Measurement of Flow in Single Blood Vessels Including Cardiac Output by Local Thermodilution

By A. Fronek, M.D., and V. Ganz, M.D.

On the basis of local thermodilution a method for measuring blood flow in a single vessel was elaborated. The measurement was accomplished by a special catheter with an injection orifice and a thermistor. The accuracy of the method was studied both in model and in vivo experiments on dogs (in jugular vein, in carotid and pulmonary artery) and good correlation was found with direct methods.

Blood flow in single vessels can be measured by direct methods such as rotameter, drop-flow meter, Rein-thermostromuhr, Venturi principle, electromagnetic flow meter and bubble-flow meter. Such methods are usually characterized by great accuracy, but their applicability is considerably limited in man by the fact that the appropriate vessel must be made accessible. Blood flow in some regions was determined by methods applying Stewart-Hamilton's principle. On this background we attempted to elaborate a method for measuring blood flow in any single vessel.

**Methods**

**Principle**

Measurement in a single vessel is made possible by mixing an indicator with blood at the site of injection, and then detecting the resulting change in the immediate neighborhood of the site of mixing. The injecting orifice and detector were located on a specially prepared catheter. For technical reasons a thermal indicator was chosen, introduced into dilution techniques by Fegler. A thermistor was used for detecting temperature changes.

**Method of Injection**

A condition for correct measurement is homogeneous mixing of the indicator with blood throughout the cross-section of the vessel. This can be done by transforming laminar into turbulent flow, if the Reynolds number of the inject is increased above a critical value. In model experiments homogeneity of mixing was judged according to whether the same dilution curves were obtained for a constant position of the injecting orifice, but with the thermistor placed at different points of the cross-section of the tube. Three methods of injection were used to achieve reliable mixing. It was found that on injection from the tip of the catheter, correct mixing could not be achieved if the tip pointed against the wall of the tube, even when the Reynolds number of the indicator was 5000. On injecting from 4 orifices, placed radially in the wall of the catheter, the mixture was also inhomogeneous if the catheter was located close to the wall of the tube. When measuring in vivo, the possibility that injection might occur against the wall of a vessel must be taken into consideration. We therefore used a catheter with a curved tip, and with an injection orifice located in the concavity (fig. 1). With this arrangement, the indicator jet is oriented towards the longitudinal axis of the vessel, against the direction of the current, at an angle of 30° to 45°. In order to satisfy this condition, the oblique orifice in the wall of the catheter must have a certain minimum length (1.5 to 2 mm.).

**The Effect of Injection on Flow**

Due to the small distance of the thermistor from the injection orifice, part of the dilution curve is registered during the injection of the indicator. In order to calculate the flow correctly, it was necessary to know how the injection of the indicator influences flow below the site of injection, i.e., in the region of the thermistor. This question was studied both in vivo and in model experiments. The changes in flow during injection were studied with a rotameter or drop-flow meter connected with the appropriate vessel, the point of injection being upstream from the flowmeter. In this way we found that during injection the flow in arteries either decreases or does not change. The decrease in the flow increases with the linear velocity of flow and the kinetic energy of the indicator. These relations were veri-
fied in model experiments. If the kinetic energy of the injected liquid indicator was smaller than 13,000 Gm./cm.²/sec., there was no change in flow in the region of the thermistor, even for a linear velocity of 356 cm./sec, which in vivo does not enter into consideration. For correct calculation, therefore, an indicator kinetic energy greater than 13,000 Gm./cm.²/sec. must not be used.

In veins, however, flow in the region of the thermistor increases during injection. An increase in flow during injection in the model experiments was achieved by narrowing the tube above the site of injection. The increase in flow in veins is probably caused by injection against the "peripheral resistance," similarly as in the model arrangement.

Indicator

As an indicator 5 per cent glucose or physiological saline at a temperature of 18 to 22 C was injected. The rate of injection was chosen so that Reynolds number was at least 3,000, while in the arteries we had to keep the condition that the kinetic energy did not exceed 13,000 Gm./cm.²/sec. The corresponding data of indicator injection are given in table 1.

