

# PEDIATRIC NEUROLOGY BRIEFS

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### VASCULAR DISORDERS

#### **TRAUMA AND INFECTION RISK FACTORS FOR STROKE**

Researchers at University of California at San Francisco (UCSF); Kaiser Permanente, Oakland, CA; and University of Utah, Salt Lake City performed a case-control study of recent exposure to trauma or infection in 126 childhood (<19 years old) cases of arterial ischemic stroke (AIS). Cases of AIS were identified from electronic records and confirmed by chart review in a cohort of 2.5 million children enrolled in a health care plan. Exposures to trauma and infection were determined from review of medical records prior to the stroke diagnosis. Twelve percent of cases of AIS (cf 1.6% of controls;  $p=0.001$ ) had encountered a medical head or neck trauma as an independent risk factor for stroke within the prior 12 weeks. More severe head trauma, with loss of consciousness in 7 cases and hospital admission of 11 cases, was strongly associated with AIS. Median time trauma to stroke was 0.5 days (range 0-2 days).

A minor acute infection in the prior 4 weeks was also an independent risk factor in 33% of cases of AIS cf 13% of controls. Two cases were exposed to both trauma and infection. A medical encounter for minor acute infection increased a child's risk of AIS by >4-fold. Common infectious diagnoses included upper respiratory infections (33%), other viral syndromes (26%), acute otitis media (19%), and acute gastroenteritis (17%). Ten percent of cases, versus 0% of controls, had a recent major acute infection (sepsis or meningitis/encephalitis). No case of AIS had a recent history of chicken pox. AIS was associated with chronic autoimmune disease in 13 cases and with cardiac disease in 10. (Hills NK, Johnston SC, Sidney S, Zielinski BA, Fullerton HJ. Recent trauma and acute infection as risk factors for childhood arterial ischemic stroke. *Ann Neurol* 2012 Dec;72(6):850-8). (Response: Dr Fullerton, Department of Neurology, Box 0114, University of California, San Francisco, 513 Parnassus Ave, 5-784, San Francisco, CA 94143. E-mail: FullertonH@neuropeds.ucsf.edu).

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COMMENT. Previous prospective multicenter studies have established pediatric stroke risk factors and associations but have lacked adequate controls and determination of causation (deVeber G. Editorial. Childhood stroke. **Ann Neurol** 2012 Dec;72(6):827-8). The current study establishes arteriopathies related to infection and trauma as independent risk factors for AIS in children, but the mechanism of the thromboembolic event is unclear. Involvement of a prothrombotic pathway with infection is suggested.

**Endothelial injury in childhood stroke with cerebral arteriopathy** was studied at Great Ormond Street Hospital for Children, London, UK. (Eleftheriou D et al. **Neurology** 2012 Nov 20;79(21):2089-96). Of 46 children with stroke (AIS), 10 had recurrence and 36 had a single AIS event. Levels of circulating endothelial cells (CECs) were significantly higher in children with AIS compared to healthy controls ( $p=0.03$ ); they were higher in children with AIS recurrence compared to those with no recurrence ( $p=0.0001$ ) and in controls ( $p=0.0001$ ). Total circulating annexin V + microparticles (MPs) were significantly greater in children with AIS recurrence than in those with no recurrence ( $p=0.020$ ). CECs and MPs reflect endothelial injury, cellular activation, and MP-mediated thrombin generation. MP-mediated thrombin generation is enhanced in children with recurrent AIS compared to those with no recurrence ( $p=0.0001$ ). These findings link inflammation, endothelial injury, and a tendency to thrombosis; they further the understanding of AIS pathophysiology.

## GENETIC RISK FACTORS FOR PERINATAL STROKE

Researchers at the University of California at San Francisco performed a population-based case-control study of births at Kaiser Permanente Northern California to explore the effect of genetic polymorphisms on the risk of perinatal arterial ischemic stroke (PAIS). Among 13 white infants with PAIS, polymorphisms were genotyped in 9 genes involved in inflammation, thrombosis, or lipid metabolism previously linked with stroke. The apolipoprotein Ee4 allele was associated with an increased risk of PAIS whereas proinflammatory and prothrombotic polymorphisms were not associated with PAIS. (Gelfand AA, Croen LA, Torres AR, Wu YW. Genetic risk factors for perinatal arterial ischemic stroke. **Pediatr Neurol** 2013 Jan;48(1):36-41). (Response: Dr Gelfand, Department of Pediatrics, UCSF, 350 Parnassus Ave, Suite 609, San Francisco, CA 94143. E-mail: GelfandA@neuropeds.ucsf.edu).

COMMENT. Apolipoprotein Ee4 allele is associated with an increased risk of PAIS in this study and is also linked to cerebral palsy in previous studies. (Kuroda MM et al. **Pediatrics** 2007 Feb;119(2):306-13). PAIS is a common cause of hemiplegic cerebral palsy. (Wu YW, et al. **Pediatr Neurol** 2006 Sep;35(3):191-6).

**Genetic deletion of CD36 enhances injury after acute neonatal stroke**, in a further study at UCSF (Woo M-S, et al. **Ann Neurol** 2012 Dec;72(6):961-70). Postnatal day 9 mice were subjected to a transient middle cerebral artery occlusion, and genetic deletion of the scavenger receptor CD36 exacerbates injury after acute focal stroke. Lack of CD36 reduces removal of apoptotic cells, enhancing injury. The injury mechanisms of neonatal stroke and those of adult stroke are compared and contrasted.