Obesity is the most common nutritional problem among children in both developed and underdeveloped countries. Despite efforts over the past decade to prevent and control obesity, data from the 2003–2006 National Health and Nutrition Examination Surveys (NHANES) show that 16.3% of children and adolescents, 2 to 19 years of age, are obese (i.e., have a body-mass index [BMI] above the 95th percentile for age and sex).  

There is strong epidemiologic evidence that obesity in childhood is associated with an increased incidence of atherosclerosis in adulthood. Postmortem studies have shown that obesity in childhood and adolescence is associated with increased evidence of atherosclerosis at autopsy, especially in males.  

1. Baker et al., using data on childhood BMI z scores and information from
found that, with each one-unit increase in BMI z score at 7 to 13 years of age in the case of boys and at 10 to 13 years of age in the case of girls, there was a significant increase in the risk of a coronary event during adulthood. Bibbins-Domingo and colleagues used data on the prevalence of overweight among adolescents in the 2000 NHANES to estimate the likely prevalence of obesity among 35-year-old persons in 2020. They then used this estimate in a computer-simulation model of coronary heart disease to predict the likely annual excess incidence and prevalence of coronary heart disease attributable to obesity from 2020 to 2035. Their model predicted that, by 2035, the prevalence of coronary heart disease in adults will increase by 5 to 16% and that more than 100,000 excess cases of coronary heart disease will be directly attributable to childhood obesity.

Despite the overwhelming evidence linking childhood obesity to adult atherosclerotic heart disease, there is also evidence that obesity in childhood does not guarantee that cardiovascular risk will be increased in adulthood. We have previously shown that among obese adolescents, an improvement in weight status and a decrease in body fatness is associated, at least in the short term (20 weeks), with a decrease in systolic and diastolic blood pressure; a decrease in total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels; an increase in high-density lipoprotein cholesterol levels; and a decrease in insulin resistance. The article by Juonala and colleagues in this issue of the Journal adds considerably to our observations by providing long-term follow-up data that suggest that cardiovascular risk in adulthood is reduced if obesity is treated or prevented in childhood. In their study of 6328 subjects, those with persistently high adiposity status from childhood to adulthood had significantly increased risks of diabetes, hypertension, dyslipidemia, and carotid-artery atherosclerosis. In contrast, the risks of all these outcomes among overweight or obese children who became nonobese as adults did not differ significantly from the risks among those who were never obese.

The study by Juonala et al. has several limitations. It was observational (with no attempt made to prevent weight gain or to reduce weight), there were differences in the acquisition of data among the four cohorts, there was a lack of comprehensive serial data, and most of the study participants were white. However, taking into account data from studies of pediatric weight-loss interventions, which have documented that weight loss is associated with a reduction in cardiovascular risk factors, I believe that the major finding in the study by Juonala et al. — that childhood obesity does not permanently increase cardiovascular risk provided that childhood obesity is successfully treated — is valid.

Given that atherosclerotic cardiovascular disease is a major driver of health care expenditures in the United States, the development of more effective strategies for treating and preventing childhood obesity is a cost-effective way of achieving a long-term reduction in atherosclerotic cardiovascular disease. To date, most studies of interventions to prevent childhood obesity have been school-based or community-based, and although these interventions are effective in modifying the diet and exercise habits of children, they unfortunately have limited value in preventing the long-term development of overweight and obesity. Juonala et al. found that, over an interval of almost 25 years, only 15% of subjects who were of normal weight as children were obese as adults, whereas 65% of those who were overweight or obese as children and 82% of those who were obese as children were obese as adults. These figures suggest that targeting interventions for obesity prevention and treatment specifically to children who are at high risk for becoming obese will prove to be a more valuable and more cost-effective strategy than targeting these interventions to whole populations of children. If we want to reduce the incidence of adult heart disease and thereby start to control the continuing escalation in U.S. health care expenditures, now is the time to do whatever it takes to develop more effective methods for both the prevention and the treatment of childhood obesity.
Systemic lupus erythematosus is a prototypical autoimmune disease that can potentially involve every organ. Its clinical spectrum is therefore extremely heterogeneous and varies from relatively mild cases (e.g., involving only the skin or joints) to life-threatening manifestations, with renal impairment, severe cytopenias, or central nervous system disease, not to mention an increased rate of thromboembolic events.

Kidney involvement (mainly glomerulonephritis) occurs in at least one third of patients with lupus and significantly affects survival. The initial clinical presentation of lupus nephritis ranges from asymptomatic proteinuria discovered on routine urinalysis to the nephrotic syndrome with or without renal impairment. Histologic examination of a renal-biopsy specimen is a pivotal step in confirming the diagnosis and guiding therapy. Immunosuppressive therapy consists of glucocorticoids combined with a cytotoxic drug (which for decades has been high-dose intravenous cyclophosphamide) to achieve a prompt response. The high rate of renal relapse (35%) justifies long-term maintenance immunosuppression. Between 10 and 20% of patients with lupus nephritis ultimately require renal-replacement therapy.

Within the past decade, clinical researchers — thanks to the outstanding collaboration of patients with lupus nephritis — have carried out well-conducted, controlled trials aimed at improving the efficacy and safety of the immunosuppressive regimen. Although the jury is still out on several issues, advances have been achieved, such as the use of a more patient-friendly, short-course induction regimen, in which low-dose intravenous cyclophosphamide is followed by long-term azathioprine maintenance therapy (as described in the Euro-Lupus Nephritis Trial), and the introduction of mycophenolate mofetil, an immunosuppressive drug used successfully in transplantation. Mycophenolate mofetil was shown to be at least equivalent to cyclophosphamide in inducing an initial renal response, thereby earning it a place in the armamentarium for the treatment of lupus nephritis, although long-term data on patients who have undergone induction therapy with mycophenolate mofetil are still eagerly awaited.

In this issue of the Journal, Dooley et al. report the results of the maintenance phase of the Aspreva Lupus Management Study (ALMS), which compared the efficacy and safety of azathioprine and mycophenolate mofetil as maintenance therapy for patients with lupus nephritis who had responded to induction therapy with either mycophenolate mofetil or intravenous cyclophosphamide. After 36 months, mycophenolate mofetil appeared to be superior to azathioprine with respect to time to treatment failure (a composite primary end point), time to renal flare, and time to rescue therapy, regardless of induction group. Withdrawals due to severe adverse events were significantly more common among the patients given azathioprine. Although the study was not powered for subset analyses, the differential effect between mycophenolate mofetil and azathioprine was more stringent in black patients. Of note, among patients given mycophenolate mofetil for maintenance, those who had previously received induction therapy with intravenous cyclophosphamide had fewer treat-