The volume of the injectate may be chosen according to the expected blood flow. For measuring blood flow in the range of tens of ml. we used up to 1 ml., in the range of hundreds up to 3 ml. and for flows in the range of liters up to 5 ml. of injectate. The dead space of the catheter must be subtracted from the injected volume. Since part of the catheter is external to the body and the contained liquid cools off, the catheter must be filled immediately before injection with uncooled blood drawn in with a second syringe. When passing through the catheter the indicator is slightly heated. The heating depends on the length of the catheter, the length of the part introduced into the vessel, the amount of indicator and its rate of flow through the catheter, and the difference in temperature between the blood and the indicator. In extreme cases the heating may be as much as 1.5 to 2.0 C, which for a temperature difference between blood and indicator of 15 to 20 C would mean an error of 10 to 13 per cent. The degree of heating of the indicator, however, can easily be determined. After completing measurements, that part of the catheter which was in the vessel is immersed in water at the temperature of the blood during measurement. After drawing in, the same amount of indicator at the same temperature as during measurement is injected into the catheter. The liquid leaving the catheter is caught in a small bowl and its temperature measured.

Example of calculation of indicator temperature after passage through catheter (tj) :

Injected, 7 ml. of indicator at temperature 2.1 C. Dead space of catheter 2 ml. Blood temperature 37 C. Temperature of liquid caught in bowl 26 C.

\[ t_j = \frac{26 - 2.1}{5 \times 7} = \text{21.6 C.} \]

Detector and Its Location

To detect the temperature changes we used a thermistor, with a temperature coefficient of 3 to 3.5 per cent. The thermistor is carefully insulated with a layer of PVC or silicone. The insulation of the thermistor is tested in the following manner: One terminal of the thermistor is connected through a microammeter to a source of d-c voltage (of the order of 5 V), while the second pole of the source is immersed in physiological saline. If a deflection appears on immersing the thermistor into this solution, the insulation must be regarded as faulty; it can easily be repaired with a thin film of PVC dissolved in cyclohexanone. Quick drying is achieved by heating to about 70 C for a few minutes. The insulating layer must be thin so that the time constant of the thermistor is as short as possible. The time constant does not influence the accuracy of measurement (calculation is carried out on the basis of the area described), but with a short time constant the curves are more ideal, and the demands made on the

<table>
<thead>
<tr>
<th>Diameter of injection orifice in mm.</th>
<th>Injection rate in ml./sec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8</td>
<td>6.5—4.0</td>
</tr>
<tr>
<td>0.7</td>
<td>5.0—3.0</td>
</tr>
<tr>
<td>0.6</td>
<td>3.5—2.5</td>
</tr>
<tr>
<td>0.5</td>
<td>2.5—1.5</td>
</tr>
<tr>
<td>0.4</td>
<td>1.5—1.0</td>
</tr>
<tr>
<td>0.3</td>
<td>1.0—0.6</td>
</tr>
</tbody>
</table>
sensitivity of the recording equipment smaller. The
time constant of thermistors used in our experi-
ments was 0.2 to 0.5". A small working current
(of the order of 1 mA) must be used, since at
higher currents the thermistor is overheated. In
this state the resistance of the thermistor depends
not only on the temperature of the medium, but
also on the velocity of the flowing blood. The re-
stance of the thermistor was measured with a
bridge circuit and changes were recorded. The
non-linearity of the calibrating curve of the ther-
miator was compensated by a logarithmic compen-
sation. In order that the flow could also be mea-
sured in shorter vessels, the thermistor was located
within 5 to 10 mm. of the injection orifice. To
prevent close contact between the thermistor and
the wall of the vessel, which might influence the
accuracy of measurements, the thermistor is also
mounted in the concavity of the catheter. If the
catheter is introduced in the direction of the stream,
the thermistor must be located distally to the in-
jection orifice (downstream catheter—fig. 1 A); when introducing the catheter against the direction
of the blood stream in a vessel the flow in which
is to be measured, the thermistor must be located
proximally to the injection orifice (upstream

catheter—fig. 1 B). As stated above, the terminal
part of the catheter should be bent. This can be
done by applying a layer of PVC to the con-
cavity of the bend.

