

# Cerebrovascular Events that are Diagnosed During the Perinatal Period

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## Description

Cardiac disorders were identified in almost one-third of children with arterial ischemic stroke. They had similar clinical presentations to those without cardiac disorders but differed in age and headache prevalence. Children with cardiac disorders more frequently had a 'cardio embolic stroke pattern' with a higher prevalence of bilateral strokes in both the anterior and posterior circulations, and a greater tendency to hemorrhagic transformation. Understanding the vascular injury pathway is crucial to developing rational strategies for secondary stroke prevention in children. The multicenter Vascular Effects of Infection in Pediatric Stroke (VIPS) cohort study will test the hypotheses that infection can lead to childhood arterial ischemic stroke by causing vascular injury and resultant arteriopathy and inflammatory markers predict recurrent stroke. The authors are prospectively enrolling 480 children (aged 1 month through 18 years) with arterial ischemic stroke and collecting extensive infectious histories, blood and serum samples (and cerebrospinal fluid, when clinically obtained), and standardized brain and cerebrovascular imaging studies. Laboratory assays include serologist (acute and convalescent) and molecular assays for herpes viruses and levels of inflammatory markers.

## Multifaceted Approach

Participants are followed prospectively for recurrent ischemic events (minimum of 1 year). The analyses will measure association between markers of infection and cerebral arteriopathy and will assess whether cerebral arteriopathy and inflammatory markers predict recurrent stroke. Stroke was once recognized so infrequently in children that it was considered a medical curiosity, and until relatively recently, our understanding of the nature of cerebrovascular disorders in children was somewhat rudimentary. Paediatric stroke is relatively rare, with approximately 1000 childhood strokes in the United States per year. However, the occurrence of stroke in children leads to significant morbidity and mortality, warranting the development proven screening tools, protocols, and treatment options. Because significant delays in seeking medical attention can occur, time to recognition of pediatric stroke in the emergency department is uniquely challenging and critical. Once recognized, a trained multidisciplinary team with a multifaceted approach is needed to provide the best possible outcome for the

patient. Key elements of the pediatric stroke protocol should include recognition tools, stroke alert mechanism, stroke order sets, timely imaging, laboratory evaluation, and treatment options. Perinatal stroke has become increasingly recognized, but the incidence is probably underestimated because of variation in the presentation, evaluation, and diagnosis. Based on estimates from population-based studies of infants with seizures, perinatal stroke occurs in approximately 1 in 4000 term births. Most perinatal strokes involve the middle cerebral artery and are caused by thromboembolism from an intracranial or extra cranial vessel, the heart, or the placenta. Cardiac disorders, coagulation abnormalities, and infection are risk factors for stroke in the perinatal period. This article discusses the epidemiology of ischemic stroke occurring in the perinatal and neonatal period, including cerebrovascular events that are diagnosed during the perinatal period and those diagnosed retrospectively, when evidence of hemiparesis or post neonatal seizures leads to later evaluation and neuroimaging.

Substantial advancements have been made in the field of pediatric stroke protocols mainly due to formation of international consortiums and clinical trial. Despite significant progress, treatment options remain controversial. The aetiologies of arterial ischemic stroke in children are diverse and often multifactorial. A large proportion occurs in children with cardiac disorders. We hypothesized that the clinical and radiographic features of children with arterial ischemic stroke attributed to cardiac disorders would differ from those with other causes. Using the large population collected in the prospective International Pediatric Stroke Study, we analyzed the characteristics, clinical presentations, imaging findings, and early outcomes of children with and without cardiac disorders. Analysis of imaging data identified significant differences in the vascular distribution (anterior vs. posterior circulation or both) between groups. Bilateral strokes and haemorrhagic conversion were more prevalent in the cardiac disorders group.

## Cell Disease

Approximately half of children presenting with stroke have a known predisposing condition, but some have unexpected pathologies such as primary cerebrovascular disease associated with congenital heart anomalies, or may have modifiable risk factors such as hypertension associated with sickle cell disease. The literature on children presenting with initially unexplained

(cryptogenic) stroke suggests that there is a daunting list of possible causes, but since the series have mainly been small, it has been difficult to evaluate the relative importance of the reported associations. This paper reviews the literature on congenital, genetic, and acquired risk factors for stroke in childhood, and includes data from the large series of patients seen at Great Ormond Street Hospital over the past 10 years. The majorities have arteriography abnormalities and there is little evidence for asymptomatic cardiac disease. Genetic predisposition, trauma, infection, and nutritional deficiencies appear to be important, although case-control studies will be required to prove causation. Appropriate screening for modifiable risk factors may lead to prevention of recurrence in some patients. Strokes associated with congenital heart disease or vasculopathy cost the most, while perinatal or idiopathic

strokes cost the least. Higher costs are correlated with worse impairment and poorer quality of life. Stroke etiology significantly influences the cost of pediatric stroke. Future cost-benefit studies must consider etiology when estimating the incremental costs associated with stroke. For children requiring mechanical circulatory support as a bridge to cardiac transplantation in North America, options previously were limited to extracorporeal membrane oxygenation. There was one late death nearly 2 years after transplant. Complications included stroke in seven patients, two of which were ultimately fatal. Five patients required re-operations for bleeding or evacuation of hematoma. Despite a disappointing rate of neurologic morbidity, our preliminary experience with the EXCOR has been very encouraging.