Type 2 Diabetes and Diabetes Risk Factors in Children and Adolescents*

Daniel E. Hale, MD

Professor of Pediatrics, Division of Endocrinology and Diabetes
Department of Pediatrics, University of Texas Health Science Center at San Antonio
Medical Director, The Children's Center at the Texas Diabetes Institute
San Antonio, Texas

Long considered a disease of older adults, type 2 diabetes mellitus (DM) is now affecting children. While the prevalence and incidence of type 2 DM are not yet established in children, the number of affected individuals continues to climb. At the same time, obesity, the primary risk factor for type 2 DM, has become epidemic, affecting all ethnic and demographic groups across the United States. The lifestyle trends contributing to both of these phenomena include changes in dietary patterns and habits, declining levels of physical activity, and increasing sedentary behaviors. In response to these problems, the medical profession must become proactive with its patients and in the community. (*Clinical Cornerstone*. 2004;6[2]:17–30)

Long considered a disease of older adults, type 2 diabetes mellitus (DM) is now a pediatric disease, and in some clinical practices presently accounts for 20% to 50% of all new cases of diabetes in individuals <18 years of age. Although disproportionately affecting minority children (eg, Native Americans, African Americans, Hispanics, and Pacific Islanders), increasing numbers of children from all racial and ethnic groups, including non-Hispanic whites, are affected by type 2 DM. The cause of this increase has not yet been firmly established; however, it is generally assumed that the increasing numbers of children with type 2 DM represent the forefront of the obesity epidemic that is sweeping across the United States and other Western countries. In turn, the problem of obesity reflects major societal trends, including changes in dietary content and habits, declining physical activity, and increasing sedentary behaviors.

PREVALENCE OF DIABETES IN THE PEDIATRIC POPULATION

Type 1 DM is well established as a pediatric disease. Population-based studies have established the prevalence of the disease in most countries and in most ethnic and minority groups. In North America, the estimated prevalence is 2 to 5 per 1000 children, and the incidence varies between 10 and 20 cases per year per 100,000 individuals aged <18 years. In contrast, no comparable population-based estimates are available on the prevalence or incidence of type 2 DM in children. Indeed, the first official acknowledgment that type 2 DM was a pediatric disease came in 2000, as a joint statement by the American Diabetes Association (ADA)[1] and the American Academy of Pediatrics (AAP).[2] Type 2 DM in adolescents was first reported in 1979 among the Pima Indians.[3] As of 1996, the estimated prevalence in the Arizona Pima aged 15 to 19 years was 50.9 per 1000, and for Pima aged 10 to 14 years was 22.3 per 1000.[4,5] Furthermore, the apparent prevalence increased 4- to 6-fold in both age groups from 1967 to 1976 and 1987 to 1996.[4,5] In the US Native American pediatric population, the prevalence is estimated to be 4.5 per 1000,[4,5] and in Canadian First Nations youth in Manitoba, Canada, the prevalence is 2.3 per 1000 (personal communication, Heather Dean, MD, 2004). In the Bogalusa Study, involving African

*This issue of *Clinical Cornerstone* contains references to off-label/unapproved uses of medications. Insulin is specifically indicated only for the treatment of hyperglycemia associated with diabetes mellitus. The above article discusses issues that are considered outside the scope of the FDA-approved indication for various drugs to treat diabetes.

American and white children, in 1992 to 1993, a survey of 3128 youth aged 5 to 17 years estimated the diabetes prevalence to be 2.6 per 1000.[6] In the National Health and Nutrition Examination Survey, performed between 1988 and 1994, among 2867 youth aged 12 to 19 years, the estimated diabetes prevalence was 4.1 per 1000.[6] The type of diabetes was uncertain in the latter 2 studies. Both the Allegheny County (Pennsylvania)[7] and the Chicago[8] diabetes registries have shown sharp increases in the incidence of diabetes among African American and Latino adolescents. Type 1 DM registries rely heavily on age at diagnosis and initial treatment, with insulin as a means of differentiating type 1 from type 2 DM. Because there has been little consideration of type 2 DM in childhood until recently,[1,2] it is possible that the pediatric registries contain children with type 2 DM who are incorrectly identified as having type 1 DM. Consistent with this, in the Allegheny County registry,[7] the incidence of diabetes among people aged 15 to 19 years was 3-fold higher among African Americans than among whites and quadrupled from 1980 to 1984 and 1990 to 1994. In the Chicago registry,[8] the annual diabetes incidence for African American adolescents was higher than anticipated, and ~20% had survived without insulin treatment.[9] Several case series have been reported. A referral center in Cincinnati, Ohio, found an incidence of 7.2 per 100,000 for African American and white children aged 10 to 19 years in 1994.[10] Type 2 DM accounted for one third of all new diagnoses in 1994.[10] Similar findings have been reported from many different sites.[11–16] Since 1994 there have been multiple reports of an increasing number of children with type 2 DM, with some clinics reporting as many as half of new diagnoses being type 2.

