Thermal-Dilution Technics

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All thermal methods for the study of the circulation depend upon the induction of a change in the heat content of the blood stream. As a result of the change, a particular time-dependent spatial distribution of temperature is developed in the blood according to the manner in which the change is brought about and as a function of the prevailing pattern of blood flow. In a general sense, any thermal method could be considered to involve thermal dilation, but, in keeping with the usual meaning of "indicator dilution," the term "thermal dilation" will be restricted to refer to those technics in which, following the artificial induction of a known change in the blood heat content at some point in the circulation, the resulting temperature change is followed at such a distance downstream that an even distribution of heat is presumed to have been developed over the whole vascular cross section.

The induced change in heat content in a thermal-dilution technic may be either positive or negative, that is, heat is either added to or abstracted from the blood stream. One may speak, instead, of positive or negative heat addition in accordance with whether an increase or decrease in temperature is induced, but it is perhaps simpler and just as acceptable to refer to the addition of heat or cold.

The change in the heat content of the blood may be achieved in several ways, for example by generation of heat within the blood itself (as is ideally the case in the diathermy-thermostromuhr of Rein), by conduction of heat across a vessel wall, by an intravascular heating or cooling device, or by the injection into the blood stream of a mass miscible with the blood and at a different temperature. Thermal dilation using this last method of changing blood heat content most closely resembles other common indicator-dilution methods from a technical point of view. It was introduced as a method for the measurement of volumetric blood-flow rate by Fegler in 1953. He called his method "thermodilution," and as the most important thermal-dilution method in use today it might well continue to be specifically identified by the name he gave it. It is to thermodilution as here defined that attention will be given.

Fegler found that following the intravenous injection of cool blood or Ringer's solution he could record temperature-time curves by means of thermocouples placed in either the pulmonary artery or the aorta and that these thermodilution curves bore a close resemblance to dye-dilution curves. He then attempted to measure the flow of water through a model circulation by thermodilution with such success when the model was contained within an air jacket that he was encouraged to try the method for the measurement of cardiac output since the pulmonary circulation might be expected to possess similar thermal insulation. He obtained remarkably close agreement between thermodilution and simultaneous dye-dilution and direct Fick measurements of cardiac output in a small series of experiments on dogs.

Despite these promising comparisons, thermodilution did not meet with ready acceptance as a reliable method for the estimation of cardiac output. Criticism came early and was based on the idea that heat exchange must occur between the blood and the heart and other adjacent tissues, thereby giving rise to misleading distortion of the dilution curve. It was also thought that the occasional general drifts in blood temperature which appeared in some of Fegler's records and upon which thermodilution curves were superimposed implied the existence of conditions likely to reduce the accuracy of the method. Subsequently Fegler re-examined thermodilution and extended its scope to include the measurement of volume rate of flow through...
single blood vessels. This second application has come to be called local thermodilution. Gradually others have studied and applied the thermodilution principle, and considerably greater confidence is now being shown in its reliability.

Calculation of Flow Rate

In principle, thermodilution is identical with other indicator-dilution methods for the measurement of blood flow. It is performed in the following way: A charge of cold liquid is injected into the bloodstream in such a way as to produce intimate commixture following which the time course of temperature change is recorded at a suitable point downstream. From this temperature-time curve and knowledge of the magnitude of the change in heat content of the blood produced by the injectate, the volume rate of flow can be calculated in a manner analogous to that used for dye and other indicator-dilution methods. In thermodilution it is heat or cold that is the indicator, the injectate being merely the vehicle for its introduction into the bloodstream. It is assumed that, as in other indicator-dilution technics for volumetric estimations of flow, there is no, or at least negligible, loss of indicator between the point of injection and the point of detection, that is, the point of temperature measurement.

