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ORIGINALS

Regional Cerebral Blood Flow and Blood Volume Measured With the Gamma Camera*

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Summary. Regional cerebral blood flow (rCBF), hemispheric blood flow (HBF), extracranial blood flow, and regional cerebral blood volume (rCBV) have been measured in a series of patients using a gamma camera equipped with a magnetic tape system for storage and retrieval. This method eliminates the need for multiple probes in measuring these parameters. ^{133}Xe and ^{99m}Tc injected into the carotid arteries were used as radioactive indicators. These measurements were carried out in patients with cerebral infarction, intracerebral hematoma, brain tumor, arteriovenous malformation, and dementia. The HBF values obtained with this method were in excellent agreement with those using the hydrogen bolus method in the same patients. The effects of 5% CO_2 inhalation, intravenous infusion of glycerol, and vasodilator drugs on rCBF and rCBV were evaluated and were found useful from diagnostic and therapeutic points of view. "Intracerebral steal" or "intracerebral squeeze" were demonstrated only in patients with space-occupying lesions such as intracerebral hematoma or brain tumor. Cerebral revascularization using a recently developed intracranial bypass procedure for the occluded internal carotid artery was found effective in increasing rCBF in selected cases where the procedure was successful.

Le flux sanguin cerebral regional et le volume sanguin mesure a l'aide de la gamma-camera

Résumé. Le flux sanguin cérébral régional, le flux sanguin hémisphérique, le flux sanguin extracrânien et le volume sanguin cérébral régional ont été mesurés chez une série de malades á l'aide de la gamma-caméra munie d'un système de bandes magnétiques pour enregistrement et relecture. Cette méthode élimine la nécessité de multiples essais pour mesurer ces paramètres. Le ^{133}Xe et le ^{99m}Tc injectés dans les artères carotides servent d'indicateurs radio-actifs. Ces mesures ont été effectuées chez des patients atteints de ramollissement cérébral, d'hématome intracérébral, de tumeur cérébrale, de malformation artério-veineuse et de démence. Les valeurs du flux sanguin cérébral hémisphérique correspondaient á celles obtenues par la technique de l'embol á hydrogène. Les effets d'inhalateurs de CO_2 á 5%, de perfusions intraveineuses de Glycérol et de vaso-dilatateurs sur le flux cérébral régional ont été déterminés et trouvés intéressants pour le point de vue diagnostique et thérapeutique. Des dérivations de sang ont été trouvées chez des malades atteints de lésions expansives (hématomes et tumeurs). Dans le cas de thrombose de la carotide interne, les mesures montrent une augmentation du glux sanguin cérébral régional lorsqu'une intervention par bypass est mise en oeuvre.

Regionaler cerebraler Blutdurchfluß- und Blutvolumen-Messungen mit der Gamma-Camera

Zusammenfassung. Nach Injektion von Xe 133 und Tc 99m in die A. carotis wurden der regionale cerebrale Blutdurchfluß und der Hemisphärenblutdurchfluß mit der Gamma-Camera bestimmt. Dabei konnten die gleichen Ergebnisse wie mit den übrigen punktförmigen Messungen nachgewiesen werden.

Numerous investigators during the last decade have measured regional cerebral blood flow (rCBF) using intracarotid injection of gamma-emitting radioisotopes and multiple scintillation detectors. These detectors, or probes, consist of small sodium iodide crystals equipped with straight bore or cone-shaped collimators and photomultipliers [1–10]. Heiss *et al.* [11] were the first to measure rCBF with the gamma camera using intracarotid injection of ^{133}Xe. We also have employed the gamma camera and a direct-store magnetic tape system which has the following advantages:

1. The gamma camera oscilloscope provides a continuous topographic display of the entire brain and extracerebral structures during the arrival and departure of radioisotopes. Occlusion and stenosis of the internal carotid artery or its major intracranial branches often can be recognized. Serial topographic photographs can be made of regional perfusion throughout the hemispheres and extracranial structures, and zones of hyperperfusion and hypoperfusion are immediately apparent. Regional desaturation curves can be selected from numerous replays of the tape without repeating the injection, so that it is possible to analyze the topographic patterns in areas of abnormal flow quantitatively.

2. After a single injection of ^{133}Xe, replays of the tape permit simultaneous measurements of rCBF from 30 or more areas of the brain and mean hemispheric blood flow (HBF). Relevant measurements of regional extracranial blood flow also can be made to determine the amount of extracranial contamination and patterns of collateral flow.

3. The high sensitivity collimator used with the gamma camera has 10000 parallel holes that provide better resolution than the $^1/_2$-inch straight bore or cone-shaped collimators commonly used with multiple probe systems. In this way, there is less overlapping of the areas measured.

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4. Though response variations over the face of a single large crystal do exist, they are relatively minor compared with those that occur with multiple small crystals.

5. Rapid sequential scintiphotography with ^{99m}Tc can be carried out during the same carotid artery puncture; thus, additional information can be obtained concerning the topographic appearance and pathology of the major cerebral vessels as well as estimates of regional cerebral blood volume (rCBV) and transit times. Repeat scintiphotography within one hour also reveals areas in which the blood-brain barrier is damaged (12—14].

