Care of Children and Adolescents With Type 1 Diabetes

A statement of the American Diabetes Association

Janet Silverstein, MD[1]
Georgeanna Klingensmith, MD[2]
Kenneth Copeland, MD[3]
Leslie Plotnick, MD[4]
Francine Kaufman, MD[5]
Lori Laffel, MD, MPH[6]
Larry Deeb, MD[7]
Margaret Grey, DRPH, CPNP[8]
Barbara Anderson, PHD[9]
Lea Ann Holzmeister, RD, CDE[10]
Nathaniel Clark, MD, MS, RD[11]

During recent years, the American Diabetes Association (ADA) has published detailed guidelines and recommendations for the management of diabetes in the form of technical reviews, position statements, and consensus statements. Recommendations regarding children and adolescents have generally been included as only a minor portion of these documents. For example, the most recent ADA position statement on "Standards of Medical Care for Patients With Diabetes Mellitus" (last revised October 2003) included "special considerations" for children and adolescents (1). Other position statements included age-specific recommendations for screening for nephropathy (2) and retinopathy (3) in children with diabetes. In addition, the ADA has published guidelines pertaining to certain aspects of diabetes that apply exclusively to children and adolescents, including care of children with diabetes at school (4) and camp (5) and a consensus statement on type 2 diabetes in children and adolescents (6).

The purpose of this document is to provide a single resource on current standards of care pertaining specifically to children and adolescents with type 1 diabetes. It is not meant to be an exhaustive compendium on all aspects of the management of pediatric diabetes. However, relevant references are provided and current works in progress are indicated as such. The information provided is based on evidence from published studies whenever possible and, when not, supported by expert opinion or consensus (7). Several excellent detailed guidelines and chapters on type 1 diabetes in pediatric endocrinology texts exist, including those by the International Society of Pediatric and Adolescent Diabetes (ISPAD) (8), by the Australian Pediatric Endocrine Group (www.chw.edu/au/prof/services/endocrinology/apeg), in Lifshitz's *Pediatric Endocrinology* (9–11), and by Plotnick and colleagues (12,13).

Children have characteristics and needs that dictate different standards of care. The management of diabetes in children must take the major differences between children of various ages and adults into account. For example, insulin doses based only on body size are likely to be incorrect; the consequences of hypoglycemic events are distinctly different between adults and children; risks for diabetic complications are likely influenced by puberty; and the targets of education need to be adjusted to the age and developmental stage of the patient with diabetes and must include the parent or caregiver.

In caring for children with diabetes, professionals need to understand the importance of involving adults in the child's diabetes management. Young children, including school-aged children, are unable to provide their own diabetes care, and middle school and high school students should not be expected to independently provide all of their own diabetes management care. Thus, the education about how to care for a child and adolescent with diabetes must be provided to the entire family unit, emphasizing age- and developmentally appropriate self-care and integrating this into the child's diabetes management (14). The goal should be a gradual transition toward independence in management through middle school and high school. Adult supervision remains important throughout the transition.

DIAGNOSIS — The diagnosis of type 1 diabetes in children is usually straightforward and requires little or no specialized testing. Most children and adolescents with type 1 diabetes present with a several-week history of polyuria, polydipsia, polyphagia, and weight loss, with hyperglycemia, glycosuria, ketonemia, and ketonuria. Glycosuria alone, especially without ketonuria, may be caused by a low renal glucose threshold. Thus, an elevated blood glucose concentration must be documented to diagnose diabetes. Similarly, the incidental discovery of hyperglycemia in the absence of classic symptoms does not necessarily in-

From the [1]Department of Pediatrics, Division of Endocrinology, University of Florida, Gainesville, Florida; the [2]Department of Pediatrics, Barbara Davis Center, Denver, Colorado; the [3]Department of Pediatrics, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma; the [4]Department of Pediatrics, Division of Endocrinology, John Hopkins Medical Institutions, Baltimore, Maryland; the [5]Department of Pediatrics, Keck School of Medicine, University of Southern California Children's Hospital, Los Angeles, California; the [6]Pediatric and Adolescent Unit, Joslin Diabetes Center, Boston, Massachusetts; the [7]Children's Clinic, Tallahassee, Florida; [8]Yale School of Nursing, New Haven, Connecticut; [9]Pediatric Metabolism and Endocrinology, Baylor College of Medicine, Houston, Texas; [10]Holzmeister Nutrition Communications, Tempe, Arizona; and the [11]American Diabetes Association, Alexandria, Virginia.

Address correspondence to Nathaniel G. Clark, MD, MS, RD, National Vice President, Clinical Affairs, American Diabetes Association, 1701 N. Beauregard St., Alexandria, VA 22311. E-mail: nclark@diabetes.org.

Abbreviations: ADA, American Diabetes Association; AER, albumin excretion rate; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; DKA, diabetic ketoacidosis; EDIC, Epidemiology of Diabetes Interventions and Complications; EMA, endomysial autoantibody; MDI, multiple daily insulin injection; NCEP, National Cholesterol Education Program; NCEP-Peds, National Cholesterol Education Program for Pediatrics; SMBG, self-monitoring of blood glucose; tTG, tissue transglutaminase.

Table 1—*Criteria for the diagnosis of diabetes*

1. Symptoms of diabetes and a casual plasma glucose ≥200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

OR

2. Fasting plasma glucose ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

OR

3. 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. The test should be performed as described by the World Health Organization, using a glucose load of 75 g anhydrous glucose dissolved in water or 1.75 g/kg body wt if weight is <40 pounds (18 kg).

In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day. The oral glucose tolerance test is not recommended for routine clinical use, but may be required in the evaluation of patients when diabetes is still suspected despite a normal fasting plasma glucose (17).

dicate new onset diabetes, especially in young children with acute illness, although the risk of developing diabetes may be increased in such children (15,16). In such cases, a prompt consultation with a pediatric endocrinologist is indicated; if this is not possible, a physician experienced in the care of children with diabetes should be consulted.

The criteria for the diagnosis of diabetes are presented in Table 1. In the asymptomatic child/adolescent who is screened because of high risk for diabetes, a fasting plasma glucose (FPG) ≥126 mg/dl or a 2-h plasma glucose/random glucose ≥200 mg/dl should be repeated on a second day to confirm the diagnosis. The child/adolescent with typical symptoms of diabetes and a random plasma glucose ≥200 mg/dl does *not* require a repeat value on another day or any further testing to diagnose diabetes. Because of the potential for rapid clinical deterioration expected in untreated children with type 1 diabetes, unnecessary delays in the diagnosis must be avoided and a definitive diagnosis should be made promptly.

Glucose tolerance testing is rarely required, except in atypical cases or very early disease, in which most plasma glucose values are normal and the diagnosis of diabetes is uncertain. Type 1 diabetes may present with symptoms ranging from incidental glycosuria to life-threatening diabetic ketoacidosis (DKA). Regardless of severity, however, the patient requires immediate medical treatment with concomitant education to provide the child and family with the knowledge and skills necessary for self-management after initial treatment. This issue is discussed more fully below.

As the incidence of type 2 diabetes in children and adolescents increases, it becomes increasingly important to differentiate newly diagnosed type 1 from type 2 diabetes. In the slender prepubertal child, one can confidently assume a diagnosis of type 1 diabetes. However, in the overweight adolescent, differentiating type 1 from type 2 diabetes may be difficult; measurement of islet autoantibodies may be useful in such patients. In children with negative autoantibody levels, the use of plasma C-peptide levels has been recommended, but the interpretation of such measurements is controversial. The differentiation between type 1 and type 2 diabetes has important implications for both therapeutic decisions and educational approaches. Regardless of the type of diabetes, the child who presents with severe fasting hyperglycemia, metabolic derangements, and ketonemia will require insulin therapy to reverse the metabolic abnormalities.

Recommendations

- Diagnosis is similar to that in adults and should be pursued expeditiously.
- Hyperglycemia alone in the setting of an acute illness and isolated glucosuria may be due to other causes.
- Differentiating type 1 from type 2 diabetes is based on patient characteristics, history, and lab tests, if appropriate.

INITIAL CARE — Whether the initial care and education is given as an inpatient or an outpatient and whether this care is provided by a pediatric endocrinologist/diabetes team, an internist endocrinologist, or the child's primary care provider will depend on the age of the child, the ability to provide outpatient education, the clinical severity of the child at presentation, and the geographic proximity of the patient to a tertiary care center. Ideally, every child newly diagnosed with type 1 diabetes should be evaluated by a diabetes team consisting of a pediatric endocrinologist, a nurse educator, a dietitian, and a mental health professional qualified to provide up-to-date pediatric-specific education and support. Such systems of care, unfortunately, are not always available. In the future, greater use of telemedicine may allow the expertise of established pediatric centers to improve the care of children in remote areas.

Regardless of the source of care, all providers caring for children with diabetes should understand the normal stages of childhood and adolescent development and how they affect diabetes management. They should also understand the different management approaches to type 1 and type 2 diabetes.

Approximately 30% of children who present with newly diagnosed type 1 diabetes are ill with DKA (18). Many require treatment in an intensive care unit. Most of the other 70% are not acutely ill and do not require hospitalization for medical management unless facilities for prolonged outpatient care and self-management education are not available.

Although outpatient initial care and education costs are substantially lower than those associated with inpatient care (9,19), hospitalization of patients, regardless of severity, is required in certain circumstances. Thus, if the center is not experienced in the outpatient management of newly diagnosed children with diabetes or is not adequately staffed to provide outpatient care because regional health care reimbursement is inadequate for initial outpatient care and education, hospitalization is necessary. Some centers are able to restrict hospitalization to only those patients who require treatment for acidosis, who require intravenous hydration, who are particularly young (e.g., <2 years), who are referred from great distances, or who present particular psychosocial challenges that preclude outpatient education.

Recommendation

- Ideally, every child newly diagnosed with type 1 diabetes should be evaluated by a diabetes team (consisting of a pediatric endocrinologist, a nurse educator, a dietitian, and a mental health professional) qualified to provide up to date pediatric-specific education and support.

DIABETES EDUCATION

Education components

Studies in children with type 1 diabetes have demonstrated that patient and family education, delivery of intensive diabetes case management, and close telephone contact with the diabetes team are associated with reduced hospitalizations, emergency room visits, and overall costs to the payer and patient (20,21). Regardless of the setting of the educational program, it should be personalized to the needs of the child and family, culturally sensitive, and paced to accommodate individual needs. One should always keep in mind the patient's sibling(s), as they may feel neglected because of the increased attention paid to the patient due to this new diagnosis.

Proper diabetes education for a child and family of a child with type 1 diabetes is intense and complex, and requires educators with a set of skills including good communication, compassion, sensitivity, humor, and in-depth knowledge of childhood diabetes. Both the information provided and the style of delivery must be pediatric-specific and should not be provided by persons experienced only in education and management of type 2 diabetes in adults. Ideally, the education should be provided by a team of certified professionals, including a physician, nurse, dietitian, and mental health professional, and dedicated to communicating basic diabetes management skills within a context that addresses family dynamics and issues facing the whole family. It is essential that substantial educational material (necessary for basic management, often referred to as "survival skills") must be conveyed to a family of a child with type 1 diabetes immediately after the initial diagnosis. The family is likely to be adjusting to the shock and perhaps anger or grief over the diabetes diagnosis and may not be able to focus on learning new material.

Education is best provided with sensitivity to the age and developmental stage of the child, with regard to both the educational approach and the content of the material delivered. For the preschooler, education likely will be directed toward the parents and primary caregivers, whereas for most adolescents (after consideration of their emotional and cognitive development), education should be directed primarily toward the patient, with parents included. Since small, albeit often insignificant inconsistencies in information can be confusing to a distraught family, education should be provided to all caregivers simultaneously if possible.

Continuing education

Education is not a one-time event that occurs at diagnosis. At diagnosis, survival skills need to be provided. Families and children need ongoing education and support as the child grows and takes on more elements of self-care. Knowledge and skills should be evaluated regularly by the diabetes educator.