Derivation of Formulae for Calculating Flow

Arterial

If the indicator is injected into the artery
against the stream with a kinetic energy of 13,000
Gm./cm.2/sec or less, flow below the site of
injection does not change. This means that in the
region of mixing the indicator replaces an exactly
corresponding amount of blood.

During homogeneous mixing, blood of initial
temperature t_b is cooled, and the indicator of tem-
perature t_i is warmed to an average resulting tem-
perature t. The blood taking part in the mixing
loses the same number of calories as are gained by
the indicator. Therefore

\[
F = \frac{m \cdot (t_b - t_i) \cdot S_b \cdot C_b}{(t_b - t_i) \cdot S_i \cdot C_i}
\]

(Caloric loss of blood) (Caloric gain of indicator)

F = flow in ml./l min., T = time in seconds be-
tween beginning and end of dilution curve, S_b, S_i =
specific heat of blood and indicator respectively
(cal/g), C_b, C_i = specific gravity of blood and
indicator respectively (g/cm.3), m = amount of
indicator in ml.

\[
t_b - t_i \text{ can be substituted by } t_b - t_i - (t_b - t)
\]

\[
t_b - t_i \text{ can be substituted by } \frac{A}{T_r} \cdot f
\]

\[
A = \text{area below dilution curve in mm.}^2, r = \text{speed of registration paper in mm./sec, } f = \text{tem-
perature change in } °C \text{ corresponding to } 1 \text{ mm. of}
curve amplitude.
\]

On substitution, the final formula for calculat-
ing the flow in arteries is

\[
F = \frac{m \cdot 60 \cdot r (t_b - t_i) \cdot S_i \cdot C_i}{A \cdot f \cdot S_b \cdot C_b}
\]

\[
F = \frac{(m-x) \cdot 60 \cdot r \cdot (t_b - t_i) \cdot S_i \cdot C_i}{A_2 \cdot f \cdot S_b \cdot C_b}
\]

\[
F = \frac{m-x}{A_1 \cdot f \cdot S_b \cdot C_b}
\]

\[
F = \frac{m-x}{A_2 \cdot f \cdot S_b \cdot C_b}
\]

On the basis of the caloric interchange between
blood and indicator, it is also possible to write
for the time T

\[
F = \frac{m-x}{A_1 \cdot f \cdot S_b \cdot C_b}
\]

After substitution

\[
F = \frac{m-x}{A_1 \cdot f \cdot S_b \cdot C_b}
\]

\[
F = \frac{m-x}{A_2 \cdot f \cdot S_b \cdot C_b}
\]

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F = \frac{m-x}{A_1 \cdot f \cdot S_b \cdot C_b}
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\]

\[
F = \frac{m-x}{A_2 \cdot f \cdot S_b \cdot C_b}
\]
Calculation of flow in an artery:

\[
f = \frac{1.5}{10} = 0.15 \text{ C/mm.};
\]

\[
r = 10 \text{ mm./sec.; } t_1 = 22 \text{ C};
\]

\[
m = 5 \text{ ml.; hematocrit : 40%}
\]

\[
F = \frac{m \cdot 60 \cdot r \cdot (t_1 - t_2) \cdot S_b \cdot C_i}{A \cdot f \cdot S_b \cdot C_b} = \frac{5 \cdot 60 \cdot 10 \cdot (37 - 22) \cdot 0.935 \cdot 1.018}{1000 \cdot 0.15 \cdot 0.87 \cdot 1.058} = 320 \text{ ml./min.}
\]

Comparison of L/D and rotameter values in model experiments.