Thermodilution is the well-known calorimetric "method of mixtures" applied to the dynamic situation existing in the circulation instead of to the usual static one. In the method of mixtures, two masses at different temperatures are intimately mixed together and the resulting equilibrium temperature is measured. Assuming that there is no change in the total heat content of the system, the heat lost by one mass equals the heat gained by the other. Thus

\[ m_1 \Delta T_1 = m_2 \Delta T_2 \]  

where \( \Delta T \) signifies the change in temperature of the appropriate mass. For the continuous injection method of thermodilution this would become

\[ M_s \Delta T = M_r \Delta T_i \]

or

\[ M_s \Delta T = M_i \Delta T_i \]

where \( M \) is the mass flow rate, \( s \) and \( i \) stand for blood and injectate respectively and \( T \) is the steady-state temperature of the mixture.

The heat-balance equation for the case of a single injection is

\[ M \Delta T = M_i \Delta T_i \]

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the thermodilution method may perhaps be seen to resemble other indicator-dilution methods more closely. If the temperature-time function is denoted by $\Delta T_b(t)$, then following the general treatment given by Meier and Zierler and considering $\Delta T_b(t)$ to be proportional to the frequency distribution of transit times for labeled particles, there can be written

$$m_1 s_1 (T_b - T_1) = \int_0^\infty \Delta T_b(t) M_b s_b dt$$  \hspace{1cm} (6)

or in volumetric terms

$$V_1 \rho_1 s_1 (T_b - T_1) = \int_0^\infty \Delta T_b(t) Q_b \rho_b s_b dt$$  \hspace{1cm} (7)

where $Q_b$ is the volume rate of blood flow, $V_1$ the volume of the injectate, $\rho$ signifies density, and the other symbols are as before. Assuming that $Q_b$ is constant (as it must be for the success of any indicator-dilution method) and also that $\rho_b$ and $s_b$ are constant, equation (7) can be written

$$Q_b = \frac{V_1 \rho_1 s_1 (T_b - T_1)}{\rho_b s_b \int_0^\infty \Delta T_b(t) dt}$$  \hspace{1cm} (8)

In practice, $T_1$ may not be constant throughout injection and so it is necessary to take a mean value for it, $\bar{T}_1$. Writing $\theta = T_b - \bar{T}_1$, and $A/rf = \int_0^\infty \Delta T_b(t) dt$, where $A$ is the area of the thermodilution curve and $r$ and $f$ are the recording-paper speed and temperature-calibration factor respectively, then

$$Q_b = \frac{V_1 \rho_1 s_1 r f \theta}{\rho_b s_b A}$$  \hspace{1cm} (9)

(If $A$ is measured, say in mm.$^2$, $r$ will be in mm./sec. and $f$ in mm./$^\circ$C).

In reality, however, $Q_b$, $\rho_b$ and $s_b$ refer to the mixture of blood and injectate. While $Q_b$ may be virtually constant, $\rho_b$ and $s_b$ will vary to some extent throughout the course of the dilution curve according to the volume of the injectate and the values of $\rho_1$ and $s_1$. As will be seen later, the time course of change of $\rho_b$ and $s_b$ will be different from that of $\Delta T_b(t)$, for, at least in the case of cardiac-output measurements in which the injectate traverses the pulmonary vascular bed, the temperature-time curve has a longer and different course than have nondiffusible indicator-dilution curves. While the errors introduced by variations in density and specific heat are generally likely to be slight, they will be for injectates such as saline in the direction that will result in an overestimation of flow rate.

In the special case that $\rho_b = \rho_1$ and $s_b = s_1$, not only will these errors be avoided but also it will be unnecessary to know the values of $\rho$ and $s$. The use of an animal's own blood as the injectate, drawn shortly before injection to minimize the effects of changing hematocrit on specific heat, would fulfill these requirements, would simplify the procedure and, in addition, would create no viscosity changes from which might result variations in blood flow rate.

