedure on the patients is essentially the same as that previously described for precordial counting.\(^1\) The anteroposterior diameter of the chest at precordial level is measured at the beginning of each study, and the heart silhouette is outlined at fluoroscopy. The TCS is then moved over the heart area, and the distance of the upper counter is adjusted to provide a 30-cm interspace between the ends of the two collimators. As a result, for a chest with an anteroposterior diameter of 20 cm, the two crystals are at the same distance from an ideal plane separating the anterior one third from the posterior two thirds of the chest, assumed to be the central plane for the heart. \(^{131}\text{I}\) as RIHSA (radioiodinated human serum albumin) and \(^{86}\text{RbCl}\) are successively injected to measure the intravascular and the intravascular + myocardial precordial radioactivity. The injections are made into the superior vena cava through a polyethylene tube having a total capacity of 0.25 ml, threaded into the median vein through a needle. From a reservoir syringe, 0.2 ml of solution of \(^{86}\text{RbCl}\) or \(^{131}\text{I}\) are transferred into the polyethylene tube, and its proximal end is clamped. Injections are made by flushing the tube with 0.5 ml of saline. This procedure has been found satisfactory for recording radiocardiographic curves.

In some cases, activity equal to that of the injectate was introduced into a 250-ml spheric container enclosed in a Perspex block that was equal in thickness to the anteroposterior diameter of the patient’s chest. The counting on the phantom was then carried out with the TCS set up as for counting over the patient (fig. 1).

Calculations

Coronary blood flow per 100 g of myocardium was calculated from MCK, as previously described.\(^1\) The successive steps of the calculations are as follows.

1. The amount of \(^{86}\text{Rb}\) extracted by the myocardium in the first 30 seconds after single injection is estimated by subtracting from the precordial counting rate between 30 and 90 seconds the contribution due to intravascular radioactivity. The latter is determined from the precordial counting rate between 30 and 90 seconds after injection of \(^{131}\text{I}\)HS, and the corresponding concentrations of \(^{86}\text{Rb}\) and \(^{131}\text{I}\)HS in arterial blood. The geometrical efficiency factors, required to make \(^{131}\text{I}\)HS measurements comparable with \(^{86}\text{Rb}\) measurements, are calculated for each case taking into account the anteroposterior diameter of the chest, as shown in the appendix.

The values thus obtained for myocardial \(^{86}\text{Rb}\) content equal the product of average myocardial concentration times the effective volume of the myocardium (volume of myocardium times average counting efficiency for it).

2. The area under the \(^{86}\text{Rb}\) radiocardiographic curve (RCG) is measured after extrapolation beyond apparent recirculation. This area equals the integral of the primary arterial concentration curve times the effective volume\(^4\) of the heart chambers including any other vessel contributing to the curve (volume of chambers times average counting efficiency for them).

3. Since the effective volumes of myocardium and the heart chambers differ very little from each other\(^1\) (see also appendix), the ratio of myocardial \(^{86}\text{Rb}\) content to area of \(^{86}\text{Rb}\)-RCG equals the ratio of myocardial \(^{86}\text{Rb}\) concentration to the area of primary arterial concentration curve.

4. Equating volume to mass units for the myocardium, the above ratio gives flow in milliliters per gram of myocardium. In fact, dimensionally,

\[
\text{Counts/g of myocardium} = \frac{\text{Counts/ml of blood} \times \text{Duration of curve}}{\text{ml of blood/g of myocardium/min}}
\]

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which multiplied by 100 gives flow in ml/100 g/min.

Coronary blood flow as a fraction of cardiac output (CBF_v) was obtained by dividing the external counting rate due to myocardial activity into the injectate activity measured on the phantom.

