The local thermal dilution method of performing serial bilateral measurements of internal jugular venous flow is significantly improved by injecting a bolus of saline rather than by using a continuous injection of saline. New thermistor catheter designs maintain the proper separation between the sites of injection and of sampling and require only a single insertion per side. The method measures mean flow rates over a two-second to three-second interval. Measurements were made in 14 patients with cerebrovascular disease. Studies of five patients are presented to illustrate the value of the method for assessing internal jugular venous hemodynamics. Positive response to injection of acetazolamide was noted in four of these five patients. Cyclic variations in jugular flow were observed in one patient with Cheyne-Stokes respiration. Occasional retrograde flow in one jugular vein was recorded in another patient.

Additional Key Words: acetazolamide, indicator dilution, total cerebral flow, cerebral venous outflow, Cheyne-Stokes respiration, thermistor

Methods

The bolus (or impulse input) method was used in these studies in contrast to the continuous infusion method previously used. The general theory of indicator dilution methods has been documented. The equation for mean flow rate using the bolus thermal dilution method is given by:

\[
F_B = \frac{Q_t}{\rho B C_B} \int_0^T (T_M - T_B) dt
\]

where \( Q_t \) is the caloric input, \( \rho B \) is the density of blood, \( C_B \) is the specific heat of blood, \( T_B \) is the temperature of blood, and \( T_M \) is the temperature of the blood indicator mixture measured downstream from the injection site as a function of time \( t \).

The accurate evaluation of the integral in this equation imposes three restrictions:

1. There is adequate mixing between the inflow and sampling sites so that a uniform temperature profile is present throughout the cross section of the sampling site at any instant of time.

2. \( T_M \) must be measured for a sufficiently long period of time to ensure that all the indicator

From the Division of Neurology, Department of Medicine, University of Alabama Medical Center, 1919 Seventh Avenue South, Birmingham, Alabama, 35233.

Supported in part by National Heart Institute Grant HE-10618 and National Institute of Neurological Diseases and Stroke Grant NS-08802.
IMPROVED THERMAL DILUTION METHOD

3. There is negligible net heat exchange from blood mixture to vessel walls between inflow and sampling sites.

Temperatures were measured by thermistors incorporated in one leg of a Wheatstone bridge as shown in figure 1. The output of the differential amplifier, $A_T$, was recorded as the transient temperature, $T_u$, as shown in figure 2. The area under this curve is directly proportional to the integral in equation 1. Although it can be obtained numerically by planimetry, because of the large number of curves (average of 100 per patient) an electronic integrator was used (Fig. 1). Since its output is proportional to the time integral of its input voltage and hence to the area under the curve, $T_M$, blood flow rate is inversely proportional to the ordinate, $h_A$, as shown by the equation (derived in appendix):

$$\frac{Q_i h_A}{h_B \rho_B C_B \tau_R R_c} = \frac{60}{\Delta R / \Delta T}$$

where $\Delta R / \Delta T$ is the thermistor slope in ohms/°C at $T_B$.

Small quantities (1.5 to 2.0 cc) of room temperature heparinized saline were injected rapidly (in approximately 0.4 second) and simultaneously into each jugular vein by an automatic injector modified to actuate two 2.5 cc syringes. The caloric input is given by:

$$Q_i = (V_{total} - V_{IV}) (T_B - T_I)$$

where $V_{IV}$ is the intravascular volume of the injecting catheter whose contents have equilibrated to blood temperature (about 0.1 cc). $T_I$ is the injectate temperature measured externally near the site of catheter insertion.

Because of the relatively high rate of injection (greater than 200 cc/min), the correction for thermal loss in the catheter during injection is quite small (less than 0.1°C) and is usually neglected.

In order to obviate two insertions in each jugular vein, several types of thermistor catheter probes were investigated. The first of these, shown in figure 3, consisted of a thermistor mounted on the exterior surface of the injecting catheter. Despite the insulation provided by the walls, epoxy, and space $S$, there was sufficient thermal coupling between thermistor and injectate when low rate continuous infusion was used to require a correction factor. Although this correction was negligible with bolus injection, the output curve was markedly distorted (prolonged decay time), because of the thermal coupling from the residual injectate at the end of injection. This effect was virtually eliminated by withdrawal of a small volume of blood immediately after injection. However, because of the added complication of this procedure as well as the possible error introduced by withdrawing some of the indicator, this design has been tentatively discarded.