It is generally assumed in indicator-dilution studies that the process of injection does not affect the blood flow being measured and in effect this is probably the case in estimations of cardiac output wherein the volume of the injectate is comparatively small. It is to be expected, however, that this assumption will not be true as far as local flow conditions are concerned. Fronk and Ganz have investigated the degree of disturbance associated with the kinetic energy of the injectate. In arteries no effect is found if the kinetic energy is less than 13,000 gin. cm.$^2$ sec.$^{-2}$, while in veins the kinetic energy required to produce satisfactory mixing of the injectate and the blood is sufficient to accelerate the flow during the period of injection to a degree that could equal as a maximum the volume rate of injection. In their local-thermodilution studies in which the points of injection and temperature measurement are only a few millimeters apart, they have found it necessary to make an allowance for this change in flow in veins during injection because the appearance time is less than that for injection. This allowance is made by dividing the dilution curve into two parts: the earlier is contemporaneous with injection and hence with accelerated flow, while during the remainder the flow rate is said to have returned to the preinjection level. By solution of a pair of
simultaneous heat-balance equations for the two parts of the curve, which eliminated the unknown fraction of the injectate that increased blood flow during injection, they derived a single equation for blood flow. In arteries they found that the volume injected displaced an equal volume of blood so that the flow rate of the mixture was identical to that which existed beforehand. The simpler formula derived for this situation is essentially that used for estimation of cardiac output, equation (9). Although Pegler employed a local-thermodilution technic in veins he made no allowance for the effects of injection, but due to technical differences this was probably entirely justifiable.

Heat Exchange

The assumption that there is no, or at least negligible, loss of indicator from the bloodstream between the sites of injection and detection if these are widely spaced appears at first sight most unlikely to be fulfilled. While there are places in which it most certainly would not be fulfilled, for example peripheral vascular beds, the degree of success attained in thermodilution measurements suggests that the assumption is fulfilled to a very great degree. The nature of heat exchange or heat transfer is so fundamental to the thermodilution method that a brief consideration of the conditions which control it is pertinent.

When a temperature difference exists between two points, heat flows down the temperature gradient. The rate of heat flow depends upon the area available for heat transfer and the thermal conductivities and thicknesses of the materials through which it takes place. The thermal conductivity of a tissue depends to a considerable degree on the blood flow through it, thermal conductivity increasing with blood flow. While the greatest surface per unit length of vessel is found in the largest vessels, the ratio of surface area to volume (and so to heat content) increases with diminishing diameter. Hence the smaller a vessel is in diameter, the more rapidly can it exchange heat per unit volume of blood contained. In summary, therefore, it may be said that for a given temperature difference across a vessel wall, the fractional rate of change of heat content will be least in large-diameter, thick-walled vessels in poorly vascularized tissues and greatest in thin-walled vessels of small diameter in highly vascularized surroundings, that is, in capillary beds.

A more complicated situation arises when a transient change in temperature occurs at some point within a vessel due to the passage of a cool volume of blood which may be regarded as a travelling temperature wave. As the temperature wave approaches, heat flows into the vessel and the wall is cooled; as the wave recedes and the blood temperature rises again, thus exceeding the wall temperature, the heat flow is reversed and the wall is rewarmed. Whether the inward and outward heat flows are the same depends on how quickly the cold wave passes the point under consideration and on the thermal diffusivity of the wall and its surroundings, that is, on their thermal conductivities, densities and specific heats. Heat exchange may be thought to take place between the blood and a surrounding volume of tissue, and the magnitude of the exchange depends on the geometry of the situation as already adumbrated, on the physical properties of the tissues, and on the rate of flow of blood. The faster the blood flow, and so the more quickly the cold wave passes a particular region, the less the opportunity for irreversible heat exchange to occur there. Heat exchange with the surroundings will result in a distortion of the temperature wave taking the form of a diminution in the height of the peak and a general prolongation of the wave when the heat exchange is reversible, and in a reduction in the area of the temperature-time curve in the case of irreversibility. In the limiting condition of no blood flow, the heat flow will be, of course, in the one direction only, and eventually temperature equilibrium will be established between the blood and its surroundings.

