Regional Cerebral Blood Flow in Patients with Intracranial Tumors

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For many years a wealth of information concerning the vascular histopathology of brain tumors and their angiographic appearance has been available. The histological appearance of abundant proliferating thin-walled vessels might suggest that these vessels allow a high blood flow value and that they possess little capacity for normal active regulation of vessel diameter. Furthermore, cerebral tumors would seem to affect the function and the circulation of neighboring cerebral structures. With these circulatory aspects of cerebral tumors in mind it was decided to study some tumor cases, applying the newly developed regional cerebral blood flow (rCBF) technique based on $^{133}$Xenon clearance measurements, in order to gain more quantitative data than that obtainable by angiography. In preliminary studies by Cronqvist, et al., abnormally high rCBF values were commonly seen in the region of cerebral tumors. Their findings have been confirmed in the present study which, in addition, emphasizes certain grossly pathological CBF responses to changes in arterial carbon dioxide tension or arterial blood pressure in the focal and perifocal regions of the brain of patients suffering from cerebral tumors.

Method

The $^{133}$Xenon clearance method has been described previously. It will therefore be presented only briefly here. Sixteen extracranial scintillation detectors with NaI (TI) crystals were used to follow the washout clearance of the radioactive inert gas administered by rapid intraarterial injection. Each crystal measured 11.5 mm in diameter and 5 mm in thickness, and the internal dimensions of the lead collimator were for each crystal 12 mm in diameter and 43 mm in length. The impulses coming from the probes, after discrimination, were stored on magnetic tape and subsequently replayed via a scaler and a ratemeter coupled to a writing potentiometer. The ratemeter and writer had a time constant of 1 sec.

A solution of 2 or 3 mCi of $^{133}$Xenon dissolved in 4 to 5 ml saline was injected over 1 to 2 sec through a polyethylene catheter into the internal carotid artery, and the clearance curves in the control state were followed for 10 min (Fig. 1). A maximal counting rate of about 25,000 counts/min was reached in most channels. From these 16 linear curves, the average blood flow of each region was calculated by the equation:

$$rCBF_{(10)} = \frac{\lambda \cdot \Delta H \cdot 100}{\Delta A} \text{ml/100 g/min,}$$

(1)

where $\lambda$ is the partition coefficient of $^{133}$Xenon between the blood and average brain tissue (a value of 1.15 being usually used in non-anemic subjects); $\Delta H$ is the difference between the maximal height of the curve at the beginning and at 10 min (the maximal impulse counting rate in counts per min minus that after 10 min of clearance); 100 is a constant that converts the flow value into the unit of flow per min for 100 g of tissue; and $\Delta A$ is the total area under the linear clearance curve for the 10 min of clearance. This value is read directly from the scaler as the sum of all of the impulses during the 10-min examination period minus the background counting rate.

To examine the normal and pathological responses of the cerebral circulation to various artificially induced stimuli, the following so-called “functional tests” have been used: hypocapnia induced by voluntary hyperven-
tilation; hypercapnia induced by inhalation of 8% CO₂ in air; hypertension induced by intravenous infusion of either Angiotensin or Aramine; hypotension induced by injecting Prozil or Ansolysen.

During the functional tests, clearance curves were logarithmically recorded for 2 min. The flow in each region was estimated from the initial slope of the clearance curve (Fig. 1),

\[ \text{rCBF}_{(\text{initial})} = 100 \cdot \lambda_x \cdot 2.30 \cdot D \text{ ml/100 g/min}, \]

where \( \lambda_x \) is the partition coefficient of ¹³³Xenon between blood and gray matter of the brain, a value selected since the initial slope is normally dominated by the blood flow of the gray matter. A standard value of 0.88 is used, as then the entire constant 100 \( \cdot \lambda_x \cdot 2.30 \) becomes simply 200. The 2.30 value is approximately equal to \( \log_{10} 10 \); it is the factor that converts decade logarithmic values (\( \log_{10} \)) to natural logarithm (\( \log_e \)) as follows:

\[ \log_e x \approx 2.30 \cdot \log_{10} x. \]

In Eq. 2, \( D \) is the numerical value of the slope of the curve in the first minute.