Studies suggest that to be effective, educational interventions need to be ongoing, with frequent telephone contact, and both in-person care and telephone availability have been demonstrated to improve A1C and to decrease hospitalization rates for acute diabetes complications (20–24).

The patient and family should receive ongoing education regarding the prevention of and screening for the microvascular and macrovascular complications of diabetes. Counseling should include the importance of optimizing blood glucose, lipid, and blood pressure treatment and avoidance of smoking.

Recommendations

- Ideally, the education should be provided by a team of certified professionals, including physician, nurse, dietitian, and mental health professional, that is dedicated to communicating basic diabetes management skills within a context that addresses family dynamics and issues facing the whole family.
- Education is best provided with sensitivity to the age and developmental stage of the child, both with regard to the educational approach and content of the material delivered.
- The patient and family should receive ongoing education regarding the prevention of and screening for the micro- and macrovascular complications of diabetes.

IDENTIFICATION — The person with diabetes should always wear identification (ID) that identifies him or her as having diabetes. This is particularly important during adolescence, when patients are often away from parent and teacher supervision and may be driving. The child who is active in sports is a case in point, and coaches need to be aware of the child's diabetes and the signs and treatment of hypoglycemia. Necklaces and bracelets are readily available in pharmacies or from organizations like MedicAlert. Use of shoe identification tags may be useful for toddlers. A wallet card is not adequate, since this card could easily be missed by paramedics or other helpers. More fashionable ID items are available. These items may be more acceptable to adolescents and may be purchased in jewelry stores or via mail. Inquiry about the use of ID should occur periodically.

Recommendation

- Children with diabetes should wear ID indicating that they have diabetes.

APPROPRIATE SELF-MANAGEMENT BY AGE —Because children and adolescents are growing and developing, their ability to participate in self-management of diabetes varies with their changing motor development, cognitive abilities, and emotional maturation. Studies (25,26) have demonstrated that parental involvement is necessary throughout childhood and adolescence to assure appropriate self-management and metabolic control. Nonetheless, there are few hard rules on what self-management capabilities children and adolescents and their families should have at various points along the developmental continuum. The management priorities and issues in self-management are summarized in Table 2.

Infants (<1 year)

When diabetes is diagnosed in infancy, the parents must adapt to the diagnosis and learn the myriad skills of daily management (27). The tremendous responsibility of care and fear of hypoglycemia are extremely stressful for families (28). Infants do not exhibit the classic catecholamine response to hypoglycemia and are unable to communicate sensations associated with hypoglycemia; thus, the risk of severe hypoglycemia, with seizures or coma, is highest in this age-group. Moreover, because the brain is still developing in infants, the adverse consequences of severe hypoglycemia may be greater than in older children (29). Parents struggle with the balance between the risk of long-term complications versus their fear of severe hypoglycemia and the risk of neuropsychological complications (30,31).

Table 2—*Major developmental issues and their effect on diabetes in children and adolescents*

Developmental stage (approximate ages)	Normal developmental tasks	Type 1 diabetes management priorities	Family issues in type 1 diabetes management
Infancy (0–12 months)	• Developing a trusting relationship/"bonding" with primary caregiver(s)	• Preventing and treating hypoglycemia • Avoiding extreme fluctuations in blood glucose levels	• Coping with stress • Sharing the "burden of care" to avoid parent burnout
Toddler (13–36 months)	• Developing a sense of mastery and autonomy	• Preventing and treating hypoglycemia • Avoiding extreme fluctuations in blood glucose levels due to irregular food intake	• Establishing a schedule • Managing the "picky eater" • Setting limits and coping with toddler's lack of cooperation with regimen • Sharing the burden of care
Preschooler and early elementary school-age (3–7 years)	• Developing initiative in activities and confidence in self	• Preventing and treating hypoglycemia • Unpredictable appetite and activity • Positive reinforcement for cooperation with regimen • Trusting other caregivers with diabetes management	• Reassuring child that diabetes is no one's fault • Educating other caregivers about diabetes management
Older elementary school-age (8–11 years)	• Developing skills in athletic, cognitive, artistic, social areas • Consolidating self-esteem with respect to the peer group	• Making diabetes regimen flexible to allow for participation in school/peer activities • Child learning short- and long-term benefits of optimal control	• Maintaining parental involvement in insulin and blood glucose monitoring tasks while allowing for independent self-care for "special occasions" • Continue to educate school and other caregivers
Early adolescence (12–15 years)	• Managing body changes • Developing a strong sense of self-identity	• Managing increased insulin requirements during puberty • Diabetes management and blood glucose control become more difficult • Weight and body image concerns	• Renegotiating parents and teen's roles in diabetes management to be acceptable to both • Learning coping skills to enhance ability to self-manage • Preventing and interventing with diabetes-related family conflict • Monitoring for signs of depression, earing disorders, risky behaviors
Later adolescence (16–19 years)	• Establishing a sense of identity after high school (decision about location, social issues, work, education)	• Begin discussion of transition to a new diabetes team • Integrating diabetes into new lifestyle	• Supporting the transition to independence • Learning coping skills to enhance ability to self-manage • Preventing and intervening with diabetes-related family conflict • Monitoring for signs of depression, eating disorders, risky behaviors

Thus, parents of infants need the support of a diabetes team that understands the difficulties of dealing with an infant with diabetes and is able to provide emotional support to manage their concerns.

Toddlers (1–3 years)

The toddler years, ages 1–3, present unique challenges for the treatment of

type 1 diabetes. As with infants, parents carry the burden of management of toddlers. Parents report that hypoglycemia is a constant fear, especially when the child refuses to eat. Important issues at this age are discipline and temper tantrums; it may be difficult to distinguish between normal developmental opposition and hypoglycemia, and therefore, parents must be taught to measure blood glucose before ignoring a temper tantrum. Parents may be overly cautious and interfere with the child's ability to try out new things, and they will need the support of the diabetes team to promote their child's healthy development.

Preschoolers and early school-aged children (3–7 years)

Children at this stage of development need to gain confidence in their ability to accomplish tasks but often lack the fine motor control, cognitive development, and impulse control necessary to be an active participant in most aspects of diabetes care. It is important to realize, however, that most children in this age-group can participate in their self-management by testing blood glucose, helping to keep records, and in some cases counting carbohydrates. For the most part, parents provide the care for preschoolers and young school-aged children, but others, such as child care providers and school nurses may also be involved in the care. Sharing care of young children with diabetes is often difficult for parents, who may fear that others will not know what to do (28). Undetected hypoglycemia remains a concern because of the variations in activity and food intake characteristic of this age-group, and because of continuing concerns regarding the adverse effects of hypoglycemia on brain development and function.

School-aged children (8–11 years)

The influence of the new diagnosis of diabetes on children in this age-group has been studied. Immediately following diagnosis, children report mild depression and anxiety, but these usually resolve by 6 months after diagnosis. After the first 1–2 years, depressive symptoms increase, and anxiety decreases for boys but increases for girls over the first 6 years after diagnosis (32). This increase in depression may be associated with the end of the physiologic "honeymoon" period, when children come to realize that the disease will not go away and that it is more difficult to manage (33).

School-aged children with diabetes can begin to assume more of the daily diabetes management tasks, such as insulin injections and blood glucose testing with supervision and support from caring and knowledgeable adults. Pump treatment is increasingly being used in this age-group, and children can learn to bolus appropriately for standard carbohydrate meals. However, they will still need significant assistance and supervision for management decisions. Several studies have shown that a child's early and independent participation in the diabetes regimen was significantly associated with poorer control (25,26). Current recommendations for care emphasize shared care responsibilities between parents and children. Children may feel that they are different from their peers because of their diabetes and may be at risk for difficulties with social competence (34). It is important to encourage school-aged children to attend school regularly and to participate in school activities and sports to facilitate the development of normal peer relationships (35). The school can present significant challenges or be a source of support to the child with diabetes. This topic is well covered in the ADA position statement "Diabetes Care in the School and Day Care Setting" (4) and the recent publication *Helping the Student with Diabetes Succeed: A Guide for School Personnel* by the National Diabetes Education Program (NDEP).

Both children and parents fear hypoglycemia and the potential for hypoglycemia to interfere with learning. Fear of hypoglycemia is a legitimate consequence of hypoglycemia in children, and the experience of severe hypoglycemia may lead patients and parents to overtreat initial symptoms and institute behavioral changes to maintain higher blood glucose levels, which result in a deterioration of metabolic control (36,37) Furthermore, fear of hypoglycemia may be associated with worse psychological status and adaptation in adult patients (38).

Adolescents

Adolescence is a period of rapid biological change accompanied by increasing physical, cognitive, and emotional maturity. Adolescents are struggling to find their own identity separate from their families. Many of the diabetes-related tasks can interfere with the adolescent's drive for independence and peer acceptance. Peer pressure may generate strong conflicts. In this age-group, there is a struggle for independence from parents and other adults that is often manifested as suboptimal adherence to the diabetes regimen.

Because adolescents have the fine motor control to competently perform most self-management activities, it is tempting for parents to turn over total diabetes management to the teenager. While adolescents can perform the tasks of diabetes management, they still need help with decision-making about insulin adjustments. Adolescents whose parents maintain some guidance and supervision in the management of diabetes have better metabolic control (26,39). Thus, continuing to involve parents appropriately, with shared management, is associated with improved control. The challenge is to find the degree of parental involvement that is comfortable for all involved, without risking deterioration in glycemic control from over- or underinvolvement (40). Such involvement in diabetes management in this developmental stage can affect parent-adolescent relationships.

Parent-child conflict has been associated with poorer diabetes outcomes in several studies (41–43). During the later adolescent years, the parents and the diabetes care team need to assist the youth to transition to more independent self-management and to adult diabetes care providers.

DIABETES CARE — The components of the initial diabetes visit are listed in Table 3. Items listed pertain to the initial presentation of a child for medical care, possibly in DKA. Continuing care visits will include many of the same components.

GLYCEMIC CONTROL — Current standards for diabetes management reflect the need to maintain glucose control as near to normal as safely possible. Based on substantial evidence of the relationship between glucose control and diabetic complications, each iteration of standards for those with diabetes during the past decade has lowered the target glucose level. Even though most target recommendations for glycemic control have been based on data obtained from studies of adult patients with diabetes, the ideal goal of near-normalization of blood glu-

Table 3—*Components of the initial visit*

Medical history
- Symptoms, and results of laboratory tests related to the diagnosis of diabetes
- Recent or current infections or illnesses
- Previous growth records, including growth chart, and pubertal development
- Family history of diabetes, diabetes complications, and other endocrine disorders
- Current or recent use of medications that may affect blood glucose levels (e.g., glucocorticoids, chemotherapeutic agents, atypical antipsychotics, etc.)
- History and treatment of other conditions, including endocrine and eating disorders, and diseases known to cause secondary diabetes (e.g., cystic fibrosis)
- Lifestyle, cultural, psychosocial, educational, and economic factors that might influence the management of diabetes
- Use of tobacco, alcohol, and/or recreational drugs
- Physical activity and exercise
- Contraception and sexual activity (if applicable)
- Risk factors for atherosclerosis: smoking, hypertension, obesity, dyslipidemia, and family history
- Review of Systems (ROS) should include gastrointestinal function (including symptoms of celiac disease) and symptoms of other endocrine disorders (especially hypothyroidism and Addison's disease)
  - Prior A1C records*
  - Details of previous treatment programs, including nutrition and diabetes self-management education, attitudes, and health beliefs*
- Results of past testing for chronic diabetes complications, including ophthalmologic examination and microalbumin screening*
- Frequency, severity, and cause of acute complications such as ketoacidosis and hypoglycemia*
- Current treatment of diabetes, including medications, meal plan, and results of glucose monitoring and patients' use of data*