From the foregoing it is possible to gauge where the greatest heat exchange will take place and where the thermodilution curve will
undergo most marked alteration in shape and area. In the large-bore, thick-walled aorta where blood velocities are high, the least heat exchange may be expected. Greater exchange rates will occur in progressively smaller arteries, in the thin-walled veins with their slower flow rates and, greatest of all, in capillary beds. The pulmonary capillaries, however, are in a special situation in so far as they are enclosed by the alveolar air which appears to be very largely protected from temperature fluctuations and entirely so from those in humidity even under the least favorable atmospheric conditions. It is to be expected that with the vast area available for heat exchange, the thinness of the alveolar walls and the low thermal capacity of air, temperature equilibration will occur between the pulmonary capillary blood, the alveolar walls and the alveolar air. Even so, the quantity of heat exchanged by the alveolar air will be negligibly small. This will not be the case, however, for the exchange between the blood and the alveolar walls. Chinard and Enns found that in its passage through the pulmonary vascular bed $D_2O$ exchanged with some volume (presumably that of the alveolar tissue) at a rate approaching half the cardiac output. On account of the high diffusibility of heat, a similar or greater volume may be expected to be available for intrapulmonary heat exchange. The existence of this large volume and the associated heat exchange will result in the prolongation of the thermodilution temperature wave, and it is in the lungs that the greatest distortion of the dilution curve is likely to occur. A second result of this heat exchange is that the thermodilution method will be unsuitable for measuring central blood volume; but it is possible that in conjunction with a reliable measurement of this volume by an independent method some idea of the mass of the lung tissue may be got if its specific heat can be measured or otherwise estimated.

It might be thought that cooling of the blood would occur in the lungs but there is little evidence in support of the idea. Small differences in temperature of the blood (usually a few hundredths of a degree) between the right and left sides of the heart have frequently been reported but many of the earlier observations must be held to be unreliable since often temperature measurements in the right side of the heart were made where the incoming venous streams of different temperature could not have been completely mixed. If consideration is limited to comparison of temperature measurements made in the pulmonary artery and either the left atrium or the proximal part of the femoral artery, only in the study of Good and Sellers was a consistent difference found and that implied the existence of a heat source somewhere in the pulmonary vascular bed. Breathing air at $-35^\circ C.$ caused no significant change in the temperature difference. Mather and co-workers found that in nine of 12 dogs the pulmonary artery was warmer than the left atrium and noted a mean increase of this difference of less than 0.02° C. on exposure to an atmosphere of $-18^\circ C.$ These findings together with those of Verzar and co-workers which showed the completeness of temperature and humidity equilibration in the respiratory tract of the dog even at low ($-5^\circ C.$) ambient temperatures, indicate that the effects of breathing on intrapulmonary blood temperature are insignificant. Even in man, in whom the air-conditioning capacity of the respiratory tract is less efficient than in the dog, maximal hyperventilation has been shown not to affect the temperature in the small pulmonary arteries.

A condition in which a considerable loss of indicator seems inevitable is pulmonary edema, and measurements of cardiac output by thermodilution will almost certainly overestimate if in fact they can be made at all. Just as undesirable transfer of heat to and from the blood is a hazard to the success of thermodilution, so also is the heat exchange that can easily occur between the injectate and its environment if any temperature difference exists between them. The injection system will usually consist of a
AORTIC THERMO-DILUTION CURVE: $t_{95} = 2.55\text{sec.}$

**FIGURE 1**

Upper Record. Typical aortic thermodilution curve obtained with a slowly responding recording system (time for 95 per cent response to an instantaneous temperature change, $t_{95} = 2.55\text{ sec.}$) following the injection of 5 ml. of normal saline at room temperature into the right atrium and showing the "tail" and the extent of recirculation assuming an exponential decay of the primary curve.

