A Method for Measuring Cerebral Hemispheric Blood Flow and Metabolism

BY JOHN STIRLING MEYER, M.D., AND YUKITO SHINOHARA, M.D.

Abstract:
A new method for measuring cerebral hemispheric blood flow together with metabolism using an injection of a 5 ml bolus of hydrogen-saturated saline into each internal carotid artery is described. This method was extensively evaluated in the monkey prior to being used in man.

Under fluoroscopic control, a catheter was inserted into each cerebral transverse sinus via the basilic veins. Hemispheric blood flow was calculated from the clearance curves of hydrogen from the transverse sinus following injection using a formula based upon the Stewart-Hamilton principle. Hemispheric metabolic index for oxygen was estimated using a new formula by assuming that the distribution of hydrogen into each transverse sinus following injection of the bolus indicates the distribution of the blood from each hemisphere into each transverse sinus.

This method has certain advantages over the conventional method for measuring cerebral blood flow, since the actual geometry of the brain in which the blood flow measured is known and simultaneous estimations of hemispheric metabolism are possible.

Abnormalities of hemispheric blood flow and metabolism have been measured in 30 patients suffering from various neurological disorders including occlusion of one internal carotid artery.

The new formula for estimating hemispheric metabolism is applicable to radioisotopic and other indicator injection methods in which blood is sampled from the cerebral transverse sinuses or internal jugular veins.

It was also shown that the transverse sinus distribution of blood derived from each cerebral hemisphere varies from one individual to another.

ADDITIONAL KEY WORDS
cerebral angiography carotid occlusion hydrogen-saturated saline cerebral transverse sinus

Introduction
Quantitative measurement of average cerebral blood flow and metabolism in man first became possible when Kety and Schmidt in 1945 introduced the nitrous oxide method. Although it is generally conceded that the Kety-Schmidt method, which utilizes the Fick principle, permits measurement of blood flow and metabolism of the brain as a whole, it is not known which parts of the brain are drained mainly by the internal jugular vein from which the blood samples are drawn.

Lassen and Ingvar first employed the intracarotid injection of an inert radioactive gas dissolved in saline in order to measure regional blood flow. This method has also been applied to estimate hemispheric blood flow. Nevertheless, the methods currently used to measure regional cerebral blood flow have
certain limitations which will be reviewed in the discussion.

The measurement of regional cerebral metabolism together with blood flow is of considerable importance because it should provide basic information concerning regional function of the brain in health and disease.

Bearing in mind the potential clinical usefulness of accurate measurements of cerebral blood flow and metabolism, a method will be described which employs the intracarotid injection of a bolus of hydrogen-saturated saline for the measurement of hemispheric blood flow (HBF) which also makes possible quantitative estimation of the metabolism of each hemisphere. This method has been extensively evaluated in the monkey prior to its use in man.4 In this communication, some illustrative results obtained in our laboratories will be presented along with a critical evaluation of the application of the method to man. Some new observations concerning the distribution of venous blood derived from each hemisphere into each transverse sinus will also be discussed.

Method
The hydrogen bolus method has been employed successfully in 46 patients, but measurements limited to the first 30 only will be reported in this paper. Twenty-four suffered from occlusive cerebrovascular disease, one had a large arteriovenous malformation of one hemisphere, three suffered from dementia, one suffered from seizures, and one had paralysis agitans. Their ages varied from 30 to 74 years with a mean of 56 years. Informed consent was obtained in writing from each patient or their responsible next of kin prior to carrying out the procedure.

Under fluoroscopic control, using an image amplifier, a catheter was inserted into each cerebral transverse or sigmoid sinus via the basilic veins of the forearms.5 Another catheter was placed into the femoral artery to obtain arterial samples. The oxygen saturation of the arterial and cerebral venous blood was monitored with CC oximeters (Kipp, Model 3), which were regularly calibrated using the manometric method of Van Slyke and Neill. The oxygen content was calculated from oxygen saturation, oxygen capacity, and the dissolved oxygen obtained from the Po2 value. Using the method described by Gotoh et al.,6 Po2, pH, respiration, and systemic blood pressure were also monitored. Electrocardiograms and electroencephalograms were recorded throughout the measurements.

