Cerebral Blood Flow and Energy Metabolism in Vascular Insufficiency

VASCULAR INSUFFICIENCY in an organ is characterized by blood flow inadequate to fulfill completely its metabolic needs, or the needs of a metabolically active region of that organ. The essential substrates must be available at any point in the tissue in a quantity that is not fixed but determined by the temporal requirements of the tissue's needs, that is, by regional functional activity.

Therefore, “cerebrovascular insufficiency” defined in terms of blood flow measurements, that is, a reduction in blood flow, does not take into account the true span of the physiological phenomena. This term and its implication must be redefined with the introduction of the new, non-invasive techniques now in use for tomographic regional evaluation of brain blood flow and energy metabolism in the same patient over time.

Obviously, the term cerebrovascular insufficiency still applies in those clinical conditions in which a reduction in blood flow (be it well documented or hypothesized) produces clinical symptoms of focal neurological deficits. In these instances the equilibrium between metabolic supply and demand has been disturbed and the insufficiency is quite apparent. In other cases the signs of insufficiency may be undetected clinically, such as those situations in which the metabolic requirements for energy production and functional brain activity are being scarcely, but still sufficiently, met by the corresponding level of blood flow in the area. This fulfillment is produced at the expense of the “reserve” possibilities of regional cerebral blood flow and autoregulation and through increasing to a maximum the extraction of the substrates from the blood stream.

No clinical, angiographic, or CBF investigation can provide as clear evidence of cerebrovascular insufficiency as does the study of local cerebral blood flow and oxygen metabolism by emission tomography with the oxygen-15 inhalation technique of Lenzi and Jones. This study gives a more complete picture and complements the clinical and angiographic information required for diagnosis, and may provide a better basis for prescribing treatment.

“Cerebrovascular insufficiency,” so defined at a sub-clinical stage, can further deteriorate and lead to the development of neurological symptoms, thus constituting the only real indication for therapy intended to increase the cerebral blood flow.

This sub-clinical condition has been demonstrated in the brain of patients with occlusive disease of the neck and/or the intracranial circulations and has been named “misery perfusion.” In this situation, there is an increase of the Oxygen Extraction Ratio well over normal values, a mechanism which allows sufficient oxygen consumption despite reduced blood flow. This compensatory mechanism reduces the reserve available for further functional demands and may lead to the appearance of neurological signs and symptoms with a general fall in blood pressure.

Unfortunately, no clinically useful medication has yet been found which is capable of correcting this situation by increasing cerebral blood flow. The reduced reserve situation leads itself to correction by the removal or circumvention of an obstruction, such as a microsurgical bypass operation where this is possible. Bypass surgery should be preceded whenever possible by the assessment of regional cerebral metabolism in order to exclude those patients with a fixed metabolic defect.

When a metabolic defect has already occurred, as in completed brain infarction, the situation is characterized by a large fall in energy requirements. Cerebrovascular insufficiency is then transformed into a luxury perfusion, be it absolute or relative. Under these circumstances, there is little value in trying to increase blood flow. However, metabolic studies have revealed an intriguing phenomenon that occurs in the areas surrounding the infarcted region which is relevant from a therapeutic and prognostic point of view. In fact, this is precisely where we can hope to achieve the maximum clinical improvement still possible, with current clinical procedures or those under study at this time.

This phenomenon, called “post-ischemic hypermetabolism,” occurs very soon after an ischemic insult to the brain and constitutes another variety of “relative” insufficiency of blood supply due to excessive post-ischemic (or post-anoxic) metabolic requirements. In these regions the “penumbra” is not determined by the decrease in rCBF, but by the excessively increased metabolic demand uncoupled from rCBF.

The post-ischemic brain is a complex mosaic of very different metabolic and hemodynamic focal situations which tend to vary considerably within the first few days. An ischemic lesion may show different perfusion
patterns, anything from persisting severe ischemia to complete restoration of the circulation with luxury perfusion and vasoparalysis.

However, these events may be entirely unrelated to oxygen consumption and completely disassociated from the metabolic requirements. Only the assessment of regional energy metabolism and circulation, and the repetition of the examination during and after the ischemia, may indicate the occurrence of these events. In the now preliminary phase of the application of these new techniques, it is not yet clear how this information will actually change strategy regarding treatment, which, in principle, should be aimed at restoring the normal balance between flow and metabolism, rather than directed only at the circulatory aspect.

Therapeutic attention might be focused at times on increasing perfusion in "true" CV insufficiency, but on other occasions or in other parts of the lesion, therapy aimed at reducing or suppressing excessive metabolic demands seems more rational.

In other instances, when the tissue's regional metabolism is depressed in spite of preserved perfusion, enhancement of the level of function through metabolic activation would be a primary therapeutic goal. This phenomenon cannot be corrected with vasoactive agents because the eventual reduction of flow is a consequence, rather than the cause of reduced neuronal activity.

The positron emission transverse tomography (PETT) research units now being developed will assist us by accurately describing the phenomena discussed above. This is necessary in order to see clearly to what extent the final outcome of an ischemic lesion can be predicted and possibly modified in terms of regional cerebral metabolism and blood flow measured together.

We are not yet ready to answer the question: "how much" these studies will benefit a patient. In the past many came to the conclusion that "what benefits CBF" in the post-ischemic phase did not have a direct influence on the final clinical outcome.

Now, we are moving one step closer to defining what is important by measuring tissue needs and viability. We are learning to define clinical or subclinical cerebrovascular insufficiency in terms of a mismatch between the tissue's needs and its blood supply.

The quality, reproducibility, and resolution of the measurements obtained with positron emission tomography, the reproducibility of the oxygen-15 inhalation technique allows us to be relatively optimistic about the clinical assistance which may be derived from these studies in spite of their cost and technical sophistication. These practical aspects could be obstacles to their broad use, but pilot centers applying this approach to the problems of cerebrovascular disease and its therapy may offer the neurological community direct evidence for a more rational approach for therapy of these disorders.

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Reference

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