KEY POINT

Type 2 DM is now a pediatric disease and a growing health concern.

CHARACTERISTICS OF AFFECTED CHILDREN

Of those children with type 2 DM, most are members of high-risk ethnic or minority groups, including Native Americans, African Americans, Hispanics, and Pacific Islanders; however, most pediatric diabetes centers are now reporting non-Hispanic white children with type 2 DM as well.

Children with type 2 DM are likely to have a close relative with the disease. While only 3% to 5% of children with type 1 DM will have a first-degree relative with type 1 DM, 48% to 99% of youth with type 2 DM will have relatives with type 2 DM.[6] At diagnosis, the majority of children with type 2 DM are ≥10 years of age. However, younger children with type 2 DM have been reported: the youngest Pima child reported was age 4 years; Mexican American, age 6 years; and African American, age 8 years. Most youth with type 2 DM present after the onset of puberty, perhaps reflecting increased production of growth hormone and the consequent increase in insulin resistance. It is possible that pubertal increases in growth hormone transform covert insulin resistance into overt type 2 DM in the overweight, genetically susceptible child.[6]

In contrast to the precipitous onset of type 1 DM, that of youth with type 2 DM may include symptoms or signs for months before these youth are diagnosed. The classic triad of polyphagia, polyuria, and polydipsia, while present, may not be recognized in an otherwise healthy teenager. Polyphagia may be interpreted as a normal response to pubertal changes and accelerated linear growth. Polyuria may not be noted by the parent because teenagers typically manage their own bathroom habits, and high-volume fluid intake is normal, particularly among teenagers in warmer climates. Weight loss, if noted, is viewed as a positive or normal event (eg, loss of "baby fat," normal response to adolescent growth spurt). While extensive descriptive studies on symptoms at onset have not been reported, most clinicians find that symptoms and signs, such as nocturia, recurrent vaginal or urinary tract infections, and unintentional weight loss in a child or adolescent who has been overweight for a prolonged period of time, are more reliable indicators of possible type 2 DM.

There are some physical findings that lead to the suspicion of type 2 DM in youth, although these abnormalities are also common in obese children. Almost all children with type 2 DM are overweight or obese at the time of diagnosis. In San Antonio, Texas, 97% of children with type 2 DM had a body mass index (BMI) >20 kg/m^2, and 83% of children had a

BMI >25 kg/m^2. Most children with type 2 DM are at or above expected height for age, and many demonstrate advanced sexual development for age. Both of these findings are likely related to hyperinsulinemia, obesity, or both. Some affected youth appear Cushingoid, with round faces, prominent cheeks, and facial redness. Occasionally, an adolescent may appear acromegalic with prominent jaws and large hands and feet. Hyperpigmentation and rugation (acanthosis nigricans) is present in many children with type 2 DM, although it is also a common finding in obese children. The most common site for acanthosis is on the posterior neck and axilla, although it has been reported on every body surface. Acanthosis is postulated to reflect insulin resistance rather than diabetes per se. Clinical experience suggests that the development of acanthosis may lag substantially behind changes in body weight. Acanthosis may be easier to detect in some groups of children (eg, Hispanics) than in others (eg, non-Hispanic whites). Physical findings may be affected by the duration of obesity, rapidity of onset, and alterations in lifestyle that have occurred prior to physician consultation. For example, recent rapid weight gain may lead to significant striae over the lower abdomen and hips, whereas slow, steady excessive weight gain over many years may occur without striae. Similarly, the adolescent who has lost 20 lbs over 6 to 8 weeks as a result of loss of β-cell function may also have substantial resolution of the acanthosis.

The clinical presentation of type 2 DM in children ranges from asymptomatic hyperglycemia to severe diabetic ketoacidosis.[1,2,6] In those who present with symptoms, glycosuria and weight loss are present in 20% to 40% and ketoacidosis is found in 5% to 10%.[1,2,6] Asymptomatic children are diagnosed as the result of routine blood or urine testing during the investigation of problems such as chronic or recurrent infections (eg, candidal vaginitis), sleep apnea, acanthosis nigricans, hyperlipidemia, hypertension, hirsutism, or dysmenorrhea. The absence of autoantibodies (ICA, GAD65) and evidence of residual insulin secretion are strongly suggestive of type 2 DM.