Hemispheric Blood Flow (HBF)
At least 15 minutes following puncture of both internal carotid arteries, a 5 ml bolus of hydrogen-saturated saline was injected by hand alternately into each artery to measure blood flow. The bolus was prepared immediately before injection using sterile technique. Repeated cultures were made to be certain that the hydrogen-saturated saline was sterile and all cultures were negative for bacteria and spore-forming organisms. The injections were made rapidly by hand, each lasting about one to two seconds. The region of brain measured was the area supplied by one internal carotid artery, i.e., the ipsilateral hemisphere. Angiography was always performed prior to the blood flow measurements to verify that the carotid artery injected supplied the ipsilateral hemisphere without demonstrable cross filling except in the cases of internal carotid occlusion.

The hydrogen electrodes are an application of the polarographical principle and were constructed in the same manner as the oxygen electrodes used in our laboratory6 except that the electrical potential of 0.68 v from the Beckman Physiological Gas Analyzers (Model 160) was reversed so that the platinum electrode acted as the anode. These electrodes have been improved upon since they were originally described7 in that the platinum wire was sealed in a glass tube and had an exposed surface area of 200 µ diameter and the surface of the platinum was lightly platinitized with platinum chloride (1% solution) and covered with a polyethylene membrane 25 µ thick rather than a Teflon membrane. Two hydrogen electrodes were used to record simultaneously the partial pressure of hydrogen in both cerebral transverse sinuses.

HBF was calculated from the clearance curves of hydrogen using a formula based on the Meier-Zierler modification of the Stewart-Hamilton principle described in an earlier report.4 When the indicator is injected at an inflow orifice and the measurement is done at the outflow orifice, the mean transit time of the indicator t may be written:

\[
 t = \frac{\int_0^\infty t \cdot C(t) \, dt}{\int_0^\infty C(t) \, dt}
\]

where t is the time after injection in minutes and C(t) is the observed concentration of the indicator at time t at exit.8 When hydrogen is used as the indicator, the partition coefficient for hydrogen, λ, is almost unity.9, 10 Therefore, we may write:4, 8
CEREBRAL HEMISPHERIC BLOOD FLOW AND METABOLISM

\[ t = \frac{\lambda}{T} = 1 \frac{t}{T} \quad (2) \]

where \( t \) is blood flow per gram of tissue.

The hydrogen concentration in the blood may be quantitatively expressed as its gas tension provided that molecular hydrogen does not combine with any of the blood constituents.\(^4\,^7\)

Hence,

\[ f = \frac{1}{T} \int_{0}^{\infty} H(t) \, dt \quad (3) \]

\[ \int_{0}^{\infty} H(t) \, dt = \int_{0}^{\infty} t \cdot H(t) \, dt \]

\( H(t) \) is the recorded partial pressure of the hydrogen at time \( t \) at exit.

In this communication, the flow values were calculated throughout ten-minute intervals following injection since the clearance was virtually complete within that time. These flow values were expressed as ml/100 gm brain tissue where brain tissue is defined as both parenchyma and blood included in the cerebral vessels.

HEMISPHERIC METABOLIC INDEX (HMI)

The conventional cerebral metabolic rate, whether it be uptake or release, was calculated from the product of blood flow and cerebral arteriovenous differences of the metabolites. However, it is common knowledge that blood in each internal jugular vein is a mixture of blood from both hemispheres; and although the blood from each internal jugular vein is fairly representative of blood derived from the ipsilateral hemisphere, the ratio of mixing is different in each individual, the evidence for which will be discussed later. The amount of metabolite from each hemisphere can be estimated from the ratio of hydrogen appearing into each transverse sinus after injection of the internal carotid artery, as suggested in an earlier paper.\(^4\)

Assuming that the venous blood derived from each hemisphere and distributed into each transverse sinus is as shown in the theoretical model in figure 1, then the total blood flow of the right and left transverse sinuses, which we will term \( F_1 \) and \( F_2 \), are:

\[ F_1 = F_R - f_1 + f_2 \quad (4) \]

\[ F_2 = F_L + f_1 - f_2 \quad (5) \]

where \( F_R \) is the total blood flow of the right hemisphere, \( F_L \) is that of the left hemisphere, and \( f_1 \) and \( f_2 \) are the blood flows leaving the right hemisphere to enter the left transverse sinus and the blood leaving the left hemisphere to enter the right sinus, respectively.