Two other designs which have worked satisfactorily for us are shown in figures 4 and 5. The "folded" thermistor probe (Teflon, o.d. = 0.021") is partially straightened to permit insertion through the Touhy-Borst adapter. The adapter is then tightened on the probe so that its

\[\text{CALIBRATION AND DILUTION CURVES FROM AMPLIFIER AND INTEGRATOR}\]

\[\text{FIGURE 2}\]

Calibration and dilution curves from amplifier and integrator.


†All thermistor probes from Wilton Webster Laboratories, P. O. Box 237, Altadena, California, 91001.
folded end just clears the distal orifice of the catheter. After catheter insertion the folded probe is inserted through the catheter until its distal end springs free from the catheter lumen. The probe is then retracted so that its fold is positioned at the distal end of the catheter (this position can be readely determined as a slight tug on the probe during retraction or by measurement). The probe is sufficiently flexible to permit complete withdrawal from an in situ catheter. The thermistor bead is located about 5 mm from the end of the probe to reduce the possibility of its lying on the vessel wall.

The "tethered" unit has a Teflon thermistor probe (o.d. = 0.027") attached to the catheter (o.d. = 0.065", i.d. = 0.040") near both of its ends. The distal end is slightly tapered to facilitate entry through the skin. The catheter is inserted over a wire guide. The thermistor is located midway in the "S" portion of the probe to avoid contact with vessel walls.

Bilateral internal jugular catheterization was accomplished percutaneously as previously described. Because of one instance in which the catheter was introduced caudally into the innominate vein, catheter position is now routinely documented by x-ray or fluoroscopy.

Results in Vitro and in Patients

The accuracy of the bolus thermal dilution method using both the folded and tethered thermistor probes was checked with in vitro studies. Comparison with flows measured by a turbine flow meter yielded a regression equation of $Y_{\text{thermal}} = 1.01X + 14 \, \text{cc/min}$ with a correlation coefficient $R = 0.99$ (range 170-1,300 cc/min, $N = 47$).

Bilateral internal jugular flow measurements using the bolus method have been made on a total of eight patients. The average number of measurements per patient was 53. Total jugular flow ranged from about 500 cc/min to 1,400 cc/min. In one patient periodic retrograde flow was observed on one side. In four patients with the head unrestrained one internal jugular vein carried more than 70% of the total flow. Positive response to intravenous injection of acetazolamide was observed in six out of seven patients. A detailed presentation of five illustrated cases is given below.

Figure 6 is a plot of separate and total internal jugular flow for patient A.G. A severe left hemiparesis developed 12 days prior to the blood flow study. A technetium brain scan was abnormal over a large area in the right hemisphere, but an EEG contained only minimal scattered nonfocal slow activity. The administration of 1 gm of acetazolamide (shown by the vertical arrow) produced a small increase in total jugular flow, manifest primarily in the left jugular vein. CMRO$_2$ values here (and in subsequent cases) are computed bilaterally from an average of flows over a 15-minute period prior to the first (A-V)O$_2$ and over a period of plus and minus ten minutes for the second (A-V)O$_2$. The effects of digital unilateral jugular compression (not shown in the graph) resulted in an approxi-
**FIGURE 5**
Tethered thermistor-catheter unit.

**FIGURE 6**
Simultaneous bilateral measurements of internal jugular venous flow. Arrow indicates time at which acetazolamide was injected. Numbers for (A-V)O₂ are located at the approximate time of blood samples. See text for computation of CMRO₂.

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>L</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-V)O₂</td>
<td>4.0</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>CMRO₂</td>
<td>27.0</td>
<td>10.0</td>
<td>37.0</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>4.0</td>
<td>39.5</td>
</tr>
</tbody>
</table>
mate 50% increase in contralateral flow. However, the total flow during compression was only about 70% of the precompression total.