Physical examination
- Height, weight, and BMI calculation (and comparison to age and sex-specific norms)
- Blood pressure determination and comparison to age-, sex-, and height-related norms
- Funduscopic examination
- Oral examination
- Thyroid palpation
- Cardiac examination
- Abdominal examination (e.g., for hepatomegaly)
- Staging of sexual maturation
- Evaluation of pulses
- Hand/finger examination
- Foot examination
- Skin examination (for acanthosis nigricans SMBG testing sites and insulin-injection sites*)
- Neurological examination

Laboratory evaluation
- *If clinical evidence for DKA:*
  - Serum glucose, electrolytes, arterial or venous pH, serum or urine ketones
- *If signs and symptoms are suggestive of type 2 diabetes:*
  - Evidence of islet autoimmunity (e.g., islet cell [ICA] 512 or IA-2, GAD, and insulin autoantibodies)
  - Evidence of β-cell secretory capacity (e.g., C-peptide levels) after 1 year, if diagnosis is in doubt
- A1C
- Lipid profile
- Annual screening for microalbuminuria
- Thyroid-stimulating hormone (TSH) levels
- Celiac antibodies at diagnosis or initial visit if not done previously

Referrals and screening
- Yearly ophthalmologic evaluation.
- Medical nutrition therapy (by a registered dietitian)
  - As part of initial team education and on referral, as needed; generally requires a series of sessions over the initial 3 months after diagnosis, then at least annually, with young children requiring more frequent reevaluations
- Diabetes nurse educator
  - As part of initial team education, or referral as needed at diagnosis; generally requires a series of sessions during the initial 3 months of diagnosis, then at least annual reeducation
- Behavorial specialist
  - As part of initial team education, or referral as needed optimally for evaluation and counseling of patient and family at diagnosis, then as indicated to enhance support and empowerment to maintain family involvement in diabetes care tasks and to identify and discuss ways to overcome barriers in successful diabetes management
- Depression screening annually for children ≥10 years of age, with referral as indicated

*Pertain only to previously diagnosed patients, at time of initial referral, assuming prior medical management.

cose levels in children and adolescents is generally the same as that for adults. However, special consideration must be given to the unique risks of hypoglycemia in young children. In addition, extensive evidence indicates that that near-normalization of blood glucose levels is seldom attainable in children and adolescents after the honeymoon (remission) period.

In the Diabetes Control and Complications Trial (DCCT) (44), a reduction of microvascular complications with improved control was observed, although it should be noted that this trial involved mostly adults with type 1 diabetes. Of note, when the cohort of adolescents included in the DCCT was analyzed separately (45), the A1C level achieved in the "intensive" group was >1% higher than the current ADA recommendation for patients in general (1).

Enthusiasm for embracing the target achieved by the intensively treated adult cohort of the DCCT is tempered by the recent results of Epidemiology of Diabetes Interventions and Complications (EDIC) (46), the follow-up study of DCCT participants. Of the DCCT trial participants, 95% participated in EDIC; of the adolescent cohort, 90% participated. Following the closeout of the DCCT, most EDIC participants were converted to or continued on intensified diabetes management (95% of the prior intensive cohort and 80% of the prior conventional cohort). This intensified management was provided in a nontrial setting, with visits every 3 months and contact with the diabetes care team initiated by the patient, as deemed necessary. The EDIC study showed an increase in A1C levels in those adolescents in the intensive treatment group (from 8.1% to 8.4%) and a decrease in those in the conventional group (from 9.8% to 8.5%) after study end. These data suggest that intensification of treatment outside of a clinical trial can decrease A1C significantly, but that it may be difficult to achieve an A1C consistently <8% without the resources of a clinical trial.

Of note, however, despite the difficulty of achieving A1C values close to 7%, results from the EDIC also suggest that intensive diabetes management has significant and long-lasting health benefits. The adolescents in the intensive treatment cohort of the DCCT had little further progression to proliferative retinopathy 4 years after the DCCT, while the previously conventionally treated group (A1C 9.8% at the end of the DCCT) had progression in an additional 15% of participants 4 years after close of the DCCT, despite their significant decline in A1C (from a mean of 9.8% to 8.5%) (46) Data from the EDIC study (47,48) suggest that 4–7 years of intensified management may have prolonged beneficial effects (49). Conversely, 4–6 years of suboptimal diabetes control, as frequently seen during adolescence, may have lasting adverse effects on the risk of micro- and macrovascular disease.

In selecting glycemic goals, the difficulty in achieving an optimal A1C must be balanced against the disadvantages of targeting a higher (although more achievable) goal that may not promote optimal long-term health outcomes. In addition, the benefits of improved glycemic control in children must be balanced with careful consideration of the child's unique vulnerability to hypoglycemia. To address these unique needs of the developing child, age-specific glycemic goals are presented for children <6 years of age, 6–12 years of age (prepubertal), and 13 years of age (or pubertal) to adulthood. As adolescents approach adulthood, the glycemic standards should approach those for adults. Although age-specific glycemic targets are provided, it is clear that hypoglycemic risk is not confined to young children (50,51), and medical professionals providing recommendations for persons with diabetes should recognize hypoglycemia as a limiting factor for many individuals in reaching optimal goals, regardless of age.

Age-specific glycemic goals

Children <6 years old. The relationship between hypoglycemia and possible neuropsychologic impairment is of far greater concern for the very young child than for older children and adolescents. Many reports describe subtle neuropsychologic or intellectual impairments with significant hypoglycemia in young children (see "Hypoglycemia" section below), whereas others report school performance to be similar to that of siblings and peers. Although many of these studies (see "Hypoglycemia" section below) describe associations between hypoglycemia and neuropsychologic dysfunction, none of these reports has resulted from longitudinal, prospective clinical trials evaluating brain or psychologic development as the outcome of the study. Nevertheless, substantial data do suggest that the developing brain is more vulnerable to detrimental effects of hypoglycemia relative to that of older children and adults. As well, the young child may be unable to mount a mature adrenergic response to hypoglycemia, and young children may be unable to effectively communicate symptoms of hypoglycemia (52). Finally, recent studies, using continuous blood glucose sensors, have documented that hypoglycemia, especially nocturnal hypoglycemia, is considerably more frequent than has been recognized by conventional capillary blood glucose measurements several times a day (53,54).

An additional confounding factor is the unpredictability of food intake and physical activity in this age-group. Toddlers may refuse food and cannot understand that failure to eat will result in hypoglycemia. Furthermore, conventional self-monitoring of glucose in small children is confounded by the frequent eating schedule of toddlers. Many toddlers are eating approximately every 2 hours except for when they get up for breakfast. Glycemic excursions may be dramatic, with reported blood glucose levels much higher than desired. Of note, however, because of the frequency of food ingestion, most blood glucose values obtained are actually postprandial values. Trying to compensate for high blood glucose with additional insulin before meals is a dangerous practice because this practice can lead to "highs" followed by "lows," a common problem in toddlers and one to be avoided. To minimize the risk of hypoglycemia as well as excessive hyperglycemia, both lower and upper targets for this age-group are provided. An A1C value between 7.5 and 8.5% is recommended.

Children 6–12 years old. The management of diabetes in this age-group is particularly challenging, because many 6- to 12-year-olds require insulin with lunch or at other times when they are away from home. Many require insulin administration while at school, which demands flexibility and close communications between the parents, the healthcare team, and school personnel (4). The lack of abstract thinking in most children of this age limits management choices and dictates that parents or other adults make most of

Table 4—*Plasma blood glucose and A1C goals for type 1 diabetes by age group*

Values by age	Plasma blood glucose goal range (mg/dl)		A1C	Rationale
	Before meals	Bedtime/overnight		
Toddlers and preschoolers (<6 years)	100–180	110–200	<8.5 (but >7.5) %	• High risk and vulnerability to hypoglycemia
School age (6–12 years)	90–180	100–180	<8%	• Risks of hypoglycemia and relatively low risk of complications prior to puberty
Adolescents and young adults (13–19 years)	90–130	90–150	<7.5%*	• Risk of hypoglycemia • Developmental and psychological issues

Key concepts in setting glycemic goals:
- Goals should be individualized and lower goals may be reasonable based on benefit–risk assessment
- Blood glucose goals should be higher than those listed above in children with frequent hypoglycemia or hypoglycemia unawareness
- Postprandial blood glucose values should be measured when there is a disparity between preprandial blood glucose values and A1C levels

*A lower goal (<7.0%) is reasonable if it can be achieved without excessive hypoglycemia

the treatment decisions. While children in this age-group may be more able to recognize and self-treat hypoglycemia, close adult supervision is still required. On the other hand, the ability of most children of this age to recognize, report, and seek treatment for hypoglycemia, combined with an absence of insulin resistance and psychological issues associated with puberty, makes this age-group perhaps the most amenable to intensive glucose control. An A1C goal of ≤8%, a level ~1% higher than the adult standard, is recommended.

Adolescents (13–19 years). This is the only age-group under discussion in whom substantial evidence-based data exist. Investigators in the DCCT were able to control diabetes in this age-group only at a level ~1% higher than that achieved by adults. That teenagers included in the DCCT were able to achieve a mean A1C level of 8.06% in an era before insulin lispro, insulin aspart, and insulin glargine were available suggests that good metabolic control is possible in at least some adolescents. Of note, however, several studies in the United States and Europe (24,55,56) have documented that mean A1C levels are generally >8.0% and with reduction comes a significant increase in the risk of severe hypoglycemia. Therefore, while an ideal target A1C identical to that for adults (<7%) could be recommended, we recognize that this level of metabolic control is not achievable in most adolescents. Concerns regarding the risks of hypoglycemia and of the potential of creating a feeling of failure in the patient and family leads us to the general recommendation of <7.5% in this group.

INSULIN MANAGEMENT OF DIABETES

— Insulin type, mixture of insulins in the same syringe, site of injection, and individual patient response differences can all affect the onset, peak, and duration of insulin activity. In general, insulins used in children are rapid-acting insulin analogs, short-acting insulin, intermediate-acting insulin (NPH and Lente), and long-acting insulin analogs. These insulins are used in combination or individually and are delivered by syringe or, in some cases, a pen or pump.

Although there is no one established formula for determining a child's insulin requirement, insulin requirements are usually based on body weight, age, and pubertal status. Children with newly diagnosed type 1 diabetes usually require an initial total daily dose of ~0.5–1.0 units/kg. In general, younger (and prepubertal) children require lower doses while the presence of ketoacidosis, use of steroids, and the hormonal changes of puberty all dictate higher doses. The small insulin needs of infants and toddlers may require diluted insulin to allow for more precise dosing and measurement of insulin in <1-unit increments. Diluents are available for specific types of insulins from the insulin manufacturers. Insulin can be diluted either at a pharmacy or at home once parent training has been completed. Insulin pens that deliver insulin in 0.5-unit increments also are available.

It is common for a newly diagnosed child's diabetes to enter a honeymoon phase with an increase in insulin production within several weeks after the initiation of insulin therapy. During this phase of diabetes, insulin requirements may fall well below the initial dose of 0.5–1.0 units/kg per day needed to maintain blood glucose targets. Children may require only minimal amounts of intermediate- or long-acting insulin, possibly combined with small amounts of rapid- or short-acting insulin. β-cell destruction continues during this honeymoon phase, and with the progressive loss of β-cell function, there is need for increased exogenous insulin to avoid elevated blood glucose levels. Insulin requirements increase with growth and, in particular, during puberty. Insulin requirements during puberty may increase to as much as 1.5 units/kg per day due to the hormonal influences of increased growth hormone and sex hormone secretion.

Children with diabetes often require multiple daily injections of insulin, using combinations of rapid-, short-, intermediate-, or long-acting insulin before meals and at bedtime to maintain optimal blood glucose control. If a large snack is consumed between meals, as often occurs in adolescents in the late afternoon, an extra injection of a rapid-acting insulin may be necessary.

