# THE PHYSIOLOGY OF THE HUMAN CEREBRAL CIRCULATION *

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DESPITE its obvious and fundamental importance, information on cerebral blood flow was not placed upon a really quantitative and therefore scientific basis until 1943, when Dumke and Schmidt (1), using an ingenious bubble flowmeter, measured the blood flow through the brain of the lightly anesthetized rhesus monkey. Their work served as the impetus for, and a means of calibrating, the nitrous oxide method developed soon afterward which was applicable to unanesthetized human beings (2, 3). This technic, which has now been employed safely in some 500 individuals, has yielded some insight into the circulation and metabolism of the human brain, although the information is still fragmentary and incomplete.

It seems pertinent, since much of what I have to say is based upon it, briefly to describe this technic as we employ it (4). Samples of blood going to and coming from the brain are readily obtained from needles placed in a peripheral artery and in the internal jugular vein just below the mastoid process. During a ten-minute period of inhalation of 15 per cent nitrous oxide these samples are taken at intervals, analyzed for nitrous oxide, oxygen and carbon dioxide, and nitrous oxide concentration curves are obtained. From the curves it is possible to calculate cerebral blood flow (CBF) per unit weight of brain per minute. The mean value for normal young men is 54 cc. of blood per 100 Gm. of brain per minute or a total blood flow through the whole brain of approximately 750 cc. per minute.

## CONTROL OF THE CEREBRAL CIRCULATION

Like the circulation to any organ in the body, that to the brain depends upon two factors: *mean arterial blood pressure* and the *local resistance to blood flow within the brain.* These are the only factors involved although they in turn depend upon a host of contributory processes.

I shall not burden you with the separate physiologic processes which

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govern the *arterial blood pressure* but consider only what may happen to the cerebral circulation when the arterial pressure falls outside of the normal limits. We have as yet little data on normotensive individuals who suffer a severe reduction in blood pressure. However, we have just completed a study in collaboration with Hafkenschiel, King and Jeffers in which hypertensive subjects suffered a drop in blood pressure as a result of differential spinal block. It is apparent from those that when the blood pressure is acutely reduced by 30 to 40 per cent of the basal value, there is an almost comparable fall in cerebral blood flow associated with a feeling of faintness, nausea or vomiting. It is reasonable to assume that when these symptoms occur in a normotensive individual whose blood pressure has fallen, they reflect a similar reduction in cerebral blood flow. We have no data as yet on the effects of an acute increase in blood pressure on the normal cerebral blood flow but it is interesting to guess that there may be a compensatory mechanism which prevents an unnecessary increase in blood flow.

If we turn to the *local resistance in the brain* in various conditions our data are more complete. We have used the expression cerebrovascular resistance (CVR) for this function and have measured it as the mean arterial blood pressure divided by the cerebral blood flow or the pressure (mm. of mercury) necessary to force 1 cc. of blood through 100 Gm. of brain in a minute. Our normal value for CVR is 1.6 mm. per cc. per 100 Gm. per minute (4).

The *blood viscosity* is an important component of the CVR and this is largely dependent on the red cell hematocrit. To cite just two examples: one patient with severe anemia and a hematocrit reading of 33 per cent, showed a CBF of 79 and a CVR of 1.0, while another with primary polycythemia and a hematocrit of 63 per cent had a CBF of 22 and a CVR of 5.0 This latter patient had the lowest cerebral blood flow and the highest resistance of any patient I have studied.

A *high intracranial pressure* would be expected to increase the resistance in the brain and to restrict the cerebral blood flow. These were exactly the findings of a study in collaboration with Drs. Shenkin and Schmidt (5). Both CVR and CBF were closely correlated with the level of intracranial pressure; one patient in the series with a cerebrospinal pressure of 840 mm. of water had a CVR of 4.2 and a CBF of 31.

The most important single factor in cerebrovascular resistance, however, is the *tone of the vessels* themselves. These we have found to be under the control of a large number of agents. *Carbon dioxide tension* and *hydrogen ion concentration* exert powerful influences on the cerebral vessels. Active or passive hyperventilation which lowered the carbon dioxide tension by 40 per cent was associated with an increase in CVR of 70 per cent and a 35 per cent reduction in cerebral blood flow (6). Conversely, the inhalation of 5 per cent to 7 per cent carbon dioxide was accompanied by a 75 per cent increase in CBF, the

result of a significant cerebral vasodilatation (7). The ability of increased acidity to dilate cerebral vessels is probably the explanation for the increased cerebral blood flow which we have observed in diabetic coma (8).

*Oxygen tension* also regulates the tone of cerebral vessels in the direction of better homeostasis. The inhalation of 100 per cent oxygen produces a 30 per cent increase in the tone of cerebral vessels while the anoxia of 10 per cent oxygen produces a 35 per cent reduction in CVR (7).