Figure 7 is a similar graph for J.D. The patient had a left hemiparesis with clinical recovery one year previously. Three days prior to the blood flow study there was a sudden onset of severe left hemiparesis, left homonymous hemianopia and mental obtundation. A technetium brain scan was normal the day after the study but ten days later revealed a focal abnormality in the right temporoparietal area. The EEG was normal. The first five measurements show the differential flow changes that can occur from changes in head position without significantly affecting total flow (head right in one, two and five, head neutral in three and four). A marked increase in total flow was noted following intravenous infusion (at arrow) of acetazolamide with maximum increase about 20 minutes after administration.

Figure 8 is a similar graph for A.M.G. Three days prior to this study the patient was admitted because of left hemiplegia and left homonymous hemianopia. The brain scan was normal. The EEG showed a slow wave focus in the right hemisphere and some lesser abnormality in the left hemisphere. Total jugular flow was substantially greater than in the two preceding patients. The positive response to acetazolamide occurred within five minutes. Right jugular compression (not shown) resulted in a 75% increase in left flow (total flow about 75% of precompression total) prior to acetazolamide and a 200% increase in left flow (total about 50% of precompression total) after giving the drug. Changes in head position increased left jugular flow by 100% but reduced total flow by about 20%.

Figure 9 is a similar flow graph which also shows systolic pressures for patient B.B. This patient had a subarachnoid hemorrhage three weeks before the blood flow study. There was coma and intermittent decerebrate rigidity, with preserved pupillary, corneal, and vestibulococular reflexes. The EEG showed diffuse slowing and voltage suppression. Arteriography
revealed bilateral internal carotid aneurysms, widespread vasospasm and a prolonged circulation time. The clinical state of the patient and the EEG were unchanged at the time of the blood flow study. Monitoring systolic blood pressure with a semi-automatic auscultatory method revealed large fluctuations in blood pressure with which the decerebrate rigidity waxed and waned. Total jugular blood flow positively followed blood pressure, but was nonetheless significantly augmented by acetazolamide. The paradoxical decrease in right jugular flow at peak total flow was probably a consequence of intrathoracic pressure or cervical muscle contraction changes during the fluctuating decerebrate rigidity.

Figure 10 shows a plot of right jugular flow and systolic pressure in patient C.L. (simultaneously measured left jugular flow was less than 60 cc/min in all measurements). This patient developed a right hemiplegia two days prior to the study. An arteriogram three days after the blood flow study revealed the occlusion of the horizontal portion of the left middle cerebral artery. The blood pressure was normal until the day of the blood flow study. The marked blood pressure elevation was discovered after initiation of the study. Appropriate antihypertensive treatment was started and bilateral jugular flow was monitored. As the blood pressure declined to normal, there was a parallel decline in total jugular blood flow and, at normotensive levels, continuing decline in blood flow and in total cerebral oxygen consumption following the administration of acetazolamide.

Pronounced temperature fluctuations bilaterally prevented obtaining quantitative flow measurements in one patient (I.T.). Blood flow was quite low in each jugular vein as shown by a delayed response to the injection and the slow indicator washout rates. Indicator was detected in one jugular vein following a single contralateral injection. This was evidence of communication between the two jugular veins. An arteriogram disclosed bilat-
Simultaneous bilateral measurements of internal jugular venous flow. Note the positive response of flow to spontaneous changes in systolic blood pressure.

Discussion

METHODOLOGICAL PROGRESS

The method described here appears to largely solve the major problems of mixing and catheter-thermistor positioning reported in our previous paper. Since the bolus injection rate is substantially greater (by a factor of seven or more) than the continuous infusion rate, the increased turbulence produces much better mixing. Moreover, the increased momentum of the injectate carries it much further upstream and thus provides an effectively longer path length between injection and sampling sites. A number of other advantages are also present.

1. The short duration of the injection means that the cumulative fluid load to the patient is less than the fluid load with continuous infusion, even though there is an increased rate of injection in the modified method. Bilateral measurements made at three-minute intervals would result in a fluid intake of about 70 cc/hr. This would correspond to...
IMPROVED THERMAL DILUTION METHOD

C.L.