After solving equations I and II, the final formula for calculating flow in veins is:

\[
F = \frac{m \cdot 60 \cdot r \cdot S_b \cdot C_i}{A \cdot f \cdot S_b \cdot C_b} = \frac{A_1 \cdot r \cdot r \cdot A_1 \cdot f}{(t_1 - t_2) + \frac{A_1 \cdot r \cdot r \cdot A_1 \cdot f}{t_1 - t_2}}
\]

The validity of the equations for blood flow in arteries and veins was confirmed on a corresponding arrangement in model experiments.

Procedure During Measurement

The measuring catheter (upstream or downstream) is introduced into the vessel, the flow of which is to be measured. The initial temperature of the blood \( t_1 \) is found by reading the resistance of the thermistor on the bridge. This value is simultaneously recorded, and eventual changes in the initial temperature of the blood up to the moment of injecting the indicator can then be read from the record. The catheter is filled with uncooled blood by drawing in with a syringe and the indicator is injected with a second syringe. The dilution curve is recorded and the resistance of thermistor is calibrated by adding an external resistance. After measurement is completed the degree of heating of the indicator during passage through the catheter is found.

Constants Needed for Calculation

5 per cent glucose: spec. heat 0.965 cal./Gm., spec. gravity 1.018 Gm./cm.\(^3\). The specific heat and specific gravity of the blood depend on the hematocrit. The values of the specific heat of the blood, calculated according to Mendlowitz's formula, are given for hematocrit values of 30 to 60 per cent in table 2. The same table gives the values for the specific gravity of the blood, calculated on the assumption that in human blood and dog's blood the specific gravity of the plasma is 1.026 and the specific gravity of the erythrocytes 1.108.

Results

Model Experiments

The model measurements were carried out to verify the accuracy of the method. Water or citrated beef blood at a temperature of 37 to 40 C flowed from a reservoir under a hydrostatic gradient in glass and rubber tubes. The magnitude of the flow was regulated by a screw clamp and read off on a rotameter, calibrated with a reproducibility of ±1 per cent. Measurements were carried out in tubes of different diameter 5, 10, 15.6, and 24.4 mm., placed during measurement in the reservoir of warm liquid. As indicator water was injected; whenever measurements were made with beef blood, 5 per cent glucose or physiological saline solution was used.

Figure 4 gives a comparison of the values

<table>
<thead>
<tr>
<th>Hematocrit</th>
<th>Specific heat of blood cal./Gm.</th>
<th>Spec. gravity of blood Gm./cm.³</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>0.89</td>
<td>1.049</td>
</tr>
<tr>
<td>35</td>
<td>0.88</td>
<td>1.053</td>
</tr>
<tr>
<td>40</td>
<td>0.87</td>
<td>1.058</td>
</tr>
<tr>
<td>45</td>
<td>0.865</td>
<td>1.061</td>
</tr>
<tr>
<td>50</td>
<td>0.86</td>
<td>1.064</td>
</tr>
<tr>
<td>55</td>
<td>0.85</td>
<td>1.068</td>
</tr>
<tr>
<td>60</td>
<td>0.84</td>
<td>1.072</td>
</tr>
</tbody>
</table>
obtained by the local thermodilution (LTD) method and those read off on the rotameter. A statistical analysis of 111 comparative measurements did not show a systematic deviation of the LTD values from the actual values of the flow either as a whole (Δ per cent = 0.189 is not significant, t<1), or as a function of the diameter of the tube in which measurement was carried out. The standard deviation of both methods was ±3.14 per cent.

**Measurement of Blood Flow in Dogs**

**Measurement in Carotid Artery**

The experiments were carried out on dogs. Both the carotid artery and the left jugular vein were dissected to a length of 5 to 6 cm. under chloralose anesthesia. A Y-shaped cannula was introduced into the right carotid artery. An upstream catheter was introduced into the artery through one arm of the cannula and the other arm was connected to the rotameter. The blood passing through the rotameter returned to the left carotid artery or to the jugular vein (in order to achieve higher flows). Coagulation of blood was prevented with heparin. After each measurement, calibration of the rotameter value was carried out at least twice with a reproducibility of about ±5 per cent.