The logarithmical clearance curve of the normal brain tissue in the first 2 min is always practically monoeponential during eucapnia. After the first 2 min the slope decreases, and typically the normal curve followed logarithmically for 10 min can be described by two exponential functions. This decrease in the initial slope after 2 min occurs earlier, after only 1.5 or even after only 1.0 min at very high flow value (CBF > 70 ml/100 g/min). This normal phenomenon is due to the more rapid desaturation of the fast component at the high flow level and called “curve transformation.” In practice it is usually not difficult to distinguish curve transformation from pathological multiexponential 2-min curves, as the latter occur at any flow level and tend to have a much more pronounced and more early bending.

In the temporal region a very fast component is seen at the start of the clearance curve due to Xenon passing rapidly through this region within the large cerebral arteries to reach cerebral tissue in other parts of the brain (Fig. 2). This shunt-like peak is here called the “carotid peak” to emphasize its origin and location.

**Normal Cerebrovascular Regulation**

In attempting to understand the alterations in rCBF which one observes with intracranial neoplasms when applying the above mentioned functional tests, it is necessary to have a basic understanding of the normal cerebral vascular regulation. A brief summary of the normal responses of the cerebral vessels is therefore given here.
Although the perfusion pressure for the CBF is provided by the systemic blood pressure, the CBF is normally independent of variations in the systemic pressure. That is, over a fairly wide range of mean arterial blood pressure (60 to 150 mm Hg) the CBF remains relatively constant (within ±10%) because of the normal autoregulation of the cerebral circulation. The normal value of the rCBF is 50 ml/100 g/min and rCBF is 55 ml/100 g/min. Under physiological conditions the arterial carbon dioxide tension exerts a profound effect upon the contractile elements of the cerebral vessels; hypercapnia increases the flow while hypocapnia results in a decreased flow. The correlation between CBF and aPCO$_2$ within the range of 25 to 60 mm Hg is approximately rectilinear. Within this range the rise in CBF per millimeter rise in aPCO$_2$ is about 3% of the CBF at aPCO$_2$ equals 40 mm Hg.

Inhalation of CO$_2$ regularly produces hypotension, the level of blood pressure increasing as the concentration of inhaled CO$_2$ increases. By comparing the response to CO$_2$ inhalation to that of pressor amine infusion, the effect of hypercapnia per se may be evaluated.

**Clinical Material**

We performed 23 examinations on 21 patients with intracranial tumors. In one patient with cerebral metastases both hemispheres were studied (Studies No. 15 and 16), and in one patient with a meningioma the tumor-involved hemisphere was studied twice (Studies No. 7 and 9). Six investiga-
### Summary of main findings in 23 investigations

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† = the patient was investigated twice in a hypertensive state.

* = Local ischemia and no hyperemia was found.

± = uncertain.

The diagnoses (3 meningiomas, 5 metastases, 4 gliomas, and 9 glioblastomas) were based on several or all of the following examinations: clinical evaluation, CSF examination, EEG, radioisotope brain scanning, serial angiography, pneumoencephalography, and operative or necropsy histopathology. It was not possible to study the correlation between blood flow data and intracranial pressure, since the latter was considered to be contraindicated by the clinical state of the patients. Considering that CSF pressure is not constant and that it is changed by the functional tests used, it would have been necessary to measure it during each of these artificially induced states to obtain data valid for comparison to the flow measurements.
Results: Control Tests

Regional CBF$_{10}$ Values in the Control State. The average blood flow for the entire hemisphere during the control state (normo-tension and normocapnia) calculated as the average of the 16 rCBF$_{10}$ values, was sub-normal in the group of patients taken as a whole. The mean of the averages was 34 ml/100 g/min (SD = 3), as compared to the normal value of 50 ml/100 g/min (SD = 4). If 42 ml/100 g/min is considered the lower limit of normality, only three cases in the entire group fell within the normal range. Of these three cases one showed extremely high rCBF$_{10}$ values (68–87 ml/100 g/min) over the tumor region and low-normal values outside the tumor region. In the second case the mean CBF was 46 ml/100 g/min but the aPCO$_2$ was 46.5 mm Hg. After correction to a normal aPCO$_2$ of 40 mm Hg, the mean rCBF$_{10}$ was therefore abnormally low even in this case. The third case was a meningioma with a mean rCBF$_{10}$ of 44 ml/100 g/min at a normal aPCO$_2$ of 39.9 mm Hg.

