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Is it the gluten or something else?

— Ivor D. Hill, MB, ChB, MD

The gluten-free diet has become the new fad diet in America, with sales of gluten-free products currently in the billions of dollars annually. Those following the diet claim resolution of a variety of symptoms, with improvement in health and well-being. Others erroneously believe a gluten-free diet will lead to weight reduction. Maintaining a strict gluten-free diet for life is mandatory for those who have celiac disease (CD). This is probably not true for the vast majority of people who are avoiding gluten today. There is little evidence that gluten (the protein fraction of wheat, barley, and rye) per se is harmful to those who do not have CD. Accumulating evidence suggests symptom resolution in patients without CD may be related to the removal of other products, such as fructans, that are present in high concentrations in wheat.

In this issue of *The Journal,* Guandalini et al provide a timely review of the subject of gluten-related disorders. They differentiate CD from wheat allergy and the entity known as nonceliac gluten sensitivity (NCGS). The need to clearly distinguish between these conditions before initiating treatment is emphasized and the rationale for doing so is described. The confusion surrounding the entity of NCGS is explored and the evidence for gluten not being the prime causative factor of symptoms in those with NCGS is analyzed. In keeping with others, the authors make a case for abandoning the term NCGS and replacing it with the more broad term of "wheat intolerance syndrome." Future well designed studies are still needed to clarify the role of wheat and related products in the causation of symptoms in people who do not have CD.

Article page 805 ▶

Beneficial effect of social advantage and detrimental effect of early postnatal CMV infection

— Sara S. Long, MD

Two prospective studies published in this issue of *The Journal* deal with neurocognitive outcome of preterm infants. The study by Manley et al from Australia took advantage of their randomized 35-center trial of caffeine for apnea of prematurity in very low birth weight infants (500g to 1250g) from 1999 to 2004, with subsequent follow-up at 31 sites to corrected age of 5 years. They aimed to determine the extent of influence of social variables in children's cognitive development. Three social advantages (higher maternal education, higher paternal education, and caregiver employment) had strong, independent, additive effects on cognitive gain between 18 months and 5 years of age.

In the second report, Brecht et al from Germany performed a longitudinal study to investigate long-term cognitive effects of early postnatally-acquired infection with cytomegalovirus (CMV) transmitted by human milk. They report the neuropsychological sequelae of a well characterized group of adolescents born very preterm (22 to 32 weeks' gestation) who had been studied prospectively to prove whether they did or did not acquire CMV through human milk in early postnatal life. They compared results of neurocognitive testing of these two groups when adolescents as well as a group of adolescents born at term (whose CMV status was not studied). Despite inevitable problems of attrition over the long study period, results in 19 adolescents with CMV compared with 23 adolescents without CMV born preterm and 24

adolescents born at term suggest adverse effect of early CMV infection on neurocognitive function. Their data also would suggest that CMV infection from breastfeeding in preterm infants could be responsible for a substantial proportion of the adverse outcomes associated with premature birth.

Should hard-to-come-by findings of this small number of well characterized study subjects change practice? Should preventive measures against transmission of CMV by human milk in preterm infants be implemented? At what potential risk? The accompanying editorial by Wright and Permar is a must read in order to place the latter study in its proper context.

Article page 834 ▶
Article page 870 ▶
Editorial page 795 ▶

Diabetes and arthritis

— Thomas R. Welch, MD

Type 1 diabetes and juvenile idiopathic arthritis (JIA) are serious chronic childhood disorders related by underlying autoimmunity. As is the case with a number of autoimmune disorders, there is evidence that these two conditions may coexist more often than would be predicted by chance.

This association in children is confirmed in this issue of *The Journal* in a study by Hermann et al from Germany, drawing from a large European registry of children with type 1 diabetes. Although both diseases are relatively rare, the incidence of children with JIA and type 1 diabetes was 3 to 4 times that of children without type 1 diabetes. There were some differences between children with type 1 diabetes who did and did not have JIA (eg, height), which may simply represent the consequence of the comorbidity. Target organ damage from type 1 diabetes (hypertension and hyperlipidemia) did not differ between the groups. Although children with JIA had somewhat lower glycosylated hemoglobin A1c levels, this could be a consequence of low-level hemolysis.

This is an interesting observation, and also is a demonstration of the power of well maintained disease registries. Indeed, such a study might have not been possible in the US.

Article page 930 ▶

Early diagnosis of biliary atresia

— William F. Balistreri, MD

Biliary atresia is the most common indication for liver transplantation in the pediatric population and the most frequent liver-related cause of death in early childhood. However, in some cases, long-term survival with the native liver can be achieved by surgical reestablishment of bile flow. The procedure of choice involves removal of the fibrotic, atretic bile duct segment and construction of a drainage route via hepatoportoenterostomy (the Kasai procedure). The outcome following hepatoportoenterostomy is closely related to the patient's age at the time of the procedure. It is universally acknowledged that the Kasai procedure performed before 60 days of age can improve the likelihood of survival with the native liver and avoid liver transplant. The problem that we continually witness in our clinical practice is late referral of patients with biliary atresia, emphasizing the importance of screening for this potentially devastating disease.

The lack of bile flow into the intestine leads to acholic stools—a reliable clue that obstruction is likely. Pale, nonpigmented stools appear within the first month after birth in patients with biliary atresia. Thus, the concept of using a stool color card for screening and parent education regarding the disease was initially introduced to the local population in Japan (Tochigi Prefecture) by Matsui et al in 1993 (*Screening* 1993;2:201-9). Their preliminary results documented the success in ensuring a prompt diagnosis and early Kasai procedure. The concept of stool color card based mass screening has subsequently been utilized in several other countries, also resulting in earlier referral of patients with biliary atresia.