8 Davidson MB. The effectiveness of nurse- and pharmacist-directed care in diabetes disease management: a narrative review. *Curr Diabetes Rev* 2007; **3:** 280–86.
9 Shojania KG, Ranji SR, McDonald KM, et al. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. *JAMA* 2006; **296:** 427–40.
10 Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2005; **43:** 521–30.
11 Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A. Cost-effectiveness of self-monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. *BMJ* 2008; **336:** 1177–80.
12 Sarol JN, Nicodemus NA, Tan KM, Grava MB. Self-monitoring of blood glucose as part of a multi-component therapy among non-insulin requiring type 2 diabetes patients: a meta-analysis (1966–2004). *Curr Med Res Opin* 2005; **21:** 173–84.
13 Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F. Use of insulin-pump therapy in the pediatric age group. *Diabetes Care* 2007; **30:** 1653–62.
14 The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 2008; **359:** 1464–76.
15 Schroeder SA. We can do better—improving the health of the American people. *N Engl J Med* 2007; **357:** 1221–28.

Type 2 diabetes in children and adolescents

The past 15–20 years have seen a dramatic increase in the prevalence of type 2 diabetes in children and adolescents. Although probably not truly epidemic in proportion,[1] the incidence of cases in high-risk ethnic populations now approaches 50% of all new cases of diabetes diagnosed in US adolescents.[2] This increased prevalence of paediatric type 2 diabetes suggests impending future morbidity from diabetic complications in a large number of relatively young adults.

These concerns have led to investigation over the past decade into the underlying pathophysiology of type 2 diabetes in children. As in adults, diabetes develops mainly in obese children, particularly within ethnic groups that are more insulin resistant, such as Hispanic, African-American, and Native American groups. In the setting of insulin resistance, progressive β-cell dysfunction leads to increasing degrees of hyperglycaemia, resulting first in prediabetes, then overt diabetes.[3,4] The transient insulin resistance of puberty might accelerate this process[5] through additional stress on β-cell compensation at a crucial period of growth and development. The specific roles of visceral adiposity, ectopic fat depots (eg, hepatic and intramyocellular), lipotoxicity, and genetic factors in progressive β-cell failure remain to be clarified. Pathogenetic mechanisms might vary depending on ethnic background, as there are clear ethnic differences in both underlying risk factors and compensatory responses to insulin resistance.[6] Fully defining the mechanisms awaits results from studies that are tracking large numbers of at-risk children over extended periods, and carries important implications for prediction and prevention of type 2 diabetes in at-risk young people. Paediatric trials are also underway with drug therapies (eg, metformin, thiazolidinediones) to reduce insulin resistance, thereby reducing β-cell demand and prolonging β-cell life, as has been effective in prediabetic adults.[7]

Treatment of children with type 2 diabetes has thus far relied on expert consensus.[8] Treatment goals include weight management, increasing physical activity, achieving glycaemic control, and managing comorbidities such as dyslipidaemia and hypertension. Optimum lifestyle approaches to weight and activity issues remain to be determined, but guidelines for management of childhood obesity can be used.[9] Lifestyle approaches must ensure a family-centred and developmentally relevant approach.

Drug therapy has relied mainly on either metformin or insulin, the only agents approved by the US Food and Drug Administration for use in children with diabetes. Insulin therapy in young people with type 2 diabetes has generally been limited to children with relatively acute onset of the disease associated with weight loss, ketosis, or ketoacidosis, as well as to children for whom lifestyle and oral hypoglycaemic agents fail to control glycaemia. Other potential uses of insulin, such as early use to preserve β-cell function,[10] as well as assessment of optimum insulin regimens in childhood type 2 diabetes, await investigation. Whilst short-term improvements in glycaemic control have been shown with oral agents,[11] ongoing single-site and multicentre, double-blind, randomised trials are now investigating the longer-term efficacy and safety of metformin, thiazolidinediones, sulphonylureas, incretin mimetics, and other agents, both as monotherapies and in combinations as treatment for newly diagnosed cases. For example, the TODAY trial[12] is randomising children

Science Photo Library

with newly-diagnosed type 2 diabetes into treatment with metformin alone, metformin plus rosiglitazone, or metformin plus intensive lifestyle intervention. Outcomes include time to treatment failure, insulin sensitivity, body composition, behavioural and psychosocial measures, and cardiovascular risk factors. The results of these ongoing trials will provide a great advance in our evidence-based approaches.