TREATMENT OF TYPE 2 DIABETES IN YOUTH

The management of type 2 DM in children must focus on the problem of insulin resistance—especially decreasing fat mass and increasing muscle mass.

KEY POINT

The characteristics that distinguish type 2 DM from type 1 DM in youth at the time of diagnosis are obesity and a strong family history of type 2 DM. Youth with type 2 DM are less likely to be significantly ill at the time of diagnosis. Severe hyperglycemia or ketoacidosis does not rule out type 2 diabetes.

Implementation of effective dietary and exercise strategies, while extremely difficult with most teenagers, is of utmost priority. These activities are buttressed by self-monitoring of blood glucose (SMBG) and self-administration of medication. All of type 2 DM management in teenagers is confounded by the psychosocial issues of adolescence and any adverse economic circumstances present in the family. Further complicating the treatment milieu is the lack of controlled clinical trials on type 2 DM in youth. However, a national study sponsored by the National Institutes of Health (National Institute of Diabetes and Digestive and Kidney Diseases) is now in the initial enrollment period.[17] When completed, this study, called Treatment Options for Diabetes Type 2 in Adolescents in Youth (TODAY), will provide crucial information on the optimal treatments for type 2 DM in children and perspective on the prevalence and progression of a range of related comorbidities.

As in most disease states, general health, established patterns and habits, family structure, culture, economic status, and belief systems have a significant impact on how families perceive and manage type 2 DM. For example, eating behaviors, food preferences, and food choices are usually established in early childhood, and are often limited by parental experience, background, and income. Similarly, obesity may be a source of social distress in one community, whereas it may be a social norm in another. Changing behavioral patterns around food intake are difficult, even for motivated, educated, middle-class adults. To implement significant change, virtually all weight-loss programs require frequent, often weekly, contact with a member of the health-care team.

For adolescents, a concerned parent or school staff member might offset the need for frequent physician visits. Adolescents have the added potential advantage of being in school, which offers the opportunity for physical activity in a safe environment.

Clarity and simplicity are the key concepts in managing adolescents with type 2 DM. Youth, like adults, have competing priorities often coupled with poor ability to undertake long-term planning. Thus, it is crucial that the diabetes care team understands the individual youth's priorities and attempts to match those priorities with those of diabetes care. For example, the female adolescent may be more concerned about the unsightliness of the acanthosis than she is about the health consequences of overweight or diabetes. However, weight loss, and the consequent reduction in insulin resistance, will benefit both her desired outcome of reduced acanthosis and the team's desired outcome of improved glycemic control. It is imperative to sharply limit the number of goals that are set at any particular time and to provide education consistent with an adolescent's life experience and education.

NONPHARMACOLOGIC CONSIDERATIONS

The goals of medical nutrition therapy are to normalize serum glucose and lipid levels, achieve weight loss or stabilization, and develop healthy and sustainable eating habits. Because there are no dietary guidelines specific to children and adolescents with type 2 DM, ADA guidelines for adults with type 2 DM are used. Because some of the more complex concepts of the guidelines for adults, such as "calorie" and "ratio and proportion" are beyond the educational level of many families, it may be more beneficial to focus on eating behaviors and portion control rather than on food choice and caloric content per se. Of direct relevance, weight stabilization or modest supervised weight loss in overweight children is safe; it is reasonable to assume that the same is true with regard to weight loss in children with type 2 DM.

Because there are no specific exercise recommendations for children with type 2 DM, guidelines developed by the AAP are used.[18] Reasonable activity guidelines are ≥60 minutes of age- and developmentally appropriate, varying physical activity each day, of which ≥30 minutes is aerobic. Physical activity should also be incorporated into all aspects of daily life, such as walking to and from school. As much as is feasible, youth with type 2 DM should also be encouraged to take advantage of the opportunities for physical activities that are provided at school. The physical activity program should be fun for the child, use available facilities, and incorporate other family members or friends as "exercise partners."

Attention should be paid to sedentary behaviors, the majority of which revolve around television, videotapes/DVDs, and video games. A goal set by the AAP is to reduce the use of television to <2 hours per day.[19] This is a reasonable goal for children with type 2 DM. The putative benefits include increasing caloric expenditure as a result of increased movement, and decreasing caloric intake due to "subconscious eating" (snacking while watching television, with little attention to portion control).