SYSTOLIC PRESSURE

RIGHT JUGULAR FLOW

LEFT JUGULAR FLOW LESS THAN 60 cc/min IN ALL MEASUREMENTS

DURATION OF CHEYNE-STOKES RESPIRATION

FIGURE 10

Simultaneous bilateral measurements of internal jugular venous flow. Bottom portion of flow scale is omitted. Left jugular flow was less than 10% of total flow in all measurements and is not plotted. Horizontal arrow indicates approximate duration of Cheyne-Stokes respiration.

TABLE 1

Unilateral Internal Jugular Blood Flow

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-acetasolamide (cc/min)</th>
<th>Post-acetasolamide (cc/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>J.S.</td>
<td>230</td>
<td>700</td>
</tr>
<tr>
<td>A.W.</td>
<td>290</td>
<td>420</td>
</tr>
<tr>
<td>W.H.</td>
<td>130</td>
<td>420</td>
</tr>
<tr>
<td>R.H.</td>
<td>300</td>
<td>720</td>
</tr>
<tr>
<td>J.W.</td>
<td>460</td>
<td>1,050</td>
</tr>
</tbody>
</table>

Flows in cc/min; cont. = continuous infusion. CLC = digital compression of contralateral jugular vein.

approximately 1.5 minutes of data per hour for continuous infusion.

2. Allowing for the increased equilibration time needed for the continuous study, the

Stroke, Vol. 2, March-April 1971
density of useful information per unit of time appears better with the bolus method.

3. The occurrence of artifact due to clot or vascular wall damping (which has been relatively infrequent) is more apparent with the bolus method.

4. As far as the computation is concerned the higher injection rate means that the correction for thermal indicator loss in the catheter is negligible.

The earlier choice of continuous infusion instead of injection of a bolus was based on the apparently simpler computation (measurement of an ordinate rather than an area) and because transient differential flow changes are readily observable. The use of an electronic integrator to compute area has effectively solved the first problem. The integrators are inexpensive and, if a stable baseline is present, provide an accuracy better than planimetry. Although the integrators are not suitable where a long segment of intravascular catheter is used (the secondary input following injection retards the return to baseline), the short dimensions involved here produce a negligible secondary input. The bolus method measures mean flow over a two-second to four-second period. Simultaneous bilateral curves can be obtained at intervals as short as ten seconds. This precludes the detection of transient flow changes that occur within this period; however, the overall advantages of the bolus method considerably outweigh this possible disadvantage.

The catheter-thermistor probe configurations shown in figures 4 and 5 provide reasonably positive control over the relative separation between injection and sampling sites. Occasionally there is some slippage of the entire assembly as a result of patient motion. The thermistor then lies below the common facial vein. This produces an increase in baseline fluctuations and the assembly should then be properly repositioned.

ANATOMICAL LIMITS OF THE METHOD
There are limitations on equating bilateral jugular blood flow with total cerebral blood flow. One limitation is contamination of jugular blood from noncerebral sources and cerebral venous outflow via alternate routes, particularly if the circumstances of the measurement cause significant unilateral or bilateral jugular venous obstruction. This occurs rather frequently with change of head position (jugular venous obstruction on the side toward which the face is turned). Obstruction of flow in one jugular vein has not always been completely compensated for by the increase in flow on the opposite side, though relatively free communication between the two jugular veins has been demonstrable in every patient. Bilateral jugular blood flow measured by the local thermal dilution method must be considered only a qualitative or semiquantitative cerebral blood flow index unless validated by measurement of total cerebral blood flow by a method which includes carotid injection.

Other cerebral blood flow measurements which depend on jugular sampling, including the Kety-Schmidt method for average cerebral blood flow and methods for total cerebral blood flow based on carotid injection, do not suffer such anatomical constraints. In these methods, blood in the jugular bulbs need only be a representative sample of the mixed cerebral venous outflow uncontaminated by blood of noncerebral origin. Provided mixing is complete, it is irrelevant how many alternate outflow channels there may be. By contrast the local indicator dilution methods, including our own, demand that all or virtually all cerebral venous outflow be via the internal jugular veins.

