Letters to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1,000 words (typed double spaced) in length, and may be subject to editing or abridgement.

Effects of Dimethyl Sulfoxide on Cerebral Arteries

To the Editor:

In an article published in *Stroke*, Pitts et al[1] present their experimental and clinical results with the use of dimethyl sulfoxide (DMSO) in brain injuries. Although their results were not unexpected, we found them extremely interesting, especially their well-conducted in vivo studies. We would like to comment on their statement "that the mechanism of action of DMSO is unknown" and to make some suggestions that may prove beneficial in clinical practice.

Central nervous system (CNS) injury is believed to result from alteration in cellular and blood vessel function. Two of the main functional alterations have been shown to be increased cellular permeability to Na^+ and K^+ and marked diminution in the caliber of arteries, capillaries, and venules, which lead to edema and impaired circulation.[2] However, theoretical and experimental evidence exists which shows that the above effects have a common cause and are due to oxidation.[3,4] Based on the above redox theory, we have conducted a number of in vitro experiments using rat aortas and dog basilar arteries and have shown that 1) simple oxidizing agents (peroxide, silver nitrate, potassium permanganate, sodium nitrate) produce vasoconstriction, 2) the concentration of agents required depends on their oxidizing potential, and 3) the vasoconstriction induced by the above agents can be inhibited and reversed by reducing agents.[5]

We used a number of simple chemical compounds whose sole common property is their capacity to donate electrons as reducing agents: citric acid, succinic acid, and glutathione. We also used DMSO because it too is a reducing agent and because it is a cheap, easily available compound empirically used in the treatment of a number of diseases. DMSO in all our experiments had the same effects as all the other reducing agents. However, its efficiency in inhibiting and reversing the vasoconstriction was consistently lower than that of the other reducing agents even though higher concentrations were used.

It is therefore likely that DMSO produces its beneficial effects in brain injury by acting as an antioxidant. This is supported by the facts that 1) in all the major CNS disorders, there is an increase in free radical concentration and a decrease in tissue antioxidant concentration,[4] and 2) apart from DMSO, a number of other antioxidants have been found beneficial in CNS disorders.[6] Our experiments suggest that a number of other reducing agents, such as succinic acid, citric acid, and reduced glutathione, may be more effective than DMSO and at lower concentrations.

Eleni Papadopulos-Eleopulos, MSc
Richard A. Fox, PhD
Department of Medical Physics
Royal Perth Hospital
Wellington Street
Perth, Western Australia 6000, Australia

References

1. Pitts LH, Young AR, McCulloch N, MacKenzie E: Vasomotor effects of dimethyl sulfoxide on cat cerebral arteries in vitro and in vivo. *Stroke* 1986;17:483–487
2. Popp AJ, et al (eds): *Neural Trauma*. New York, Raven Press, 1979
3. Papadopulos-Eleopulos E: A mitotic theory. *J Theor Biol* 1982;96: 741–758
4. Demopoulos HB, Flamm ES, Pietronigro DD, Seligman ML: The free radical pathology and the microcirculation in the major central nervous system disorders. *Acta Physiol Scand Suppl* 1980; 492:91–119
5. Papadopulos-Eleopulos E, Knuckey N, Dufty A, Fox RA: Evidence that the redox state has a role in muscular contraction and relaxation. *Physiol Chem Phys Med NMR* 1985;17:407–411
6. Suzuki J, Fujimoto S, Mizoi K, Oba M. The protective effect of combined administration of anti-oxidants and perfluorochemicals on cerebral ischemia. *Stroke* 1984;15:672–679

The following letter is in reply:

To the Editor:

We appreciate the comments of the above authors. Although we are well aware of the proposed role of antioxidants in the treatment of nervous system injuries, it is not clear that they are involved in the vasodilatation seen in our experiments. During the micropipette instillation of DMSO around small cerebral arteries, we believe that we maintained a normal brain and perivascular environment and that there would have been no abnormal concentrations of free radicals in or around the vessels. In the preceding letter, the authors note that oxidizing agents can constrict vessels and that antioxidants can reverse this constriction. However, we know of no data demonstrating that in the absence of oxidant-induced vasoconstriction antioxidants cause vasodilatation specifically by their antioxidizing properties. In our study, we suggested that the dilatation seen with DMSO can be explained by its osmolarity and noted similar effects seen with hypertonic saline.[1]

Papadopulos-Eleopulos and Fox cite interesting reports concerning chronic or prolonged vasoconstriction in which oxidants may play a role. However, in the acute vasodilatation of normal vessels that we reported, we cannot be sure that DMSO exerts its effects by an antioxidant role.

Lawrence H. Pitts, MD
Department of Neurological Surgery
San Francisco General Hospital
4M-39, Box 0870
San Francisco, CA 94143-0870

References

1. Wahl M, Kuschinsky W, Bosse O, Thurau K: Dependency of pial arterial and arteriolar diameter on perivascular osmolarity in the cat. *Circ Res* 1973;32:162–169

Is the Circadian Change in Hematocrit and Blood Viscosity a Factor Triggering Cerebral and Myocardial Infarction?

To the Editor:

Increased frequency of onset of cerebral and myocardial infarction in the morning hours has been reported.[1–3] Numerous physiologic factors, such as arterial blood pressure,[4] plasma catecholamine,[5] and blood fibrinolytic activity,[6] in addition to physical and mental stress occurring after waking,[3] have been proposed as causes attributable to the circadian variation. Since hematocrit and blood viscosity are important factors influencing cerebral blood flow,[7] we examined their circadian change with relation to the occurrence of cerebral and myocardial infarction.

Thirty nonsmoking and normotensive individuals (mean age 65, range 33–86 years) were included in this study. Fifteen (11 men and 4 women) were patients who had a history of cerebral infarction at least 3 months before but were living a normal life in spite of neurologic impairment. Ten of the 15 patients had the stroke between 5 AM and noon. None were receiving drugs. Informed consent was obtained from each patient. The daily schedule was: wake at 7 AM; breakfast at 8 AM; lunch at noon; dinner at 5 PM; and to sleep at 9 PM. They were confined to bed throughout the period of this study. Bathing was not allowed, and drinking beverages was forbidden except for those provided at 10 AM and 3 PM. They were all relaxed and comfortable and slept well. Blood samples of 2 ml were obtained from a right forearm vein using EDTA-2K as anticoagulant at 4-hour intervals from 8 AM one day until 8 AM the

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Is the circadian change in hematocrit and blood viscosity a factor triggering cerebral and myocardial infarction?

K Kubota, T Sakurai, J Tamura and T Shirakura

Stroke. 1987;18:812-813
doi: 10.1161/01.STR.18.4.812.b
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628