Type 1 Diabetes in Children and Adolescents: A Position Statement by the American Diabetes Association

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POSITION STATEMENT

Since the American Diabetes Association (ADA) published the Position Statement "Care of Children and Adolescents With Type 1 Diabetes" (1) in 2005, innovations have transformed the landscape and management of type 1 diabetes: novel autoantibodies, sophisticated devices for delivering insulin and measuring glucose, and diabetes registries. However, strategies to prevent or delay type 1 diabetes in youth remain elusive, and meanwhile the number of affected children continues to grow. The SEARCH for Diabetes in Youth (SEARCH) study found a 21.1% rise in the prevalence of type 1 diabetes from 2001 to 2009 in youth aged 0 through 19 years, with increases observed in all sex, age, and race/ethnic subgroups except those with the lowest prevalence (0–4 years old and American Indians) (2). Incidence has also increased; the adjusted risk for developing type 1 diabetes increased 1.4% annually between 2002 and 2012, with significant increases in all age-groups except those 0–4 years old (3).

One theme of this Position Statement is that "children are not little adults"—pediatric-onset diabetes is different from adult diabetes because of its distinct epidemiology, pathophysiology, developmental considerations, and response to therapy (4,5). Diabetes management for children must not be extrapolated from adult diabetes care. In caring for children and adolescents, clinicians need to be mindful of the child's evolving developmental stages and must adapt care to the child's needs and circumstances. Timely anticipatory guidance and care coordination will enable a seamless child/adolescent/young adult transition for both the developing patient and his or her family.

Although the ADA stopped developing new position statements in 2018 (6), this Position Statement was developed under the 2017 criteria (7) and provides recommendations for current standards of care for youth (children and adolescents) with type 1 diabetes. It is not intended to be an exhaustive compendium on all aspects of disease management, nor does it discuss type 2 diabetes in youth, which is the subject of an ADA Position Statement currently under review. While adult clinical trials produce robust evidence that has advanced care and improved outcomes (8), pediatric clinical trials remain scarce. Therefore, the majority of pediatric recommendations are not based on large, randomized clinical trials (evidence level A) but rely on supportive evidence from cohort/registry studies (B or C) or expert consensus/clinical experience (E) (Table 1). Please refer to the ADA's "Standards of Medical Care in Diabetes" for updates to these recommendations (professional.diabetes.org/SOC).

DIAGNOSIS

Recommendations

- Diagnosis of type 1 diabetes should be pursued expeditiously. **E**
- A pediatric endocrinologist should be consulted before making a diagnosis of type 1 diabetes when isolated glycosuria or hyperglycemia is discovered in the setting of acute illness and in the absence of classic symptoms. **C**
- Distinguishing between type 1 diabetes, type 2 diabetes, monogenic diabetes, and other forms of diabetes is based on history, patient characteristics, and laboratory tests, including an islet autoantibody panel. **B**

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Table 1—ADA evidence-grading system for "Standards of Medical Care in Diabetes"

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

Type 1 Staging

Prospective longitudinal studies of individuals at risk for developing type 1 diabetes have demonstrated that the disease is a continuum that progresses sequentially at variable but predictable rates through distinct stages before the onset of symptoms. According to a new staging classification system, type 1 diabetes develops in three stages (Table 2). Stage 1 is defined as the presence of β-cell autoimmunity as evidenced by two or more islet autoantibodies with normoglycemia and is presymptomatic. Stage 2 is the presence of β-cell autoimmunity with dysglycemia and is presymptomatic. Onset of symptomatic disease resulting from insulin deficiency in children with type 1 diabetes occurs at stage 3. Adoption of this staging classification provides a standardized taxonomy for type 1 diabetes and may aid the development of therapies and the design of clinical trials to prevent symptomatic disease, promote precision medicine, and provide a framework for an optimized benefit/risk ratio that will impact regulatory approval, reimbursement, and adoption of interventions in the early stages of type 1 diabetes to prevent symptomatic disease.