**Body versus Coronary Extraction**

A Goodale Lubin catheter was inserted into the coronary sinus, and a no. 7 Courand catheter into the right ventricle. The proximal ends of the two catheters and the indwelling brachial artery needle were connected to three syringes mounted on a slightly modified Harvard pump. Injection of the $^{86}$RbCl was made into the right branch of the pulmonary artery through a no. 5 Courand catheter to avoid contamination of the right ventricular blood with primary circulating radioactivity. The connecting tube between the arterial needle and the pump was led through a shielded NaI scintillation counter with a hole drilled in it, and the output of the counter was fed to a ratemeter and recorder. Sampling was started 5 seconds before injection and continued for 90 seconds afterward.

**Calculations.** The average radioactivity concentration in each syringe was equal to

$$\tilde{x} = \frac{X}{Ft} = \frac{\int_{t_0}^{t} x(t) \, dt}{Ft}$$

where $X$ and $\tilde{x}$ are respectively the total activity and the mean radioactive concentration in the syringe, $F$ is the rate of withdrawal and $t$ the duration of sampling.

The integral represents the area of the concentration curve from beginning to end of sampling. Multiplication of $\tilde{x}$ by $t$ yields this area.

In the record, the primary arterial concentration curve was completed by extrapolation beyond apparent recirculation; its area was then calculated and subtracted from the total area from beginning to end of sampling.

**Comparison of the Nitrous Oxide Method with MCK**

Coronary blood flow was measured by the nitrous oxide saturation method as modified for the coronary circulation. The coronary sinus was cannulated with a Goodale-Lubin catheter. MCK was measured with the usual technique immediately before and after the measurement of coronary blood flow with nitrous oxide.

**Studies Performed**

Sixty-three patients were studied: 43 were young subjects with normal cardiovascular systems; 13 had hypertensive heart disease (HHD) and seven had ischemic heart disease (IHD) without arterial hypertension. The diagnosis had been established on the basis of clinical and electrocardiographic data.

In all cases MCK was measured under basal conditions. In 12 cases (nine normal subjects and three with IHD), a second measurement was performed under the same conditions, from 10 to 20 min after the first one.

In 18 cases (11 normal subjects and seven with HHD), the injectate activity was measured as indicated above for the evaluation of fractional CBF, which was then calculated.

In 11 cases (eight normal subjects and three with IHD) $N_2O$ measurement of coronary blood flow was performed: in 10 cases between two MCK measurements; in one case, after a single MCK measurement. Finally, in two additional cases the average body extraction was compared with the myocardial extraction.

**Results**

**Coronary Blood Flow Values by the MCK Method**

Basal values for MCK averaged 80.3 ± 18.5 (SD) ml/min/100 g of myocardium in the normal group, 56.8 ± 7.0 (SD) ml/min/100 g of myocardium in the HHD group, 46.8 ± 4.9 (SD) ml/min/100 g of myocardium in the IHD group. The average values for both HHD and IHD groups differ significantly from the mean normal value ($P < 0.001$). The distribution of the results obtained is shown in the histograms of figure 2.

**Reproducibility of MCK Values**

In figure 3 MCK values obtained in two successive measurements performed in the same subject are plotted one against the other. The substantial agreement is evident. The mean difference between the two measurements averages 6.98% of their mean values.

**Body versus Myocardial Extraction of $^{86}$Rb**

The results of the two studies performed are shown in table 1. Average body extraction over the first 90 seconds after injection exceeded myocardial extraction of 6.0% in the average of the two cases. Assuming no loss of indicator in the pulmonary circulation, mixed venous recirculation was subtracted from arterial activity to calculate the integral.
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CARDIOVASCULAR NORMALS

HYPERTENSIVE HEART DISEASE

ISCHAEMIC HEART DISEASE

Figure 2
Distribution of values of coronary flow per 100 g of myocardium (Qm) as measured from MCK. Continuous line represents the Gaussian distribution for normal subjects calculated from observed mean value and standard deviation.

of the primary arterial circulation. When calculated in this way, recirculating activity during the first 90 seconds after injection was 34.5% of total arterial activity during the entire period in both cases.

This figure compares well with the value of 31% obtained in one case by direct measurement of the primary arterial circulation from the recorded curve, thus confirming the negligible loss of indicator in the pulmonary circulation within the time of observation.