MEDICAL THERAPY

The ADA Consensus Panel[1,2] has recommended that asymptomatic or mildly symptomatic children should initially be managed with medical nutrition therapy and lifestyle changes. If treatment goals (glycosylated hemoglobin [A1C] level <7% and fasting plasma glucose [FPG] level >100 and <126 mg/dL) are not met, pharmacologic therapy is indicated. The only oral agent approved for the treatment of type 2 DM in children is metformin. In a 16-week, double-blind, placebo-controlled trial of metformin in new-onset type 2 DM in children, metformin resulted in a significantly lower A1C level (7.5% vs 8.6%, $P < 0.001$) and lower FPG level (–43 mg/dL vs 21 mg/dL, $P < 0.001$) compared with placebo.[20] Metformin was well tolerated, with adverse-event rates similar to those observed in the adult population. Intensification of therapy is recommended if 3- to 6-month monotherapy with metformin is unsuccessful.[1,2]

For the child who is symptomatic at presentation, with evidence of severe insulin deficiency, with greatly elevated blood glucose and A1C levels, and with or without ketonuria, insulin is the first choice for therapy. Once glycemic control has been established, metformin therapy should be added to the treatment regimen, with tapering of insulin therapy if feasible.

There is little pediatric experience with the thiazolidinediones (TZDs), rosiglitazone and pioglitazone, although pediatric clinical trials are currently under

way. In adult clinical trials,[21–23] TZDs were effective and well tolerated, not only when used as monotherapy but also when used in combination with a sulfonylurea or metformin. A potential advantage of the TZDs is that they may preserve β-cell function by ameliorating lipotoxicity and lowering free fatty acid levels. However, adult trials with TZDs have demonstrated weight gain; fluid retention; and, in some elderly patients, heart failure.[21–23]

Glipizide or other insulin secretagogues were first-line therapy for type 2 DM in adults throughout most of the past 2 decades. However, insulin secretagogues are now more commonly used as adjunctive therapy. They are well tolerated in adolescents but may result in symptomatic hypoglycemia, especially in youth who have successfully lost weight, recently instituted a vigorous exercise program, or gone for prolonged periods without eating while continuing to use medication.

Monitoring of Therapy

SMBG is an important tool to achieve glycemic control in youth with type 2 DM treated with diet and/or oral agents, and is essential for safety in insulin-treated patients. *Two measurements per day—immediately before breakfast and 2 hours after supper—may be sufficient in most cases*, although children receiving insulin therapy or those with deteriorating glycemic control may require the "4-or-more" premeal, prebedtime schedule more typical of patients with type 1 DM. The goals for glycemic control are fasting blood glucose <110 mg/dL 85% of the time (on 6 of 7 consecutive mornings), 2-hour postprandial blood glucose <140 mg/dL 85% of the time (on 6 of 7 consecutive evenings), and A1C <7%, consistent with ADA guidelines.[1,2]

The goals of medical monitoring are to promote or ensure normalization of A1C, lipids, blood pressure, and body weight; to screen for diabetes complications, including retinopathy and nephropathy, or complications related to medical therapies; and to identify potential barriers to the management plan. Monitoring every 3 months is warranted in children and adolescents, given the probable duration of diabetes and the benefits of having multiple objective assessment parameters. Ideally, the A1C level should be within the normal range for nondiabetic individuals. The ADA practice guidelines recommend lipid monitoring (total cholesterol, high-density lipoprotein cholesterol, and triglycerides) at least once per year if the lipid profile is normal on initial evaluation (more frequently if abnormal or if pharmacologic therapy is used). Additional recommendations by the ADA for individuals diagnosed with type 2 DM are a dilated eye examination and a urine test for microalbuminuria, both at or near the time of diagnosis and repeated on an annual basis.[24] Twenty-four–hour urine specimens to test for microalbuminuria are difficult to obtain and have largely been replaced by spot urine samples for albumin/creatinine ratios.

KEY POINT

For children receiving oral therapy for type 2 diabetes, ≥2 blood glucose tests per day are required. Teaching families to use the glucose results to tailor eating and activity patterns is crucial to achieving good control.

