Letters To The Editor

Ischemic Edema in Stroke

To the Editor:

Dr. Harrison claims that locally decreased BBB function is seen 24–72 hr after the ictus in patients with hemiparesis due to cerebral infarction. The increased activity of the radioisotope Tc99m on ECT scans might well indicate such a qualitative change. The degree of BBB disturbance at this time is not reported.

Intracellular water accumulation (edema) may be indicated by increased adenylyl kinase (AK) activity in the CSF. AK is a relatively small enzyme (MW 21 500) of intracellular origin. The GSF/serum ratio is about 0.015 compared to 0.004 for albumin. This higher quotient for a smaller molecule is in accordance with the general physical principles of passive transfer over the BBB. The CSF/serum ratio is gradually increased when the BBB damage progresses, equaling 1 at complete breakdown. The rapid rise of the CSF-AK activity in comparison to the discrete and late increase in CSF-albumin concentration may not be explained by passive transfer from serum. In addition, the curves for CSF-AK and -albumin cross each other in individual patients. Also linear regression analysis revealed no correlation at all (r = 0.038) between CSF-AK and CSF-protein obtained within 48 hr after the stroke. This finding contradicts a possible co-migration of protein (albumin) and AK from the blood plasma compartment.

Thus, cell leakage due to energy shortage with intracellular water accumulation (edema) remains the most plausible explanation to the early rise in AK-activity.

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References


Concerns Voiced on Focal Cerebral Hyperemia Paper

To the Editor:

Lassen and colleagues continue in the forefront of technological advance in the imaging and quantification of cerebral blood flow. In their recent publication on focal cerebral hyperemia laboratory technology is advanced; especially impressive are the flow maps which beautifully document the zones of hyperemia. Nevertheless, two aspects of their report trouble me:

1) Clinical information is collected but omitted from the report. Did these patients have TIAs in the same vascular territory before their stroke? The presence of TIAs would support a mechanism of in situ thrombosis. Did some patients have sudden onset deficits? Were there either cardiac lesions, or carotid plaques which might serve as an embolic source? Were these patients stable, improving, or worsening at the time of the investigations? Although angiography was performed, the findings are not detailed. Were there proximal carotid occlusions, stenosis, or plaques? Without inclusion of the clinical and angiographic data it is impossible for the clinician to interpret the setting of these elegant laboratory findings.

2) The authors assume in their discussion of possible therapeutic implications of the results that hyperemic borderzones are a "threatened area with a potential to survive." This idea is speculative. They provide no data that would clarify the clinical significance of the hyperemia. In most well studied instances of tissue injury (trauma, inflammation, ischemia), a zone of increased blood flow surrounds the injured tissue. The customary interpretation is that the hyperemia brings needed blood and nutriments to the injured zone, and helps in the repair and healing of the injury. I know of no evidence that the increased blood flow within or around the injured zone is in any way harmful. Yet the discussion invites therapies aimed at controlling the hyperemia, some of which might diminish blood flow.

Much work remains before the clinical significance of hyperemic zones is clarified. Until then, it seems prudent not to embark on ill conceived treatments aimed at strangling the curious genic hyperemia, at least until we know if the genie is good, bad, or indifferent. Clarification will only occur if the patient and his clinical findings and course are kept in the center of focus and related to the laboratory findings.

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Reference


To the Editor:

Dr. Caplan discusses two aspects of our paper "Focal cerebral hyperemia in acute stroke": 1) The (inadequate) clinical presentation of the patients and 2) the therapeutical implications as they were suggested by us.

1) We completely agree that the patient in one way or another always must be the center of focus of all medical scientific work. However, we deliberately omitted the clinical data from the paper. First of all because a detailed description of clinical and angiographical features would increase the length of the paper exceeding what is normally accepted. Second because we intended to focus and draw attention to a normally occurring feature of rCBF in acute stroke — the hyperemia which in our opinion has attracted too little attention during recent years.

Although Dr. Caplan’s questions probably are a few among many, we will answer briefly. The patient population was practically consecutively and nonselected, and we consider the findings representative for a normal stroke population in a large city hospital. Only one patient had had two TIA’s (in the same vascular territory as the stroke). All patients had sudden onset of the neurological deficits, 8 were fairly stable in the acute state when the CT-scan, rCBF and angiography were performed, 3 were improving and 5 were worsening, 3 of these only temporarily. Occlusions were present only in the middle cerebral artery. Atherosclerosis in the internal carotid artery (ICA) was seen in different degrees in 13 patients. ICA plaques were the possible embolic source in 3 patients, a cardiac lesion the possible source in 3, and in 10 the embolic source was impossible to determine.

2) We certainly hope that our discussion of possible therapeutical implications is considered only as a contribution to the current discussion of the treatment of acute stroke patients. As the findings were obtained from a patient population and as focal hyperemia were consis-
tently seen in the patients in which the hyperemias were accessible for reliable rCBF investigations, we found it justified to discuss therapeutic possibilities.