Comparison with the N2O Saturation Method

Coronary blood flow values obtained with the N2O saturation method and those obtained with external counting immediately before and after are reported in table 2 and in figure 4. All the values but one are comprised within the lines of ±20% deviation from identity. The average values with the N2O and the

\[ \text{MCK} = \frac{m(\tau)}{A_1} \]  

where \( m(\tau) \) indicates the myocardial concen-

\[ \text{Qm} \]

\[ \text{ml/min/100 g} \]

\[ +15\% \]

\[ -15\% \]

\[ \text{IDENTITY} \]

\[ \text{ml/min/100 g} \]

\[ \text{Qm (2)} \]

Figure 3
Comparison of two successive measurements of coronary flow per 100 g of myocardium from MCK values.

\[ {\text{Rb}}^8 \text{ method were } 72.0 \pm 16.8 \text{ (SD) and } 68.6 \pm 16.1 \text{ (SD) ml/min/100 g of myocardium, respectively.} \]

CBF as Fraction of Cardiac Output

As shown in table 3 CBF was found to represent 5.91 ± 0.79% of the cardiac output in 11 normal subjects and 6.67 ± 1.29% in seven hypertensive subjects. The difference between the two groups did not reach statistical significance.

Discussion

Consideration of the Method

The basic assumption of the present method for the measurement of coronary blood flow is that the fraction of the injected indicator taken up by the myocardium early after injection equals the fraction of the cardiac output perfusing the myocardium.

The validity of this assumption in rats and dogs was shown by Sapirstein, and it was explained by the small difference between the average body and myocardial extraction of indicator early after injection.

The actual expression for MCK is:

\[ \text{MCK} = \frac{m(\tau)}{A_1} \]  

where \( m(\tau) \) indicates the myocardial concentra-

Comparison of two successive measurements of coronary flow per 100 g of myocardium from MCK values.
Table 1

Integrals of Arterial (A), Mixed Venous (\(\bar{V}\)) and Coronary Sinus (\(V_m\)) Concentrations from 0 to 90 Seconds after Injection of \(^{86}\)RbCl into the Pulmonary Artery (in Percentage of A)

<table>
<thead>
<tr>
<th>Case</th>
<th>A</th>
<th>(\bar{V})</th>
<th>(V_m)</th>
<th>(A_1)</th>
<th>(\Delta V)</th>
<th>(\sigma_{MCK}), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>278</td>
<td>100</td>
<td>34.5</td>
<td>35.9</td>
<td>65.5</td>
<td>-1.4</td>
<td>2.14</td>
</tr>
<tr>
<td>279</td>
<td>100</td>
<td>34.5</td>
<td>40.5</td>
<td>65.5</td>
<td>-6.0</td>
<td>9.16</td>
</tr>
<tr>
<td>Avg</td>
<td>100</td>
<td>34.5</td>
<td>38.2</td>
<td>65.5</td>
<td>-3.7</td>
<td>5.65</td>
</tr>
</tbody>
</table>

\(A_1\), Integral of primary arterial concentration curve = A - \(\bar{V}\), \(\Delta V = \bar{V} - V_m\)

\(\sigma_{MCK}\) = error in estimate of \(Q_m\) from \(MCK\) due to \(\Delta V \neq 0\)

Table 2

Comparison of MCK with Coronary Blood Flow Measured by \(N_2O\)

