

COMMENT. This study is similar to a multicenter study of language regression in a different cohort published earlier by the same investigators (Shinnar S et al. *Pediatr Neurol* 2001;24:183-189; see *Ped Neur Briefs* May 2001;15:37-38). As in the earlier publication that involved 177 children with early onset language regression, reports of a triggering event, frequently associated autistic symptoms, and the inordinately long delay in referral to a neurologist or language specialist are the most noteworthy findings. In patients with associated autism, one third show language regression between 18 and 24 months of age, and 95% before age 3 years, whereas in the majority of children with an associated epilepsy, as in Landau-Kleffner syndrome (LKS, acquired epileptic aphasia), regression begins after age 3 years (Deonna TW. *J Clin Neurophysiol* 1991;3:288-298). In a 10 year follow-up of children with LKS, children who showed language regression before 5 years of age were most likely to have severe language deficits (Bishop DVM. *Dev Med Child Neurol* 1985;27:705-712), and children with LKS or autism who were speaking at 5 years of age had a better prognosis.

The age-dependent characteristics of language regression are important in diagnosis and emphasize the need for early evaluation and treatment intervention. Children who show regression or a plateau in language development before 24 months of age should receive a neurologic examination that includes an electroencephalogram. EEG epileptiform discharges may occur in 16% of routine recordings and in 33% with prolonged video-EEG monitoring. Seizures temporally related to the onset of language regression should be treated with antiepileptic medication (AED). The response to conventional AEDs is variable (Paquier PF et al. *Arch Neurol* 1992;49:354-359), and a course of ACTH is more likely to result in remission of both seizures and aphasia. Treatment of LKS with ACTH or corticosteroids has been successful when given early; seizures and EEG epileptiform discharges were controlled within 3 weeks whereas complete remission of the acquired aphasia was delayed up to 8 months (Lerman P et al. *Dev Med Child Neurol* 1991;33:257-266). (See *Progress in Pediatric Neurology II*, PNB Publishers, 1994;pp223-226).

INFECTIOUS DISORDERS

INFLUENZA-ASSOCIATED ENCEPHALOPATHY AND FEBRILE CONVULSIONS

The transcription of cytokine genes in peripheral blood leukocytes (PBL) of 23 children (mean age 3.2 years) with influenza (mostly type A) complicated by encephalopathy (11 patients) or febrile convulsions (12 patients) was compared with systemic cytokine responses in 23 (mean age 5.0 years) with influenza but without neurologic complications, in a study at Nagoya University Graduate School of Medicine, Japan. WBCs were significantly higher in patients with encephalopathy than in patients with febrile convulsions or without neurologic complications ($P=.02$ and $P=.002$, respectively). A quantitative polymerase chain reaction (PCR) showed that transcription of the interleukin (IL)-6, IL-10, and tumor necrosis factor (TNF)- α genes was up-regulated more in patients with encephalopathy than in those without ($P=.049$, $P=.049$, and $P=.098$, respectively). Of 3 patients with encephalopathy and extremely high concentrations of IL-10, 2 died. IL-10 and TNF- α transcriptions were also higher in patients with febrile

convulsions than in those without neurologic complications ($P=.006$ and $P=.078$, respectively). Plasma IL-6 levels were higher with encephalopathy ($P=.071$, ANOVA) but not with febrile convulsions. Virus load, quantified by a real-time PCR applied to throat swab samples, was similar in patients with or without encephalopathy or febrile convulsions, and was not correlated with transcription of cytokine genes or plasma cytokine concentrations. Influenza-associated encephalopathy and febrile convulsions may be a consequence of systemic immune responses and are independent of the severity of the influenza virus infection. (Kawada J-I, Kimura H, Ito Y et al. Systemic cytokine responses in patients with influenza-associated encephalopathy. *J Infect Dis* September 2003;188:690-698). (Reprints: Dr Jun-ichi Kawada, Dept of Pediatrics, Nagoya University Graduate School of Medicine, 65 Tsurumaicho, Showa-ku, Nagoya 466-8550, Japan).

COMMENT. Influenza may activate peripheral immune cells to cause an increased cytokine response in patients who develop encephalopathy or FC. A cytokine response after FCs is reported previously with various infections other than influenza (Straussberg R et al. *Pediatr Neurol* 2001;24:49-53; see *Ped Neur Briefs* April 2001;15:32). Compared to 11 controls with fever but no convulsion, the secretion of IL-6 and IL-10 is greater in those with FCs. Interleukin 1 receptor antagonist (IL-1Ra) allele 1, one of the first cytokines to be discovered, and an endogenous pyrogen, is increased in Taiwanese children with FC and is a useful marker for predicting susceptibility to FC (Tsai F-J et al. *Arch Pediatr Adolesc Med* 2002;156:545-548).