Let us consider the case of injection of a bolus of indicator into the right carotid artery (A). The indicator injected at A appears at B after perfusing the right hemisphere and then passes into D and D' where the blood is drawn. Let the ratio of the areas under the hydrogen clearance curve, if it be the indicator, appearing at D compared to that appearing at D' following the right carotid bolus be called \( a \). The relationships between the concentration of hydrogen at time \( t \) and located at B, which we will call \( H_B(t) \), and located at D and D', which we will call \( H_D(t) \) and \( H_{D'}(t) \), respectively, are expressed in the following equations assuming flow to be constant:

\[ F_2 \int_{0}^{\infty} H_2(t) \, dt = f_1 \int_{0}^{\infty} H_R(t) \, dt \quad (6) \]

\[ F_1 \int_{0}^{\infty} H_1(t) \, dt = (F_R - f_1) \int_{0}^{\infty} H_R(t) \, dt \quad (7) \]

\[ F_1 = F_R - f_1 + f_2 \quad (4) \]

\[ F_2 = F_L + f_1 - f_2 \quad (5) \]

\( F_R \) is the total blood flow of the right hemisphere, \( F_L \) is that of the left hemisphere, and \( f_1 \) and \( f_2 \) are the blood flows leaving the right hemisphere to enter the left transverse sinus and the blood leaving the left hemisphere to enter the right sinus, respectively.

**FIGURE 1**

Schematic model of the blood distribution from each hemisphere into each transverse sinus. (See text for explanation of abbreviations.)
Therefore, the ratio of concentration $a$ following the right carotid bolus is:

$$a = \frac{\int_0^\infty H_1(t) \, dt}{\int_0^\infty H_2(t) \, dt} = \frac{F_2}{F_1} \cdot \frac{(F_R - f_1)}{f_1} \quad (8)$$

Similarly, the ratio of the appearance of hydrogen in $D'$ and $D$ following injection of the left carotid bolus $b$ is:

$$b = \frac{F_1}{F_2} \cdot \frac{(F_L - f_2)}{f_2} \quad (9)$$

Hence,

$$f_1 = \frac{aF_L (b-1) - F_R (a-1)}{(ab-1)(a-1)} \quad (10)$$

$$f_2 = bF_R (a-1) - F_L (b-1)}{(ab-1)(b-1)} \quad (11)$$

if

$$(F_R - f_1) \neq 0, \quad (F_L - f_2) \neq 0.$$ 

The concentration of oxygen at time $t$ at $B$, $V_R(t)$, and at $B'$, $V_L(t)$, and at $D'$, $C_1(t)$, and at $D$, $C_2(t)$ may be written:

$$F_1 \cdot C_1(t) = (F_R - f_1) \cdot V_R(t) + f_2 \cdot V_L(t) \quad (12)$$

$$F_2 \cdot C_2(t) = f_1 \cdot V_R(t) + (F_L - f_2) \cdot V_L(t) \quad (13)$$

From equations 10, 11, 12, and 13 the following formulas may finally be derived:

$$V_R(t) = \frac{bC_1(t) - C_2(t)}{b-1} \quad (14)$$

$$V_L(t) = \frac{aC_2(t) - C_1(t)}{a-1} \quad (15)$$

The advantage of these final formulas is that they are not affected by the values of total blood flow or mixing of interhemispheric venous blood. The hemispheric metabolic index for oxygen consumption (HMI-O$_2$) was, therefore, calculated by multiplying HBF by hemispheric arteriovenous oxygen difference in volume percent using formulas 14 and 15 and expressed as ml/100 gm brain/min.

**Results**

**CEREBRAL TRANSVERSE SINUS CATHETERIZATION**

Bilateral transbasilic catheterization of the cerebral transverse sinuses was successfully performed in 80% of patients. In some patients anatomical abnormalities involving the angle of the subclavian vein in relation to the internal jugular vein made it difficult to slide the catheter into the internal jugular vein of the ipsilateral side, so the catheter was manipulated through the brachiocephalic vein into the internal jugular vein of the opposite side. In two cases radiopaque dye injected through the catheter revealed atresia or a venous plexus formation in the distribution of the internal jugular vein high in the neck. In these two cases, only one catheter could be inserted into an unusually large cerebral transverse sinus on the opposite side.

**EFFECTS OF INJECTING THE HYDROGEN BOLUS**

An actual recording of the cerebral venous blood gases and pH during injection of the bolus of 5 ml saline saturated with hydrogen is shown in figure 2. There were no significant alterations in transverse sinus blood P$_{O_2}$, oxygen saturation, P$_{CO_2}$, or pH, nor did the bolus injection significantly alter respiration, systemic blood pressure, or the electrocardiogram or electroencephalographic recordings.