In 13 cases (56%) the rCBF$_{10}$ values over the tumor region were significantly higher than in the non-tumor regions. The rCBF$_{10}$ values were more than 15% higher than the mean value in two or more neighboring channels (Fig. 3); in three cases the deviation was greater than 30% in more than two channels.

Three cases (13%) showed only equivocal focal hyperemia in that more than a +15% deviation was shown by only one channel or the deviations were less than 15%. In six cases (26%) there was no significant difference in rCBF$_{10}$ between tumor and non-tumor regions. In one patient (5%) with a cystic and poorly vascularized tumor, the lowest rather than the highest rCBF values were observed in the tumor region. Surrounding the tumor region was an area of relative hyperemia.

Shape of the Logarithmically Recorded 2-min Clearance Curves in the Control State. In 20 investigations, abnormal non-monoexponential logarithmic 2-min clearance curves were found over and immediately surrounding tumor regions (Fig. 2, see also Fig. 4 and 5). In many of the tumor cases, extremely steep initial slopes were seen, and this was particularly notable in the group of glioblastomas. If this steep initial slope is expressed in terms of the rCBF$_{10}$, a relatively hyperemic tissue component was revealed over the tumor region of these studies.

Fig. 3. Focal hyperemia over a cerebral tumor. Circled numbers represent the per cent deviation from the average of the rCBF$_{10}$ values in each region and the hatched area represents the tumor locus. (Study No. 11)

Following this steep initial component, the “second component” of the 2-min clearance curve over the tumor regions usually indicated lower flow than the mean flow over the non-tumor regions (Fig. 2). Over highly vascularized tumors, an extremely fast flow component lasting only a few seconds was frequently observed (Fig. 2). These extremely fast components, the so-called “shunt peaks,” were followed by a less fast intermediate component. Finally, a third component was observed which was almost always lower than the average flow for the hemisphere. This intermediate component has never been seen in association with the previously mentioned normal “carotid peak,” seen over the temporal region (Fig. 2).

In three studies only monoexponential 2-min curves were seen during the resting state. During the functional tests, however, multieponential curves also appeared in each of these cases.

Apart from the above mentioned abnormalities in the descending portion of the 2-min logarithmically recorded clearance curves, alterations were frequently seen in the ascending and maximum portion of the curves. A brief plateau at the maximum of the curve and a delayed maximum of the curve (see Fig. 2), have been frequently
Fig. 4. Focal hyperemia over a cerebral tumor. The initial part of the logarithmically recorded clearance curve demonstrating the steeper initial rate of clearance in areas 2, 6, and 9. (Study No. 22)

Fig. 5. Logarithmic recording of 16 clearance curves during resting state. The hatched area represents the tumor locus. (Study No. 11)
found in our clinical material. Both types of alterations have also been found occasionally in normal cases therefore they cannot be considered as unquestionable pathological signs. Due to a fairly low counting rate a time constant shorter than 1 sec could not be used in our studies. For this reason a more detailed analysis of the initial curve segment could not be made. It seems to be very likely that these plateaus and delayed maximums are caused by some kind of irregularity in the regional inflow and outflow of blood.

**Results: Functional Tests**

The multiexponential configuration of the logarithmic 2-min clearance curves tended to be somewhat accentuated during hypertension and hypocapnia, whereas hypotension and hypercapnia usually decreased the bending of the curves. In the three cases in which multiexponential curves were not observed in the resting state, all showed such curves during the functional tests. Thus, in all 23 studies, gross intracranial pathology was revealed by simple inspection of the curves. The typical responses to the functional tests as expressed by the alteration of the initial slope are given in Fig. 6.

![Fig. 6. The typical responses to the functional tests as expressed by the alteration of the initial slope of the logarithmically recorded clearance curves.](image)

**Changes in the Arterial Carbon Dioxide Tension.** Hypercapnia was induced in nine cases and in all nine the CBF in non-tumor
Fig. 7. Flow decrease by vasodilator. Alteration of the initial slope of the logarithmically recorded clearance curves in "intracerebral steal" phenomenon.