 Altogether 70 comparative measurements in a flow range of 21.5 to 538 ml./min. were carried out on 5 dogs. Figure 5 gives a comparison of the values obtained by the LTD method and those read from the rotameter at the moment of injecting the indicator. According to statistical analysis the 2 methods did not differ systematically (Δ per cent = +0.071 per cent, not significant, t<1). The standard deviation of both methods was ±4.61 per cent with a maximum deviation of +10.95 per cent and −11.1 per cent.

**Figure 5**

Comparison of LTD and rotameter values in the carotid artery.

**Figure 6**

Comparison of LTD and control method values in the jugular vein.

Altogether 108 comparative measurements were carried out for a range of flows from 9.6 to 204 ml./min. (fig. 6). The values calculated by the LTD method did not deviate systematically from those found rotometrically (Δ per cent = +0.096 per cent, not significant, t<1). The standard deviation of...
Comparison of Fick and LTD values.

Both methods was ±5.23 per cent, the maximum deviations being +11.85 per cent and -12.2 per cent.

Measurement in Pulmonary Artery

On 7 dogs under chloralose narcosis 86 comparative measurements were carried out. Fick method: Pure oxygen was led through a tracheal cannula and consumption was determined by a Roth-Benedict spirometer. A deflection of the spirometer pen by 1 mm. represented a consumption of 20.4 ml. of oxygen. To test for leaks, at the end of each experiment the apparatus was run for 10 min. with the dead dog in the circuit. Heparin (10 mg./Kg.) was used as anticoagulant. Mixed venous blood samples were drawn with a catheter from the root of the pulmonary artery for 1 min. and arterial blood from the femoral artery. Oxygen saturation was determined on a hemoreflectometer according to Brinkman and Zijlstra. The hemoglobin was determined photoelectrically for each sample of arterial blood.

LTD method: A downstream catheter was introduced from the jugular vein under X-ray and blood pressure control into the root of the pulmonary artery. The following procedure proved suitable for preventing the shifting of the catheter into a branch of the pulmonary artery as a result of ventricular contraction: on introducing the catheter the position at which a change from ventricular to arterial blood pressure occurs is determined. The catheter is then pushed further into the branch and again drawn out so that the tip of the catheter is about 1 cm. distally from the position ascertained. With this procedure the loop of the catheter in the right ventricle is much smaller, and the probability of a shift of the catheter into the branch is minimized. However, occasional control of the position of the catheter is recommended. As indicator, 3 ml. of 5 per cent glucose at room temperature was injected.

Blood could not be drawn simultaneously with the recording of the dilution curves as the indicator was injected through the same catheter into the pulmonary artery. The spirometer being constantly attached to the circuit, we measured cardiac output by both methods at 15 min. intervals. Cardiac output was decreased by repeated removal of blood in amounts of 30 to 300 ml.

Calculation of the flow in the pulmonary artery from the thermodilution curves obtained was carried out according to the formula valid for arteries.

Since the flow in the pulmonary artery exhibits rapid periodic fluctuations, we regularly made 3 to 4 LTD measurements a minute or 5 to 8 measurements in 2 min. The average of the values obtained in this way was compared with the value calculated according to the Fick method, which represents the average flow over a few minutes.

The fluctuation of the different LTD values about the average was ±6.7 per cent. Figure 7 gives a comparison of the values of cardiac output determined by both methods.*

*The table representing these data can be sent on request to the authors.
Figure 9
Changes of arterial blood pressure and coronary sinus flow, recorded by LTD method, after 0.1 mg adrenaline.

ard deviation of the 2 methods was ±9.30 per cent with greatest deviation +23.0 per cent and —22.4 per cent. There was no systematic difference between the two methods (Δ per cent = +0.49, insignificant, t<1). Figure 8 represents the percentage deviation of the thermodilution values from the average value obtained from the two methods.