Our assumption of hyperemic borderzone as threatened areas with a potential to survive is derived from our own findings of impaired autoregulation, false autoregulation, and impaired CO$_2$-response in some of the hyperemic areas investigated. Experimental findings of histopathological changes in hyperemic brain tissue are available and quoted in the paper. Early surgical recanalisation of occluded arteries in stroke are known sometimes to produce hemorrhagic infarction and worsening the clinical outcome. Unlike other organs, the brain is placed within a closed skull. Focally increased blood volume and edema affect, therefore, the tissue pressure in the surrounding tissue much more in the brain than in other organs. Finally the type of hyperemia reported in our study seems to disappear within the first week after the stroke. It is not comparable to the hyperemias seen 2-4 weeks after the stroke which serves in the reabsorption process of necrotic material from the infarct.

Much work remains before the nature and clinical significance of cerebral hyperemia is clarified. The findings in our study indicate that acute cerebral infarction is not only a matter of cerebral ischemia. Hyperemia is quite as common and the entire infarct is sometimes even hyperemic without being hemorrhagic. We find it worthwhile to include the presence of focal hyperemia in therapeutical considerations.

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Important Points in Treatment of Progressing Stroke

To the Editor:
We found the editorial on "Treatment of progressing stroke" by Drs. Norris and Lassen in Stroke 12, 397-409, 1981 both interesting and controversial.

The opening sentence of the article implies that progressing strokes are defined by their progression over minutes. When questioned closely, patients with strokes of apparently "sudden" onset will often describe an evolution of their symptoms over minutes. We feel that progressing strokes are better defined as showing deterioration over an hour than the process is usually completed within one day. Deterioration over days on the other hand is also seen in a large minority of acute stroke patients. The pathogenesis of these three evolutionary types of acute stroke may be the determining factor in their differing temporal profiles.

The authors state that anticoagulants may be helpful in progressing ischemic strokes but the implied progressing "thrombosis" may be a theoretical concept which needs revising. Cerebral edema is the most powerful adverse factor in the first few days of acute cerebral infarction and serial CT scans in such patients in the acute and sub-acute periods usually show no extension of the area of infarction.

Patients who progress or deteriorate in the acute stage usually reveal a mass effect of brain swelling on CT, the suddenness simply representing mechanical decompenation within the bony confines of the skull. Models of experimental brain edema suggest that more edema accumulates outside than inside the infarction once the blood-brain barrier has been breeched. Attacking this problem may prove more fruitful than using anticoagulant therapy for which therapeutic effectiveness has yet to be demonstrated.

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To the Editor:
The letter from Drs. Norris and Lassen provides an opportunity to emphasize again three of the many points made in our article "Treatment of Progressing Stroke." I

1. Over the decades it has become apparent that many physicians have a problem in dealing with the concept of the minute to minute uncertainty produced by the changing quality and quantity of neurologi­cal deficit which is the hallmark of "progressing stroke" (stroke-in­evolution). Physicians who deal with acute illness in patients in intensive care units soon become familiar with the notion of frequent re-examination (every 30 minutes in our cerebrovascular intensive care unit) of the salient abnormality. Thus, a determination can be made as to whether the trouble is worsening, static or improving. For instance, a patient seen at 10 a.m. with mild left upper extremity weakness (history of onset at 9 a.m. that day), re-examined at 10:30 a.m. and found to have severe weakness of that extremity, would be classified as "progressing stroke," but if the deficit had disappeared the categorization would be "transient ischemic attack." The clinical stage designation may change several times for the same patient. This extreme variability in the natural history, when added to the diverse pathogenetic mechanisms causing the focal situation, admittedly does produce a complex set of variables with which the physician must grapple.

In our review, we wrote that "18 to 24 hours without progression is needed to be sure that further progression is unlikely," for infarction in brain supplied by the carotid system, while in the vertebralbasilar system a longer period (up to 72 hours), should pass. This natural history is so variable that we included numerous details to illustrate those differences.

2. The use of anticoagulant, to prevent progression, is only recom­mended when there is accurate diagnosis and there is incomplete impair­ment of function. If the patient is hemiplegic and/or has a depressed level of consciousness, it can be assumed that maximum ischemia is probably past and progression of focal ischemia is unlikely. In this situation, it is not advisable to start heparin. In a number of centers, where there is extensive experience with acute occlusive stroke, anticoagulant therapy is used frequently.

3. Cerebral edema which can follow cerebral infarction is the most serious threat to life. In the same issue of "Stroke" in which our paper appeared, Bounds et al. reported that transtentorial herniation was the cause of death in 31% of 100 cases of acute cerebral infarction in the brain supplied by the internal carotid artery studied at autopsy, and 60% had some other cause of death. At that same cerebrovascular center the mortality for acute occlusive disease stroke (carotid system) is 11%. Those who work with animal models of experimental brain edema are working with and producing severe lesions. This is an entirely different population than patients with stroke coming to a clinical cerebrovascular service. In the latter situation, many patients have minimum focal brain damage when admitted — the objective is to keep focal brain damage from progressing to an extreme state as often represented by the experimental brain edema models.

A number of therapies are reviewed in our paper for treatment of progressing stroke — selection must be made depending on the mecha-
Ischemic edema in stroke.
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The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/13/3/402.2.citation

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