**HEMISPHERIC BLOOD FLOW**

Typical clearance curves of the hydrogen from both cerebral transverse sinuses are shown in figures 3, 4, and 5. Following a rapid saturation phase, the clearance curve persisted for about ten minutes. Values for the partial pressure of hydrogen were read manually from the curves at five-second intervals and recorded on a graph in arbitrary units. In some patients, using a digital recorder (Hewlett Packard, model N28 562A), values were taken at intervals of one, two, ten, 20, and 30 seconds as well as at five seconds. The calculated blood flow values were in excellent agreement whether computed at intervals of one, two, five, or even ten seconds (table 1). Therefore, a sampling interval of five seconds for calculating blood flow appeared justified.

Table 2 contains a summary of the HBF measurements in 30 human subjects. Detailed information regarding the clinical manifestations in these patients has been described elsewhere.$^{11}$

HBF was calculated simultaneously from the clearance curves obtained from both transverse sinuses if the height of the curves...
was sufficient to read. Table 3 shows that the values obtained simultaneously from the ipsilateral and contralateral sinuses are in excellent agreement (r = 0.79, P < 0.01). However, HBF values shown in table 2 were those obtained routinely from the ipsilateral sinus because in many cases the curves from the contralateral side were too low to read accurately. The shapes of the desaturation portion of the two curves from each transverse sinus were also similar despite the differences in scale, supporting the assumption that each hemisphere represents a single mixing chamber. Figure 6 illustrates that following injection of the bolus the hydrogen does not recirculate into the arterial blood.

One of the advantages of this method is that blood flow can be measured in cases of internal carotid artery occlusion. In those patients in whom angiography revealed occlusion of one internal carotid artery (figure 6, table 2, cases with one asterisk) with collateral
circulation apparently through the external carotid artery, hydrogen injected into the common carotid artery appeared in the transverse sinus but usually the ascending part of the curve was slower than usual. One should bear in mind that in such cases the region being measured is only that supplied by the collateral circulation.

In some patients, a 15 ml bolus was injected retrograde into the right brachial artery. Although the clearance curve that appeared in the cerebral venous blood after this type of injection is almost identical to that following carotid injection, the region measured is that perfused by the ipsilateral carotid and vertebral arteries. Values obtained following both right brachial and carotid artery injection in the same patient were similar, but as might be expected the correlation was not statistically significant (table 4, \( r = 0.39, 0.4 > P > 0.3 \)) since the cerebellum and brain stem flow were combined with the hemispheric measurements. It is also possible to measure the blood flow of the left vertebral territory, i.e., the cerebellum and brain stem, with a left brachial bolus injection.

**Table 1**

Values of HBF Calculated at Variable Sampling Intervals

<table>
<thead>
<tr>
<th>Sampling Intervals (in seconds)</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBF (ml/100 gm brain/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flow value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>49.2</td>
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<td>46.2</td>
</tr>
<tr>
<td>4</td>
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<td>47.9</td>
<td>47.9</td>
<td>47.9</td>
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<td>44.5</td>
</tr>
<tr>
<td>5</td>
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<td>45.5</td>
<td>45.4</td>
<td>45.4</td>
<td>46.7</td>
<td>48.8</td>
</tr>
<tr>
<td>6</td>
<td>55.0</td>
<td>55.0</td>
<td>55.2</td>
<td>54.8</td>
<td>53.8</td>
<td>51.9</td>
</tr>
</tbody>
</table>
CEREBRAL HEMISPHERIC BLOOD FLOW AND METABOLISM

LEFT CAROTID BOLUS

R. Trans. Sinus

L. Trans. Sinus

HBF = 246.3 ml/100g brain/min

MINUTES

RIGHT CAROTID BOLUS

R. Trans. Sinus

L. Trans. Sinus

HBF = 53.6 ml/100g brain/min

MINUTES

FIGURE 4

Hydrogen clearance curves from both cerebral transverse sinuses in patient with huge left cerebral arteriovenous malformation. A large difference in HBF is shown.

COMPARISON WITH HYDROGEN INHALATION METHOD

Average cerebral blood flow was also measured in nine patients in this series during the desaturation phase employing the hydrogen inhalation method. The average CBF values were in reasonable agreement with the mean of both HBF values (table 5). However, in one patient in whom the hemispheric venous blood distribution into the transverse sinuses was almost exclusively from each hemisphere into its ipsilateral transverse sinus, the average CBF agreed only with the HBF values measured on the same side from which the cerebral venous blood was drawn during the inhalation measurements (table 5, case nine).