DIABETES RISK FACTORS IN THE PEDIATRIC POPULATION

As in adults, type 2 DM in youth is due to the combination of insulin resistance and relative β-cell failure. There are many genetic and environmental risk factors for insulin resistance and limited β-cell reserve. However, the rise in the prevalence of type 2 DM in children most closely parallels the well-documented burgeoning of obesity in the pediatric population and mirrors the well-substantiated decrease in physical activity.[25–28]

Obesity

Obesity has been identified as a major risk factor for type 2 DM in children. Over the past 4 decades, there has been a dramatic increase in obesity in youth. The proportion of adolescents aged 12 to 17 years with a BMI ≥85th percentile increased from 15.2% in the 1970s to 25% in the 1990s.[25] Youth at highest risk for obesity are also at highest risk for type 2 DM and include Hispanics, African Americans, and Native Americans. The preponderance of obese youth will become obese adults and, as a consequence, will have increased long-term morbidity and mortality.[26,27] In

1998, the cost of obesity accounted for 5.7% of the US health-care dollar.

Several studies[29–32] have shown that aggressive lifestyle interventions can prevent type 2 DM in adults. While these studies were conducted in self-selected volunteers who were likely motivated to make lifestyle changes, there is reason to anticipate that youth might have a similar positive response to a comprehensive intervention combining diet and physical activity changes, if they can be motivated to make health-related lifestyle changes.

Poor Diet and Nutrition

Poor eating and drinking habits are risk factors for obesity.[33–35] Childhood obesity is associated with excessive consumption of sweetened beverages, fruit drinks, and fruit juices due to the kilocalories they contribute to the diet.[36,37] Although the brevity of this article precludes extensive discussions, a few examples of the changes in diet over the past several decades have provided insight into the evolution of eating and drinking habits among US youth. For instance, the average male adolescent now consumes 50 fluid ounces of sweetened beverages per day,[38] or an estimated intake of 400 to 600 excess calories. This is more than double the intake of sweetened beverages reported in the 1970s. At the same time, the intake of fruit and vegetables by children has fallen; it is less than half of the recommended goal of 5 servings per day.[39,40]

A diet high in fruits, vegetables, and whole-grain products and low in total calories and dietary saturated fat and sodium is likely protective against both obesity and type 2 DM.[41] An inverse relationship between fruit/vegetable consumption and dietary fat intake has been demonstrated.[42,43] These and many other observations suggest that the promotion of increased fruit, vegetable, and whole-grain intake, coupled with a decreased intake of sweetened beverages, could reduce the risk for obesity and the subsequent progression to diabetes. However, studies reported to date have not been particularly promising. For example, in a 2-year study in rural Nebraska, 200 elementary school children were provided enhanced physical activity, nutrition education, and school lunches with reduced fat and sodium content. The study showed no significant difference in body weight, body fat, insulin, or glucose levels.[44] A pilot study of 8 months' duration, designed to reduce diabetes risk factors in Mexican American children through health education, improved eating habits and increased diabetes health knowledge but did not reduce body fat.[45] The Zuni, a Native American tribe, Diabetes Prevention Program employs diabetes education, a school-based wellness center, supportive social networks, and modification of the food types available to teens.[46,47] In a 3-year study of the program, investigators found a significant reduction in soft-drink consumption and a decrease in fasting insulin levels, with no significant change in FPG levels.[47] Similarly, the Child and Adolescent Trial for Cardiovascular Health (CATCH)[48] improved eating habits but still did not make a significant difference in obesity rates or in cholesterol levels.

Sedentary Behaviors

The amount of physical activity affects total energy expenditure and consequently energy balance. Low physical activity levels (ie, sedentary behaviors) are associated with obesity in youth and may be both the cause and consequence of overweight.[49–51] The use of media, especially television, is highest among those demographic groups that are also at highest risk for diabetes, including the economically disadvantaged, minorities, and children whose parents have had little education.[52–54] As a consequence of an increasingly sedentary lifestyle, the level of physical activity of children and adolescents has declined in many countries during the past few decades.[55,56] The obesity risk of a child has been correlated with time spent viewing television in 2 studies.[57,58] The influence of sedentary behaviors on obesity risk might reflect the combination of physical inactivity, snacking behaviors, and specific personality and socioeconomic factors.

Regular vigorous physical activity helps develop and maintain healthy bones, muscles, and joints in youth. It is also useful in increasing lean muscle mass, reducing body fat, and controlling body weight. There may be psychological and cognitive benefits as well, but these have been less well documented. In 1999, a survey[59] of a representative sample of youth in grades 9 to 12 showed that 35% did not participate regularly in vigorous physical activity, 44% did not play on any sports teams, and 44% were not enrolled in a physical education (PE) class. Only 29% attended

daily PE classes. Activity decreases with increasing age, especially among female adolescents.[59] The survey also showed that in teenagers, regular participation in vigorous physical activity dropped from 73% of 9th graders to 61% of 12th graders, and enrollment in PE dropped from 79% in 9th grade to 37% in 12th grade. Many states no longer have mandatory PE requirements beyond elementary school, or they permit the substitution of less strenuous activities, such as band, for PE.

