VASCULAR DISORDERS

STROKE PREVENTION TRIALS IN SICKLE CELL ANEMIA

As part of an International Pediatric Stroke Study launched in 2002, the Stroke Prevention Trial in Sickle Cell Anemia (STOP) reports a reduction in the number of overt clinical strokes in children with critically high transcranial Doppler velocities (>200 cm/sec) who were regularly transfused. Of 130 patients with an abnormal transcranial Doppler ultrasound, 65 were randomly allocated to receive transfusions and 65 were controls. Clinical stroke, defined as a new focal neurologic deficit lasting more than 24 hours, was the end point. This study was discontinued early, a Clinical Alert being issued because of the observed benefit of Doppler screening and transfusion and reduction in stroke (Adams RJ for STOP investigators. **N Engl J Med** 1998;339:5-11). STOP II was designed to study the safety of discontinuing prophylactic transfusion in children whose Doppler velocities had remained normal for at least 30 months. STOP II was halted early because of reversions to high risk or stroke in the halt transfusion group. Children with Doppler velocities >200 cm/sec should be transfused indefinitely (Adams RJ et al. **N Engl J Med** 2005;353:2769-2778). A Silent Infarct Transfusion trial, designed to determine whether children with SCD and silent cerebral infarcts (20%) will be benefited by regular blood transfusion therapy, involves 200 patients from 24 sites in US, Canada, and UK, and will take 6.5 years. Children with Doppler velocities >200 cm/sec are excluded, receiving transfusion as standard of care. Neurologic exam and cognitive assessments using Wechsler scales will be repeated every 12-18 months. Low-dose aspirin and overnight respiratory support trials are also under review. (Kirkham FJ, Lerner NB, Noetzel M et al. Trials in sickle cell disease. **Pediatr Neurol** June 2006;34:450-458). (Respond: Dr Kirkham, Reader in Paediatric Neurology, Neurosciences Unit, Wolfson Centre, Mecklen burgh Square, London WC1N 2AP, UK).

COMMENT. Stroke is common in patients with SCD, occurring in 25% of those with homozygous SCA and 10% of those with hemoglobin SC-disease. The distal internal carotid and proximal middle and anterior cerebral arteries are mainly affected. Covert or "silent" infarcts revealed on MRI without clinical stroke occur in 20% of SCD patients by adolescence, and are associated with cognitive deficits. Recent reports suggest that stroke may be predicted by using transcranial Doppler ultrasound, MRI, or pulse oximetry.

EEG hyperventilation and stroke in SCD. The potential risk of stroke attending the practice of hyperventilation during EEG in SCD patients should probably be emphasized, and the American EEG Society precautionary guidelines more widely publicized (Millichap JG. **Ann Neurol** 2005;58:972; **Clin EEG and Neuroscience** July 2006; in press). Voluntary routine hyperventilation during EEG recording is contraindicated in both SCD and SC trait patients (AEEGS guideline one. **J Clin Neurophysiol** 1986;3 (suppl 1):1-6). Generalized slowing in the EEG during hyperventilation results from cerebral hypoxia caused by constriction of cerebral vessels. Arterial constriction is a response to HV-induced hypocapnea, and results in decreased cerebral blood flow. In SCD, multiple areas of cerebral ischemia or infarction due to intravascular sickling may be precipitated by HV-induced cerebral hypoxia. In states of severe hypoxia, SC trait patients are also susceptible to stroke.