We would like to suggest another factor, namely, that of decreased platelet aggregation, which may contribute to their observation. We studied platelet aggregation in 25 newly diagnosed patients with Parkinson’s disease and 25 age- and sex-matched controls. None were diabetic, hypertensive, smokers, or on any treatment. Citrated blood was collected by venipuncture and centrifuged at 205g for 10 minutes, and the supernatant platelet-rich plasma was obtained. Platelet counts were measured using a platelet counter (Contraves, Switzerland). No patient had a low platelet count. Platelet aggregation was measured by the Born method using a four-channel aggregorecorder (Daichi-PA 3220, Kyoto, Japan). Adenosine diphosphate (2.5 μM/ml), collagen (2.5 μM/ml), and epinephrine (3 μM/ml) were used as inducers. The stock solution was diluted with 0.85% saline. The aggregation was studied at fixed intervals of 5 minutes for collagen and 10 minutes each for adenosine diphosphate and epinephrine. The absorbance was measured as % aggregation. The results were analyzed statistically using Student’s t-test.

Platelet aggregation induced by adenosine diphosphate and epinephrine was significantly decreased (32% and 60%, respectively) in Parkinson’s disease cases, while collagen-induced aggregation was unchanged.

To the best of our knowledge, these findings have not been recorded elsewhere. We hypothesize that decreased platelet aggregation in Parkinson’s patients may be a significant contributory factor for the reduced incidence of ischemic stroke.

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Glycerol Infusion Rates Warrant Caution

To the Editor:
We wish to comment on the assertion by Nau and colleagues1 that very high intravenous infusion rates of glycerol (>500 ml of 10% solutions given over 4 hours) are required to exert any significant osmotic effect on cerebral edema associated with acute stroke.

The most important side effect of such dosages is intravascular hemolysis.2 We conducted a critical evaluation of the latter adverse effect and its possible mechanism in the course of a large, randomized, double-blind clinical trial of intravenous glycerol treatment in patients with acute stroke. This in vivo and in vitro study3 suggested that hemolysis resulted from glycerol at the site of infusion rapidly entering red cells and from destruction of the latter in more central veins due to osmotically induced swelling beyond a critical limit. Moreover, so long as the infusion rate was not allowed to exceed 125 ml/hr, even temporarily, clinically significant hemolysis was avoidable.

Japanese investigators and clinicians have reported that use of glycerol solutions containing small amounts of fructose can overcome this problem associated with more rapid infusion rates.4,5 Moreover, in vitro studies in our institution (Figure 1) are also consistent with such a possibility.

Thus, regardless of the possible benefits before embarking on further studies to evaluate the value of more rapid glycerol infusions in managing acute stroke, it is important to address this anticipated and alarming degree of intravascular hemolysis.

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Multiple Aneurysms Caused by Hemodynamic Stress and Hypertension

To the Editor:
Increased hemodynamic stress is possibly a factor in the development of cerebral aneurysms. The clinical basis for this possibility includes the development of aneurysms in feeders of arteriovenous

Figure 1. Graph showing percentage of lysed red blood cells from two subjects after resuspension in normal saline following primary exposure in varying concentrations of glycerol in saline only (-----) and glycerol plus fructose in saline (-----). Red blood cells from three other subjects yielded similar findings. Primary exposure in the presence of fructose mitigates against saline resuspension hemolysis.

Multiple Aneurysms Caused by Hemodynamic Stress and Hypertension

To the Editor:
Increased hemodynamic stress is possibly a factor in the development of cerebral aneurysms. The clinical basis for this possibility includes the development of aneurysms in feeders of arteriovenous
malformations and along the collateral circulation of the occlusion of major cerebral arteries.\textsuperscript{1,2} However, we believe that multiple aneurysms have never been observed in the contiguous circulation associated with the occlusion of a major cerebral artery until our recent patient.

A 67-year-old woman, who had suffered from untreated hypertension for 6 years, had cerebral angiography demonstrating occlusion of the right middle cerebral artery at its origin. The area normally fed by the occluded right middle cerebral artery was compensated by collateral circulation from the ipsilateral anterior cerebral artery via the leptomeningeal anastomosis. Three saccular aneurysms had developed in the peripheral portion of the anterior cerebral artery proximal to the leptomeningeal anastomosis, in a direction consistent with blood flow.

The anterior communicating artery is a frequent location for the development of cerebral aneurysms associated with the occlusion of a major cerebral artery. Aneurysms in the terminal portion of the basilar artery and the junction of the posterior cerebral and basilar artery have also been reported in a patient with internal carotid artery occlusion.\textsuperscript{1} However, the present aneurysm in the peripheral portion of the anterior cerebral artery is the first described, and multiple aneurysms associated with occlusion of a major cerebral artery have been reported in only two cases.\textsuperscript{1,2} In both cases, the aneurysms were located in different arteries, in contrast to this case.

Several investigators consider that both hemodynamic stress and hypertension play an important role in the development of cerebral aneurysms. Experimentally, Hashimoto et al\textsuperscript{3} induced cerebral aneurysms in rats and monkeys using unilateral or bilateral carotid artery ligation and hypertension without \textbeta-aminoproprionitrile.\textsuperscript{5} Thus, these investigators\textsuperscript{3,5} showed experimentally that, in addition to increased hemodynamic stress, stress on the arterial wall caused by hypertension will promote the development of cerebral aneurysms. Our findings also suggest that increased hemodynamic stress and the development of aneurysms are related.

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**Future of Stroke Management**

To the Editor:

The simple, but elegant, experiments recently reported by Kaplan et al\textsuperscript{1} emphasizing similar recent findings by others\textsuperscript{2} give both reason for despair and reason for hope to clinicians dealing with ischemic stroke.

The despair arises from the fact that, as the experiments from the Cornell group indicate, infarction and edema are maximal at 3 hours and do not change much even at 24 hours, suggesting a therapeutic window even briefer than generally believed, at least in rats. Only a tiny minority of patients could be delivered to primary care facilities for treatment in this short time, based on the present system for deployment of ambulance and emergency facilities in most hospitals.

There is reason for a glimmer of optimism, however. Just because pathological effects are maximal at 3 hours does not mean that the clinical effects cannot be reversed after several hours since other factors are involved, some of which are probably reversible (e.g., the ischemic penumbra). There is also the implication that almost no drug trials have ever really been tried in ischemic stroke, since most published studies have had therapeutic windows of days, not hours (there are a few exceptions, such as the Italian Ganglioside Study\textsuperscript{4}). Thus all previous stroke trials need to be repeated.

Most important of all, the facts of these reported experiments emphasize that physicians, hospital administrators, ambulance services, and the public will need a new perspective of stroke care in much the same way that "coronary care" and cardiac arrest care have been revised in recent years.\textsuperscript{4} If ischemic stroke is a potentially reversible state, these patients must be delivered to health care facilities as medical emergencies, which is opposite to the way in which they are viewed in most of the world at present.

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Multiple aneurysms caused by hemodynamic stress and hypertension.
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http://stroke.ahajournals.org/content/22/12/1608.2.citation