In the study reported herein, rCBF, HBF, extracranial blood flow, and rCBV were measured in 49 patients using the gamma camera and intracarotid injection of ^{133}Xe and ^{99m}Tc. Seven of these patients underwent an intracarotid bypass procedure to restore blood flow to the area supplied by the occluded internal carotid artery.

Method

Premedication in each patient consisted of meperidine hydrochloride (Demerol®) 50 mg and atropine sulfate 0.4 mg. A conventional 19-gauge Cournand needle was used for selective puncturing of the internal carotid artery high up in the carotid triangle under local anesthesia. In a small number of patients in whom selective internal carotid puncture was technically difficult, common carotid puncture and selective catheterization of the internal carotid was done using a thin polyethylene catheter. Ten patients had common carotid injection for measurement of extracranial blood flow. The patient's head was securely positioned with adhesive tape so that the lateral surface was against the camera. The landmarks of the head were recorded on the camera oscilloscope with a capsule containing a small amount of ^{99m}Tc and then traced with a grease pencil on a plexiglass plate overlaying the scope. Four millicuries (2 ml) of ^{133}Xe were then injected into the internal carotid artery and blood flow data were recorded for 10 min on a magnetic tape. Serial photographs were obtained at 2-second intervals of the initial passage of isotope through the head. Ten min after the injection of ^{133}Xe, 2 mc of ^{99m}Tc (2 ml) were injected through the same needle, and data were recorded for 60 seconds. Serial photographs were obtained at 1-second intervals during the first passage of the isotope. Blood pressure and arterial pCO_2 were measured at intervals during the procedure. Appropriate correction of CBF for $PaCO_2$ variations were made in a few patients who had abnormal $PaCO_2$, using Reivich's formula [15].

When the study was completed, the tape was replayed and the data recorded on analogue charts. Regional curves for ^{133}Xe and ^{99m}Tc were recorded routinely from seven to eight standard areas over the cerebral hemisphere and from one area over the angle of the mandible to represent extracranial flow. Fig. 1 shows a typical ^{133}Xe clearance curve. The mean HBF for the entire hemisphere also was measured. In certain cases in which the topographic display revealed regional areas of special interest, detailed measurements were obtained by replaying the tape.

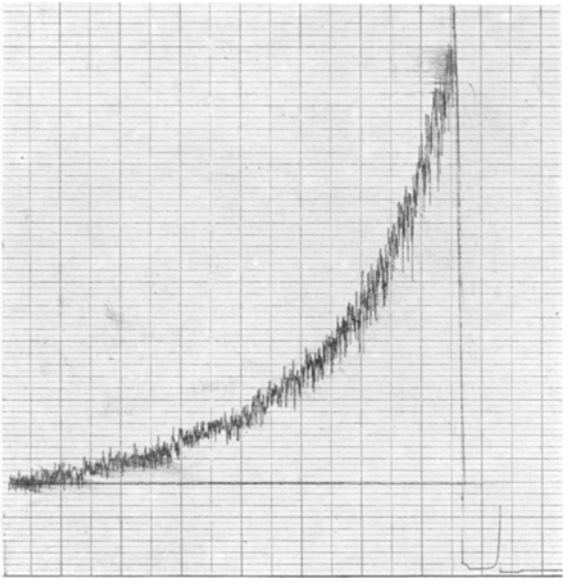

Fig. 1. Typical regional ^{133}Xe clearance curve

rCBF was calculated from the clearance curves of ^{133}Xe using the following formulas:

Stochastic (height over area) method

$$\text{rCBF}_{(10\text{ min})} = 100\ \bar{\lambda}\ \text{H/A ml/100 g brain/min}$$

where $\bar{\lambda}$ is the mean partition coefficient of ^{133}Xe for the whole brain adjusted for the hemoglobin content of the patient [7, 16—18]. H represents height of the clearance curve and A represents the area of the clearance curve.

Flow initial

$$\text{rCBF}_{(\text{initial 2 min})} = 100\ \bar{\lambda}\ \text{of cortex}\ \frac{0.693}{T^1/_2\ (\text{initial segment})}\ \text{ml/100 g brain/min}$$

where $\bar{\lambda}$ is the partition coefficient for cortex (grey matter) adjusted for hemoglobin content.

Regional cerebral blood volume. Regional cerebral blood volume was calculated using a formula based on theoretical considerations described by Fieschi *et al.* [19] and by Lassen [20].

$$t = \frac{V}{F}$$

where t is the transit time of ^{99m}Tc activity curves. V is rCBV and F is rCBF determined in ml/100 g brain/min by the ^{133}Xe method using H/A calculation. Hence, rCBV equals rCBF in ml/100 g brain/min times t in minutes; t is determined from the cerebral

curves of ^{99m}Tc using the method adopted by Fieschi *et al.* [19].