Fig. 8. Flow increase by vasoconstrictor. Alteration of the initial slope of the logarithmically recorded clearance curves in "intracerebral inverse steal" phenomenon.
Regional Cerebral Blood Flow with Brain Tumors

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Flow Decrease During Hypertension

Normotension

Hypertension

Partial

Total

Flow Increase During Hypotension

Normotension

Hypotension

Partial

Total

Fig. 9. Paradoxical reactions. Alteration of the initial slope of the logarithmically recorded clearance curves in hypertensive and hypotensive states.

areas was increased. An observation of particular interest was that in five of these cases the flow decreased (Fig. 7) in the tumor region ("intracerebral steal" by hypercapnia, see discussion). In two other cases the hypercapnic CBF values were extremely high and an increased flow was found even in the tumor region; however, this increase near a tumor region was much less than that in other regions in both patients. The remaining two cases showed no focal abnormality. In one of these cases (No. 7) we have evidence that the tumor lay outside the field covered by the probes; in the other case (No. 20) no focal abnormality of CO₂ response was found.

Hypocapnia was studied in five cases and gave the reverse picture. In four cases the normal response, decrease of blood flow, was found over the non-tumor regions while a pathological increase in flow was found over the tumor region. We have termed this pathological response the "inverse intracerebral steal" (see discussion and Fig. 8). In two of these patients this paradoxical response was seen in practically all channels, but the tumor was very extensive in both.

The channels with such responses probably even in these cases represent the tumor and peritumor region. The patient showing no paradoxical reaction was Case 7, where the probes were not lying over the tumor region.

Changes in the Systemic Blood Pressure.

The effect of induced hypertension was studied in 14 cases. Autoregulation was lost in all 14. In four cases this was confined to the tumor region, whereas in 10 cases autoregulation was lost in the entire hemisphere. The changes of the blood flow in hypotensive state was studied in two cases; both had loss of autoregulation over the entire hemisphere.

Paradoxical focal reactions to pressure changes were seen in five cases. In three patients the flow was increased over the entire hemisphere during induced hypertension. Flow decreased markedly in channels near the tumor in the two patients in whom hypotension decreased flow in the hemisphere. As a whole, the channels near the tumor region showed a marked flow increase (Fig. 9). These reactions were clearly related to the paradoxical reactions to PCO₂ changes: in four of the five cases where CO₂ reactivity
studies were performed, paradoxical CO₂ reactions also occurred in the tumor region.

Twelve patients were investigated both with changes of the PCO₂ and of the arterial blood pressure. All showed a normal reaction to hypercapnia/hypocapnia in non-tumor regions, the pathological reactions being present only locally. On the other hand, in nine of these cases the autoregulation was diffusely lost over the entire hemisphere, while only three showed a local impairment of this responsiveness.

Repeated “control” clearance studies were performed in three patients after one or more functional tests to determine whether the control state of the cerebral circulation was affected by the functional tests. No significant difference as compared to the values of rCBF<sub>init</sub> has been found.

**Variations in rCBF between Tumor Types.** In our three meningioma cases, the angiographic study showed that the tumors were not supplied via the internal carotid artery. Hence, it is highly unlikely that any ¹³³Xenon reached the tumor tissue itself. Autoregulation was diffusely impaired during hypertension in all three cases, the impairment being especially marked over the tumor region. The pathological areas determined by the location of multiexponential clearance curves and their response to the functional tests were not sharply outlined, and the abnormalities were found over quite extensive areas. As the tumor itself did not receive any ¹³³Xenon, the pathological changes represent the conditions in the brain tissue affected by the tumor. These tissue regions were apparently larger than the meningioma itself.

In each of the five metastasis and the four glioma (Grade I-III) cases, moderately fast flow components with multiexponential initial curve configurations were observed over the tumor region (see Fig. 4). In one of the gliomas, which was a cystic tumor, a local ischemic zone was found over the tumor region, while the probes around the tumor showed relative hyperemia.

A rather unique observation was made in the course of studying a patient with clinical signs of metastasis to the right cerebral hemisphere. Here rCBF studies (No. 16), angiograms, and brain scans pointed to a right-sided tumor. We then proceeded to study the left asymptomatic hemisphere (No. 15) where the scan was considered normal. Here an abnormal vasomotor reaction (intracerebral steal) in three adjacent channels revealed a frontally located tissue abnormality. At necropsy a pea-size metastasis with considerable peri-tumoral edema was found.