The benefits of exercise, with relevance to diabetes and diabetes risk factors, are well documented. In adults, exercise at 40% of maximal capacity performed for ≥20 minutes each day results in a lowering of insulin levels.[60–62] Exercise training can enhance the glycemic status of healthy individuals[63,64] and patients with type 2 DM.[65,66] In children, the effects of exercise on glycemic status are less well established[67–69]; however, it appears that moderate-intensity exercise for 8 to 15 weeks results in improvement in glycemic status, particularly in obese youth.

KEY POINT

Ongoing information and education about nutrition, sedentary behaviors, and activity should be provided throughout childhood.

Nonmedical Treatment of Obesity

The initial aim of obesity treatment is normalization of body weight and body fat content, with the long-term goal of achieving a pattern of behaviors and attitudes that will sustain a healthy body weight over the course of a lifetime. Obviously, a perceived improvement in quality of life is highly desirable during both the treatment and maintenance phases. There is a need to minimize adverse physical and psychological consequences.

Most types of obesity treatment in children and adolescents emphasize improved dietary habits and composition, increased physical activity, decreased sedentary behaviors, and extensive familial support. Most obesity treatment programs in both adults and children report short-term success. However, maintenance of weight loss for a protracted period of time is relatively uncommon. The long-term outcome may be better in children than in adults.[70] The more favorable outcome in children may be related to the fact that their behaviors are less well established and therefore more amenable to modification. Greater family support and the potential for additional longitudinal growth may also enhance outcome. The treatment of obesity in childhood most likely offers greater disease-preventive effects in view of the longer life expectancy.[71]

Rigorous dietary limitations are not associated with better long-term success than moderate dietary modifications and are considerably more difficult to maintain for long periods.[71] However, rigorous restrictions may be useful for a limited period of time to provide initial success for the child and family. In the pediatric population, there are additional concerns about adversely affecting growth,[72] although this is primarily a concern for children who are not yet sexually mature. A highly restrictive diet and constant adverse food messages may increase the risk for later disturbances of eating patterns, eating disorders, and other adverse psychological effects.[73] Combination diet-and-exercise programs are associated with better outcomes than either component alone in terms of both weight reduction and weight maintenance.[74] More studies are needed to determine the types of exercise programs that would be most appropriate for use in obese children and adolescents. These may vary widely based on the social, economic, and ethnic background of the child and the environment in which the child functions.

Behavioral weight-management programs enhance physical activity and healthy eating habits, stabilize and reinforce health-promoting behavior, and strengthen self-confidence and independence. These programs have been successful in several large cohorts of children.[75,76] Such programs are relatively intense, often involving ≥20 weekly sessions with a psychologist or trained interventionist. While individually quite successful, this approach is not amenable to the usual office practice of physicians.[70]

Simple measures, such as reducing children's television, videotape/DVD, and video game use, can decrease the prevalence of overweight in children. These approaches may be more directly applicable to the general pediatric practice. A number of organiza-

tions, such as the AAP, have created educational materials for physicians and families about obesity, changes in diet, and increasing activity. Many such materials are readily accessible via the Internet. The AAP has recommended several practical steps that can be accomplished within the context of the primary care physician's practice.[77] These steps include:

- Identifying children at risk for diabetes and overweight based on family history and demographic factors
- Tracking the BMI to identify children with excessively rapid weight gain
- Promoting breastfeeding in infants and healthy eating behaviors in children
- Modeling and encouraging all forms of physical activity
- Limiting or eliminating television viewing and other nonacademic sedentary behaviors

Medical Intervention

A number of sites around the United States are developing pediatric bariatric surgery units to investigate the efficacy and safety of this approach in the management of severely obese children, especially those who are approaching the point at which the obesity is acutely life-threatening. There is a growing interest in pharmacologic interventions for obesity, but safe and effective medications have not yet been identified or approved for use in pediatric patients except metformin. However, future developments are likely to confer new options for useful pharmacologic treatment aids in young patients.