Influenza virus A is a frequent cause of febrile convulsions in Japan and China, whereas in the US and Europe, except for one epidemic in the UK (Brocklebank JT et al. *Lancet* 1972;2:497-500) with a 50% incidence of FCs, influenza is an uncommon cause. In the Japanese influenza seasons (1999-2002) 12 of 46 (25%) patients recruited for the present study had febrile convulsions. In Hong Kong, influenza A infection accounted for 10 to 21% in 1997 and 1998, and up to 35% to 44% of FC during peak influenza months, while parainfluenza and adenovirus were less frequently (6 to 10%) associated with FC admissions (Chiu SS et al. *Pediatrics* 2001;108:E63).

Herpesvirus-6 infection is a more frequent cause of FC than influenza in the US, accounting for one third of all first-time febrile seizures in children up to 2 years of age. The risk of FC with HHV-6 infection was 29% (17% had HHV-6 and roseola) compared to only 9% with non-HHV-6 infections (with otitis or fever of undetermined origin). (Hall CB, Epstein LG et al. *N Engl J Med* 1994;331:432-438). The risk of FC with HHV-6 is correlated with a high fever, and with low immunoglobulins, IgA and IgM. FCs with HHV-6 may be prolonged and complex and, like those complicating influenza, a possible encephalitis/encephalopathy etiology is suspected in some (Suga S et al. *Ann Neurol* 1993;33:597-603). With HHV-6 and roseola, the height of the fever is exceptional and is often considered sufficient to explain the FC. In the Japanese study of influenza cases, the number with repeated febrile seizures (complex FC) during a 24-hour period (28%) is higher than that usually expected (<20%), and fever alone seems an unlikely explanation. The authors propose that the pathogenesis of FCs is similar to that of encephalopathy, and encephalopathy with convulsion may be difficult to differentiate from a complex FC (Millichap JG. *Febrile Convulsions*. Macmillan, 1968). Both simple or complex FC may occur with a viral infection and positive CSF viral isolation. Children with a proven viral

infection and FC have no worse prognosis than those without (Rantala H et al. J Pediatr 1990;116:196-199).

Do complex FCs have a different mechanism from the simple FC or do they both result from fever and infection which, in the complex FC, is neurotropic and encephalopathic and associated with a greater cytokine response? Future studies in the etiology of FCs should emphasize the role of viral infection and cytokines and require the expertise of the specialist in infectious disease. It is appropriate that influenza vaccination is now recommended in infants ages 6-35 months as well as older children.

ATTENTION DEFICIT DISORDERS

FINE AND GROSS MOTOR ABILITY IN MALES WITH ADHD

Both fine and gross motor abilities were evaluated in 10-year-old males with attention deficit hyperactivity disorder (ADHD) and compared to a group of control children at the School of Psychology, Curtin University of Technology, Perth, Australia. Movement ability was assessed using the Movement Assessment Battery for Children (MABC) and the Purdue Pegboard test. Children with ADHD had impaired movement ability compared to controls. Comparison of the Total Impairment scores derived from the MABC and fine motor ability scores showed that the ADHD-predominantly inattentive (-PI) group (n=50), and ADHD-combined (-C) group (n=38) were significantly impaired ($p<.001$), whereas the ADHD-hyperactive/impulsive (-HI) group (n=16) was less affected. The percentage of children with motor impairment consistent with developmental coordination disorder (DCD) was 10% in controls compared to 42% in ADHD-PI, 31% in ADHD-HI, and 29% in ADHD-C. Poorer fine motor ability in ADHD was not attributed to deficits in attention and concentration, and the evaluation of motor ability should be included in the diagnostic criteria for ADHD. (Pitcher TM, Piek JP, Hay DA. Fine and gross motor ability in males with ADHD. *Dev Med Child Neurol* August 2003;45:525-535). (Respond: Jan P Piek PhD, School of Psychology, Curtin University of Technology, GPO Box U1987, Perth 6845, Australia).

COMMENT. The relation between ADHD and motor coordination difficulties, as envisioned in the syndrome of minimal brain dysfunction (MBD) (Clements SD. 1966), has been neglected in favor of a symptomatic approach to diagnosis. Swedish research has emphasized the association of Deficits in Attention, Motor Control, and Perception (DAMP), and Gillberg (1998) suggests that children with DAMP meet criteria of DSM-IV ADHD and Developmental Coordination Disorder. Huttenlocher PR et al (1990) and Millichap JG (1974) have reported the predictive value of subtle neurologic abnormalities for learning disabilities and ADHD. Poor fine motor ability in children with ADHD is not the result of ADHD symptomatology but rather reflects a comorbid developmental coordination disorder and neurologic deficit. The recognition of coordination problems as a frequent (50%) and integral part of the ADHD syndrome would lead to early physical and educational accommodations and improved prognosis. (see [Progress in Pediatric Neurology III](#), PNB, 1997;pp195-205, for ADHD and brain dysfunction).