Case Material

The clinical diagnoses of the 49 patients in whom rCBF measurements were made are shown in Tab. 1. Diagnosis of arteriosclerotic dementia was made in elderly patients with progressive dementia, with the following clinical features: 1. waxing and waning character of mental functions; 2. stuttering progression; 3. associated hypertension, transient ischemic attacks, transient global amnesia, vertebrobasilar insufficiency, and cardiac dysfunction; and 4. focal neurological signs. The injection of ^{133}Xe was repeated at the end of five minutes of inhalation of 5% CO_2 in

Table 1. *Clinical diagnoses in patients in whom ^{133}Xe and ^{99m}Tc studies were performed*

Diagnosis	No. of patients
I. Stroke	
1. hemispheric infarction	19
2. complete internal carotid artery occlusion	7[a]
3. spontaneous hypertensive intracerebral hemorrhage	3
4. brain stem infarction	1
II. Dementia	
1. presenile type	2
2. arteriosclerotic type	14
III. Brain tumor	
1. primary glioma (astrocytoma)	2
IV. Arteriovenous malformation	1

[a] All 7 patients underwent intracranial bypass surgery.

9 patients with recent stroke, 1 with brain tumor, and 1 with arteriosclerotic dementia. In 2 of the 3 patients with spontaneous intracerebral hematoma, rCBF measurements were repeated after surgical evaluation of the hematoma.

Glycerol, 500 ml of a 10% solution, was administered intravenously in 2 patients with recent hemispheric infarction, 1 with intracerebral hematoma, and 1 with brain tumor and injection of ^{133}Xe was repeated. Serial rCBF studies were performed in 20 patients during a double-blind evaluation of a cerebral vasodilator drug. Measurements were performed in all patients before and during the drug trial. These measurements were made before surgery in the 7 patients who underwent the intracranial carotid bypass procedure for correction of complete occlusion of the internal carotid artery. This was done by injecting ^{133}Xe into the contralateral unoccluded internal carotid artery and monitoring the radioactivity from the hemisphere corresponding to the side of the occluded internal carotid artery. Postoperative measurements were made by injecting the radioisotope into the graft. Four patients had measurements made postoperatively, and rCBF measurements were repeated in 2 at intervals up to 3 months.

Results

In 13 patients with hemispheric infarction, the hydrogen bolus technique [21] also was used to measure HBF for purposes of comparison of results with the ^{133}Xe determinations (Tab. 2).

Table 2. *Comparison of Hemispheric blood flow measurements with the Hydrogen Bolus and ^{133}Xe methods in patients with hemispheric Infarction*

Case No.	Hydrogen Bolus method	^{133}Xe method
1	35.6	39.4
2	37.3	39.0
3	35.0	35.0
4	33.8	30.7
5	35.0	33.1
6	32.5	34.0
7	31.9	28.7
8	33.6	40.3
9	36.7	30.8
10	34.7	28.7
11	33.5	30.8
12	31.6	33.8
13	38.2	39.5
Mean	34.6	34.1
S.D.	±2.1	±4.2

Table 3. *Coefficient of interregional variation*

	Hemispheric infarction	Arteriosclerotic dementia
$rCBF_{10}$ (H/A_{10})	10±1.1%	13±1.2%
rCBF	23±2.2%	24±1.9%

The ^{133}Xe injection was repeated after 10 min in 5 patients with arterial pCO_2 and blood pressure measurements at the same level in order to check the reproducibility of the method. The second injection indicated an average reduction of 5.5% with a range of 3—10%.

Since several published reports [6, 8—10] were based on 2-min or initial rCBF values, a comparison was made of $rCBF_{10}$ (H/A_{10}) and $rCBF_{initial}$ in patients with hemispheric infarction and arteriosclerotic dementia. From the results obtained, an interregional difference exceeding 10—13% in $rCBF_{10}$ and 23—24% in $rCBF_{initial}$ may be considered abnormal (Tab. 3).

Correlation of rCBF values with clinical and angiographic features. The $rCBF_{10}$ values, in general, correlated well with the clinical and angiographic findings. Areas of greatly reduced rCBF corresponded well with angiographically demonstrated vascular occlusion. Reduced rCBF also was observed in stroke patients with neurologic deficits but in whom the arteriograms appeared normal. In all 3 patients with spontaneous intracerebral hemorrhage, areas of reduced rCBF corresponded with the site of hematoma which had been diagnosed clinically and confirmed by angiography and lumbar puncture.

In 2 patients with astrocytomas, there were distinctive regional abnormalities in perfusion rates. Vascularity was increased in the tumor in 1 patient, and the ^{99m}Tc injection indicated damage to the blood-brain barrier. A regional increase in rCBF occurred in one area of the tumor, but the mean HBF and blood volume were below normal due to increased intracranial pressure. In the second patient with a slowly growing, relatively avascular, cystic astrocytoma, the blood-brain barrier had sustained less damage and there was reduction in rCBF, HBF and rCBV.