Lower Record. Temperature of the injectate within the tip of the injecting catheter placed in the right atrium showing the time course of temperature during injection and the subsequent rewarming of the contents of the catheter as recorded with a rapidly responding system ($t_{95} = 0.2\text{ sec.}$). Note that the injection was half completed before the temperature of the injectate reached a constant value (room temperature).

Despite these several hazards, all of which stem from unwanted heat exchange, the thermodilution method offers a number of attractions for the measurement of blood flow. These are: It is technically simple both from procedural and instrumental aspects; it gives exact information on the shape of the

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the dilution curve since intravascular detection of the indicator is used; it requires neither blood sampling (and hence is applicable to very small animals) nor the introduction of any foreign material; and, on account of the rapid disappearance of the indicator from the circulation in peripheral vascular beds, it allows frequent measurements to be made.

The Shape of the Thermodilution Curve

The general configuration of a thermodilution curve recorded from the aorta after intravenous injection of a suitable cool liquid is similar in the main to that of dilution curves obtained with the usual nondiffusible indicators. There are, however, some differences which are typical of the diffusible indicator. These are the usual absence of a secondary or later peaks due to the small recirculation of indicator, and a greatly protracted recovery slope which gives a long "tail" to the curve (fig. 1). When the speed of response of the recording system is sufficiently fast the smooth curve, as would be expected, takes on a step-like structure, each step corresponding to a stroke volume of roughly homogeneous temperature distribution. In some curves, however, transient fluctuations in temperature are seen at the leading and trailing edges of each step (fig. 2). These may be due to incomplete mixing in the left ventricle as demonstrated by Swan and Beck. Fegler’s records and those of Goodyer and his associates show that following intravenous injection the pulmonary-artery thermodilution curve has a much more rapid time-course than has that from the aorta. Moreover, the records of Goodyer and associates show that in the aorta the thermodilution curve has a more extended course than has the simultaneously recorded dye-dilution curve even without allowing for the inevitable prolongation of the dye curve that must have occurred in the sampling catheter. This clearly suggests that it is in the lungs that the thermodilution curve develops its longer course. That sufficiently great intrapulmonary heat exchange occurs for this to be so can be seen from figure 2. Fegler showed by serial recordings along the length of the aorta that neither change in shape nor change in area of the thermodilution curve occurred before the bifurcation. Simultaneous measurements would have given more weight to this report, but, as can be seen in figure 3, curves recorded simultaneously from the arch and the bifurcation of the aorta do in fact have the same area and the same time constant for the die-away portion. It seems, therefore, that entirely adequate records can be obtained from the lower aorta, but distal to it conditions of heat exchange will progressively militate against satisfactory measurement. Recirculation of indicator, as Fegler and Goodyer and associates have shown, is very slight but prolonged.

Cardiac Output Measurements

Four series of measurements of cardiac output in which thermodilution was compared with both a dye-dilution technique and the direct Fick method have been reported in the literature. In these the cool injectate was given intravenously and the thermodilution curve was recorded from the aorta and, in some, from the pulmonary artery as well. Fegler and Kussmann and associates used injectates at room temperatures and allowed for the dead space (presumably the intravascular dead space) of the catheter. Goodyer and his associates, using iced saline as the injectate, made a standard correction by calorimetry for the heat gain of the injectate in the catheter during injection. All of these authors reported close agreement among the three techniques, and thermodilution was apparently without systematic deviation with respect to the other two. The high degree of correlation observed in these comparative studies was not found, however, between the calculated values for simultaneously measured outputs of the right and left sides of the heart. This can best be explained by incomplete mixing of the injectate and blood in the right side of
AORTIC AND BRONCHIAL THERMO-DILUTIONS

Simultaneous records of temperature changes in the aortic arch and a secondary bronchus obtained with rapidly responding thermistors \( (t_{95} = 0.2 \text{ sec}) \) following injection of 2 ml of saline at room temperature into the right atrium. The aortic record shows transient temperature fluctuations on the leading and trailing edges of the steps. The bronchial record shows a slow wave of similar time course but earlier appearance than does the aortic curve, indicating the extent of heat exchange between the pulmonary capillary blood and the alveolar air. The superimposed spikes occur at the respiratory frequency and are probably due to cooling of the air in a primary bronchus by an adjacent pulmonary artery.