HEMISPHERIC METABOLIC INDEX FOR OXYGEN

The hemispheric metabolic index for oxygen (HMI-O²) was calculated by the use of formulas 14 and 15 and expressed as ml O²/100 gm brain (table 6). Table 6 also displays the ratio for the areas under the hydrogen clearance curves for ipsilateral transverse sinus to contralateral sinus. In all except five patients the ratio was much higher following right carotid injection than after left carotid injection. The difference is statistically significant (P < 0.05). In the isolated case (case nine) in which the hydrogen clearance curve was found exclusively in the ipsilateral side, since f₁ and f₂ equal 0, HMI-O² was calculated directly from the product of HBF and the ipsilateral arterial transverse sinus oxygen difference in volume percent. In only three of the total of 32 injections were the areas under the curve of hydrogen clearance greater on the contralateral than on the ipsilateral side. In other words, the clearance of hydrogen from each hemisphere was predominantly via the ipsilateral transverse sinus.

These data prove that diffusible gases
such as hydrogen are not mixed completely in the sagittal sinus or torcular Herophili.

**Discussion**

Using the method described here, blood flow of the tissue supplied by one internal carotid artery was measured, i.e., almost exclusively the ipsilateral hemisphere. This method avoids certain difficulties inherent in the Kety-Schmidt method, namely, sampling from one internal jugular vein the distribution of which is not known—a problem which makes the nitrous oxide method unsuitable for comparisons of blood flow between the two hemispheres.

Other methods employing isotopes for measuring HBF also have limitations, such as self-absorption of the radioisotope and uncertainty of the exact area measured due to the inverse square law and Compton scattering.

For the hydrogen method to be valid, the blood distribution from one hemisphere into each transverse sinus and the HBF should be constant during the time interval of measurement (ten minutes). In this series of patients, the clearance curves simultaneously recorded from both transverse sinuses were parallel (figs. 4 and 5), a finding also noted by Nylin et al. using the injection of thorium-B-labeled erythrocytes. The HBF values calculated from both transverse sinus curves were in good agreement (table 3). Clearance curves from repeated injections of hydrogen in the same patient were highly reproducible. It has been reported previously that repeated average cerebral blood flow measurements in the same individual in the steady state have given extremely constant results. This observation was also found to be true for measurement of HBF in the monkey. These findings provide...
CEREBRAL HEMISPHERIC BLOOD FLOW AND METABOLISM

LEFT CAROTID BOLUS

Femoral Artery

L. Trans. Sinus

HBF=32.5 ml/100 g brain/min

RIGHT CAROTID BOLUS

L. Trans. Sinus

HBF=34.7 ml/100 g brain/min

FIGURE 6

Hydrogen clearance curves from left transverse sinus in patient with right internal carotid occlusion. After injection of left carotid bolus, no hydrogen was recorded from femoral artery. After right carotid injection, hydrogen was distributed in the brain through collateral circulation and recorded in the transverse sinus.

strong evidence that in the steady state blood distribution from each hemisphere into each transverse sinus is constant as well as the HBF.

An additional advantage of the method is that in patients with internal carotid occlusion it is possible to measure the blood flow through the collateral channels. The possibility of extracerebral contamination using this method can be virtually excluded for the following reasons:

1. The tip of the venous catheter was placed high enough to avoid significant contamination of extracerebral origin.

2. Calculated blood flow values were higher than those reported as the extracranial blood flow.18

3. In one patient, after administration of a new cerebral vasodilator drug (hexobendine), the collateral blood flow via the external carotid artery was markedly increased without increase in systemic blood pressure.

4. In another patient, not included in the present series, with occlusion of the internal carotid artery and no collateral circulation demonstrated by arteriography, there was no recorded hydrogen clearance in the cerebral venous blood after injecting the bolus into the common carotid artery.

Comparison of the hydrogen bolus method with the inhalation method reveals certain limitations of the latter technique. The appearance of identical hydrogen clearance curves but at different partial pressures in both sinuses indicates incomplete side-to-side mixing of blood, which has been reported previously by other investigators.13, 14, 19-20 In one case, for example, the injected hydrogen appeared only in the ipsilateral sinus. Similar observations were reported by Nylin et al.21, 22 and Hedlund.23 In such cases, average cerebral blood flow using the inhalation method is heavily weighted in favor of hemispheric blood flow from the side sampled in spite of the fact that Kety and Schmidt24 found no significant differences in cerebral blood flow during simultaneous measurements from both internal jugular veins. In another study conducted in

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our laboratory in monkeys, the results of both the bolus and inhalation methods were in good agreement. This is to be expected since the monkeys were normal and there was probably little difference in blood flow between hemispheres.