In patients with classic symptoms, measurement of blood glucose is sufficient to diagnose diabetes (symptoms of hyperglycemia or hyperglycemic crisis plus a random plasma glucose [PG] ≥200 mg/dL [11.1 mmol/L]). Classic symptoms, typically occurring for several days to a few weeks prior to diagnosis, may include polyuria, polydipsia, weight loss, polyphagia, fatigue, and blurred vision from lens swelling caused by the osmotic effects of chronic hyperglycemia (9). Perineal candidiasis is a common symptom in young children and girls (10). Approximately one-third of cases present with diabetic ketoacidosis (DKA) and, unfortunately, the numbers are increasing (11). The characteristic biochemical features—hyperglycemia, glucosuria, ketonemia, and ketonuria—usually make the diagnosis of stage 3 diabetes obvious. Because a low renal glucose threshold may cause glycosuria without hyperglycemia or ketonuria, an elevated PG concentration must be documented in a laboratory to diagnose diabetes. The ADA's criteria for the diagnosis of stage 3 diabetes are shown in Table 3. Blood glucose rather than A1C should be used to diagnose acute onset of type 1 diabetes in individuals with symptoms of hyperglycemia (9). Clinical diagnostic criteria are the same for type 1 and type 2 diabetes.

Because the metabolic state of untreated children with type 1 diabetes can deteriorate rapidly, a definitive diagnosis should be made immediately. Delays in diagnosis and initiation of medical treatment, including insulin replacement therapy (see below), must be avoided. A glucose tolerance test is seldom required except in atypical cases or very early in the disease when PG values may be normal or only mildly abnormal and the diagnosis may be uncertain.

Table 2—Staging of type 1 diabetes

	Stage 1	Stage 2	Stage 3
Stage	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• ≥2 autoantibodies • No IGT or IFG	• ≥2 autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Table 3—Criteria for the diagnosis of diabetes (9)

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 1.75 g/kg up to a maximum of 75 g anhydrous glucose dissolved in water.*

OR

A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified† and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random PG ≥200 mg/dL (11.1 mmol/L).

Definitions are based on venous PG levels. WHO, World Health Organization. *In the absence of unequivocal hyperglycemia, the first three criteria should be confirmed by repeat testing. †See www.ngsp.org.

Screening and Testing for Type 1 Diabetes in Asymptomatic Children

Screening for type 1 diabetes in asymptomatic children with a panel of autoantibodies is currently recommended only in the setting of research studies in first-degree family members of a proband with type 1 diabetes (9). The incidental discovery of hyperglycemia without classic symptoms does not necessarily indicate new-onset diabetes, especially in young children with an acute illness who may experience "stress hyperglycemia." The risk of eventually developing diabetes, however, may be increased in some children with incidental or stress hyperglycemia, especially those with immunological, metabolic, or genetic markers for type 1 diabetes (12–14), and consultation with a pediatric endocrinologist is indicated.

In the asymptomatic child or adolescent screened because of a high risk for diabetes, a test with fasting plasma glucose (FPG) ≥126 mg/dL (7 mmol/L), 2-h PG ≥200 mg/dL (11.1 mmol/L), or A1C ≥6.5% should be repeated on a separate day to confirm the diagnosis. The ADA recommends that the same test be repeated without delay using a new blood sample (9). The diagnosis is also confirmed if two different tests (such as A1C and FPG) are both above the diagnostic threshold; however, if the results are discordant, then the test whose result is above the diagnostic cut point should be repeated. The child or adolescent with typical symptoms of diabetes and a random PG ≥200 mg/dL (11.1 mmol/L) does not require a repeat value on another day or any further testing to diagnose diabetes. Glucose meters (and urine ketone tests) are useful for screening in clinics and physicians' offices, but the diagnosis of diabetes must be confirmed by measurement of venous PG on an analytic instrument in a clinical chemistry laboratory.