In most centers, the majority of children with diabetes are treated with two or three doses of rapid-acting or short-acting insulin combined with intermediate-acting insulin. However, many patients require more frequent insulin administration in order to achieve and maintain good glycemic control, especially after the honeymoon period is over. Cross-sectional epidemiological studies have been unable to document improved control with increasing numbers of insulin injections per day, indicating that the number of injections alone is not sufficient to achieve optimal glycemic control (24). However, greater flexibility provided by multiple daily insulin injections (MDIs) per day, combined with carbohydrate counting and dose determined using an insulin-to-carbohydrate ratio, makes this an attractive therapeutic regimen for most middle school and high school students.

The basal/bolus insulin regimen uses a long-acting insulin analog (glargine) combined with a rapid-acting insulin analog given before meals and snacks and has been documented to result in stable glycemic control and less hypoglycemia compared with regimens using intermediate and short insulin regimens (55, 57,58).

Because many young children and teenagers may consume multiple snacks throughout the day, an ideal basal/bolus regimen may consist of as many as six to seven insulin injections per day. Many families are reluctant to commit to this many doses per day; therefore, a combination of rapid-acting insulin with small amounts of intermediate-acting insulin to allow coverage for snacks may be an appropriate alternative to the strict basal/bolus plan. For example, children who have lunch at a consistent time and are willing to eat a consistent amount of carbohydrate at lunch often do well with a breakfast dose of NPH given to provide coverage for lunch (55) in addition to a bedtime dose of a long-acting insulin analog. Although an MDI regimen with carbohydrate counting allows flexibility of eating times and amounts, the number of insulin injections required may be a barrier to good control; thus, many choose an insulin pump if it is an option financially and the patient and family are prepared for the training.

Adjusting insulin based on the carbohydrate content of meals has been shown to improve glycemic control in adults (59). The principles of using carbohydrate counting and an insulin-to-carbohydrate ratio tailored to each individual is a principle that is applied to both insulin injection therapy and insulin pump therapy.

The DCCT demonstrated that patients on basal/bolus insulin therapy (MDIs and pump) achieved better metabolic control compared with those on traditional twice-daily insulin dosing. However, it should be emphasized that the diabetes therapy used in the intensively treated cohort of the DCCT included not only different approaches to insulin dosing, but also more intensive blood glucose monitoring, improved medical nutrition therapy, and insulin adjustments for exercise. These are now recognized to be important components in any diabetes management approach.

Because two or three doses of mixed rapid-acting or short-acting insulin with intermediate-acting insulin generally cannot maintain A1C levels within the target range for 50–70% of the pediatric diabetes population (60), recommendations now support moving toward a basal/bolus insulin regimen for most patients, especially after the honeymoon period.

Additional specific details of insulin treatment and dosage adjustments appropriate for the pediatric population are discussed in detail in several books published by the ADA, including *Medical Management of Type 1 Diabetes* (61) and *Intensive Diabetes Management* (62).

Basal bolus insulin regimens

The combination of rapid-acting insulin analogs and a long-acting peakless insulin offers an excellent option for basal and bolus insulin administration. Glargine is the first long-acting analog to have received Food and Drug Administration (FDA) approval. It is an almost peakless insulin, with a duration of action of 20–24 h. Usually it is given at bedtime, although administration at other times of the day may result in similar levels of coverage and glycemic control. In some patients glargine may not last 24 h, and anecdotal experience has suggested dividing the dose into two daily injections. Glargine has been approved for use in pediatric patients ≥6 years of age. Ongoing clinical studies in the pediatric population will define the most effective use of this insulin preparation in young children. Because there is some increase in effective insulin action (a small peak) during the initial 3–5 h after administration, nocturnal hypoglycemia, in theory, may be reduced in young children by administering glargine in the morning or before supper.

In a basal-bolus regimen, the premeal rapid (or short-acting) insulin dose is generally based on three factors: the current blood glucose level, the anticipated consumption of carbohydrate in the meal, and the expected level of physical activity in the coming hours. Basal/bolus regimens have been shown to result in lower fasting blood glucose levels with less nocturnal hypoglycemia than regimens that use intermediate-acting NPH insulin in children/adolescents (54,57) as well as in adults (63). The obvious downside of a strict basal/bolus regimen in the pediatric population is the number of injections required to accommodate the frequent meals and snacks that many children and adolescents require for adequate caloric intake.

Studies have demonstrated the feasibility of administering lispro insulin after meals in very young children (64). Dosing with lispro after meals allows a care provider to more accurately titrate the insulin doses for an erratic eater, with the goal of matching actual food intake and insulin more closely and minimizing the potential for hypoglycemia. Other studies have shown that in the child with more predictable eating habits, premeal insulin dosing results in lower postprandial blood glucose values (65).

Pumps

Pump use is increasing rapidly in the pediatric population (66). There is no best predetermined age to initiate insulin pump therapy. As with all diabetes management issues, individualized treatment plans that consider the needs of the patient as well as those of the family are best. Currently, there are fewer young children than preadolescents and adolescents using insulin pumps (67,68). Adult support at both home and school is essential for success with all diabetes management but especially with pump treatment until the child is able to manage the diabetes independently (69).

Recommendations

- Insulin requirements are usually based on body weight, age, and pubertal status.

- A basal-bolus insulin regimen using either and MDI regimen or an insulin pump should be considered.

BLOOD GLUCOSE MONITORING — Self-management of diabetes is the ultimate goal for all patients with diabetes, with insulin dosing decisions based on interpretation of blood glucose results. Self-monitoring of blood glucose (SMBG) allows people with diabetes and their families to measure blood glucose levels rapidly and accurately. All basal/bolus diabetes management regimens and all self-management skills rely on frequent SMBG.

Blood glucose monitoring in general has been extensively reviewed by the ADA and is summarized in the ADA consensus statement "Self-Monitoring of Blood Glucose" (70). For children with type 1 diabetes, four or more tests per day are generally necessary.

SMBG is necessary for individuals to achieve optimal glycemic control; there is a good correlation between frequency of monitoring and glycemic control (71). Multiple blood glucose measurements should be done each day to determine patterns of hypoglycemia and hyperglycemia and to provide data for insulin dose adjustments. Preprandial blood glucose levels are important, but postprandial and overnight levels are also valuable in determining insulin dose adjustments. Special attention should be addressed to the preschool and early school-aged child who may be unable to identify and self-report episodes of hypoglycemia. Safe management of these children requires more frequent blood glucose testing. Monitoring at anticipated peaks in insulin action may be necessary, particularly if a child has not eaten well at the preceding meal. Additional testing during periods of increased physical activity is also very important.

Most blood glucose meters contain a memory chip, and the manufacturer can provide software to print out monitoring results, which can be used to examine blood glucose patterns or to validate the accuracy of SMBG logs. Several of the newer meters allow alternate-site testing (e.g., the arm or leg) to decrease the discomfort of fingersticks. A concern has been raised, however, as alternate-site testing may not reflect arterial glucose measurements as quickly as fingerstick capillary blood glucose measurments, thus creating a delay in documentation of hypoglycemia when the glucose level is changing rapidly (72–74).

Interpretation of blood glucose monitoring results and their use for dose calculations are of major importance for achieving good metabolic control. It is these skills that make intensive diabetes management possible. If results are not reviewed frequently, patterns are easily missed and opportunities for changes in the regimen are also missed.

Newer technologies are now allowing near continuous blood glucose monitoring (75). These devices may hold promise for improved assessment of metabolic control and are approved for use in pediatric patients (76,77). Further improvements of products are in development.

Recommendations

- Use glucose levels to make insulin dose adjustments acutely for rapid- or short-acting insulins and after observing patterns over several days to adjust doses of long-acting insulins
- Use insulin-to-carbohydrate ratios and correction doses for high and low blood glucose levels
- Test at least four times a day
- Periodically test postprandial, before- and after-exercise, and nocturnal glucose levels.

NUTRITION FOR CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES — Nutrition recommendations for children and adolescents with type 1 diabetes should focus on achieving blood glucose goals without excessive hypoglycemia (78–81), lipid and blood pressure goals, and normal growth and development. This can be accomplished through individualized meal planning, flexible insulin regimens and algorithms, SMBG, and education promoting decision-making based on documentation and review of previous results.

Nutrient recommendations are based on requirements for all healthy children and adolescents (82–86) because there is no research on the nutrient requirements for children and adolescents with diabetes. Children and adolescents should adopt healthful eating habits to ensure adequate intake of essential vitamins and minerals. In general, U.S. children are not eating recommended amounts of fruits and vegetables (87), although children with diabetes may be doing somewhat better than the general population in some areas. A 1996 report on dietary intake of 4- to 9-year-old children with type 1 diabetes found that energy, vitamin, and mineral intakes were adequate while fiber intake was less than recommended (88). However, many children consumed levels of saturated fat well above the National Cholesterol Education Program (NCEP) recommendations (89).

MEDICAL NUTRITION THERAPY — Medical nutrition therapy plays a major role in the management of type 1 diabetes in children, although it is often one of the most difficult aspects of treatment. Consultation with a registered dietitian with experience in pediatric nutrition and diabetes is recommended. Meal plans must be individualized to accommodate food preferences, cultural influences, physical activity patterns, and family eating patterns and schedules. The meal planning approach selected must assist families to learn the effect of food on blood glucose levels. The system must also be comprehensible and one that can be implemented within the context of the family's lifestyle and eating patterns.

There is some evidence that total carbohydrate content of meals and snacks is most important in determining the postprandial glucose response and, thus, in determining the premeal insulin dosage (90). The Dose Adjustment for Normal Eating (DAFNE) study group documented a decrease in HbA_{1c} and an increase in patient satisfaction in adults after initiating diabetes management using carbohydrate counting for meal and snack carbohydrate content and insulin-to-carbohydrate ratio to determine the insulin dose (59). Consistency of food intake (carbohydrate) is important for children and adolescents who are on fixed insulin regimens and do not adjust premeal insulin dosages.

Consideration of a child's appetite must be given when determining energy requirements and the nutrition prescription. Adequacy of energy intake can be evaluated by following weight gain and growth patterns on the Centers for Disease Control and Prevention (CDC) pediatric growth charts (http://www.cdc.gov/growthcharts) on a regular basis. Many children with type 1 diabetes present at diagnosis with weight loss that must be restored with insulin initiation, hydration, and adequate energy intake. As energy requirements change with age,

physical activity, and growth rate, an evaluation of height, weight, BMI, and nutrition plan is recommended at least every year (91). Good metabolic control is essential for normal growth and development (78). However, withholding food or having the child eat consistently without an appetite for food in an effort to control blood glucose is discouraged. BMI should be monitored and calories restricted if the child becomes overweight. Nutrition therapy has been extensively reviewed by the ADA (92,93).

Recommendations

- Consultation with a dietitian to develop/discuss the medical nutrition plan is encouraged
- Evaluate height, weight, BMI, and nutrition plan annually
- Calories should be adequate for growth and restricted if child becomes overweight.

EXERCISE — Exercise offers many health-promoting benefits for people with and without diabetes, and intervention strategies that promote life-long physical activity should be encouraged. Clinical practice guidelines for exercise in adult patients have been published by the ADA (94). Benefits of exercise in type 1 diabetes are detailed in an ADA Technical Review (95) and include a greater sense of well-being, help with weight control, improved physical fitness, and improved cardiovascular fitness, with lower pulse and blood pressure and improved lipid profile (95,96). These advantages apply to children as well as to adults, as indicated by studies demonstrating the beneficial effect of physical fitness on lipid and lipoprotein levels in adolescents (96). The effects of improved metabolic control on cardiovascular fitness is controversial, with most recent studies showing no relationship between physical fitness and A1C levels (97,98).

Of hypoglycemic episodes in the pediatric population, 10–20% are associated with exercise, which is generally of greater than usual intensity, duration, or frequency. Increased hepatic glucose output in association with vigorous exercise secondary to both β- and α-adrenergic stimulation may cause hyperglycemia during and immediately after exercise, followed by hypoglycemia within 1–6 h of completion of exercise due to hepatic glycogen depletion (99).