The nine glioblastoma cases showed the most striking changes in blood flow. Shunt peaks were found solely over these tumors (Fig. 5). The size of any shunt peak was probably related to the actual volume of blood being shunted through the particular region. All of the curves having shunt peak showed also a transient fast flow component. Five of these cases were investigated during changes of aPCO₂ tension, and four showed an intracerebral steal or inverse steal. Autoregulation was most markedly impaired in and around the tumors in this group of patients.

**Comments.** The pathological changes in the circulation revealed by the ¹³³Xenon method were in general more extensive than the lesions shown by the other neuroradiological investigations. This was particularly so regarding the cerebral metastases (see study No. 16), and the incongruity was seen especially clearly when comparing the rCBF data to the angiographical picture. Over tumors showing pathological vessels and shunts in the angiographical picture, shunt peaks could be revealed in the rCBF study; otherwise no close correlation has been found between the angiographical appearance and the rCBF study of the tumor.

With regard to the size of the hot spots in the brain scans, the rCBF study always showed more extensive pathological changes, and no correlation between the intensity of the hot spot and the pathological flow changes could be found.

In three patients localization of the tumor on the basis of the rCBF study was not possible; in one of these cases (No. 4) the investigation was performed only in the resting state; in another (No. 7) the tumor was not seen by the probes; in the third case (No. 14) a glioblastoma was investigated only in hypertension, and the autoregulation was diffusely lost.

**Discussion**

Previous studies of the cerebral blood flow in patients with brain tumors have been
based on the inert gas method of Kety and Schmidt, which gives an average value for the brain. These studies have shown a gross correlation between increase in cerebrospinal fluid pressure and subnormal cerebral blood flow values. With this method, regional differences in the CBF remained unexplored.

The regional $^{133}$Xenon clearance method used in our study allows some degree of spatial resolution of flow measurements. The clearance curve of a single probe represents a summation of all the labelled tissues within its field of vision. This superposition plus the Compton scatter from the neighboring regions undoubtedly conceal minor changes of regional flow. Thus the resolution of the $^{133}$Xenon clearance method is far from ideal.

The resolution of the clearance method could be improved by using $^{135}$Xenon which has a photopeak at 250 keV compared to the 81 and 31 keV photopeak of $^{133}$Xenon. Therefore, the Compton scatter will be significantly reduced with $^{135}$Xenon. However, $^{135}$Xenon has some disadvantages compared to $^{133}$Xenon. The half life of $^{135}$Xenon is only 9 hours compared to 5.2 days for $^{133}$Xenon. Furthermore, $^{135}$Xenon with the higher energy of the $\gamma$-ray will give more problems with radiation doses to the personnel.

If a curve does not show abnormalities, it does not mean that the flow in the given region is normal. One can only say that no pathological sign could be discovered. It is also appropriate to emphasize that hyperemic tissues are especially well seen by this method because the initial part of the curve shows mostly the fast flow components. These conceal the underlying slow components, which also receive less isotope per unit weight. Totally ischemic tissue areas are not reflected either in the initial slope or in the rCBF$_{10}$ values.

With these comments in mind it may be concluded that a very uneven perfusion is typical for brain tumor cases. Neither the anatomical extension nor the degree of unevenness is fully recorded in this study.

The incongruity between the angiographical and rCBF findings is due to the fact that the two investigations are basically different; angiography demonstrates anatomical changes in the cerebral vasculature, and the transit time of the injected contrast material gives only a rough index of the CBF. On the other hand, the $^{133}$Xenon clearance method reflects microcirculatory changes in tissue perfusion. This explains why peritumoral functional alterations of flow and flow regulation, are best revealed by the $^{133}$Xenon method.

**Regional rCBF$_{10}$ Values.** Our experience suggests that localization of cerebral tumors based on the presence of a relatively hyperemic zone as evidenced by the rCBF$_{10}$ values is only reliable when the differences in regional values are significant and sharply circumscribed. An exact localization of the tumors in this manner was possible in only 56% of the cases.