Shenkin et al.\textsuperscript{19} injected dye into the internal carotid artery of one side only and concluded that two-thirds of the blood supplied to the hemisphere was drained through the ipsilateral jugular bulb. According to Hellinger et al.,\textsuperscript{25} about 60\% of the blood in the internal jugular vein comes from the ipsilateral hemisphere.

Although most investigators have assumed that the ratio of the concentration of the indicator in each jugular vein indicates the blood distribution from the injected hemisphere, this is only justified if the blood volume of each vein is the same. If this assumption is correct, our studies reveal that about 85\% of the blood derived from the right carotid territory and 65\% of the blood from the left carotid territory flow out through the ipsilateral jugular vein.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
Case no. & Age & Clinical diagnosis & Right HBF (ml/100 gm brain/min) & Left HBF (ml/100 gm brain/min) \\
\hline
1 & 60 & L. cerebral infarction & 30.5 & \\
2 & 62 & R. cerebral infarction & 36.3 & 36.7 \\
3 & 30 & R. cerebral infarction & 37.7 & 51.3 \\
4 & 49 & R. cerebral infarction & 42.2 & 47.0 \\
5 & 61 & L. cerebral infarction & 46.5 & \\
6 & 69 & L. cerebral infarction & 39.8 & 33.3 \\
7 & 43 & R. cerebral infarction & 35.0 & 36.3 \\
8 & 54 & R. cerebral infarction & 41.0 & 44.3 \\
9 & 57 & R. cerebral infarction & 31.4 & 41.2 \\
10 & 57 & R. cerebral infarction* & 38.2 & 44.0 \\
11 & 62 & R. cerebral infarction & 32.3 & \\
12 & 57 & R. cerebral infarction & 35.2 & \\
13 & 44 & L. cerebral infarction & 45.3 & 41.1 \\
14 & 52 & R. cerebral infarction & 35.1 & 47.5 \\
15 & 56 & R. cerebral infarction & 34.2 & 36.4 \\
16 & 59 & R. cerebral infarction & 38.7 & 38.8 \\
17 & 70 & R. cerebral infarction & & 37.0 \\
18 & 39 & R. cerebral infarction & 27.8 & 37.3 \\
19 & 74 & R. cerebral infarction & 34.7 & 32.5 \\
20 & 63 & L. cerebral infarction & 40.5 & 43.1 \\
21 & 42 & R. cerebral infarction & 36.7 & 40.2 \\
22 & 64 & Superior cerebellar artery syndrome & 39.8 & 38.9 \\
23 & 56 & Bilateral subcortical infarction* & 46.8 & 41.8 \\
24 & 55 & Bilateral subcortical infarction & 44.1 & \\
\hline
Mean & & & 38.6 & 39.4 \\
S.D. & & & ±5.0 & ±5.4 \\
\hline
25 & 46 & L. AV malformation & 53.6 & 246.3 \\
26 & 40 & Convulsive disorder & 41.5 & 40.8 \\
27 & 50 & Presenile dementia & 41.3 & 43.1 \\
28 & 67 & Arteriosclerotic dementia & 30.5 & 35.2 \\
29 & 60 & ALS with dementia & 37.5 & 37.4 \\
30 & 67 & Parkinson's disease & 36.7 & 31.5 \\
\hline
Mean & & & 37.5 & 37.6 \\
S.D. & ±10 & & ±4.5 & ±4.6 \\
\hline
\end{tabular}
\caption{HBF Values in Subjects with Neurological Disorders}
\end{table}

\footnotesize*Right internal carotid occlusion shown angiographically.  
†Amyotrophic lateral sclerosis.
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TABLE 3

Comparison of HBF Calculated from Left and Right Transverse Sinus Clearance Curves Simultaneously

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Ipsilateral sinus (ml/100 gm brain/min)</th>
<th>Contralateral sinus (ml/100 gm brain/min)</th>
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</thead>
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<tr>
<td>2</td>
<td>36.7</td>
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</tr>
<tr>
<td>Mean</td>
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<td>43.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>±5.6</td>
<td>±4.2</td>
</tr>
</tbody>
</table>

r = 0.79
P < 0.01

*Measurement made after administration of hexobarbital.