The heart. A very recent study comparing thermodilution and dye-dilution measurements of cardiac output using an injectate at room temperature has revealed a systematic difference in thermodilution measurements of +4 per cent with respect to the dye-dilution technique as standard. As with the earlier studies, a similar high coefficient of correlation between the two methods was found but in addition a considerably better agreement between outputs of the left and right sides of the heart was found than had been found by the other workers. No obvious reason for this can yet be seen. It was found also that the output of the left side of the heart systematically exceeded that of the right by 2 per cent, suggesting a loss of indicator in the pulmonary circulation.

These results of Evonuk's group should, however, be considered in the light of a comparable study by Bussingthwaite and Edwards using a dye-dilution technique. They found a similar difference (4 per cent) between the simultaneously measured outputs of the left and right sides of the heart after injection into the inferior vena cava and a considerably greater difference (9 per cent) when the injection site was the same as that used by Evonuk's group, namely the superior vena cava. Since the results of

\( \Delta T \text{ in } ^\circ \text{C} \)

Pig, 8.6 kg: 2ml. saline (20°C) injected into R.A.
Bassingthwaighte and Edwards suggest progressively more homogeneous distribution of the indicator with increasing distance from the site of injection, it may well be that the significantly closer agreement for outputs of the left and right sides of the heart found by Evonuk and his associates implies the more rapid spread of heat, a process that depends to a greater extent on diffusion than is true for dyes. The considerably better results obtained by Evonuk’s group for outputs of the right side of the heart over those obtained by Rapaport and Ketterer, who used ice-cold Ringer’s solution, again emphasize the value of using an injectate at room temperature. Thermodilution has also been used successfully in two studies of ventricular-washout characteristics, and closely comparable results for the ratio of end-systolic volume to end-diastolic volume were obtained.

From consideration of the aforementioned studies, it appears that use of the thermodilution method for the measurement of output of the left side of the heart is reliable under normal circulatory conditions, especially when intravenous injection is employed, but in so far as the accuracy of a method can be estimated only to the order of accuracy of the standard no matter how great the precision employed, a definitive study of the thermodilution method with rigid control of all methodological variables and a direct measurement of the particular blood flow being examined as a standard remains to be carried out. Such an undertaking would be difficult as errors are likely to appear in the thermodilution method whenever blood vessels or conduits are exposed to temperatures differing from their contents. In general, it seems that for the measurement of cardiac output by thermodilution to the same order of accuracy as is achieved with other indicator-dilution methods, the precautions taken against heat exchange in most studies to date are sufficient. Nevertheless, a full awareness of possible shortcomings of the method should be retained and the method not be applied without adequate controls to conditions different from those in which it has up till now shown successful application. As emphasis to this caution it should be noted that Fegler found that after severe hemorrhage the output of the left side of the heart consistently appeared to exceed that of the right by about 50 per cent.

Local Thermodilution

Following his original work on measurement of cardiac output, Fegler extended his method to the measurement of flow in single blood vessels and made studies in tubes, in the Ringer-perfused inferior vena cava of the cadaver, and in vivo in the superior and inferior venae cavae. He also studied flow in the hepatic veins, and with Hill in the portal vein. Poorest results were obtained in the model in which fairly rapid heat exchange might be expected, but uniformly good results were obtained in the perfused vena cava and in the living animal in which the blood was collected from a cannula in the vessel. The directly measured and the calculated flows did not differ significantly. However, a systematic overestimation of flow rate of 5 per cent was found by Linzell using very similar technic in his measurements of blood flow in exteriorized veins in skin loops, and this indicates that in local thermodilution also, heat exchange can be a danger and especially so, as he also showed, at very low flow rates.