In the single case of a relatively large cystic glioma the probes "seeing" the center of the tumor showed relatively low flow values, suggesting that in these regions flow was dominated by perfusion of the poorly perfused tumor and brain areas. The surrounding probes showed relatively high values, demonstrating a hyperemic zone in the neighborhood of the tumor.

**CBF Initial.** In 90% of our cases there were pathological multieponential logarithmic 2-min curves over and adjacent to the tumor region in the control state. This type of curve configuration was never seen in normal cases or over non-tumor regions. The size and shape of the pathological tissue peaks and shunt peaks were variable, and in all probability depended on the amount of pathological tissue and its blood flow as seen by the probe. The height of the peaks is related to the amount of $^{133}$Xenon flowing through the pathological tissue, and the slope of the new components reflects the rate of this flow. In general the greater the volume and the faster the rate of the pathological flow, the slower was the second component (between 1.0 and 2.0 min of clearance), in other words the value of the first component was always greater and the second component almost always less than the mean flow value for the hemisphere. This fact suggests the existence of hyperemia and ischemia within the same region. It seems likely that there may be a "steal" within any one region, so that blood may be "stolen" by the hyperemic tissue (see discussion below).

In 10% (two cases) the 2-min logarith-
mic clearance curves in the resting state were monoexponential over the tumor. If the flow rates in the pathological and in the normal tissue seen by any one probe do not differ significantly in the control state, or if one of the two components dominate the curve, the 2-min clearance curve may be monoexponential. In the first case, stressing the cerebral circulation with one or more of the functional tests, will be expected to provoke a difference in flow between the normal and abnormal tissue, and the clearance curve will become biexponential. In the second case if, for example, the curve is dominated by the pathological tissue-flow, the monoexponential pathological curve responds as a whole without becoming biexponential. In the two cases here discussed, the monoexponential curves in the pathological area became multiexponential during the functional tests.

Shunt Peaks. The extremely fast components at the beginning of the curves, the so-called “shunt peaks,” seem to represent that part of the bolus of injected $^{133}Xe$ flowing very rapidly through the pathological shunts in the tumor region, thus having no chance to diffuse into the tissue. The passage of the large arteries in the counting field could also account for these peaks. The duration of the shunt peaks was never more than the time of the intravascular transit time. The peaks were only observed over glioblastomas which showed pathological shunts in the angiography. The changes in the height of these shunt peaks was usually determined by the intravascular pressure. The bigger the pressure, the higher the shunt peak.

CO$_2$ Reactivity. During hypercapnia the CBF increased over the whole hemisphere, except in the tumor region where a diminished response or even a paradoxical local flow decrease was found in most cases. This may be explained in the following manner. In the nontumor region hypercapnia results in vasodilatation with the fall in cerebrovascular resistance allowing increase in flow. The arterial blood pressure in the arteries going to the pathological tumor and peritumor areas tends to decrease because of this dilatation. At the same time the pressure in the intracranial veins rises in parallel with the marked intracranial hypertension elicited by the increase in blood volume. The perfusion pressure to the vasoparalytic tumor areas thus decreases, and the blood flow consequently drops. This pathological effect of carbon dioxide inhalation or other vasodilators is termed “intracerebral steal.” It has recently been demonstrated experimentally$^{2,3}$ and also preoperatively in patients with intracranial space-occupying lesions.$^4$

The observed “inverse intracerebral steal,” blood flow increase elicited by a vasoconstrictor agent, seen during hypocapnia in several of our patients may be explained in a similar manner. If the aPCO$_2$ tension is lowered, the CBF normally decreases because of vasoconstriction. If the vessels of the pathological tissue area are unable to constrict, then the blood will be deviated into this area, especially since the venous pressure and the intracranial pressure will have fallen during the test.

This inverse steal effect was expected on the basis of the above cited literature demonstrating the steal mechanism. It may help explain the beneficial effect of hyperventilation in patients suffering from some kind of local brain damage. Depression of the flow in healthy parts of the brain may increase the flow to poorly perfused areas.

Autoregulation. In four cases it was only the pathological area which showed a pathological response while in the other 10 cases studied, autoregulation was lost over the entire hemisphere. Two patients were investigated during hypotension. Both showed a diffuse decrease in flow, namely, total loss of autoregulation.