The seasonal alteration in sports activities and types of sports in which children are involved may require frequent dose adjustments to allow the child to participate in school, team, and individual sports. Initially, frequent blood glucose monitoring will be required to determine how to best adjust insulin and food for the sports activity. It is recommended that blood glucose monitoring be done before and at the termination of exercise and at hourly intervals during episodes of prolonged strenuous activity. Fifteen grams of carbohydrate may be administered as a readily absorbed sugar if blood glucose levels are <100 mg/dl during the period of exercise. Parents will need to ensure that the school personnel and coaches are aware of the risk of hypoglycemia with exercise, the child's symptoms of hypoglycemia, and the use of emergency glucose sources to treat hypoglycemia. The parent is responsible for providing blood glucose monitoring equipment and glucose tablets or juice. The use of a readily absorbable carbohydrate source, such as an electrolyte-containing sports drink, may be very helpful in preventing hypoglycemia both during and after exercise.

Decreasing insulin dose for planned exercise, rather than increasing calories, should be considered as part of appropriate weight management for all children with diabetes, although this strategy may be difficult in the very young child whose physical activity is more sporadic than planned. With prior planning, all children with diabetes should be able to enjoy the many benefits of physical activity, and their diabetes should not be a deterrent.

With the increased prevalence of overweight and obesity in children and adolescents, children and adolescents with type 1 diabetes may also be overweight or obese. For these children, exercise is particularly encouraged as an important component of a weight management strategy. Studies in pediatric populations have shown that discouraging sedentary activities, especially time spent in front of the TV or computer monitor, is an effective method to increase physical activity and encourage weight loss in inactive children.

Recommendations

- Children and adolescents with type 1 diabetes should adhere to the CDC and American Academy of Sports Medicine recommendations for a minimum of 30–60 min of moderate physical activity daily
- Blood glucose monitoring before exercise is recommended with a suggested intake of 15 g of carbohydrate (amount may need to be less in younger children—10 g, for example) for a blood glucose level below target range before exercise; for vigorous physical activity expected to be >30 min, an additional 15 g of carbohydrate may be necessary
- For prolonged vigorous exercise, hourly blood glucose monitoring during the exercise, as well as blood glucose monitoring after completion of exercise, is recommended to guide carbohydrate intake and prospective insulin dose adjustment for recurring exercise events
- At the onset of a new sports season, frequent blood glucose monitoring during the 12-h postexercise period should be undertaken to guide insulin dose adjustments
- In the child or adolescent (particularly if overweight/obese), physical exercise should be encouraged and sedentary activity discouraged.

ASSESSMENT OF CHILD AND FAMILY RISK FACTORS AT DIAGNOSIS — It is well-documented that over the first few years after the diagnosis of type 1 diabetes in childhood, child adherence to the diabetes regimen, family diabetes-related behavior patterns, as well as glycemic control tend to become established or "track" and are difficult to change (81). Therefore, it is important to assess both the risk factors and the strengths of the child and family at the time of diagnosis, with the hope of intervening before child and family behavior patterns become firmly established.

PSYCHOSOCIAL ISSUES AFFECTING THE DIABETES CARE PLAN — Certain characteristics of the child/adolescent and their parents predict an increased risk for difficulties with diabetes management. Findings in the child include the presence of other health problems (e.g., asthma, eating disorders), poor school attendance, learning disabilities, and emotional and behavioral disorders, including risk-taking behaviors resulting in delin-

quent behavior and depression (100,101).

Likewise, certain family characteristics have been identified as risk factors for poor diabetes control and repeat hospitalizations. These include a single-parent home, chronic physical or mental health problems in a parent or other close family member (including substance abuse,) a recent major life change for the parent (e.g., loss of a job or a death in the family), lack of adequate health insurance, complex child care arrangements, and health/cultural/religious beliefs that make it difficult for the family to follow current diabetes treatment plans (71,102). Additional barriers to care may be found in a family with intimate experience with diabetes. A parent with diabetes may be committed to outdated treatment ideas or information more pertinent to adult diabetes care. Personal knowledge of the acute and chronic complications of diabetes may result in anxiety and/or depression, impairing the ability to learn the tools needed to succeed in diabetes management and hindering the care of the child with diabetes.

Conversely, a child and family with established peer and family support who have met other life challenges well in the past will frequently be able to draw on these strengths to manage successfully the challenge of diabetes.

Recommendation

- Patient and family characteristics predicting difficulty with diabetes management should be sought and addressed.

ACUTE COMPLICATIONS

Growth assessment

Normal linear growth and appropriate weight gain throughout childhood and adolescence are excellent indexes of health in general and reasonable markers of metabolic control in particular. Although weight loss just before a diagnosis of type 1 diabetes is the rule, rapid weight gain and normal linear growth should ensue rapidly upon initiation of appropriate treatment. Height and weight measurements are essential components of the physical exam in healthy children, including children with diabetes, and should be plotted on appropriate growth charts at each clinic visit (http://www.cdc.gov/growthcharts). One of the main goals of treating children and youth with diabetes is to maintain normal physical growth to include normal gains in height and weight and normal timing of the onset and tempo of puberty, including normal timing and magnitude of the pubertal growth spurt. Chronic undertreatment with insulin with resultant long-standing poor diabetes control often leads to poor growth and weight loss and a delay in pubertal and skeletal maturation. Overtreatment with insulin can lead to excessive weight gain. In addition, impaired linear growth or poor weight gain should raise suspicion of the coexistence or development of a comorbidity, including hypothyroidism or celiac disease. Longitudinal evaluation of the patient's height, weight, and BMI plotted on standard growth curves will allow for early recognition of any deviations from normal, which can then be evaluated and treated.

Recommendations

- All children and adolescents should have height and weight plotted on the CDC growth curves at each clinic visit
- Thyroid function (serum TSH levels) should be monitored at diagnosis and every 1–2 years thereafter or obtained at any time growth rate is abnormal
- Evaluation for celiac disease should be considered if there is unsatisfactory weight gain that cannot be explained by poor metabolic control.

DKA

DKA is a consequence of absolute or relative insulin deficiency resulting in hyperglycemia and an accumulation of ketone bodies in the blood, with subsequent metabolic acidosis. DKA is generally categorized by the severity of the acidosis, with mild DKA defined as a venous pH <7.3 and bicarbonate <15 mmol/l; moderate DKA as a pH <7.2 with a bicarbonate <10; and severe DKA as a pH <7.1 and bicarbonate <5. DKA is a potentially life-threatening condition. In the United States, the overall mortality for a child with DKA is 1–3% (18), although recent reports from tertiary care centers suggest lower mortality rates (103,104). The risk for morbidity and mortality is higher in severe DKA. These patients require close physician monitoring, frequently utilizing central venous and intra-arterial pressure monitoring as well as frequent blood chemistry determinations to direct therapy. Physicians experienced in the care of children with DKA (pediatric endocrinologists or pediatric intensivists) should direct management, whenever possible (105).

1. DKA at diagnosis. DKA may occur in a variety of circumstances. The most common is the initial presentation of type 1 diabetes. Approximately 30% of new-onset patients present in ketoacidosis (18). This percent increases with decreasing age of the child (<4 years of age), lower socioeconomic status, and children from families who are not familiar with the signs and symptoms of diabetes (i.e., those without a first-degree relative with type 1 diabetes (106).

2. DKA after diagnosis. In a child with known diabetes, the most common cause is omitted insulin injections. Intercurrent illnesses (105), trauma, surgery, or other causes of physiologic stress may result in DKA if adequate insulin dose adjustments are not made. Emotional stress may be a clue to insulin omission.

Children are at higher risk for developing cerebral edema during treatment. Cerebral edema is an important cause of DKA-associated deaths in childhood and for 20% of all deaths in children with diabetes <20 years of age (107). While cerebral edema has been reported in individuals in the fourth decade of life, it is most common in patients <15 years old who are severely dehydrated (103,108), acidotic, and hyperosmolar. Newly diagnosed patients <5 years of age seem to be at the greatest risk.

A consensus conference on management of DKA in children took place in June 2003. Recommendations from that conference have been published and are concordant with the recommendations below (109).

3. Recurrent DKA. A child or adolescent with recurrent episodes of ketoacidosis needs special attention. Recurrent DKA is almost always due to insulin omission. These children have a higher incidence of psychiatric illness, especially depression, and were more likely to miss insulin doses, to come from single parent homes, and to be underinsured than their peers (110,111). Long-term follow-up studies have shown that the frequency of eating disorders is more common in adolescents with recurrent episodes of DKA (112). Diabetes morbidity and mortality is also significantly greater in those with recurrent DKA compared with patients without episodes of DKA (112). Psychological coun-

seling is recommended for all children with recurrent DKA and their families.

Because of the significant mortality and morbidity associated with DKA, prevention is of paramount importance. Prevention can be achieved by:

- Public awareness of the signs and symptoms of untreated diabetes
- Education of friends, roommates, and other caregivers about the signs and symptoms of early DKA
- Increased recognition that insulin omission due to psychological problems and lack of financial resources is the most common cause of DKA in patients with established diabetes
- Improved detection of families at risk
- Education about ketone monitoring
- 24-h telephone availability and encouragement to contact the healthcare team when blood glucose levels are high, when there is ketonuria or ketonemia, and especially during intercurrent illness.

Recommendations

1. Monitoring

- Hourly heart rate, respiratory rate, blood pressure, and neurologic status
- Hourly accurate fluid input and output
- Electrocardiogram monitoring for assessment of T-waves for evidence of hyperkalemia/hypokalemia
- Hourly capillary glucose
- Laboratory tests: electrolytes, blood glucose, and blood gases should be repeated every 2–4 h.

2. Fluids and electrolytes

- Intravenous fluids should be given to replace fluid deficits over 48 h
- Hypotonic fluids (<0.45N NaCl) should never be given as initial therapy
- Potassium levels should be monitored closely and replaced as soon as urine output is established.

3. Insulin replacement

- Initial insulin therapy should be given intravenously in a dose of 0.1 unit · $kg^{-1} \cdot h^{-1}$.

4. A flow sheet should be maintained documenting clinical observations, intravenous and oral fluids, insulin dosing, and laboratory results.

Hypoglycemia

The desire to avoid hypoglycemia is one of the major barriers to achieving near-normal glycemic control (113). Both children and parents fear hypoglycemia, especially if the child has a history of hypoglycemic seizure. Even mild hypoglycemia causes acute alterations in cognitive function, especially associative learning, attention, and mental flexibility (114). The definition of hypoglycemia is controversial, but studies have shown cognitive impairment at blood glucose concentrations <60 mg/dl (115). Counterregulatory hormone responses to falling blood glucose levels and associated symptoms occur at higher blood glucose levels than adults; children with chronic hyperglycemia may have symptoms of hypoglycemia at normal blood glucose levels (116). On the other hand, a single episode of hypoglycemia lowers the plasma glucose threshold for autonomic activation, resulting in increased potential for further acute events (117).

Neurologic abnormalities associated with the acute phase of hypoglycemia include transient reduction in mental efficiency, altered electroencephalogram, and increased regional cerebral blood flow. Some cognitive deficits may persist beyond the acute phase. Several investigations have found that while diabetes itself is not associated with cognitive deficits, cognitive dysfunction may be increased in children and adolescents who have experienced severe hypoglycemia, especially if the hypoglycemia occurred before 5 years of age (118–120). Recent data suggest that some of the learning difficulties in children who have experienced severe hypoglycemia earlier in life may be due to difficulties in delayed spatial memory (121).

Hypoglycemia is more frequent in children with lower A1C levels, a prior history of severe hypoglycemia, and higher insulin doses and in younger children (122). In addition, longer duration of diabetes and male sex have been associated with increased risk of hypoglycemia. Because of the deleterious effects of severe hypoglycemia in children <5 years, glycemic goals are higher in this age-group.