The results of these and other less defined influences permit a delicate adjustment in cerebral blood flow in response to the demands of *cerebral metabolism.* Our data in man are incomplete in this regard but studies in the rhesus monkey clearly indicate a correlation between cerebral blood flow and cerebral metabolism (9). During a metrazol convulsion there was an 80 per cent increase in metabolism accompanied by a doubling of the cerebral blood flow, while a 36 per cent reduction in cerebral metabolism from pentothal was associated with a comparable decrease in blood flow.

The *neurogenic control* of cerebrovascular tone in man is at present under investigation. Harmel and associates have completed a series of studies on the effect of bilateral stellate ganglion block on cerebral blood flow (10). Although in some cases this procedure has resulted in a measurably increased flow, this has not been a constant or significant finding. Shenkin, in some studies on tilting, has evidence pertinent to a possible role of the carotid sinus reflex in the control of cerebrovascular tone (11). There is need for much further investigation in this aspect of human cerebrovascular control.

There are two conditions which we have investigated in which changes in cerebrovascular resistance are the result of obvious anatomical defects. In *cerebral hemangioma* we have observed three-fold increases in cerebral blood flow as the result of low resistance shunts in the tumor (12). We have recently completed a study on *cerebral arteriosclerosis* in which were found a significantly higher cerebrovascular resistance and a moderate to severe restriction in cerebral blood flow (13).

We come finally to a group of conditions in which there is a striking increase in cerebrovascular tone for reasons which are at present unknown. In *essential hypertension* we have observed a consistent and quite marked increase in CVR, averaging 88 per cent above normal (14). This occurs with no known change in oxygen or carbon dioxide tension or hydrogen ion concentration, and Hafkenschiel and his associates have evidence that this increased tone is not mediated by way of the stellate ganglion. Some humoral agent may be responsible, a possibility which is strongly suggested by the fact that every vascular bed in hypertension is constricted equally. McCall and his associates at Jefferson Medical College have recently reported an excellent study

on the cerebral circulation in *eclampsia* (15) in which they found a significant increase in cerebral vascular tone.

Before closing, I should like to add a few words about *cerebral metabolism* which measurement of cerebral blood flow makes it possible to calculate. In healthy young men we have found an average value for cerebral oxygen consumption of 3.3 cc. of oxygen per 100 Gm. of brain per minute or about 45 cc. of oxygen per minute by the whole brain (3). In all of our studies we have been impressed with the close correlation between the level of consciousness and the rate of oxygen consumption by the brain. In patients who are comatose for whatever reason, cerebral oxygen consumption falls to a value of less than 2.0 cc. per 100 Gm. per minute, while in those who are semistuporous or confused, the value lies between 2.5 and 3.0. It seems clear that mental function is closely dependent on an adequate cerebral metabolism. This latter function may be impaired in at least three ways: *a deficient circulation, the absence of essential nutrients,* or some *intracellular interference with metabolic processes.*

We have observed two conditions in which cerebral metabolism and its resultant mental state were probably impaired by a deficient cerebral circulation: the *senile dementia* associated with cerebral arteriosclerosis (13), and the coma or semicoma of those patients in whom a *high intracranial pressure sufficiently* embarrassed the blood flow to the brain (5).

Although we have not studied a degree of anoxia severe enough to impair the cerebral metabolism, we have no doubt that such a phenomenon could and does occur. An opportunity, however, was presented to study schizophrenic patients during insulin shock (16). In these individuals there was a profound fall in the utilization of oxygen and glucose by the brain (44 per cent and 82 per cent reduction respectively), probably the result of the practical absence of this important nutrient from the arterial blood.

Finally, we have data on two conditions in which a depressed cerebral metabolism was found which must be attributed to some interference with cellular oxidations. In *diabetic coma* (8) there is a profound fall in cerebral oxygen utilization to 1.7 cc. per 100 Gm. per minute, although there is no deficiency in circulation, oxygen or glucose. During *pentothal* anesthesia, both we and Himwich and associates (17) have observed a marked fall in cerebral utilization of oxygen which in our study represented a 44 per cent decrease. Work is now in progress to amplify these studies in anesthesia and to observe the effects of different anesthetic agents on cerebral blood flow and metabolism.

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## MEETING OF THE PHILADELPHIA SOCIETY OF ANESTHESIOLOGISTS

MEDICAL AMPHITHEATRE OF THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

OCTOBER 7, 1949—8:00 P.M.

SYMPOSIUM ON ANESTHESIA IN THE GERIATRIC PATIENT

"Preanesthetic Medication," by Robert D. Dripps, M.D.
"Penthothal Nitrous Oxide Curare Anesthesia as a Method of Choice in the Elderly Patient," by Ellis K. Hultzman, M.D.
"Spinal Anesthesia for Hip Fractures," by J. Eugene Rubin, M.D.
"Choice of Anesthesia for Upper Abdominal Surgery in the Elderly Patient," by Leroy Krumperman, M.D.