Extracranial blood flow. ^{133}Xe was injected into the common carotid artery in 10 patients, and blood flow measurements were made in an area supplied entirely by the external carotid artery, i.e., over the distribution of the facial artery at the mandibular angle, to obtain extracerebral blood flow determination. Since we were measuring the blood flow over the masseter muscle, a lambda of 0.7, partition coefficient of ^{133}Xe in the muscle was used for calculation [16]. The average extracranial blood flow was 16 ± 1.1 ml/100 g tissue/min, or approximately 30% of the normal HBF. When the injection was made via a catheter or by selective puncture into the internal carotid artery, the average extracranial blood flow was much less — — 5 ± 1.3 ml/100 g/min, or approximately 10% of normal cerebral blood flow.

Activation tests of rCBF by inhalation of 5% CO_2. In 11 patients ^{133}Xe injection was repeated after 5 min of 5% CO_2 inhalation. The diagnoses and patterns of response are shown in Table 4.

Table 4. *Effect of 5% CO_2 inhalation on rCBF*

No. of Patients	Diagnosis	Pattern of response
3	Spontaneous intracerebral hemorrhage	Regional reduction in area of hemorrhage with increase in normal areas
6	Hemispheric infarction	Generalized increase in all areas but degree of increase less in infarcted regions
1	Brain tumor	Regional reduction in region of tumor with increase in normal regions
1	Arteriosclerotic dementia	Generalized increase in all areas

Arterial pCO_2 was estimated before and after inhalation. In the patient with arteriosclerotic dementia, rCBF was increased in all areas measured, confirming that the reactivity of the cerebral vessels is retained in patients with this disease [22].

Intracranial pressure at the time of the initial rCBF measurement was high (CSF pressure above 220 mmH_2O) in all 3 patients with intracerebral hemorrhage. A regional reduction of rCBF after CO_2 inhalation occurred in each patient in the area of the intracerebral hematoma. In 2 patients in whom the hematomas were evacuated surgically, ^{133}Xe measurements repeated 3—4 weeks later showed that the regional reduction of rCBF in response to CO_2 had disappeared (Figs. 2 and 3).

There was no detectable regional reduction in rCBF in response to CO_2 inhalation in any of the 6 patients with ischemic hemispheric infarction; *e.g.*, no "intracerebral steal" or "intracerebral squeeze" [23] was apparent.

Effect of reducing intracranial pressure by intravenous infusion of glycerol on rCBF. Measurement of rCBF with ^{133}Xe was repeated in 2 patients with

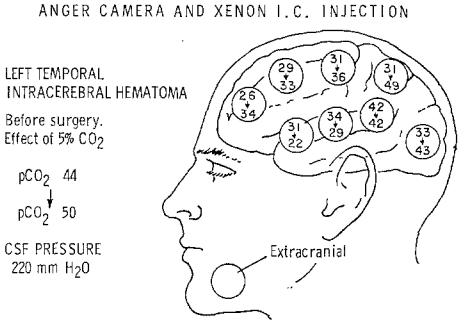

Fig. 2. rCBF values in a patient with spontaneous hypertensive intracerebral hematoma in the left temporal region before surgical evancuation. Lower figures are rCBF values after inhalation of 5% CO_2

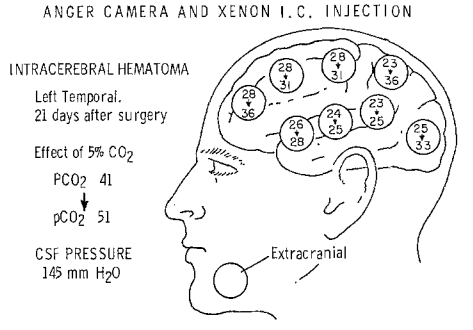

Fig. 3. Same patient as shown in Fig. 2 21 days after surgical evacuation of hematoma. Note the disappearance of regional reduction in rCBF in the area of the hematoma

cerebral hemispheric infarction, 1 with astrocytoma, and 1 with intracerebral hematoma after intravenous infusion of 50 g of glycerol (500 ml of a 10% solution in 5% dextrose) [24] over a period of 45 min. CSF pressure was reduced in all patients following the infusion. The mean rCBF in all regions measured increased 14.5%, and in areas of maximum infarction the mean increase was 31.9%. Mean HBF increased 11.9%. The effect of glycerol on the rCBF and CSF pressure in a patient with acute cerebral infarction is shown in Fig. 4.

rCBF measurements in the dementias. In all 16 patients with dementia (2 presenile and 14 arteriosclerotic) HBF and rCBF values were below normal, ranging from 22 to 41 ml/100 g brain/min. The regional reduction was strikingly characteristic of the disease,

with minimal values recorded from frontal and temporal regions. Typical rCBF values in a patient with arteriosclerotic dementia are shown in Fig. 5. The quantitative degree of reduction in HBF and rCBF in all patients correlated well with the degree of dementia as determined by a battery of neuropsychological tests. The arteriograms in these patients revealed diffuse irregularities of the cerebral vessels or no abnormality at all; thus, the rCBF determinations were