Nocturnal hypoglycemia is common, with reported incidence of 14–47%, and may be due, in part, to impaired counterregulatory response to hypoglycemia during sleep (123). It may be asymptomatic or be associated with subtle symptoms and signs, such as nightmares, restless sleep, low fasting blood glucose levels, and headache, confusion, or behavior changes on awakening. Bedtime blood glucose levels are poor predictors of nocturnal hypoglycemia (124).

Hypoglycemia may be categorized according to severity. Mild hypoglycemia is associated with mild adrenergic or cholinergic symptoms (sweating, pallor, palpitations, and tremors) and occasional mild symptoms of neuroglycopenia (headache and behavior changes) and can usually be treated by the child or adolescent with 15 g (amount may need to be less in younger children—10 g for example) of an easily absorbed carbohydrate followed by a protein-containing snack. Adjustments in amount should be based on blood glucose levels. Moderate hypoglycemia requires that someone other than the patient administer treatment, but the treatment can be administered orally. Symptoms usually consist of neuroglycopenia (e.g., aggressiveness, drowsiness, and confusion) and autonomic symptoms, and usually require 20–30 g of glucose to restore the blood glucose levels to >80 mg/dl. Severe hypoglycemia requires treatment with glucagon or intravenous glucose and is associated with altered states of consciousness, including coma, seizures, or inability of the patient to take glucose orally because of disorientation. A glucagon dose of 30 mcg/kg subcutaneously to a maximum dose of 1 mg will increase blood glucose levels within 5–15 min but may be associated with nausea and vomiting. A lower dose of 10 mcg/kg results in a smaller glycemic response, although blood glucose levels at 20 min are not significantly different than with a dose of 20 mcg/kg, and is associated with less nausea (125). Repeated episodes of hypoglycemia or long diabetes duration may result in abnormality of the counterregulatory system, with failure of adrenergic responses (defective glucose counterregulation). This results in hypoglycemic unawareness and requires frequent blood glucose monitoring to avoid recurrent episodes.

Recommendations

- Frequency of hypoglycemia should be determined at every visit
- Presence of hypoglycemia unawareness should be assessed at every visit
- If hypoglycemia unawareness is present

or if symptomatic hypoglycemia is frequent, blood glucose targets should be reassessed
- Severe hypoglycemia in children <5 years of age may be associated with cognitive deficits; thus, blood glucose goals are higher for this age-group
- Recognition of hypoglycemia symptomatology is developmental and age-dependent; the limitations of infants and toddlers to detect such symptoms may influence treatment goals and monitoring frequency
- Treatment of hypoglycemia requires the administration of rapidly absorbed glucose, glucagon, and intravenous glucose with treatment based on the severity of the hypoglycemia

IMMUNIZATION — Children with diabetes and children who have family members with type 1 diabetes should receive all immunizations in accordance with the recommendations of the American Academy of Pediatrics (126). Large studies have shown no causal relationship between childhood vaccination and type 1 diabetes (127). In the fall, vaccination against influenza should be given to children with diabetes who are >6 months of age (128).

CHRONIC COMPLICATIONS

Nephropathy

The first manifestation of diabetic nephropathy is microalbuminuria, an elevated albumin excretion rate (AER). The presence of persistent microalbuminuria predicts progression to gross proteinuria within 6–14 years. Hypertension, or even a rise in blood pressure within the normal range, may accompany progression to microalbuminuria, although limited data exist in children (129), or becomes manifest after the recognition of persistent microalbuminuria (130). However, hypertension generally precedes macroalbuminuria and overt proteinuria.

Risk factors for nephropathy include poor glycemic control (44,45), smoking (131,132), having a parent with essential hypertension, or a family history of cardiovascular disease (132).

Microalbuminuria is a sign of early nephropathy at a stage when nephropathy may be reversible with careful glycemic and blood pressure control (2,133,134). Some data suggest that lowering LDL cholesterol may also provide benefit (133). Even in the absence of hypertension, therapy with an ACE inhibitor reverses increased albumin excretion or delays the rate of progression to macroalbuminuria (135–137). Screening provides an opportunity to detect microalbuminuria early, to initiate ACE inhibition therapy, and to encourage meticulous attention to achieving glycemic goals during the reversible phase of diabetic nephropathy.

The definition of microalbuminuria may vary depending on the laboratory and the collection method.

- Albumin-to-creatinine ratio (ACR) 30–299 mg/g in a spot urine sample; slightly higher values can be used in females because of the difference in creatinine excretion (138)
- Timed overnight or 24-h collections: AER of 20–199 mcg/min.
- Because exercise, smoking, and menstruation can affect the results and albumin excretion can vary from day to day, an abnormal value should be repeated. The diagnosis of persistent abnormal microalbumin excretion requires documentation of two of three consecutive abnormal values obtained on different days (2).
- When persistently elevated microalbumin excretion is confirmed, non–diabetes-related causes of renal disease should be excluded with further evaluation determined by the physical examination and clinical situation. Borderline values may indicate an increased risk for progression and should be repeated more frequently (139,140). Following renal evaluation, treatment with an ACE inhibitor should be initiated, even if the blood pressure is not elevated. Microalbumin excretion should be monitored at 3–6 months intervals, and therapy should be titrated to achieve as normal an ACR as possible.

Recommendations

Screening

- Annual screening for microalbuminuria should be initiated once the child is 10 years of age and has had diabetes for 5 years; more frequent testing is indicated if values are increasing
- Screening is done with a random spot urine sample analyzed for microalbumin-to-creatinine ratio; a timed overnight or a 24-h analysis can be done in follow-up, if indicated
- Because exercise, smoking, and menstruation can affect the results and albumin excretion can vary from day to day, an abnormal value should be repeated; the diagnosis of persistent abnormal microalbumin excretion requires documentation of two of three consecutive abnormal values obtained on different days (2).

Treatment

- Confirmed, persistently elevated microalbumin levels should be treated with an ACE inhibitor titrated to normalization of microalbumin excretion (if possible)
- Patients should be educated about the importance of attention to glycemic control and avoidance or cessation of smoking in preventing and/or reversing diabetic nephropathy
- If hypertension exists, rigorous attention to normalization of blood pressure is important for reversal or delay of progression of nephropathy
- Rigorous treatment of elevated LDL cholesterol may offer some benefit
- If medical treatment is unsatisfactory, referral to a nephrologist should be considered.

Hypertension

Hypertension is a common comorbidity of diabetes, which, in adults, is to be associated with development of both microvascular and macrovascular disease. Clinicians who care for children with diabetes often pay little or no attention to blood pressure, and management of hypertension in children with diabetes is often delayed until adulthood. At each visit, determination and review of the patient's blood pressure history can reveal not only early hypertension, but also an upward trend within the normal range, which may indicate the need for further evaluation. Studies have shown that parental hypertension is a major risk factor for elevated blood pressure in childhood (141). Thus, a family history of hypertension is important in the evaluation of a child with diabetes. Because the parents of children with diabetes may be young, periodic reassessment of family history is necessary. If hypertension is documented, pathologic causes other than diabetic nephropathy should be excluded. Laboratory examination should include

evaluation of renal functional status (urinalysis, serum creatinine, and blood urea nitrogen) and urinary albumin excretion (if not obtained within the previous 6 months). Further investigations are determined by the physical examination and clinical situation. In adults (133,142), and presumably in children and adolescents (143), treatment of blood pressure is also critical in reducing both microvascular and macrovascular complications of diabetes. For these reasons, aggressive efforts at diagnosis and management of hypertension in children and adolescents with diabetes are indicated (143).

Definition of hypertension.

- Hypertension is defined as an average systolic or diastolic blood pressure ≥95th percentile for age, sex, and height percentile measured on at least 3 separate days
- "High-normal" blood pressure is defined as an average systolic or diastolic blood pressure ≥90th but <95th percentile for age, sex, and height percentile measured on at least 3 separate days
- Normal blood pressure levels for age, sex, and height are available online at: www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf
- Norms for height are available online at www.cdc.gov/nchs/about/major/nhanes/growthcharts/charts.htm
- Blood pressure should be measured according to recommended standardized techniques, specific for children, with instructions accessible online at www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf.

Treatment. Patients with hypertension should initially be placed on a diet consisting of no added salt and be encouraged to exercise if they are sedentary. The importance of achieving glycemic goals should be reviewed and reinforced. As part of general education on cardiovascular health, counseling should be given for smoking cessation, or encouragement given to not begin the use of tobacco products, since smoking increases microvascular complications, including hypertension (131,144).

There is good evidence that ACE inhibitor treatment of hypertension decreases the rate of decline of renal function in adults (134,135). Decrease in AERs independent of their antihypertensive effects has been described with the use of enalapril and captopril in adolescents, and there have been no reports of significant side effects (135–137). Furthermore, use of ACE inhibitors in adults decreases progression of retinopathy (145) and cardiovascular disease (146). The salutatory effects appear to be from the class of medication rather than any particular agent. Use of ACE inhibitors in children is safe and efficacious. There are no data available on the use of angiotensin receptor blockers in children or adolescents with diabetes.

Recommendations

- Blood pressure determination, using an appropriately sized cuff and with the patient relaxed and seated, should be part of every diabetes physical examination.
- If an elevated blood pressure is detected and confirmed, non–diabetes-associated causes of hypertension should be excluded.
- Treatment of high-normal blood pressure (systolic or diastolic blood pressure consistently above the 90th percentile for age, sex, and height) should include dietary intervention and exercise, aimed at weight control and increased physical activity, if appropriate. Dietary intervention consists of eliminating added salt to cooked foods and a reduction in foods high in sodium content. If target blood pressure is not reached within 3–6 months of lifestyle intervention, pharmacologic treatment should be initiated.
- Pharmacologic treatment of hypertension (systolic or diastolic blood pressure consistently above the 95th percentile for age, sex, and height or consistently >130/80 mmHg, if 95% exceeds that value) should be initiated as soon as the diagnosis is confirmed.
- ACE inhibitors should be considered for the initial treatment of hypertension, with dose titrated to achieve a blood pressure (both systolic and diastolic) consistently <130/80 mmHg or below the 90th percentile for age, sex, and height, whichever is lower. A once-daily formulation is recommended to promote adherence.
- If target blood pressure is not reached with an ACE inhibitor alone, additional antihypertensive medications should be considered
- ACE inhibitors are contraindicated during pregnancy.

Dyslipidemia

Cardiovascular disease (CVD), cerebrovascular disease, and peripheral vascular disease resulting from atherosclerosis are leading causes of morbidity and mortality in adults with type 1 diabetes (147,148). There is unequivocal evidence that atherosclerosis is well established in some patients by adolescence (149,150) and that dyslipidemia is a major risk factor for atherosclerosis (151,152).

According to the National Cholesterol Education Program for Pediatrics (NCEP-Peds) (153), factors contributing to atherosclerosis in children and youth, in addition to elevated plasma lipid concentrations, include smoking, hypertension, obesity, family history of heart disease, and diabetes (153,154). Diabetes is an independent risk factor for CVD in adults, conferring a two- to fourfold increased incidence of cardiovascular disease (155–157).

The few reports of studies done in children and youth with diabetes assessing carotid artery intima-media thickness (IMT) indicate a significant increase in IMT, which correlated with lipid levels (mainly LDL cholesterol), in youth with diabetes compared with age and sex-matched control subjects (150,158–163).

According to NCEP (156), in adults there is ample evidence that elevated LDL cholesterol is most closely associated with CVD and that therapy that lowers LDL levels reduces CVD risk. Therefore, the primary goal of therapy and the determinant for initiating treatment are stated in terms of LDL cholesterol (1,164).