Further research is needed to investigate innovative behavioural, educational, lifestyle, and other non-drug approaches to management, particularly in view of the major developmental differences between paediatric and older adult populations. Smaller proof-of-concept studies are needed to investigate efficacy before launching into large expensive trials. The lifelong risk of comorbidities, such as cardiovascular and fatty-liver disease, means we must also investigate the safety and efficacy of long-term use of lipid-lowering and antihypertensive agents, with intermediate outcome measures such as cardiovascular risk factors and carotid intima media thickening. Whilst we have learned much in response to the huge increase in type 2 diabetes in young people, we have a long way to go to ensure that our understanding, prevention efforts, and treatment of this disease are optimum for paediatric patients.

*Marc J Weigensberg, *Michael I Goran*
Departments of Pediatrics (MJW, MIG), Preventive Medicine (MIG), and Physiology and Biophysics (MIG), University of Southern California, Los Angeles, CA 90089, USA
Goran@usc.edu

We declare that we have no conflicts of interest.

1 Goran MI, Davis J, Kelly L, et al. Low prevalence of pediatric type 2 diabetes: where's the epidemic? *J Pediatr* 2008; **152:** 753–55.
2 Dabelea D, Bell RA, D'Agostino RB Jr, et al. Incidence of diabetes in youth in the United States. *JAMA* 2007; **297:** 2716–24.
3 Goran MI, Lane CJ, Toledo-Corral CM, Weigensberg MJ. Persistence of pre-diabetes in overweight Hispanic children: association with progressive insulin resistance, poor β-cell function, and increasing visceral fat. *Diabetes* 2008; **57:** 3007–12.
4 Weiss R, Taksali S, Tamborlane W, Burgert T, Savoye M, Caprio S. Predictors of changes in glucose tolerance status in obese youth. *Diabetes Care* 2005; **28:** 902–09.
5 Goran MI, Gower BA. Longitudinal study on pubertal insulin resistance. *Diabetes* 2001; **50:** 2444–50.
6 Goran MI, Bergman RN, Cruz ML, Watanabe R. Insulin resistance and associated compensatory responses in African-American and Hispanic children. *Diabetes Care* 2002; **25:** 2184–90.
7 Buchanan TA, Xiang AH, Peters RK, et al. Preservation of pancreatic β-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk Hispanic women. *Diabetes* 2002; **51:** 2796–803.
8 Rosenbloom A, Silverstein J, Amemiya S, Zeitler P, Klingensmith G. ISPAD clinical practice consensus guidelines 2006–2007: type 2 diabetes mellitus in the child and adolescent. *Pediatr Diabetes* 2008; **9:** 512–26.
9 August GP, Caprio S, Fennoy I, et al. Prevention and treatment of pediatric obesity: an Endocrine Society clinical practice guideline based on expert opinion. *J Clin Endocrinol Metab* 2008; **93:** 4576–99.
10 Weng J, Li Y, Xu W, et al. Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. *Lancet* 2008; **371:** 1753–60.
11 Jones KL, Arslanian S, Peterokova VA, Park JS, Tomlinson MJ. Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial. *Diabetes Care* 2002; **25:** 89–94.
12 The TODAY Study Group. Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes. *Pediatr Diabetes* 2007; **8:** 74–87.

Continuous glucose monitoring in type 1 diabetes mellitus

When first introduced, continuous glucose monitoring was hailed as having the potential to revolutionise the safety and effectiveness of intensive treatment of type 1 diabetes.[1] With this new tool, basal insulin replacement could be optimised and meal-related insulin requirements accurately defined. Alarms could alert patients to impending hypoglycaemia and bolus doses adjusted depending on the direction of change in glucose levels before the meal.

The first generation of continuous glucose-monitoring systems had suboptimum sensor accuracy and were either too difficult to use or could only be used for retrospective review.[2,3] Accuracy and usability of real-time monitoring devices has improved such