The differences in localization of abnormal responses such as the focal response to CO$_2$, or the diffuse response to blood pressure, demonstrate that autoregulation may be lost, while the CO$_2$ responsiveness is maintained. One of the meningioma cases demonstrated this pattern particularly convincingly; in the whole hemisphere studied the cerebral vasoconstriction to a blood pressure increase was lost, while the cerebral vasoconstriction to hypocapnia was preserved.$^4$

As mentioned in the section on the results of blood pressure variations, local paradoxical responses were found in some cases. These
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The loss of autoregulation means a pressure passive cerebral blood flow. This means that cerebral blood flow must be expected to be markedly influenced by variations of the intracranial pressure. Thus, a rise in the intracranial pressure without concomitant blood pressure rise will tend to cause a decrease of the CBF since it is not compensated for by vasodilatation as in the normal brain. Focal decreases can, as has been demonstrated, also follow an increase in blood pressure and in aPCO₂. It follows from this that such increases that are harmless in normal man may be critical for a tumor patient.

Conclusions

From the present study emerges the picture of a grossly heterogenous regional circulation in the brain with neoplastic disease. With our technique small tissue components with increased flow (hyperemia) were detected especially well. Other techniques that identify ischemic areas better have demonstrated areas of reduced flow in and around tumors. With the external recording techniques employed in these various studies one cannot avoid some degree of superimposition of different tissue layers in any one region studied. Hence one must conclude that the true heterogeneity of blood flow is probably even much more pronounced.

This picture is not different, qualitatively speaking, from what has been known for a long time from angiographic studies. Two points, however, appear to be of special interest. First the circulatory derangements may not be coextensive with the tumor. To what extent peritumoral abnormalities of brain perfusion or volume (edema) may complicate the angiographic delineation of a tumor is difficult to know in any individual case. The point we make is that such abnormalities do occur and that they are important in the interpretation of angiograms.

Second the circulatory derangement in and around the tumor is characterized by very abnormal (paradoxical) vasomotor reactions. This phenomenon is so characteristic, being present in practically all cases studied, that we do not hesitate in expressing the opinion that it may be of diagnostic value as a supplement to angiography in borderline cases.

The deranged vasomotor responses may be of some value in conventional angiographic studies. It appears quite certain that certain borderline abnormalities could be demonstrated by performing angiograms during functional tests as here used. We especially recommend comparison of a control state angiogram (normocapnia, normotension) to one performed during hyperventilation, when the fraction of contrast material going to the tumor region should increase. These comments are also pertinent to the semiquantitative CBF studies currently being attempted with γ-camera techniques.

We have noted a tendency to a decrease in maximal counting rate in the regions where intracerebral steal occurs and the converse in the “inverse steal.” Comparing changes in maximal regional counting rates during functional tests circumvents geometrical factors. Our analysis of such changes have, however, given a much less precise picture of the flow derangements than has the clearance approach reported in this paper.

In the eventual diagnostic use of the rCBF technique its sensitivity recommends itself. Apparently no other neuroradiological technique is able to detect such subtle functional derangements. However, the Xenon method not only has a fairly poor resolution but also is not specific. Patients with cerebrovascular diseases may show exactly the same changes as those seen in brain tumor cases. In fact, such cases may be considered, physiologically speaking, as “acute tumors,” the brain reacting in a stereotype fashion to a space-occupying lesion. The most specific lesions seen with the rCBF technique are in arteriovenous aneurysms and glioblastomas, but these abnormalities are readily detected angiographically.

Summary

Regional cerebral blood flow (rCBF) has been investigated in 21 patients with brain tumors, using the intraarterial Xenon clearance method. In the resting state local hyperemia and multiexponential logarithmic
clearance curves have been found in the tumor regions. In artificially induced hypocapnic states, there is a paradoxical decrease in the regional flow ("intracerebral steal") while in hypocapnic states there is a paradoxical increase in the regional flow ("inverse intracerebral steal") in the region of the tumor. In artificially induced hypertensive and hypotensive states, a local or diffuse loss of autoregulation could be demonstrated. We conclude that regional circulation in the presence of a brain tumor is grossly uneven and its regulation massively deranged.

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