In its statements on "Standards of Medical Care in Diabetes" (1) and "Management of Dyslipidemia in Children and Adolescents With Diabetes" (165), ADA suggests that a lipid profile be performed on prepubertal children with type 1 diabetes >2 years of age after diagnosis of diabetes if the family history for CVD is positive or unknown. If family history is known and negative, screening should begin at puberty. In either case, screening should be done after glucose control has been established. Borderline (LDL 100–129 mg/dl) or abnormal (LDL ≥130 mg/dl) values should be repeated. If values fall within the accepted risk levels (LDL <100 mg/dl), assessment should be repeated every 5 years based on CVD risk status (164).

Treatment of dyslipidemia in chil-

dren with diabetes has not been rigorously studied. For the general pediatric population, the NCEP-Peds (153) recommendations are mainly nutritional; pharmacotherapy is reserved for subjects with severe hypercholesterolemia. Medical nutrition therapy is aimed at a general decrease in the amount of total and saturated fat in the diet (166). Dietary management of lipid abnormalities recommended by the NCEP includes a reduction in total fat, saturated fat, and cholesterol for children >2 years of age. The current recommendation for children with abnormal lipid levels restricts saturated fat to <7% of calories and cholesterol to <200 mg/day. Lifestyle changes identical to those recommended for hypertension (i.e., weight control, increased physical activity, avoidance of tobacco products, and attention to glucose control) are also recommended to optimize lipid levels.

If diet therapy and lifestyle changes are not successful, pharmacotherapy is suggested if the LDL is >160 mg/dl. If the LDL is 130–159 mg/dl, medication should be considered based on the child's CVD risk profile. It is unknown whether these goals are adequate in the presence of diabetes, and there are no trial data in children addressing the efficacy of LDL reduction in regard to CVD risk. The American Heart Association's recommendation for prevention of heart disease in children recommends that the LDL goal for children with diabetes should be <100 mg/dl (167).

The mainstays of drug therapy for the treatment of dyslipidemia in children have been the bile acid sequestrants, cholestyramine and colestipol (153). However, these agents have only modest effects on cholesterol (with a lowering of 10–25%), they are not well tolerated, and compliance is poor. The introduction of bile acid sequestrants in tablet form may improve adherence. Short-term trials of HMG-CoA reductase inhibitors in youth have confirmed their safety and efficacy (168,169) in youth with familial hypercholesterolemia. These agents are approved for use in children ≥10 years of age with familial hypercholesterolemia. There have been no large long-term pediatric trials. A new class of agents (e.g., Ezetimibe) acts at the small intestine brush border to inhibit absorption of cholesterol, and is also approved for use in children ≥10 years of age. These two classes of drugs work at different sites in the cholesterol pathway and may have additive benefits. Therefore, if the cholesterol goal is not achieved with a statin alone, the addition of Ezetimibe is recommended. Rigorous studies to prospectively evaluate the effectiveness of HMG-CoA reductase inhibitors, fibric acid derivatives, and inhibitors of cholesterol absorption should be expanded in the pediatric population.

Treatment with low-dose aspirin to reduce hypercoagulability is recommended in adults with diabetes. However, aspirin therapy is not recommended for those <21 years of age due to the increased risk for Reye's syndrome (1,170).

Recommendations

Screening

- Prepubertal children: a fasting lipid profile should be performed on all children >2 years of age at the time of diagnosis (after glucose control has been established) if there is a family history of hypercholesterolemia (total cholesterol >240 mg/dl) or a history of a cardiovascular event before age 55 years, or if the family history is unknown. Borderline or abnormal values should be repeated for confirmation. If values fall are within the accepted risk levels (LDL <100 mg/dl), a lipid profile should be repeated every 5 years. If family history is not of concern, the first lipid screening should be performed at puberty (>12 years).
- Pubertal children (>12 years old): a fasting lipid profile should be performed at the time of diagnosis (after glucose control has been established). If values fall within the accepted risk levels (LDL <100 mg/dl), the measurement should be repeated every 5 years.

Treatment

- Treatment should be based on fasting lipid levels (mainly LDL) obtained after glucose control is established.
- Initial therapy should consist of optimization of glucose control and medical nutrition therapy aimed at a decrease in the amount of total and saturated fat in the diet, as well as encouragement of lifestyle changes to control weight, increase exercise, and if applicable, discontinue tobacco use.
- The addition of pharmacologic lipid-lowering agents is strongly recommended for LDL >160 mg/dl and is also recommended in patients who have LDL cholesterol values 130–159 mg/dl after failure of medical nutrition therapy and lifestyle changes based on the patient's CVD risk profile. Further studies are needed to determine recommendations for children with LDL values <130 mg/dl.
- The goal of pharmacologic therapy is an LDL value <100 mg/dl.
- Youth at risk for pregnancy should be counseled about lipid-lowering agents, and drug therapy should be stopped immediately if pregnancy is suspected.

Retinopathy

Retinopathy has been reported to be present with diabetes duration of 1–2 years (171,172); however, it usually is not recognized before 5–10 years of diabetes duration (80,172–174). Although retinopathy is most commonly described after the onset of puberty, retinopathy can occur in prepubertal children (175). Pre-DCCT epidemiological data suggest that background retinopathy is present in 34–42% of adolescents (176) and in 9% of children <13 years (177). Follow-up of children with retinopathy found progression in 11% and regression in 5% of patients (178). In children and adolescents, most patients with any degree of retinopathy have either background or preproliferative retinopathy. Proliferative retinopathy is rare but may occur in patients <20 years of age (173). In one study, the relative risk of retinopathy in a pubertal versus prepubertal child was 4.8 (175).

Hypertension (179,180), poor metabolic control (44–48,49,182), presence of albuminuria, hyperlipidemia, smoking (183), duration of diabetes (172), and pregnancy all confer increased risk of developing retinopathy (184). Early identification can lead to appropriate treatment and prevention of loss of vision (185).

In the DCCT, improvement in metabolic control with intensification of diabetes management resulted in a significant decreased risk of new retinopathy as well as retinopathy progression (44,45), and as reported in EDIC, these effects persisted over 3–8 years (49,182). The use of ACE inhibitors slows progression of retinopathy, even in normotensive patients (145). The Early Treatment of Diabetic Retinopathy Study (185) and the Diabetic Vitrectomy Study (186) have shown that

laser photocoagulation surgery, although unable to reverse the disease process, can prevent additional visual loss and significantly prolong the period of useful vision. Rapidly improving metabolic control may be associated with an initial worsening of diabetic retinopathy (187) with subsequent long-term improvement (44,184).

Referrals should be made to eye care professionals with expertise in diabetic retinopathy, an understanding of the risk for retinopathy in the pediatric population, as well as experience in counseling the pediatric patient and family on the importance of early prevention/intervention. Early referral to a specialist before the onset of retinopathy may be less traumatic for the patient and family and set expectations that eye examination is part of routine diabetes care (3,188). The goals for early referral are to establish an appropriate referral pattern for ophthalmologic examination and to educate and engage the pediatric patient and his/her family in the management of diabetes and its comorbidities. The young woman who is planning a pregnancy should have an ophthalmologic examination before conception, during the first trimester, and at physician discretion contingent on the results of the first trimester exam.

Fundus photography may be an additional helpful educational tool for the adolescent.

Recommendations

Screening

- Ophthalmological screening evaluations should be reviewed and regular examinations scheduled with an eye care professional skilled in the care of children and adolescents with diabetes.
- The first ophthalmologic examination should be obtained once the child is ≥10 years of age and has had diabetes for 3–5 years.
- After the initial examination, annual routine follow-up is generally recommended. Less frequent examinations may be acceptable on the advice of an eye care professional.
- The young woman who is planning a pregnancy should have an ophthalmologic examination before conception, during the first trimester, and at physician discretion contingent on the results of the first trimester exam.

Foot care

The ADA has published clinical practice recommendations for preventive foot care in adults with diabetes (1,189). Although foot problems are rare in children and adolescents, it is valuable for young patients to learn how to care for their feet and develop good foot care skills. It is recommended that children with type 1 diabetes have their feet examined beginning at puberty and then at least annually for protective sensation (with a 5.07 nylon [10 g force] monofilament), pulses, skin integrity, and treatable nail problems such as ingrown toenails. The importance of use of appropriate footwear and proper monitoring of feet, including nail and skin care, should be reviewed periodically, especially during adolescence. Risks to the feet for diabetic neuropathy and atherosclerosis should be included in the diabetes education plan. Patients should call their health care clinicians if a foot lesion shows signs of infection or poor healing. Patient education should include information on the importance of meticulous glycemic control when a foot infection is present to optimize timely healing. Antibiotic therapy is indicated if there is extension of infection.

Recommendation

- Annual foot exams should begin at puberty.

ASSOCIATED AUTOIMMUNE CONDITIONS

Thyroid disease

The prevalence of autoimmune thyroid disorders in association with type 1 diabetes is ~17% (190). It is the most common autoimmune disorder associated with type 1 diabetes; patients with thyroid autoimmunity may be euthyroid, hypothyroid, or hyperthyroid (191–193). Hyperthyroidism alters glucose metabolism potentially resulting in deterioration of metabolic control.

Patients with type 1 diabetes should be screened for autoimmune thyroid disease at diabetes diagnosis. Measuring thyroid autoantibodies is used to identify thyroid autoimmunity, and measurement of TSH may be the most sensitive way to identify patients with thyroid dysfunction (190,194). Subclinical hypothyroidism has been associated with an increased risk of symptomatic hypoglycemia (195) and with reduced linear growth (196).

Recommendations

- Thyroid function should be monitored after metabolic control has been established for several weeks. This should be done with a TSH measurement. If TSH is abnormal, free T4 and, if indicated, total T3 can be measured. Thyroid function tests should be obtained at any time clinical thyroid dysfunction is suspected and in any patient who has thyromegaly.
- Patients with previously normal TSH levels may be rechecked every 1–2 years or obtained at any time the growth rate is abnormal.
- The presence of thyroid autoantibodies (antithyroid peroxidase [TPO] and antithyroglobulin [TG]) identifies patients at increased risk for thyroid autoimmunity.
- Patients with elevated TSH levels should be treated with thyroid hormone replacement therapy.
- Comprehensive evaluation and treatment of hyperthyroidism should be initiated in patients with suppressed TSH and elevated T4/T3 levels.

Celiac disease

Celiac disease is an immune-mediated disorder that causes malabsorption in genetically susceptible individuals. Patients with type 1 diabetes are at an increased risk for celiac disease, with a prevalence of 1–16%, compared with 0.3–1% in the general population (197,198). Recent data indicate that 5.4% of individuals with type 1 diabetes in the United States have circulating autoantibodies to tissue transglutaminase (an immune marker for celiac disease) (199). Immune-mediated damage to the mucosa of the small intestine occurs after exposure to the gliadin moiety of gluten, leading to destruction of the villi of the small intestine. Gluten is found in wheat, rye, barley, and oats. Symptoms of celiac disease include diarrhea, weight loss or poor weight gain, growth failure, abdominal pain, chronic fatigue, irritability, an inability to concentrate, malnutrition due to malabsorption, and other gastrointestinal problems (200). Symptoms of celiac disease in patients who also have diabetes may include unpredictable blood glucose levels, unexplained hypoglycemia, and deterioration in glycemic control (201–203).

The current approach to diagnosis is based on testing for circulating IgA autoantibodies to tissue transglutaminase (tTG), followed by a small-bowel biopsy in those with elevated autoantibody levels. If the tTG assay is not available, the endomysial autoantibody (EMA) assay may be used. It is not as sensitive for celiac disease but may be more specific (199,204). The antigliadin antibody is less specific than the tTG or EMA test, and is not recommended for screening. IgA deficiency is present in 1 in 500 in the population (205), but in 1–3% in patients with celiac disease (206), and will be associated with falsely low levels of the IgA tTGA or EMA assay. Therefore, a quantitative serum IgA level should be obtained at the time of celiac disease screening. IgA tTG levels may fluctuate over time; accordingly, a confirmatory test is always necessary.