Discussion
The principle of local dilution and local detection, which forms the basis of this method for measuring blood flow in a single vessel, required the solution of 2 main problems: 1) mixing at the site of injection, and 2) influence of indicator-injection on flow.

Mixing
When measuring cardiac output by the classical indicator-dilution method, mixing is not a particular problem. The indicator is thoroughly mixed with the blood in the cardiac chambers and in the pulmonary bed. Despite some theoretical objections, the mixing is obviously sufficient since the cardiac output can be measured with satisfactory accuracy. When measuring blood flow in a single vessel, however, homogeneous mixing must take place immediately at the site of injection. A condition of this is turbulent flow. However, calculations and experiments have shown that there is probably turbulent flow only in some sections of the vascular bed, e.g., in the root of the aorta. The linear velocity of the blood stream in vessels therefore had to be greatly increased in order to exceed the critical Reynolds number at which laminar flow is transformed into turbulent flow. With injection of the indicator into the blood stream, however, turbulence can also be obtained by increasing the Reynolds number of the indicator above the critical limit (about 1000). Under the present condition, the Reynolds number of the indicator was 3,000 to 5,000; moreover, injecting the indicator against the blood stream is a further factor facilitating mixing. For reliable mixing throughout the cross-section, however, particularly in wider vessels, suitable spatial orientation of the indicator jet also had to be ensured, i.e., the direction in relation to the axis of the vessel. This was done by bending the terminal part of the catheter, as described above.

The Effect of Injection of Indicator on Blood Flow
Because of the proximity of the thermistor and injection orifice, part of the dilution curve is recorded while the indicator is still being injected. It was necessary to investigate how, and under what conditions, blood flow in arteries and veins changes as a result of injecting the indicator. The data enabled us to derive relations for calculating flow both in arteries and in veins. As a result of these a maximum permissible kinetic energy of injection into arteries was determined. Atten-
tion must also be paid to the changes in blood flow, arising when using modifications of the classical dilution principle with constant injection of the indicator, where injection and detection occur simultaneously.

This method enables flow to be measured in any part of the vascular bed into which a catheter can be introduced under more physiological conditions than has been possible up to now. When measuring in small vessels, of course, a catheter of an appropriate size must be used so that its presence should not affect the flow in the vessel to any great extent. Measurement of blood flow can be repeated several times a minute, and one can thus study rapid changes in flow (fig. 9).

Evaluation of the dilution curves is facilitated by the fact that no ascertainable recirculation of the indicator occurs even when injecting into the pulmonary artery. This fact can be explained, apart from the considerable dilution of the indicator, by its escape from the vascular bed and by heat conduction from the vessels and their surroundings on passage of the indicator into further sections of the vascular bed.

Summary

A method was elaborated for measuring blood flow in single blood vessels on the basis of local thermodilution. Measurements were carried out with a specially prepared catheter with an injection orifice and a thermistor for detecting temperature changes.

The method was elaborated in model experiments (s.d. ± 3.14 per cent) and verified by comparative measurements in the carotid artery (s.d. ± 4.61 per cent), jugular vein (s.d. ± 5.23 per cent) and pulmonary artery (s.d. ± 9.30 per cent). The method permits flow to be measured in any vessel into which a catheter can be introduced, and enables rapid changes in flow to be studied.

Summario in Interlingua

Esseva elaborate un metodo pro le mesuracio del fluxo de sanguine in vasos individual super le base de thermodilution local. Le mesurationes esseva efectuate per medio de un specialmente preparate catheter con un orificio de injection e un thermistor pro le detection de alteraciones de temperatura. Le metodo esseva elaborate in experimentos con modellos (deviation standard ±3.14 pro cento) e verificata in mesuraciones comparative in canes in le arteria carotidic (deviation standard ±4.61 pro cento), le vea jugular (deviation standard ±5.23 pro cento), e le arteria pulmonar (deviation standard ±9.30 pro cento). Le metodo permetto le mesuracio del fluxo in omne vaso in que un catheter pote esser introducito. Ilo rende possibile le studio de alteraciones rapide del fluxo.

References

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