Recently, in the interesting report already referred to, have appeared the results of Fronek and Ganz obtained from single blood vessels in which the points of injection and temperature measurement were separated by a centimeter or less, the detecting thermistor being mounted on the injection catheter. Using the formulas previously mentioned, they found that neither in models using water and blood nor in the carotid artery and jugular vein, wherein blood flows were measured by rotameter and collection respectively, was any systematic difference found between the calculated flows and the standards of comparison. In another series of observations comparing their local-thermo-
dilution method in the pulmonary artery with simultaneous direct Fick estimations, from five to eight local-thermodilution measurements were averaged to smooth out the effects of the intermittent nature of pulmonary arterial blood flow. While there was no significant difference between the outputs of the right side of the heart that were observed by the two methods, the standard deviation was about 9 per cent and the maximal deviation 23 per cent. Allowing for the vagaries of the direct Fick method as a standard of comparison, this fairly wide scatter of results by local thermodilution, each of which required as many as eight single measurements for its determination, does not suggest that in this situation the technic offers any advantage over the more conventional single-injection method with more distant separation of injection and detection sites.

The lack of precision in measurements where intermittent or pulsatile flows occur raises the question of the calibration of local-thermodilution methods. In Fegler's studies, perfusions were carried out with steady flows while in those experiments in which blood was collected from the inferior vena cava the normally occurring fluctuations in flow must have been obliterated or at least greatly diminished. Similarly, the insertion of a rotameter with its associated tubing into the carotid artery and the opening of the jugular vein for blood collection in the experiments of Froněk and Ganz must have considerably reduced the natural pulsations. While the calculated flows under these conditions showed good agreement with the direct measurement there is as yet no evidence that measurements can be made with the same accuracy in intact vessels with phasic flow. It may be, however, that since the course of local-thermodilution curves takes many seconds to reach completion, it

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is long enough to extend over several of
the longest cycles of flow pulsation (pre-
sumably respiratory) resulting in a smoothing
out of the effects of the fluctuations. The
problem remains to be elucidated.

One major difference exists between the
local-thermodilution method of Fegler and
that of Fronek and Ganz for the measure-
ment of venous flows; namely, Fegler used
the same formula as for cardiac output while
Fronek and Ganz allowed for local changes
in flow in their special formula. Technically
the two methods differ in that while Fronek
and Ganz made their injections within 1 cm.
of the thermistor, Fegler’s injection and
detection sites were separated by several
centimeters. Since, however, with the latter
arrangement the appearance time would be
likely to exceed the period of injection,
probably no correction need be made for
temporary changes in flow rate. Where allow-
dance does require to be made, its nature
requires some attention. The implication that
the duration of accelerated flow is invaria-
tely identical with the build-up time of the
local-thermodilution curve at all rates of
flow needs to be qualified. It can be shown
in experiments in models (fig. 4) that this
desirably uniform relation does not always
hold and that the end of the injection may
precede the peak of the curve by an appreci-
able interval thereby introducing a con-
siderable error into the calculated flow rate.
If, however, the injection time is sufficiently
long and the injection and detection sites
are close enough together, the discrepancy
may be minimized even at low flow rates and
the use of the special “venous” formula
be fully validated. Strict adherence to the
instructions for injection given in the origi-
nal paper is apparently necessary for the
success of the method.