If IgA tTG levels are very elevated, and confirmed, the patient should be referred to a gastroenterologist for further evaluation, which typically includes a small-bowel biopsy. IgA tTG levels at the time of the small-bowel biopsy correlate well with the degree of damage (207). Low to moderately positive IgA tTG levels should be interpreted in the context of symptoms and, in many instances, should be followed with repeat IgA tTG testing every 6–12 months (199). Many children with type 1 diabetes who have elevated tTG levels are either asymptomatic or have subtle gastroenterologic symptoms (208,209). A small-bowel biopsy may be recommended in patients with positive tTG, even in the absence of symptoms, to confirm the diagnosis of celiac disease. If changes to the absorptive surfaces of the villae are present, a gluten-free diet may prevent unexpected hypoglycemia due to absorptive abnormalities, and may prevent the other nutritional, metabolic, and oncologic consequences of celiac disease.

To date, there are no controlled trials to guide recommendations for asymptomatic individuals with elevated autoantibody levels and normal small-bowel biopsies. Likewise, there is little literature to guide the optimal frequency of repeat antibody screening of these individuals or repeat antibody testing of those with negative antibody levels.

At present, the only treatment for celiac disease is a gluten-free diet. Families of children with diabetes and celiac disease should receive nutritional counseling from a registered dietitian who has experience with both diabetes and celiac disease. Gluten-free substitutes are often very high in carbohydrates; additionally, assistance in finding acceptable gluten-free products is essential to maintaining a gluten-free diet (210).

Recommendations

- Patients with type 1 diabetes should be screened for celiac disease, using tTG antibodies, or EMA, with documentation of normal serum IgA levels. Testing should occur soon after the diagnosis of diabetes and subsequently if growth failure, failure to gain weight, weight loss, or gastroenterologic symptoms occur.
- Positive antibody levels should be confirmed.
- Individuals with confirmed elevated tTG, or EMA, antibodies should be referred to a gastroenterologist for consultation and will usually require a small-bowel biopsy.
- Individuals with type 1 diabetes and confirmed celiac disease should follow a gluten-free diet.
- Consultation with a registered dietitian experienced in managing both diabetes and celiac disease in children should be obtained.
- Consideration should be given to periodic rescreening of patients with negative antibody levels.

ADJUSTMENT AND PSYCHIATRIC DISORDERS —

Diabetes is a risk factor for adolescent psychiatric disorders (211,212). Compared with adolescents without diabetes or with other chronic conditions, adolescents with diabetes have a threefold increased risk of psychiatric disorders, with rates as high as 33% (211). This increased morbidity is primarily associated with the incidence of major depression (~27.5%) (213) and generalized anxiety disorder (18.4%), rather than psychiatric behavioral disorders (212). Further, a substantial number of adolescents with diabetes consider suicide after the onset of the disease (214). Although the rate of suicidal ideation has been found to be higher than would be expected (26.4%), the number of suicide attempts was only 4.4%, which is a rate comparable to the general population of adolescents (215). In addition, adolescents who have recurrent diabetic ketoacidosis may be more likely to have psychiatric disorders, especially anxiety and depression, than those without recurrent hospitalization (216). These studies emphasize that psychiatric illness is a serious complication of diabetes and is often associated with poor metabolic control and adaptation. Thus, regular screening for psychiatric disorders in adolescents with diabetes is warranted.

Recommendations

- Youth with difficulties achieving treatment goals or with recurrent DKA should be screened for psychiatric disorders.
- Routine screening of psychosocial functioning, especially depression and family coping, should be performed.
- Youth with positive screening should be referred promptly for treatment.

Eating disorders

Eating disorders are associated with diabetes in adolescents. Several studies have suggested that adolescents with diabetes are at no higher risk for eating disorders than their peers without diabetes, (217,218), whereas other studies have found rates of both anorexia and bulimia to be higher in youth with type 1 diabetes and have described insulin omission as a specific type of eating disorder to control weight (219,220). Youth, especially girls, with such eating disorders are more likely to have poor metabolic control (221,222) and recurrent hospitalizations (223). A recent cross-sectional study found that the mortality rate was almost fivefold higher for adolescents with comorbid anorexia and diabetes, as compared with anorexia alone, and almost 16-fold higher than for diabetes alone (112). Any adolescent who has poor metabolic control or has recurrent hospitalizations for DKA should be screened for eating disorders by an experienced mental health professional.

Recommendations

- Failure to achieve treatment goals, particularly but not exclusively, in an underweight patient should prompt screening for eating disorders by a mental health professional.

SPECIAL SITUATIONS

Sick day management

The goals of sick day management are prevention and early treatment of hypo-

glycemia, significant hyperglycemia and ketosis, and prevention of DKA. Management of sick days requires frequent monitoring of blood glucose and urine (or blood) ketone levels, monitoring food and fluid intake, and adult supervision. Sick day management should not be left to a child or to a teenager alone. Parental involvement and telephone availability of the diabetes clinician are essential for success. In addition to the management of diabetes, the underlying illness must be appropriately evaluated by the child's primary care clinician. Effects of illness on insulin requirements are variable. Appetite often resulting in decreased caloric intake whether due to decreased appetite during illness or nausea and vomiting may lead to a decrease in insulin needs. On the other hand, the stress of illness may cause increased release of counterregulatory hormones, resulting in increased insulin needs. In very young children (<6 years), in whom brisk counterregulatory responses may not be well developed, decreased calories and excess insulin action may cause hypoglycemia. In older, especially pubertal children, however, a stressful illness is usually characterized by relative insulin deficiency and hyperglycemia.

Frequent monitoring will help determine how to proceed. Ketones must be monitored no matter what the blood glucose level is, as acidosis can sometimes occur without elevated glucose levels, especially if oral intake is poor.

Use of sugar-containing liquids and minidose glucagon (224) is helpful in children with nausea and vomiting. If vomiting persists or if home treatment cannot correct hypoglycemia, significant hyperglycemia, or ketosis, then an emergency department (ED) visit is needed for evaluation and treatment.

Diabetes care at school and day care

Children usually spend 4–8 h and sometimes up to 12 h each day in school and/or extended day care. To optimize the child's diabetes management, school/day care personnel must be knowledgeable about diabetes care issues and provide an environment that promotes excellence in diabetes management. The student with diabetes should be able to participate fully in all school activities while performing blood glucose testing, eating appropriately, and administering insulin as needed. The ADA position statement "Care of Children With Diabetes in the School and Day Care Setting" (4) outlines the responsibilities of the child, the parent, and the school/day care to ensure a safe learning environment for the child. This position statement and the recent publication *Helping the Student with Diabetes Succeed: A Guide for School Personnel* by the National Diabetes Education Program (NDEP) also contains an example of a diabetes medical management plan, which may be used to provide the school/day care with the information needed to care for a child with diabetes. A safe environment includes, at a minimum, the ability to measure blood glucose levels; to recognize and treat hypoglycemia, including the ability to administer glucagons; and to recognize impending DKA. Knowledgeable individuals must be present to assist the student during the school day and after-school activities.

Over the past 10 years, diabetes management of children has intensified, including use of MDIs and insulin pumps in young children and school-aged children. This has put a greater burden on schools and day care settings to provide appropriate care to children with diabetes. The use of insulin pens and pumps may make insulin administration in the schools safer and more acceptable to school personnel (225).

ADOLESCENCE — The onset of puberty causes insulin resistance and psychosocial challenges to achieving optimal metabolic control. In addition to the hormonal changes of adolescence that cause insulin resistance and the corresponding need for larger doses of insulin, (226) adolescent rebellion/experimentation results in reduced adherence to the treatment regimen (81). Adolescence is also marked by feelings of ambivalence, impulsiveness, and mood swings; the struggle to separate from parents; and the need to be accepted by peers. Adolescents typically engage in experimentation and risk-taking behaviors that may adversely affect self-care and clinical outcomes (71). Metabolic control tends to deteriorate in adolescence.

Recommendations

- Routine annual screening for depression of all youth ≥10 years of age with type 1 diabetes.
- The adolescent should gradually assume greater responsibility for diabetes management tasks.
- Parents should be encouraged to maintain a partnership with youth for diabetes decisions important for optimal diabetes control.
- Transition to adult care providers should be planned and negotiated among the patient, the family, the pediatric diabetes team, and the adult care providers.

ADHERENCE TO SELF-MANAGEMENT — Adolescence complicates the decision-making required for appropriate self-management. Adolescents who fail to adhere to a regimen of diabetes self-management have less motivation and less support and believe that nonadherence is an issue of personal freedom (227).

Numerous studies have focused on enhancing adherence during the adolescent years. In well-controlled studies, interventions such as coping skills training (228,229) and peer support (230) have been demonstrated to lead to improved adjustment or quality of life, as well as improved metabolic control. Coping skills training is designed to modify coping styles and patterns of behavior into more constructive behaviors.

Studies of family intervention include those in which the intervention targeted family members, primarily parents, and did not focus on outcomes in children, adolescents, or parents alone. Multifamily group intervention with parent simulation of diabetes (231) and Behavioral Family Systems Therapy (232) have been demonstrated to improve parent and child outcomes. As parents and children negotiate responsibilities in diabetes management, and as these responsibilities change over time, it is likely that parent-adolescent conflict will develop. An office-based intervention aimed at maintaining parent-adolescent teamwork in diabetes management tasks, without increasing diabetes-related family conflict, assisted youth to achieve better metabolic control and decreased parent-child conflict. Incorporation of such approaches into routine clinical care of adolescents with diabetes is recommended.

Recommendation

- Behavioral interventions that enhance the ability of youth and families to self-

manage diabetes should be incorporated into routine care.

RISK BEHAVIORS — Youth with diabetes frequently experiment with diabetes mismanagement through nonadherence. They may also engage in other risky behaviors, including use of tobacco and recreational drugs and unprotected sexual intercourse. Many of these behaviors can also interfere with diabetes self-management. Females are more likely to participate in diabetes mismanagement, whereas boys are more likely to engage in risky behaviors (227,233,234). Alcohol use is a particular problem, as it can be associated with severe hypoglycemia several hours after drinking, if adequate food is not ingested. Adolescent risk behaviors should be routinely assessed by the diabetes team and counseling provided.

Driving has the potential for significant morbidity and mortality in adolescents. Most of the research on driving risk and hypoglycemia has been conducted with adults, but the same risks occur in adolescents. Indeed, the risks may be higher in adolescents, as their sense of invulnerability may make it less likely that they will assess hypoglycemia regularly before driving. Clarke et al. (235) found that ~50% of adults would drive at least 50% of the time when their blood glucose was <70 mg/dl (3.9 mmol/l). At 40 mg/dl, only 22% of subjects could accurately assess their ability to drive safely (236). Further, despite the fact that progressive hypoglycemia has been associated with cognitive-motor and driving impairments, most patients do not take corrective action, and those who do not treat have more neuroglycopenia and less perceived need to self-treat. It seems prudent to suggest that all adolescents test blood glucose before driving and take corrective action to avoid hypoglycemia.

Many adolescents experiment with sexual behavior, which may lead to pregnancy. Before initiating sexual activity, all adolescent girls should be given preconception counseling, including the risk of diabetes complications and the risk of any medications and poor glycemic control to the fetus (237). Prevention of pregnancy is desirable in the adolescent age-group, and most teens tolerate low-dose estrogen birth control preparations. Barrier methods to prevent sexually transmitted diseases should also be discussed and Depo-Provera (Pharmacia & Upjohn) should be offered to girls who are not likely to adhere to daily medication regimens.

Recommendations

- Providers should counsel adolescents to test blood glucose before driving, to carry a source of glucose in the car while driving, and to stop immediately should symptoms of hypoglycemia occur; this counseling should be documented in the record.
- Preconception counseling should be provided to all girls contemplating sexual activity
- Information about risk of fetal malformations and of diabetes in offspring should be provided to all sexually active adolescents.

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