

PSEUDOTUMOR CEREBRI

VITAMIN A AND IDIOPATHIC INTRACRANIAL HYPERTENSION

Vitamin A levels were measured in the cerebrospinal fluid of a total of 78 patients having idiopathic intracranial hypertension (IIH;n=20), elevated pressure of other causes (E-ICP;n=19), and normal pressure (N-ICP;n=39), in a study at the University of Utah, Salt Lake City, UT. Higher CSF vitamin A levels found in some patients with IIH were significantly correlated ($p=0.036$) when compared with control E-ICP and IIH patients. Higher levels were marginally significantly associated with female gender ($p=0.094$) and younger age ($p=0.069$). Multivitamin use was not associated with the levels of vitamin A. High vitamin A levels in patients with IIH and high average vitamin A levels in patients with breakdown of the blood-brain barrier are suggestive of a toxic effect of CSF retinol on the arachnoid granulation resorption mechanism in IIH. (Warner JEA, Bernstein PS, Yemelyanov A et al. Vitamin A in the cerebrospinal fluid of patients with and without idiopathic intracranial hypertension. Ann Neurol November 2002;52:647-650). (Respond: Dr Warner, Department of Ophthalmology and Visual Sciences, John A Moran Eye Center, 50 North Medical Drive, Salt Lake City, UT 84132).

COMMENT. Some patients with idiopathic intracranial hypertension have significantly higher levels of vitamin A in the CSF than patients with normal pressure or those with increased pressure due to other causes. Serum retinol-binding protein (RBP) and retinol are also elevated in some patients with IIH (Jacobson DM, Berg R, Wall M, et al. Neurology 1999;53:1114-1118). Vitamin A may have a specific transport mechanism into the CSF, and it becomes toxic when the level exceeds the RBP binding capacity. Study of patients with breakdown of the blood-brain barrier may elucidate the transport mechanism of CSF vitamin A and pathogenesis of IIH.

The role of vitamin A intoxication in the pathogenesis of IIH is discussed in an editorial by Fishman RA. (Polar bear liver, vitamin A, aquaporins, and pseudotumor cerebri. Ann Neurol November 2002;52:531-533). It is speculated that vitamin A increases CSF volume and pressure by an effect on aquaporins present in membranes of the choroid plexus that control CSF secretion.

ATTENTION DEFICIT DISORDERS

BRAIN VOLUME ABNORMALITIES IN ADHD

Regional brain volumes have been compared at initial MRI scans and their change over time in 152 medicated and previously unmedicated male and female patients (age range, 5-18 years) with attention-deficit/hyperactivity disorder (ADHD) and 139 age- and sex-matched healthy controls. In a case-control study conducted from 1991-2001 at the National Institute of Mental Health, Bethesda, MD, total cerebrum, cerebellum, gray and white matter for the four major lobes, and caudate nucleus volumes were measured by automated methods. On initial scan, patients with ADHD had significantly smaller brain volumes in all regions, amounting to a 3% decrease. Compared with controls, previously unmedicated ADHD children had significantly smaller total cerebral volumes, cerebellar volumes, and especially white matter volumes. In these unmedicated patients, white matter volumes were also smaller when compared with medicated ADHD children. Abnormal volumes persisted with age, except for caudate volumes which decreased in both patients and controls during adolescence. Male and female

ADHD patients showed comparable abnormalities in regional brain volumes, and the changes correlated significantly with parent- and physician-rated severity of ADHD. It is concluded that brain volumetric and development changes related to genetic and/or early environmental factors in children with ADHD are fixed and nonprogressive through adolescence, and are unrelated to stimulant medication. (Castellanos FX, Lee PP, Sharp W, et al. Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. *JAMA* October 9 2002;288:1740-1748). (Reprints: F Xavier Castellanos MD, New York University Child Study Center, 577 First Ave, New York, NY 10016).

COMMENT. It should be emphasized to parents that these quantitative MRI studies are only appropriate in research and not applicable to the diagnostic assessment and management of ADHD. The decreases in brain total and regional volumes in ADHD patients appear to reflect neurobiological insults or genetic factors that have influenced brain development early. The 3% disparity in brain volume stays constant through adolescence. In later childhood and adolescence, for the most part these decreases in brain volumes remain static and nonprogressive and are not influenced by medications or behavioral interventions. The previously emphasized frontal-striatal brain abnormality in ADHD is not confirmed in this study. Never medicated ADHD children have smaller white-matter volumes than those with ADHD who receive stimulants and compared to normal controls. These findings appear to further support arguments in favor of using medications for ADHD.

AUTISTIC SPECTRUM DISORDERS

EVALUATION OF MMR VACCINATION AND AUTISM LINK

A retrospective cohort study of autism in all children born in Denmark from January 1991 through December 1998 and those receiving measles, mumps, and rubella (MMR) vaccination is reported from the Danish Epidemiology Science Center, Aarhus, Denmark. Of 537,303 children in the cohort, 440,655 (82%) had received the MMR vaccine, 316 children were identified with a diagnosis of autistic disorder, and 422 with other autistic-spectrum disorders. The relative risk of autistic and other autistic-spectrum disorders in vaccinated compared to unvaccinated children was 0.92 and 0.83, respectively. No association was detected between age at time of vaccination, time since vaccination, and date of vaccination and development of autistic disorder. It is concluded that the evidence is against the hypothesis that MMR vaccination causes autism. (Madsen KM, Hviid A, Vestergaard M et al. A population-based study of measles, mumps, and rubella vaccination and autism. *N Engl J Med* November 7, 2002;347:1477-1482). (Reprints: Dr Madsen, Danish Epidemiology Science Center, Department of Epidemiology and Social Medicine, Vennelyst Blvd 6, DK-8000, Aarhus C, Denmark).

COMMENT. It has been suggested that a reported increase in the incidence of autism in California may be linked to the widespread use of MMR vaccine. Symptoms of developmental regression and gastrointestinal disorders have coincided with MMR vaccination, and measles virus has been detected in the terminal ileum of these patients. Although these proposed associations may be suggestive of a causative role of MMR in autism, this retrospective cohort study fails to confirm the hypothesis and shows no temporal or other association between MMR and the onset of autism. The prevalence rates in 8-year-old children born between 1991 and 1998 in the Danish cohort were 7.7 per 10,000 for autistic disorder and 22.2 per 10,000 for other autistic-spectrum disorders. These