eral transverse sinus. This high ratio for the right side is especially true in cases of right internal carotid artery occlusion with collateral flow via the external carotid artery. Excluding the three cases of internal carotid occlusion (cases two, ten, and 23), after right carotid injection the calculated mean value of hydrogen distribution was about 75% in the ipsilateral transverse sinus and was not statistically significantly different from comparable values after left carotid injection. Although our finding differs from the results of the studies of Nylin et al. and Shenkin et al., whose tables of results and figures we carefully checked, it is noticeable that in many of their cases following right carotid injection the distribution of the indicator to the ipsilateral side is larger than after the injection on the left side. Nylin et al. also pointed this out in a later study.

From the above considerations, we have concluded that the conventional method for calculating cerebral metabolic rate using average cerebral blood flow or HBF multiplied by arteriovenous differences measured from one jugular vein may not always be correct. To eliminate such errors, the use of formulas 14 and 15 for measuring hemispheric metabolism are recommended. In the formula, if the ratio a or b equals 1, it is not possible to use the formula to calculate the hemispheric venous concentrations. However, such a situation would mean that mixing was complete, and in none of our patients did this occur. While anatomical factors play a part, it seems likely that flow in the sagittal sinus and, to some extent, in the confluence remains laminar, so that blood from one hemisphere drains mainly into the ipsilateral transverse sinus, as many investigators using different methods have pointed out. In cases in which f1 and/or f2 is 0 (as in case nine), the formula need not be used, but the hemispheric metabolic index can be calculated from HBF \times ipsilateral arterial transverse sinus differences for oxygen.

The blood sampled from the transverse sinus or internal jugular vein also contains some blood from the territory of the vertebrobasilar system. For this reason, the term “metabolic index” was used instead of “metabolic rate.” However, because of the limitations of the conventional method for measuring cerebral metabolic rate, the new formula for estimating hemispheric metabolism is believed to be more accurate than other methods.

All measurements discussed in this paper were done in the steady state and tabulated as mean values for each ten-minute interval. Simultaneous measurements of arteriovenous concentration differences for metabolites may be used, therefore, as valid estimates of hemispheric metabolism, despite the fact that the transit time of oxygen through the hemispheres is unknown.

Acknowledgment

The authors would like to express their appreciation

TABLE 4

Comparison of Right Carotid Bolus and Right Brachial Bolus

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Right carotid bolus (ml/100 gm brain/min)</th>
<th>Right brachial bolus (ml/100 gm brain/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>39.8</td>
<td>38.9</td>
</tr>
<tr>
<td>9</td>
<td>31.4</td>
<td>41.5</td>
</tr>
<tr>
<td>13</td>
<td>45.3</td>
<td>40.8</td>
</tr>
<tr>
<td>26</td>
<td>41.5</td>
<td>43.0</td>
</tr>
<tr>
<td>27</td>
<td>41.3</td>
<td>42.4</td>
</tr>
<tr>
<td>28</td>
<td>30.5</td>
<td>33.5</td>
</tr>
<tr>
<td>29</td>
<td>37.5</td>
<td>47.7</td>
</tr>
<tr>
<td>Mean</td>
<td>38.2</td>
<td>41.1</td>
</tr>
<tr>
<td>S.D.</td>
<td>±5.5</td>
<td>±4.3</td>
</tr>
</tbody>
</table>

r = 0.39
0.4 > P > 0.3
### TABLE 5
Comparison of HBF and Average CBF

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Right (ml/100 gm brain/min)</th>
<th>Left (ml/100 gm brain/min)</th>
<th>Mean of both HBF (ml/100 gm brain/min)</th>
<th>Average CBF (ml/100 gm brain/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>36.3</td>
<td>36.7</td>
<td>36.5</td>
<td>42.8(r)</td>
</tr>
<tr>
<td>3</td>
<td>37.7</td>
<td>51.3</td>
<td>44.5</td>
<td>47.9(r)</td>
</tr>
<tr>
<td>4</td>
<td>42.2</td>
<td>47.0</td>
<td>44.6</td>
<td>42.4(r)</td>
</tr>
<tr>
<td>23</td>
<td>46.8</td>
<td>41.8</td>
<td>44.3</td>
<td>44.1(r)</td>
</tr>
<tr>
<td>6</td>
<td>39.8</td>
<td>33.3</td>
<td>36.6</td>
<td>42.5(l)</td>
</tr>
<tr>
<td>9*</td>
<td>31.4</td>
<td>41.2</td>
<td>36.3</td>
<td>32.6(r)</td>
</tr>
<tr>
<td>26</td>
<td>41.5</td>
<td>40.8</td>
<td>41.2</td>
<td>40.3(l)</td>
</tr>
<tr>
<td>10</td>
<td>38.2</td>
<td>44.0</td>
<td>41.1</td>
<td>39.4(l)</td>
</tr>
<tr>
<td>29</td>
<td>37.5</td>
<td>37.4</td>
<td>37.5</td>
<td>41.2(r)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td></td>
<td>Mean of both HBF</td>
<td>40.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>S.D.</td>
<td>±3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>r = 0.54</td>
<td>0.2 &gt; P &gt; 0.1</td>
</tr>
</tbody>
</table>