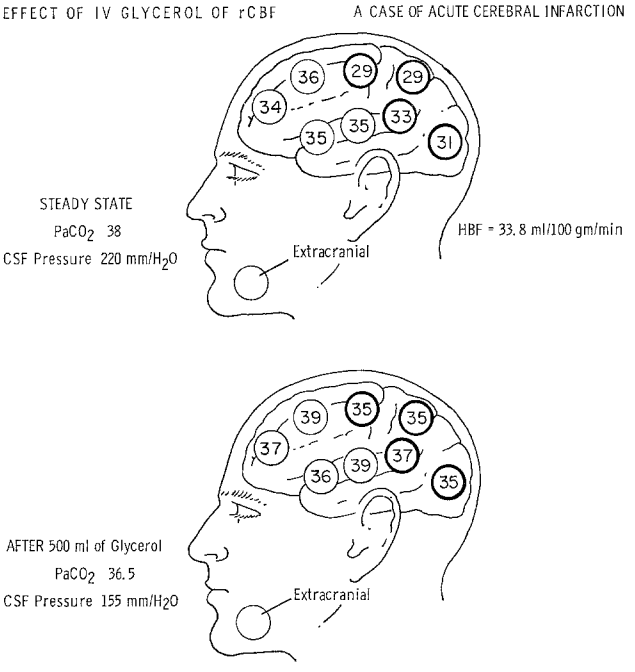

Fig. 4. The effect of intravenous injection of glycerol in a patient with acute cerebral infarction

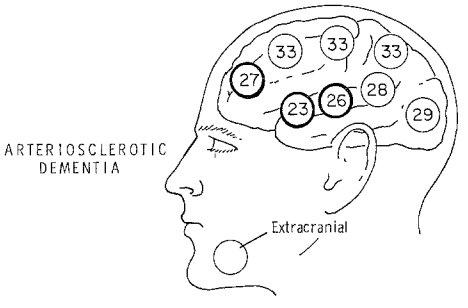

Fig. 5. Typical rCBF values in a patient with arteriosclerotic dementia. The circles with darker outlines indicate areas of minimum blood flow

of value in making a more definitive diagnosis. In 1 patient with arteriosclerotic dementia, rCBF increased approximately 30% during 5% CO_2 inhalation. In a double-blind evaluation of the effect of the cerebral vasodilator drug, hexobendine, on rCBF and HBF in patients with dementia, we found improvement of rCBF and HBF with long-term treatment. The results are published elsewhere [25].

Cerebral revascularization for occlusion of the internal carotid artery by intracranial bypass. In the past 6 months, 7 patients with occlusion of the cervical portion of the internal carotid artery and consequent cerebral infarction have undergone bypass grafts from the common carotid to the intracranial carotid artery with a segment of the saphenous vein in an attempt to revascularize the brain. rCBF studies were performed in all of them prior to the procedure, as described

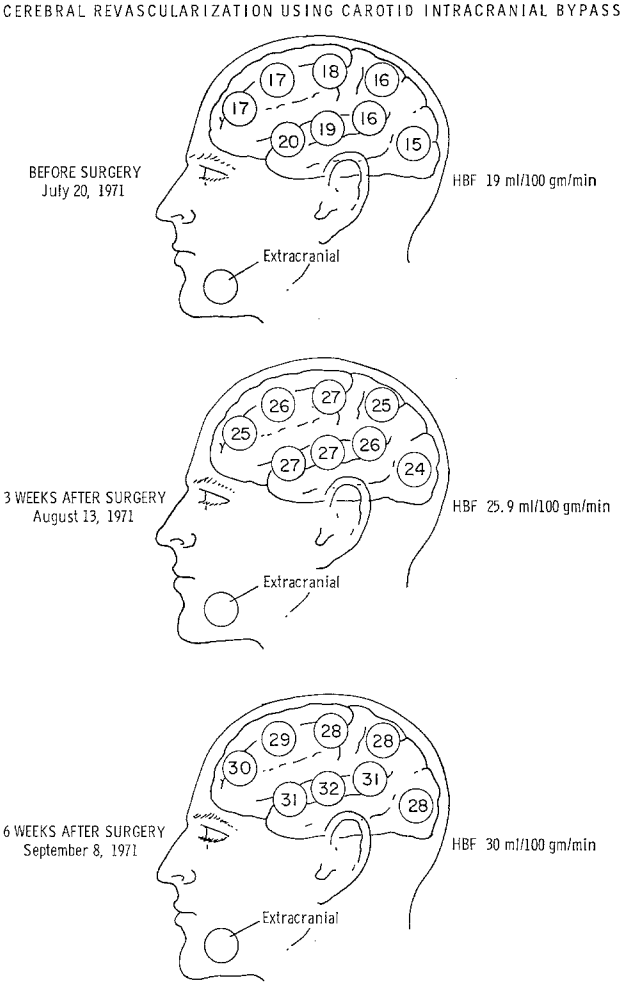

Fig. 6. rCBF measurements in a patient with complete occlusion of the internal carotid artery treated surgically by intracranial bypass procedure show a progressive increase in blood flow

before. The average rCBF on the occluded side in these patients was 19 ± 1.4 ml/100 g brain/min. The rCBF measurements were performed again in 4 patients after bypass surgery by injecting ^{133}Xe into the graft. In 2 patients in whom the procedure was successful, HBF and rCBF increased and continued to increase with the passage of time (Fig. 6). For example, the rCBF study repeated 3 weeks after surgery in 1 patient showed an increase of 41%, and after 6 weeks the increase was 58%.