Public Health Approaches

Given the high prevalence of overweight children and of children at risk for overweight, there have been some efforts to take a public health approach to the problem.[50] These efforts, still in the early stages, may ultimately have the greatest benefit for the lowest cost. For example, several states have passed initiatives that change the school environment by decreasing the availability of unhealthful foods, increasing the availability of healthy alternatives, and/or increasing PE requirements. There have been successful attempts to implement programs, such as CATCH, in the school environment.[48] Some urban areas have developed public campaigns to promote walking, while others have attempted to develop safe places for children and their families to play (eg, sidewalks, parks, and walking trails). There are many advocacy roles that the primary care provider can undertake outside the medical office that may have benefit for children and adults, including:

- Supporting groups that advocate for safe places for children and families to play (eg, sidewalks, parks, and walking trails)
- Encouraging inclusive physical-activity programs in school (eg, walking programs, jogging clubs)
- Opposing the provision of unhealthy foods within the context of school (eg, no soda machines)
- Providing information to policymakers about the problem of obesity and the need for resources to prevent and treat it
- Advocating activities that promote a positive health message to children (eg, be active, be fit)
- Being a positive role model by developing and maintaining positive health habits and sustaining a healthy body weight

KEY POINT

Good nutrition and vigorous physical activity not only promote general health in children but also establish habits that reduce the risk for diabetes and related comorbidities.

CONCLUSION

Type 2 DM and related risk factors are pervasive in the pediatric population. In response, primary care pediatricians must recognize the national crisis of pediatric obesity. Furthermore, they need to support local, regional or national efforts that implement preventive strategies in their practice and community.

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Address correspondence to: Daniel E. Hale, MD, Department of Pediatrics, 7703 Floyd Curl Drive, San Antonio, TX 78229. E-mail: hale@uthscsa.edu

Dialogue Box

EDITORIAL BOARD
What is the mechanism for the development of diabetic ketoacidosis in a child with type 2 DM?

HALE
The mechanism revolves around the concept of glucose toxicity. It is thought that protracted, prolonged high glucose levels, coupled with elevated levels of lipids in the bloodstream, produce marked dysfunction of the β-cells and severe enough impairment of insulin secretion to initiate the cascade of events responsible for causing ketoacidosis.

EDITORIAL BOARD
To what do you attribute the growing prevalence of type 2 DM among specific minority ethnic groups in the United States?

HALE
There is little doubt that it stems from the obesity epidemic in our society. Although type 2 DM is a problem that is seen in all segments of society, its higher prevalence among certain minority groups likely stems from these groups being overrepresented among that segment which has always been the most affected by obesity (ie, the poor and disenfranchised). Those are the exact same ethnic groups experiencing a high prevalence of type 2 DM in children. This obesity problem was particularly evident in the findings of a recent study we just completed involving almost 3000 children in Rio Grande City. Rio Grande City, on the border between Texas and Mexico, is in Stark County, which is the poorest county in the United States. Alarmingly, we found that slightly more than 50% of the children living there had a BMI, starting at age 4, above the 85th percentile and >10% had a BMI above the 99th percentile for age and gender.

EDITORIAL BOARD
How has the growing number of pediatric patients with newly diagnosed DM who have type 2 DM impacted your diagnostic evaluation of such patients?

HALE
There has long been the assumption that if a patient is under the age of 18 years and presents with DM, that child has type 1 until proven otherwise. My advice now is that if the patient is under 18 and has DM, one has to at least entertain the possibility that you might be dealing with a type 2 diabetic patient. Although I don't routinely screen for antibodies in all patients with presumed type 2 DM, I do screen for antibodies, insulin, and C peptide in those patients who do not quite fit the phenotype; for example, the child who is not substantially overweight (ie, BMI >20–25), the child who has only minimal acanthosis nigricans, or the child with a strong family history of type 2 DM.

EDITORIAL BOARD
Is type 2 DM more common among females than males?

HALE
It may be. Our experience in South Texas, where we deal predominantly with a Hispanic population, suggests that 2 of every 3 new cases of type 2 DM occur in females. For the most part, our experience seems to mirror the experience of other centers that deal primarily with minority populations. Although this might be related to gender, I suspect that there is also a strong detection bias arising from the fact that females are more likely to have contact with the medical system. Males between the ages of about 13 and 25 years tend to go to the doctor only for traumatic injuries, whereas females more frequently seek medical attention for issues related to pregnancy, menstrual irregularity, hirsutism, urinary tract infections, and vaginal infections. As a result, females are much more likely to be tested for hyperglycemia. The existence of such a detection bias is supported by population-based surveys of middle school–aged children, which have shown the preva-

Dialogue Box

lence of hyperglycemia (ie, an FPG >110 mg/dL) to be similar between the boys and the girls.