*See text.
†( ) sampling side.

### TABLE 6
HBI-O₂ Index in Patients with Neurological Disorders

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Cerebral transverse sinus oxygen content</th>
<th>Arterial O₂ content</th>
<th>Ratio</th>
<th>HBI-O₂ (ml O₂/100 gm brain/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>volume %</td>
<td>volume %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusive cerebrovascular disease</td>
<td>12.05</td>
<td>12.50</td>
<td>17.46</td>
<td>22.80</td>
</tr>
<tr>
<td>7</td>
<td>9.19</td>
<td>9.58</td>
<td>17.52</td>
<td>1.66</td>
</tr>
<tr>
<td>8</td>
<td>8.51</td>
<td>8.76</td>
<td>14.47</td>
<td>1.90</td>
</tr>
<tr>
<td>9</td>
<td>12.14</td>
<td>11.28</td>
<td>17.64</td>
<td>∞</td>
</tr>
<tr>
<td>10</td>
<td>11.48</td>
<td>11.17</td>
<td>17.45</td>
<td>16.04</td>
</tr>
<tr>
<td>13</td>
<td>8.83</td>
<td>8.77</td>
<td>13.48</td>
<td>2.31</td>
</tr>
<tr>
<td>14</td>
<td>9.13</td>
<td>9.61</td>
<td>14.81</td>
<td>1.39</td>
</tr>
<tr>
<td>16</td>
<td>8.76</td>
<td>8.15</td>
<td>15.77</td>
<td>2.65</td>
</tr>
<tr>
<td>18</td>
<td>9.39</td>
<td>9.59</td>
<td>15.29</td>
<td>1.45</td>
</tr>
<tr>
<td>21</td>
<td>7.99</td>
<td>7.84</td>
<td>13.76</td>
<td>0.50</td>
</tr>
<tr>
<td>22</td>
<td>7.63</td>
<td>7.66</td>
<td>13.41</td>
<td>9.95</td>
</tr>
<tr>
<td>23</td>
<td>11.38</td>
<td>11.41</td>
<td>16.42</td>
<td>23.30</td>
</tr>
<tr>
<td>Arteriovenous malformation</td>
<td>14.80</td>
<td>15.90</td>
<td>17.50</td>
<td>2.86</td>
</tr>
<tr>
<td>Other neurological disorders</td>
<td>14.80</td>
<td>15.90</td>
<td>17.50</td>
<td>2.86</td>
</tr>
<tr>
<td>27</td>
<td>9.84</td>
<td>10.09</td>
<td>14.16</td>
<td>3.38</td>
</tr>
<tr>
<td>28</td>
<td>11.50</td>
<td>12.02</td>
<td>19.51</td>
<td>4.47</td>
</tr>
<tr>
<td>29</td>
<td>10.64</td>
<td>10.94</td>
<td>16.03</td>
<td>2.03</td>
</tr>
<tr>
<td>Mean</td>
<td>±10.20</td>
<td>±10.20</td>
<td>15.92</td>
<td>6.45†</td>
</tr>
<tr>
<td>S.D.</td>
<td>±1.91</td>
<td>±2.06</td>
<td>±1.82</td>
<td>±7.85</td>
</tr>
</tbody>
</table>

*For age and diagnosis see table 2.
†Mean value was calculated except case 9.

References


Fukuuchi, and N. Kok, who assisted in some aspects of this work.
CEREBRAL HEMISPHERIC BLOOD FLOW AND METABOLISM


A Method for Measuring Cerebral Hemispheric Blood Flow and Metabolism
JOHN STIRLING MEYER and YUKITO SHINOHARA

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