Measurement of rCBV. In the patients with cerebral infarction, the average rCBV was 4.2 ± 0.5 ml/100 g/min, with marked reductions limited to the areas of infarction. The rCBV in patients with dementia, however, was diffusely reduced, predominantly in the frontotemporal regions, with an average value of 3.8 ± 0.4 ml/100 g/min.

In general, our measurements indicated that both rCBF and rCBV were reduced moderately in areas of cerebral infarction and greatly reduced in intracerebral hematoma accompanied by increased CSF pressure. In patients with brain tumor and intracerebral hematoma, CO_2 inhalation caused a further reduction in rCBV and rCBF in the area of the lesion by increasing the intracranial pressure. This "intracerebral steal" or "squeeze" phenomenon is reversed when the hematoma is evacuated.

Discussion

Although external monitoring of radioactivity after intracarotid injection of gamma-emitting radioactive substances does have certain limitations such as Compton scatter, absorption of radioactive material by extracerebral tissue, and problems due to recirculation, the method is still the most suitable of the currently available techniques for measuring rCBF. It is a practical diagnostic test suitable for widespread clinical use. The greater resolution and other advantages of the gamma camera over the multiple probe system are now well extablished [11, 12], and have been described in detail in the introduction.

In 13 of our patients with infarction of one hemisphere, the HBF values obtained using the hydrogen bolus technique and calculated by means of the Meier-Zierler equation were compared with the values obtained with the ^{133}Xe and gamma camera technique. The results of the two methods were in excellent agreement. Since the hydrogen bolus method [21] does not require the use of partition coefficients ($\bar{\lambda}s$) for the calculation of HBF and comparable results are obtained with the two methods, certain assumptions concerning $\bar{\lambda}$ for ^{133}Xe appear justified and the reliability of the ^{133}Xe method also is established.

The average decrease of 5.5% in mean rCBF obser-v ed during the second injection was thought to be due to recirculation of ^{133}Xe and incomplete clearance from the white matter. Paulson [26] observed an average reduction of 13% (range 3—27%) in $rCBF_{initial}$ values after repeat injections.

In the present study, after the second injection of ^{133}Xe into the common carotid artery, the average reduction was in the range of 25% due to the absorption of a considerable amount of radioisotope by the tissues supplied by the external carotid artery. This high reduction in rCBF, together with the fact that average external carotid artery flow monitored from the mandibular angle is approximately 30% of normal HBF, emphasizes the need for selective internal carotid artery injection in order to avoid fallacious results. Even after selective injection of the internal carotid artery, there was measurable blood flow in the external carotid territory. This may be accounted for partly by reflux into the common carotid artery with retrograde filling of the external carotid system and partly by the normal anastomotic communications between the external and internal carotid arterial systems.

Rees *et al.* [27], in a recent study, compared rCBF determinations analyzed with the stochastic method with those determined from 2-compartmental analysis and the $rCBF_{initial}$ methods. They concluded that in normal subjects the stochastic method (H/A_{10}) is satisfactory for determining rCBF, and the correlation between the results obtained with the 2 methods is good in normal persons; however, in disease states such as infarction, the correlation is less satisfactory.

In the present study, in patients with hemispheric infarction and those with arteriosclerotic dementia, the interregional coefficient of variation determined by the stochastic method was in the range of 10—13%, while with the $rCBF_{initial}$ method it was 24%. Paulson [26] found in a control group of 11 patients without cerebrovascular disease that the average interregional coefficient of variation with the $rCBF_{10}$ method was 8.5% and the average with the $rCBF_{initial}$ method was 10.6%. Since all of our patients had cerebrovascular disease or some other form of intracranial involvement, a high value for regional coefficient of variation is not surprising. In order that the results of functional and therapeutic tests such as CO_2 inhalation, glycerol infusion, and vasodilator therapy could be compared, the $rCBF_{10}$ method rather than the $rCBF_{initial}$ method was used since the latter method has a high interregional coefficient of variation.

Paradoxical responses to 5% CO_2 inhalation were demonstrated only in patients with space-occupying lesions. CSF pressure was elevated in all these patients. These paradoxical responses with the phenomenon of focal reduction of rCBF after 5% CO_2 inhalation can be explained only by a further increase in intracranial pressure caused by vasodilatation in normal brain or increased edema in abnormal brain which "squeezed" blood from the mass lesion or both. For these reasons, the term "intracerebral squeeze" better defines this paradoxical effect than "intracerebral steal." In our patients with cerebral infarction, even when in the acute stage, there was no evidence of a paradoxical response to 5% CO_2 inhalation. McHenry *et al.* [28] likewise rarely if ever observed "intracerebral steal" with 5% CO_2 inhalation or vasodilator drugs in patients with cerebral infarction. In our patients with cerebral infarction, 5% CO_2 significantly increased HBF and rCBF, although the degree of increase in the regions of infarction was not as great as in normal brain. Dynamic data of this type obtained during 5% CO_2 inhalation are of diagnostic value in differentiating space-occupying lesions from ischemic areas.