EDITORIAL BOARD

Seeing that insulin resistance plays an important pathogenic role in female patients with polycystic ovarian syndrome (PCOS), have you thought of routinely starting such patients on an insulin sensitizer, such as metformin?

HALE

Let me begin by stating that there often is a gap between what one might do in clinical practice and what is evidence supported by carefully performed clinical trials. On one side there are very clear data in adults, at least from the Diabetes Prevention Trial (DPT), that the use of metformin in people with impaired glucose tolerance slows the progression of DM by 30% to 35%. In addition, there are also data in adults that suggest that the use of metformin substantially improves the androgenic profile in females with the androgenic profile consistent with PCOS. Furthermore, clinical experience suggests that, for girls who have substantial menstrual irregularity, who are obese, and/or who are hirsute, metformin offers as much benefit on their androgenic profile as oral contraceptives or bedtime prednisone. The problem with using metformin in such patients is that carefully controlled clinical trials in the pediatric population haven't been done yet.

EDITORIAL BOARD

Given this chasm, what are pediatric endocrinologists like yourself doing in clinical practice?

HALE

I think what most clinicians do is emphasize the other interventions studied in the DPT—that is, they push intensive lifestyle modification with weight loss and regular aerobic exercise; in that trial, these measures were found to be even more effective in slowing the progression to DM in people who have impaired glucose tolerance than pharmacologic therapy. Although the DPT was conducted in adults, the interesting thing in the pediatric population is that while many parents will not change their lifestyle to benefit themselves, they are much more inclined to change their way of living for the benefit of their children. I have found parents to be fairly receptive to changing dietary habits and incorporating physical activity in the home once they're told that their child has impaired glucose tolerance or hyperandrogenism and that the youth would greatly benefit from such interventions as a means for facilitating weight reduction.

EDITORIAL BOARD

When would you use an insulin sensitizer in a patient with PCOS?

HALE

When lifestyle measures fail in pediatric patients with impaired glucose tolerance or who have an androgenic profile consistent with PCOS, I will sit down with the family and discuss it as a potential option. I convey to them that a substantial amount of literature, albeit in adults, would support the off-label use of this agent in such a situation.

EDITORIAL BOARD

What is the natural history of acanthosis nigricans with regard to glucose tolerance?

HALE

We don't know since no natural history data on this exist. I have an RO-1 grant designed to study the prevalence of progression of DM risk factors in Mexican American children, and one of the things we'll be looking at is that issue. With regard to this, I find it somewhat surprising that the ADA recommended that a fasting blood glucose be used initially as a screening test in children. I say this because our study children have incredible β-cell function, and until they develop β-cell failure, the detection of glucose intoler-

Dialogue Box

ance is more likely accomplished with an oral glucose tolerance test (OGTT) as opposed to a fasting glucose. These children are profoundly insulin resistant, and their peak insulin may rise as high as 700 μU/mL when stressed. However, if they fast 8 to 10 hours, their blood sugar will likely return to normal. As a result, if I am truly suspicious of the possibility of type 2 DM on the basis of symptoms or family history or BMI, I will routinely do a 2-hour OGTT because the 2-hour value just seems far more likely to demonstrate DM than a fasting blood sugar test.

EDITORIAL BOARD

In the pediatric population, why do the Centers for Disease Control and Prevention (CDC) continue to favor the percentile classification to delineate optimal body weight as opposed to using a more quantitative method, such as the BMI in adults?

HALE

The problem is that the interpretation of what would be an appropriate BMI would change with the child's age. For example, a BMI of 20 when you are 15 years of age has a very different meaning than a BMI of 20 when you are 7. That is why they still focus on using percentiles.

EDITORIAL BOARD

As America gets more obese, won't this cause the weight linked to any given percentile to also increase to a number higher than appropriate?

HALE

That is a very interesting question. It should be noted, however, that in developing the current growth charts, the CDC actually made an effort to factor that in. Although it relied on contemporary heights for the chart, it chose not to use contemporary weights. Instead, it used contemporary weight from some time in the mid-1980s, before the huge rise in obesity in the United States. The prevalence of obesity in the pediatric population was fairly stable from the 60s to the 80s, and then suddenly in the 90s it made a huge jump, which has largely been attributed to "fast foods" and a lack of physical activity.