Measurement of Temperature

Since the measurement of temperature is
fundamental to the thermodilution method,
a brief excursion into this field is apposite.
Two types of temperature-sensitive device
are suitable for measurement and recording
of intravascular temperature. These are
thermocouples and thermistors. Thermo-
couples, though pleasingly simple to make,
produce only a small electromotive force
(approximately 40μV./°C.) and so must be
used in low-resistance circuits with sensitive
galvanometers of long period unless suitable
amplification can be arranged. Moreover, if
an absolute measure of temperature is re-
quired, the reference junction must be main-
tained at an accurately controlled tempera-
ture varying by not more than a few
hundredths of a degree. The calibration curve
of thermocouples is essentially linear. Ther-
mistors have a high negative temperature
coefficient of resistance and an almost loga-
rithmic temperature-resistance characteristic.
Over a small range in temperature this
may be considered to be sufficiently linear
but the characteristic can be made virtually
linear over a much greater range and the
sensitivity (ohms/degree), though reduced,
adjusted to any convenient value by shunt-
ing the thermistor with a fixed resistance
of appropriate value. Used as one arm of
either a Wheatstone bridge or of a suitable
alternating-current bridge circuit (for exam-
ple, transformer ratio-arm bridge), the cur-
rent through the thermistor must be kept
small enough to produce no appreciable heat-
ing, otherwise the thermistor becomes sensi-
tive to variations in blood flow rate and so
gives spurious indications of temperature.
The smaller the thermistor, the more easily
can it dissipate the heat it generates, and,
in addition, its thermal inertia to tempera-
ture changes decreases. Thus the smaller it
is the better will be its dynamic-response
characteristic. If rapid responsiveness is re-
quired, the thermosensitive element (ther-
mistor or thermojunction) must be enclosed
in as little insulating material as is prac-
ticable and the associated amplifying and
recording apparatus must have at least as
rapid response characteristics as the de-
tector. When the detector is mounted on
the injection catheter, as for local thermo-
dilution, it may well be influenced by the
temperature of the injectate within the
catheter during injection. This can be overcome by supporting the detector on a little bridge, for example its own lead wires, so that a gap is left between it and the catheter wall. Direct-current bridge circuits are more easily constructed and operated than are alternating-current bridge circuits on account of the necessity with the latter for capacitive balancing, in addition to resistive balancing, making difficult the determination of absolute temperatures. Whichever type of bridge is employed, the energizing voltage must be kept constant or calibration errors will be introduced.

It is a common finding in thermal measurements in vivo that considerable drifts in temperature occur and this is particularly likely in anesthetized animals. Provided the drift is constant, it need offer no deterrent to the making of thermodilution measurements on condition that the heat exchange to which the drift is due is not taking place between the site of injection and the site of temperature measurement, for then the thermodilution curve would no longer be representative of the flow rate. Automatic compensation for drifts in blood temperature can be accomplished to some extent by placing the reference junction of the thermocouple, or a second thermistor in the arm of the bridge adjacent to the measuring thermistor, at some site in the body at which the temperature is drifting at roughly the same rate and in the same direction as that of the blood. It may be conveniently placed at a point upstream from the injection site or anywhere that it will not be affected by either the primary dilution process or the recirculation of indicator, for example subcutaneously or in muscle. The rectum is not a very satisfactory site for the temperature compensator, as rectal tem-
perature changes usually lag behind those of aortic blood by as much as 20 minutes and rectal and aortic temperatures may at times be changing in opposite directions. Unsteady or rapid changes in blood temperature imply unsteady conditions generally and any indicator-dilution estimation, though particularly thermodilution measurements, would then be in error to an unknown degree.

Notwithstanding the necessity for certain precautions in its application, thermodilution, by its technical simplicity and satisfactory comparison with longer established methods for quantification of blood flow, seems to be a method of considerable promise for the investigation of the circulation under normal conditions. With due regard to the circumstances in which it may be expected to fail, its range of application may be extended to include the study of at least some pathologic conditions; a start has already been made in this direction by its employment for the detection of cardiac and other circulatory shunts.27 28 It is to be hoped, however, that in whatever other fields it may yet be of service it will continue to receive the attention which its simplicity and elegance merit and that with further improvement and verification of its usefulness the modest claims first made for it will be upheld.

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