Meyer *et al.* [29] demonstrated that reduction of cerebral edema in experimental cerebral infarction increased cerebral blood flow. In a therapeutic trial using intravenous glycerol, the mortality rate was reduced in patients with cerebral edema due to acute cerebral infarction [24]. The effect of intravenous glycerol in reducing cerebral edema and intracranial pressure and increasing rCBF in zones of infarction and hemorrhage was a consistent finding not only in the 4 patients described in this paper but also was observed in a study of a large group of patients with acute stroke in whom cerebral blood flow and metabolism was measured with the hydrogen bolus method [30]. The increase in rCBF in the areas of focal cerebral edema in the present series was striking.

Reduction of rCBF in patients with dementia has been reported by a number of workers [22, 31, 32]. In all of our patients with presenile and arteriosclerotic dementia, rCBF and HBF values were low. The reductions were predominantly in frontotemporal regions in both groups, although there were some exceptions. In addition, focal reduction in rCBF in various areas corresponding to clinical focal neurological abnormality could be found in cases of arteriosclerotic dementia. Simard *et al.* [22] reported that reduction in rCBF in frontotemporal regions was characteristic of presenile dementia. The increases in rCBF after 5% CO_2 inhalation or long-term administration of vasodilator drugs confirm the reports of others that the vascular reactivity in patients with dementia is preserved [22]. Such uniform observations are clinically relevant since long-term treatment of these patients with vasodilator drugs early in the course of the disease may prevent or retard the dementing process. Extensive clinical trials to test this hypothesis are in progress at the moment in this stroke center.

The progressive increase in rCBF and HBF noted in patients who have undergone cerebral bypass procedures for occlusion of the internal carotid artery can be explained by progressive increases in cerebral metabolism and revascularization of previously ischemic areas since these changes are associated with improvement of cerebral function.

Finally, rCBV measurements combined with rCBF measurements also are of value in diagnosis. Normal rCBV ranges from 5—6 ml/100 mg/min. Zones in which rCBF and rCBV are increased are likely to be involved by arteriovenous malformations, hyperemia, or neovascularization in tumors with arteriovenous shunting. Zones of decreased rCBF and rCBV are probably infarcted or atrophic. In zones of infarction, this pattern of reduced blood flow and blood volume is regional, while in the case of presenile or arteriosclerotic dementia it is diffuse with a frontotemporal preponderance.

References

1. Lassen, N.A., Ingvar, D.H.: The blood flow of the cerebral cortex determined by radioactive krypton. Experientia **17**, 42—43 (1961).
2. Fieschi, C., Agnoli, A., Battistini, N., Bozzao, L.: Regional cerebral blood flow in patients with brain infarcts. A study with the ^{85}Kr clearance technique. Arch. Neurol. (Chicago) **15**, 653—663 (1966).
3. Fieschi, C., Agnoli, A., Battistini, N., Bozzao, L., Prencipe, M.: Derangement of regional cerebral blood flow and of its regulatory mechanism in acute cerebrovascular lesions. Neurology (Minneap.) **18**, 1166—1179 (1968).
4. Agnoli, A., Fieschi, C., Battistini, N., Prencipe, M.: Autoregulation of cerebral blood flow. Studies during drug-induced hypertension in normal subjects and in patients with cerebral vascular disease. Circulation **28**, 800—812 (1968).
5. Cronqvist, S.: Regional cerebral blood flow and angiography in apoplexy. Acta radiol. (Diagn.) (Stockholm) **7**, 521—534 (1968).
6. Høedt-Rasmussen, K., Skinhøj, E., Paulson, O., Ewald, J., Bjerrum, J.K., Fahrenkrug, A., Lassen, N.A.: Regional cerebral blood flow in acute apoplexy. The "luxury perfusion syndrome" of brain tissue. Arch. Neurol. (Chicago) **17**, 271—281 (1967).
7. Høedt-Rasmussen, K., Sveinsdottir, E., Lassen, N.A.: Regional cerebral blood flow in man determined by intra-arterial injection of radioactive inert gas. Circulat. Res. **18**, 237—247 (1966).
8. Høedt-Rasmussen, K.: Regional cerebral blood flow: The intra-arterial injection method. Acta neurol. scand. **43** (suppl. 27), 1—79 (1967).
9. McHenry, L.C., Jr., Jaffe, M.E., Goldberg, H.I.: Regional cerebral blood flow measurement with small probes. I. Evaluation of the method. Neurology (Minneap.) **19**, 1198—1206 (1969).
10. Jaffe, M.E., McHenry, L.C., Jr., Goldberg, H.I.: Regional cerebral blood flow measurements with small probes. II. Application of the method. Neurology (Minneap.) **20**, 225—237 (1970).
11. Heiss, W.-D., Kvicala, V., Prosenz, P., Tschabitscher, H.: Gammacamera and multichannel analyzer for multiocular rCBF measurements. In: Brock, M., Fieschi, C., Ingvar, D.H., Lassen, N.A., Schürmann, K. (Eds): Cerebral blood flow: Clinical and experimental results, 29—30. Berlin-Heidelberg-New York: Springer 1969.
12. Powell, M.R., Anger, H.O.: Blood flow visualization with scintillation camera. J. Nucl. Med. **7**, 729—732 (1966).
13. Kennady, J.C., Potter, R., Chin, F., Swanson, L.: Assessment of cerebral lesions by rapid sequential scintiphotography. J. Nucl. Med. **9**, 423—425 (1968).
14. Penning, L., Front, D., Beekhuis, H.: Differentiation of brain lesions by sequential gamma camera studies. J. Neurol. Sci. **14**, 1—13 (1971).
15. Reivich, M.: Arterial pCO_2 and cerebral hemodynamics. Amer. J. Physiol. **206**, 25—35 (1964).
16. Conn, H.L.: Equilibrium distribution of radioxenon in tissue: Xenonhaemoglobin association curve. J. Appl. Physiol. **16**, 1065—1070 (1961).
17. Isbister, W.H., Schofield, P.F., Torrance, H.B.: Measurement of the solubility of xenon-133 in blood and human brain. Phys. Med. Biol. **10**, 243—250 (1965).
18. Veall, N., Mallett, B.L.: The partition of trace amounts of xenon between human blood and brain tissues at 37 degrees C. Phys. Med. Biol. **10**, 375—380 (1965).
19. Fieschi, C., Agnoli, A., Battistini, N., Bozzao, L.: Relationships between cerebral transit time of non-diffusible indicators and cerebral blood flow. A comparative study with krypton-85 and radioalbumin. Experientia **22**, 189—190 (1966).
20. Lassen, N.A.: Regional cerebral perfusion studied by intraarterial injection of Kr^{85} or Xe^{133}: Theoretical

