# PEDIATRIC NEUROLOGY BRIEFS
## A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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## INFECTIOUS DISORDERS

### NEONATAL INFAMMATORY CYTOKINES AND CEREBRAL PALSY

The association of inflammatory, autoimmune and coagulation factors with cerebral palsy (CP) was examined at the National Institutes of Health, Bethesda, MD, and the Immunochemistry Laboratory, George Washington University Medical Center, using dried, preserved neonatal blood spot specimens of 31 children enrolled in the California Birth Defects case-controlled study of spastic CP and compared to 65 control children.

Concentrations of interleukins 1, 8, 9, tumor necrosis factor-x, and RANTES were elevated in the neonatal blood specimens of children with CP. CP children with lower Apgar scores and those with known intrauterine exposure to infection immediately prior to birth had especially high values of inflammatory cytokines. Spastic diplegia was associated with higher mean concentrations of inflammatory cytokines and chemokines than hemiplegia. Higher concentrations of antibodies to antiphospholipid, antithrombin III, factor V Leiden mutation, and to proteins C and S were found in the blood analytes of CP children compared to controls. (Nelson KB, Dambrosia JM, Grether JK, Phillips TM. Neonatal cytokines and coagulation factors in children with cerebral palsy. Ann Neurol October 1998;44:665-675). ((Respond: Dr Karin B Nelson, 7550 Wisconsin Ave, Room 714, Bethesda, MD 20892).

COMMENT. In children born at term with low Apgar scores and without known prenatal cerebral pathology, the etiology of a subsequently diagnosed spastic cerebral palsy may be explained by a prenatal or perinatal inflammatory or coagulation abnormality. Elevated cytokine concentrations detected in the neonatal blood of CP children are known to be neurotoxic and can trigger changes in immune, coagulation, and neuroendocrine factors. The role of autoimmune and coagulation disorders in neonatal encephalopathy and seizures and as a cause of CP requires further study. Factor V Leiden mutation has been linked to in utero ischemic infarction and congenital hemiplegic CP (see Ped Neur Briefs Oct 1997;11:75). This continuing NIH study of causes of CP, emphasizing involvement of infectious and coagulation disorders, supports previous

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conclusions that factors other than birth asphyxia may be more important in etiology (see Progress in Pediatric Neurology III, PNB Publ, 1997;p377). The reliability of dried neonatal blood spot samples for immunoassay of inflammatory cytokines may permit a correlation between prenatal or perinatal infection and the development of childhood neurobehavioral disorders, including ADHD, often associated with subtle neurologic abnormalities.

**Criteria for inclusion of cases in CP Registers** are discussed in an article from the University of Western Australia (Badawi N, Stanley F et al. What constitutes cerebral palsy? Dev Med Child Neurol Aug 1998;40:520-527). As generally accepted, CP is a motor impairment resulting from brain pathology that is non-progressive and is manifested in early childhood. Exclusion criteria are those motor disorders caused by neurodegenerative diseases, neuromuscular disorders, spinal neural-tube defects, and brain tumors. The MRI and other laboratory investigations have permitted an etiological approach to classification of cases of CP that was formerly regarded as a "waste-basket" diagnosis.

## ACUTE TRANSVERSE MYELITIS: CAUSES AND TREATMENT

Clinical manifestations, laboratory findings, management, and course of nine children diagnosed with acute transverse myelitis (ATM) between 1993 and 1996 are reported from the Children's University Hospital, Wurzburg, Germany. Spinal cord functions, including sensation, motor activity, and sphincter control, were affected in differing degrees, and neurologic symptoms and signs were often preceded by non-specific fever, nausea, and muscle pain. The peak of the illness and paraplegia was generally seen within 10 days and no later than 4 weeks. The thoracic spinal cord was principally involved in 80% of cases. Initially, tone and reflexes were decreased, and later, paralyses were associated with spasticity and hyperreflexia. CSF pleocytosis and/or elevated protein levels occurred in 4 patients. Peripheral nerve conduction velocity was normal, but muscle action potential amplitudes were decreased. An infectious causative agent was found in only 2 cases, with increasing antibody titers against echovirus 25 in one and *Borrelia* in one other. A para-, postinfective, postvaccinal myelitis was suspected in 7 cases. A review of the literature found bacterial, parasitic, and systemic lupus collagen disease as rare causes of ATM. A 3-day high-dose IV steroid pulse therapy (20 mg/kg/day prednisone) offered the most promising response in therapy. MRI excluded tumors, abscess, and vascular malformation. Multiple sclerosis, Guillain-Barre syndrome, and spinal cord infarction were more difficult to exclude. Of 6 patients followed up, 1 had a good recovery and 5 had a fair outcome. (Knebusch M, Strassburg HM, Reiners K. Acute transverse myelitis in childhood: nine cases and review of the literature. Dev Med Child Neurol September 1998;40:631-639). (Respond. Hans M Strassburg MD, Universitats Kinderklinik, Josef-Schneider-Str. 2 D-97080 Wurzburg, Germany).

COMMENT. Diagnostic criteria for acute transverse myelitis include: 1) acute paraplegia and sphincter disturbance with maximum impairment within 4 weeks; 2) bilateral segmental sensory impairment; 3) exclusion of spinal cord compression or systemic neurologic disease; and 4) consistent MRI and laboratory EMG findings. Prognosis is variable and residual sequelae are common.

## *ASPERGILLUS* MYELOPATHY

Three children, ages 14 - 15 years, who developed myelopathy as the first manifestation of invasive aspergillosis are reported from the Children's Hospital Los Angeles, University of Southern California. All were immunosuppressed because of chemotherapy and antibiotics for treatment of leukemia. Symptoms