PHYSIOLOGICAL OBSERVATIONS
The administration of acetazolamide, a potent short-acting cerebral vasodilator, was selected as a simple qualitative test of whether this method is a valid index of cerebral blood flow. In four of the five patients studied, total jugular flow did increase. In two of the five (A. M.G. & C.L.) cerebral oxygen metabolism decreased following administration of acetazolamide, and in one patient (angiographically proved middle cerebral artery occlusion), autoregulation also appeared defective as suggested by a decrease in total jugular blood flow associated with a decrease in blood pressure. Whether these abnormalities are due to a regional or general defect in circulatory dynamics is a matter for speculation. Some investigators have suggested that regional abnormalities may be reflected by changes in average or total cerebral oxygen or glycolytic metabolism. This hypothesis has not been subjected to the necessary test of simultaneous...
measurement of regional and either total or average cerebral blood flow and metabolism.

In one patient repetitive blood flow measurements were made at various points of the cycle of Cheyne-Stokes respirations. The highest flow rates were recorded (mean 1,100 cc/min) toward the end of hyperventilation and early in the apneic period, while the lowest values (mean 600 cc/min) were near the end of apnea and at the beginning of hyperventilation. The physiological interpretation of this observation must await additional observations in other patients. This observation demonstrates one of the advantages of this method. A complete measurement can be made in a few seconds, while other methods applicable in man require several minutes for completion.

Conclusions

An improved method for the simultaneous bilateral measurement of internal jugular venous flow by thermal dilution is presented. The previously encountered difficulties of indicator mixing and thermistor-catheter spacing have been largely overcome by the use of bolus injection and new thermistor-catheter configurations. The use of a simple electronic circuit provides an on-line measure of the dilution curve area which is inversely proportional to flow rate. The data from patients confirm our earlier findings of some diversion of internal jugular venous flow to other venous channels as a result either of digital compression of one jugular vein or of changes in head position. Thus the measurement of total jugular flow would require simultaneous bilateral measurements with the head in a relatively neutral position. Since the method measures mean flow rate over a two-second to three-second period and since measurements can be repeated at about ten-second intervals, the method affords good opportunity for the study of dynamic changes in total internal jugular venous flow following pharmacological intervention or as a result of various pathophysiological conditions (e.g., Cheyne-Stokes respiration). It will facilitate further study directed to determining the degree to which total internal jugular flow is an index of total cerebral flow.

References


Appendix

BRIDGE-AMPLIFIER-INTEGRATOR CALIBRATION:

Referring to figs. 1 and 2, prior to each measurement or calibration the bridge is balanced by the 10-turn dial potentiometer, R₀. Blood temperature, T₀, and thermistor slope ΔR/ΔT at T₀, are obtained from thermistor calibration tables. Calibration is obtained by the insertion of resistor, Rₛ, in series with the thermistor for a time duration, tₛ. The integrator outputs are

Calibration

\[ h_c = K V_c t_c \]  \hspace{1cm} (A-1)

Curve

\[ h_A = K \int_0^T (T_M - T_B) dt \]  \hspace{1cm} (A-2)

Eliminating K we have

\[ \int_0^T (T_M - T_B) dt = \frac{V_c [CM] t_c [SEC] h_A [CM]}{h_c [CM]} \]  \hspace{1cm} (A-3)
To convert from units of cm-sec to °C-sec, note that

\[(T_M - T_B) \ [°C] = \frac{(T_M - T_B) \ [cm]}{V_e [cm]} \cdot \frac{R_e [OHMS]}{\Delta R/\Delta T [OHMS/°C]} \]  

so that

\[\int_0^T (T_M - T_B) \ dt \ [°C\cdot sec] = \frac{t_c \cdot R_e \cdot h_A}{h_e \cdot \Delta R/\Delta T} \]  

Flow is then given by

\[F_B = \frac{Q_t \cdot \Delta R/\Delta T \cdot h_e}{h_A \cdot \rho_B \cdot C_B \cdot t_e \cdot R_e} \]  

The integrator is returned to zero output by means of a switch after each calibration or measurement.
An Improved Thermal Dilution Method for Measuring Jugular Venous Flow
EDWIN M. WILSON and JAMES H. HALSEY, JR.

Stroke. 1971;2:128-138
doi: 10.1161/01.STR.2.2.128

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/2/2/128