<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>MCK, ml/min/100 g</th>
<th>CBF ((N_2O)), ml/min/100 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>251</td>
<td>Resolved acute gastroenteritis</td>
<td>1 74.3</td>
<td>71.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 81.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>78.1</td>
<td></td>
</tr>
<tr>
<td>252</td>
<td>Cardiac neurosis</td>
<td>1 94.8</td>
<td>90.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 108.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>101.5</td>
<td></td>
</tr>
<tr>
<td>254</td>
<td>Rheumatoid arthritis</td>
<td>1 55.7</td>
<td>66.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 59.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>57.8</td>
<td></td>
</tr>
<tr>
<td>255</td>
<td>Cardiac neurosis</td>
<td>1 65.5</td>
<td>84.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 77.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>71.3</td>
<td></td>
</tr>
<tr>
<td>259</td>
<td>Psychoneurosis</td>
<td>1 79.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 80.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>79.8</td>
<td>91.7</td>
</tr>
<tr>
<td>260</td>
<td>Gastroduodenitis</td>
<td>1 66.8</td>
<td>71.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 64.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>65.8</td>
<td></td>
</tr>
<tr>
<td>261</td>
<td>Lumbar scoliosis</td>
<td>1 75.3</td>
<td>69.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 65.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>70.4</td>
<td></td>
</tr>
<tr>
<td>262</td>
<td>Salmonella infection</td>
<td>1 72.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 82.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>77.4</td>
<td>90.0</td>
</tr>
<tr>
<td>265</td>
<td>Ischemic heart disease</td>
<td>1 52.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 64.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>58.3</td>
<td>56.7</td>
</tr>
<tr>
<td>267</td>
<td>Ischemic heart disease</td>
<td>1 48.9</td>
<td>54.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 56.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>52.7</td>
<td></td>
</tr>
<tr>
<td>268</td>
<td>Ischemic heart disease</td>
<td>1 41.9</td>
<td>46.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>41.9</td>
<td></td>
</tr>
</tbody>
</table>
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the expression for coronary blood flow per unit mass of myocardium is:

\[ Q_m^\prime = \frac{m(\tau)}{A_1 + (\bar{V} - V_m)} \]  

(3)

where \( \bar{V} \) and \( V_m \) are the concentration integrals for the mixed venous and coronary sinus recirculation, respectively.\(^1\) From equations 2 and 3 it is evident that MCK equals \( Q_m \) provided \( (\bar{V} - V_m) = 0 \). It is easy to show that differences between \( \bar{V} \) and \( V_m \) will be reflected in erroneous estimates of \( Q_m \) from MCK in the following way:

\[ MCK = \Delta V / A_1 \]  

(4)

The average error in estimate of \( Q_m \) from this difference in the two cases examined amounts to \(-5.65\%\). To cause a 10\% error, the coronary integral would need to exceed the mixed venous integral of about 20\%. It seems unlikely, therefore, that this source of error may be of relevant importance.

The second set of assumptions deals with

![Figure 4](image)

Comparison of coronary blood flow (CBF) as measured from MCK (\(^{86}\)Rb) and the \( N_2O \) method.

Table 3

<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>MCK, ml/min/100 g</th>
<th>CBF(_r), % of cardiac output</th>
</tr>
</thead>
<tbody>
<tr>
<td>219</td>
<td>Cardiac neurosis</td>
<td>90.8</td>
<td>6.1</td>
</tr>
<tr>
<td>220</td>
<td>Psychoneurosis</td>
<td>69.0</td>
<td>5.6</td>
</tr>
<tr>
<td>221</td>
<td>Chickenpox</td>
<td>109.6</td>
<td>4.2</td>
</tr>
<tr>
<td>222</td>
<td>Resolving thrombophlebitis</td>
<td>87.5</td>
<td>6.3</td>
</tr>
<tr>
<td>223</td>
<td>Cervico-arthrosis</td>
<td>68.1</td>
<td>5.3</td>
</tr>
<tr>
<td>228</td>
<td>Irritable colon</td>
<td>105.1</td>
<td>6.0</td>
</tr>
<tr>
<td>229</td>
<td>Resolving bronchitis</td>
<td>109.4</td>
<td>5.4</td>
</tr>
<tr>
<td>230</td>
<td>Pleurisy</td>
<td>80.9</td>
<td>6.7</td>
</tr>
<tr>
<td>231</td>
<td>Psychoneurosis</td>
<td>65.9</td>
<td>6.4</td>
</tr>
<tr>
<td>232</td>
<td>Hysteria</td>
<td>56.5</td>
<td>6.1</td>
</tr>
<tr>
<td>235</td>
<td>Psychoneurosis</td>
<td>80.6</td>
<td>6.9</td>
</tr>
<tr>
<td></td>
<td>( \bar{m} )</td>
<td>83.9</td>
<td>5.91</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>( \pm 18.7 )</td>
<td>( \pm 0.79 )</td>
</tr>
<tr>
<td>224</td>
<td>Renal hypertension</td>
<td>48.2</td>
<td>5.3</td>
</tr>
<tr>
<td>225</td>
<td>Renal hypertension</td>
<td>70.0</td>
<td>7.8</td>
</tr>
<tr>
<td>226</td>
<td>Renal hypertension</td>
<td>50.3</td>
<td>4.8</td>
</tr>
<tr>
<td>227</td>
<td>Essential hypertension</td>
<td>58.1</td>
<td>6.0</td>
</tr>
<tr>
<td>233</td>
<td>Renal hypertension</td>
<td>54.1</td>
<td>7.3</td>
</tr>
<tr>
<td>236</td>
<td>Essential hypertension</td>
<td>61.8</td>
<td>7.9</td>
</tr>
<tr>
<td>237</td>
<td>Essential hypertension</td>
<td>57.6</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>( \bar{m} )</td>
<td>57.1</td>
<td>6.67</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>( \pm 7.6 )</td>
<td>( \pm 1.29 )</td>
</tr>
</tbody>
</table>