considerations. In: Eichhorn, O., Lechner, H., Aurell, K.-H. (Eds): Scientific and clinical research on the cerebral Circulation; summary of the Second International Salzburg Conference, 159—165. Wien: Verlag Brüder Hollinek 1964.
21. Meyer, J.S., Shinohara, Y.: A method for measuring cerebral hemispheric blood flow and metabolism. Stroke **1**, 419—431 (1970).
22. Simard, D., Olesen, J., Paulson, O.B., Lassen, N.A., Skinhøj, E.: Regional cerebral blood flow and its regulation in dementia. Brain **94**, 273—288 (1971).
23. Welch, K.M.A., Meyer, J.S.: Control of cerebral blood-flow. Lancet **1970 II**, 1316
24. Meyer, J.S., Charney, J.Z., Rivera, V.M., Mathew, N.T.: Treatment with glycerol of cerebral oedema due to acute cerebral infarction. Lancet **1971 II**, 993—997.
25. — Mathew, N.T., Shimazu, K.: Clinical management of cerebral ischemia. In: Cerebral vascular diseases. Proceedings of the 8th Princeton Conference. New York: Grune & Stratton (in press).
26. Paulson, O.B.: Regional cerebral blood flow in apoplexy due to occlusion of middle cerebral artery. Neurology (Minneap.) **20**, 63—77 (1970).
27. Rees, J.E., Bull, J.W.D., DuBoulay, G.H., Marshall, J., Ross Russell, R.W., Symon, L.: The comparative analysis of isotope clearance curves in normal and ischemic brain. Stroke **2**, 444—451 (1971).
28. Jaffe, M.E., McHenry, L.C., Jr., Goldberg, H.I.: Regional cerebral blood flow studies in middle cerebral artery occlusion and stenosis. Circulation **38** (suppl. 6), 106 (1968).
29. Meyer, J.S., Teraura, T., Marx, P., Hashi, K., Sakamoto, K.: Brain swelling due to experimental cerebral infarction. Changes in vasomotor capacitance and effects of intravenous glycerol. Brain (submitted).
30. Meyer, J.S., Fukuuchi, Y., Shimazu, K., Ohuchi, T., Ericsson, A.D.: Effect of intravenous infusion of glycerol on hemispheric blood flow and metabolism in patients with acute cerebral infarction. Stroke **3**, 141 (1972).
31. Ingvar, D., Obrist, W., Chivian, E., Cronqvist, S., Risberg, J., Gustafson, L., Hägerdal, M., Wittbom-Cigén, G.: General and regional abnormalities of cerebral blood flow in senile and "presenile" dementia. Scand. J. Lab. Clin. Invest. (suppl. 102), **XII**: **B** (1968).
32. Obrist, D.W., Chivian, E., Cronqvist, S., Ingvar, D. H.: Regional cerebral blood flow in senile and presenile dementia. Neurology (Minneap.) **20**, 315—322 (1970).

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