been shown to decrease levels of adiponectin.[5] Thus, a combination of increased TNF-α and decreased adiponectin leads to severe insulin resistance, which in turn leads to NAFLD. Various treatments for NAFLD (e.g., weight loss or use of drugs such as thiazolidinediones) serve to increase adiponectin levels.[5,6]

Adams and associates,[1] in their discussion of the inflammatory and fibrotic mediators of NAFLD, suggest that adiponectin promotes liver fibrosis in NAFLD, but the evidence indicates that the opposite is true. Some clarification seems warranted.

Pankaj Madan
University College of Medical Sciences
Guru Teg Bahadur Hospital
Delhi, India

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Leon Adams and associates[1] provide an excellent and up-to-date review of NAFLD in adults,[1] but they do not discuss the condition in children. Childhood NAFLD has been reported globally since our first large clinical series from the Hospital for Sick Children in Toronto was published in 2000.[2] In part this recent reporting reflects the increasing prevalence of obesity in childhood.[3,4] NAFLD is typically diagnosed in children 12–14 years old, but serious liver disease associated with NAFLD has been reported in children as young as 5 years of age.[5,6]

In adults NAFLD must be differentiated from alcoholic liver disease, but in children NAFLD must be distinguished from various rare metabolic disorders that cause fatty liver (such as Wilson disease). The typical child suffers from overnutrition, is asymptomatic or has vague abdominal pain, and may have abnormal results on liver biochemistry testing. As in adults, an important feature of childhood NAFLD is hyperinsulinemia associated with relative insulin resistance, as shown by clinical studies using the homeostasis model of insulin resistance.[5] Whether oxidative damage to the liver is prominent in childhood NAFLD is now being investigated.

NAFLD in adults can progress to cirrhosis with chronic liver failure requiring liver transplantation or to hepatocellular carcinoma, but the long-term outcome for children with NAFLD is unknown. Cirrhosis has been reported in a few children.[6] Although simple steatosis (hepatic fat accumulation without inflammation and fibrosis) carries a benign prognosis in adults, the long-term outcome for children with simple steatosis is uncertain. Current treatment strategies in NAFLD are aimed at eliminating or reducing the risk factors associated with NAFLD: they involve weight loss and increased physical activity. Few pediatric data are available regarding pharmacologic interventions such as vitamin E, ursodiol and metformin.[7-9] Well-designed prospective studies in children are urgently needed to determine the best overall medical management.

Childhood NAFLD may be the hepatic manifestation of the metabolic dysregulation leading to type 2 diabetes, hypertension and cardiovascular disease. Given that childhood NAFLD is highly prevalent — estimated at 3% to 10% of obese children — we need to intervene now so as to avoid cirrhosis, as well as these other diseases, in the current generation of children.

Diana Mager
Eve Roberts
Division of Gastroenterology,
Hepatology and Nutrition
Metabolism Research Program
The Hospital for Sick Children
Toronto, Ont.

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