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1. 

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tration of the indicator at the time of measurement, and \( A_1 \) the integral of the primary arterial concentration curve. On the other hand,
the feasibility of using external counting to estimate the myocardial content of indicator. In the case of the measurement of MCK the relevant assumption is that the "effective volume" contributing counts from the heart cavities and vessels is the same as the "effective volume" contributing counts from the myocardium.\textsuperscript{4} It has been shown that the difference is contained within narrow limits even for relatively large volumes in case of precordial counting; the conditions are improved further with the TCS which has a much greater uniformity of counting efficiency.

In the case of fractional CBF the relevant assumption is that of the adequacy of simulating self-absorption and scattering of radiation within the chest of the patients by counting on Perspex phantoms. Model experiments reported in the appendix suggest that the external counting rate is essentially unaffected by variations in heart size and depth, at least within the range of interest.

These elements, derived from physical considerations and phantom studies, are presently the only ones in support of the latter assumption. However, the significance of the results obtained is an indirect supporting argument that will be examined in the next paragraph.

**Considerations of the Results**

CBF values per gram of myocardium in normal subjects agree well with previous estimates with the indirect Fick method\textsuperscript{6, 7, 8} and with our previous series with precordial detectors.\textsuperscript{4} The results obtained in the ischemic group agree with the expectancy on the basis of clinical and ECG findings. Data in the hypertensive group also show a significant reduction of CBF per unit heart mass. This latter finding is in agreement with postmortem perfusion studies in hypertrophied hearts,\textsuperscript{9} and with current knowledge concerning vascularization of hypertrophied myocardium. On the other hand, previous studies with N\textsubscript{2}O\textsuperscript{10, 11} have failed to demonstrate reduction of flow per gram of myocardium in hypertensive cases. As Gregg and Fisher pointed out, however, limitations inherent in the indirect Fick method as applied to CBF may account for the results in cardiac hypertrophy.\textsuperscript{12, 13}

The reproducibility of the measurements appears quite satisfactory in the series examined: it will be noted that the second estimates tend systematically to exceed slightly the first one. No satisfactory explanation is presently available for such tendency.

Comparisons with N\textsubscript{2}O values, measured during the same study, also seem to be highly satisfactory. The agreement was excellent over the entire range of values explored, from 40 to 110 ml/min/100 g myocardium.

Fractional CBF values may be compared only with similar estimates in rats and dogs by Sapirstein.\textsuperscript{2} CBF in man has been admitted to vary between 5 and 10% of the cardiac output,\textsuperscript{12} and this is in agreement with the results of some attempts to use the dilution principle to measure CBF.\textsuperscript{14}

The average values obtained in the groups examined are within this range, but this statement is obviously of limited value. At the moment, no elements are available to validate the significance of our estimates of fractional CBF, but it is nevertheless of some importance that the values be distributed within the range of expectancy.

It should be pointed out that CBF in absolute value and the mass of the heart could be derived from fractional CBF and MCK provided cardiac output is measured at the same time.

**Advantages and Disadvantages of the Method**

During the last few years a large number of new methods or variants have been proposed for the measurement of coronary blood flow. This probably reflects the inadequacy of currently available methods to meet the requirements for CBF measurement in man.

Precordial measures of myocardial uptake during intravenous infusion of \textsuperscript{86}Rb have been used by Love and Burch\textsuperscript{12} in the attempt to estimate coronary flow. Difficulties in determining the uptake of the heart alone, separated from surrounding organs, and the reduction of myocardial extraction with time\textsuperscript{14}

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have prevented development of this approach into a practical technique. Some of the technical difficulties may be overcome by infusing the positron-emitting $^{88}$Rb, in place of $^{86}$Rb as proposed by Bing and associates.$^{18}$ This latter method, however, yields a “coronary flow equivalent” which may be of clinical value, but, as pointed out by its authors, it does not represent a procedure for quantitative measurement of coronary flow.

Excluding the methods that demand direct injections in the coronary arteries or in the myocardium, which can be only of limited practical value, the indirect Fick method, with $\text{N}_2\text{O}$, inert radioactive gases or $^{131}$I-antipyrine, seems the best available approach. More recently, thermodilution seems to be a promising approach to the problem of directly measuring coronary sinus outflow.$^{17}$

An evaluation of the potential merits and disadvantages of the present method in comparison with indirect Fick and thermodilution may be attempted.

The main and immediately evident advantage of the present technic over the other two is the avoidance of coronary sinus catheterization. While this feature may enhance the practical value of the method, its limitation is inherent in the fact that any investigation of myocardial metabolism demands coronary sinus catheterization anyhow. However, insofar as changes in oxygen requirements of the heart are essentially met by changes in flow,$^{18-20}$ a CBF measurement may be of value per se.

The second unique feature of the present technique is that of measuring the average flow to the entire myocardial mass, independently of the venous drainage. Unperfused areas, which do not contribute to the Fick values since they do not extract the indicator, contribute to the MCK or CBF values by the present method, in which the indicator content of the entire heart is averaged, so that areas with no indicator actually contribute with their zero value to the obtained average.

The third, and probably most significant point, is that the flow value measured by MCK undoubtedly represents actual flow to true capillaries. The relevance of this feature is best appreciated if considered in the light of the demonstration of arteriovenous anastomotic circuits in the myocardium$^{21}$ recently confirmed to occur from the arterioles and meta-arterioles to the venules.$^{22}$ To our knowledge no estimates are presently available of the relative importance of flow shunting circuits in the coronary vascular bed, nor about their modifications in changing states. However, the occurrence of such circuits and the demonstration of nerve endings at the sphincteric structures of the anastomotic vessels$^{22}$ are suggestive of the potential importance of diversion of flow from true capillaries in the response of the coronary circulation to different stimuli.

Should this flow pattern be of some importance, most of the presently accepted conclusions concerning the physiology, pathophysiology, and pharmacology of the coronary circulation would require reinvestigation, on the basis of a method capable of assessing true capillary flow.

A further advantage of this method in comparison with Kety’s technique is its independence from prolonged steady state conditions: the fact that the entire measurement may be completed in 90 seconds is an obvious advantage in comparison with the indirect Fick method, which demands long equilibration periods. Repeatability at time intervals as short as 5 minutes is an important feature that stems from the previous considerations, although from this point of view the method can obviously not compete with thermodilution.

The main present drawback to the method, which also limits its repeatability in the same patient, stems from dosimetric considerations. The small percentage of $\gamma$-radiations emitted by $^{86}$Rb demands the use of relatively large radioactive doses, which limit the number of measurements that may be performed in the individual patient to a maximum of two. The use of $^{42}$K cuts down the patient dose by an important factor, but the shortness of its physical half-life makes $^{42}$K a somewhat impractical isotope to use.
Appendix

Geometrical efficiency factors required to make precordial measurements of $^{131}$I radioactivity from RIHSA comparable with $^{86}$Rb measurements were calculated by using a Perspex phantom.

The phantom was made up of Perspex slices of variable thickness (0.5 to 1 cm) that could be superimposed to simulate different chest diameters. Spheric containers of variable volumes (100 to 1000 ml) filled with radioactive solution can be included in the Perspex phantom in different positions.

The following experiments were performed counting with the TCS on the phantom:

**Effect of Source Volume**

The same amount of radioactivity was diluted in water-filled spheric containers of sizes ranging from 100 to 1000 ml, placed at the center of the phantom, the thickness of which along the TCS axis was 20 cm. When the results are expressed as percentage differences from the counting rate for a 100-ml volume, it is seen from figure 5 that deviations are always smaller than 5% for both $^{131}$I and $^{86}$Rb, and smaller than 2.5% up to 700 ml.

**Effect of Source Depth**

The radioactivity-filled spheric containers were counted in the same Perspex phantom, having been placed along the TCS axis but close to one of the surfaces of the phantom (0.5 to 1.5 cm of Perspex between the radioactive container and the phantom surface). When the results are expressed in percentage difference from the counting rates obtained for the same size container in central position, it is seen from figure 6 that the maximal deviation is about 5% for $^{131}$I, and about 5% for $^{86}$Rb, both occurring for the smallest volumes. For larger volumes, from 200 ml up, deviations are smaller than 5%.

**Relative Effect of Chest Thickness on $^{131}$I and $^{86}$Rb Counting**

Two 250-ml spheric containers, filled with $^{131}$I and $^{86}$Rb activity of known concentration, were counted in the Perspex block at thicknesses ranging from 17.4 to 22.0 cm, assumed to cover the expected range for anteroposterior chest diameters of adults. Counting was performed with 30-cm interspace between the collimators, as used for in vivo measurements, and with the center of the 250-ml container at the junction of the upper one third with

*Figure 6*

Change of TCS counting rate for maximal displacement along the TCS axis of spheric containers of increasing size, from the central position in the phantom. Differences are expressed as percentage of the counting rate from the same container in the central position. Closed circles, $^{131}$I; open circles, $^{86}$Rb.

*Figure 5*

Changes of TCS counting rate on Perspex phantom for the same amount of activity in spheric containers of increasing size, placed at the center of the phantom, on the counter axis. Changes are expressed as percentage of the counting rate for a 100 ml container. Closed circles, $^{131}$I; open circles, $^{86}$Rb.
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Figure 7

Geometrical efficiency factor \( a \), required to correct \(^{131}\)I external counting rates for difference in counting efficiency in comparison with \(^{86}\)Rb, counting as a function of the anteroposterior chest diameter, expressed in centimeters.

the lower two thirds of the Perspex block. Results were expressed as:

\[
\frac{^{86}\text{Rb(TCS)}}{^{86}\text{Rb(well)}} \times \frac{^{131}\text{I (well)}}{^{131}\text{I (TCS)}} = a
\]

in which TCS and well, respectively, indicated external counting on phantom and concentration measurement in well counters; \( a \) is the factor required to make precordial measurements with \(^{131}\)I comparable with \(^{86}\)Rb measurements. As represented in figure 7 the values of \( a \) show a progressive, although small increase for increasing phantom thickness, due to the progressively greater loss of \(^{131}\)I gammas in respect to the more energetic \(^{86}\)Rb gammas.

Geometrical factors for MCK calculation were derived from this graph in all cases on the basis of anteroposterior chest diameter; frequent controls were made of the constancy of the counting performances of the instruments used for in vivo and in vitro counting.

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L. DONATO, G. BARTOLOMEI, G. FEDERIGHI and G. TORREGGIANI

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