There is still debate over whether A1C and the same A1C cut point as in adults should be used to diagnose type 1 diabetes in children and adolescents (15). The studies that formed the basis for recommending A1C for the diagnosis of diabetes included only adults, primarily those with type 2 diabetes. Also, A1C alone may be a poor diagnostic tool for prediabetes and type 2 diabetes in obese children and adolescents (16). In a cohort of newly diagnosed children and adolescents with type 1 diabetes, all had an A1C value >6.6% (measured with a point-of-care [POC] device), whereas A1C levels in children with transient hyperglycemia were between 4.5% and 6.1%. An A1C cutoff level of 6.35% had a 100% sensitivity and specificity for the diagnosis of type 1 diabetes (17). Data from four separate prospective studies of high-risk subjects <21 years of age—the Diabetes Prevention Trial–Type 1 (DPT-1), The Environmental Determinants of Diabetes in the Young (TEDDY), Trial to Reduce IDDM in the Genetically at Risk (TRIGR), and Type 1 Diabetes TrialNet Natural History Study (A1C measured within 90 days of a diagnostic oral glucose tolerance test [OGTT] or fasting PG ≥126 mg/dL)—show that A1C ≥6.5% is a highly specific but not sensitive early indicator of type 1 diabetes diagnosed by OGTT or asymptomatic hyperglycemia (18).

Although POC A1C assays may be certified by the NGSP (formerly the National Glycohemoglobin Standardization Program), proficiency testing is not mandated for performing the test; accordingly, POC assays for diagnostic purposes are not recommended. Further details on factors that may impact hemoglobin glycation and thus the A1C test, including age, race, and hemoglobinopathies, can be found in "Standards of Medical Care in Diabetes" (19).

Distinguishing Diabetes Type

One often correctly assumes a diagnosis of type 1 diabetes in the slender prepubertal child with classic symptoms and without a family history suggestive of a monogenic form of diabetes. However, observational studies show increasing numbers of overweight and obese children and adolescents with type 1 diabetes (20), similar to the general population, and recent data from the T1D Exchange clinic registry indicate that in more than 11,000 U.S. children and adolescents with type 1 diabetes, 24% are overweight and an additional 15% are obese (21). Moreover, in patients aged 10–17 years with a type 2 diabetes phenotype, 10% have evidence of islet autoimmunity (22) and some patients have pathophysiological features of both type 1 and type 2 diabetes (i.e., insulin deficiency and increased insulin resistance). Distinguishing between type 1 and type 2 diabetes in an overweight or obese adolescent, therefore, may be challenging, especially in ethnic/racial minorities. In such patients, a detailed family history and measurement of islet autoantibodies is recommended, and plasma or urinary C-peptide concentrations also may be helpful (22–24).

Monogenic diabetes, which may account for ~1.2–4% of pediatric diabetes (25), is frequently misdiagnosed as type 1 diabetes and inappropriately treated with insulin (26). The minimum prevalence of monogenic diabetes in the U.S. pediatric population is approximately 2.1 per 100,000 (26). Clinicians should be alert to the possibility of maturity-onset diabetes of the young (MODY), particularly in antibody-negative youth with diabetes (26), and neonatal diabetes, particularly in children diagnosed with diabetes in the first 6 months of life. Making the diagnosis of MODY or neonatal diabetes has important implications for treatment of the patient and other affected family members (27) (see Table 4). The online probability calculator

Table 4—Characteristics of prevalent forms of primary diabetes in children and adolescents

	Type 1 diabetes	Type 2 diabetes	MODY*	Atypical diabetes**
Prevalence	~85%	~12%	~1–4%	≥10% in African American
Age at onset	Throughout childhood and adolescence	Puberty; rare <10 years	<25 years	Pubertal
Onset	Acute severe	Insidious to severe	Gradual	Acute severe
DKA at onset	~30%	~6%	Not typical	Common
Affected relative	5–10%	60–90%	50–90%	>75%
Female:male	1:1	1.1–1.8:1	1:1	Variable
Inheritance	Polygenic	Polygenic	Autosomal dominant	Autosomal dominant
HLA-DR3/4	Association	No association	No association	No association
Ethnicity	All, Caucasian at highest risk	All¶	All	African American/Asian
Insulin (C-peptide) secretion	Decreased/absent	Variable	Variably decreased	Variably decreased
Insulin sensitivity	Normal when controlled	Decreased	Normal	Normal
Insulin dependence	Permanent	Variable	Variable	Intermittent
Obesity	No†	>90%	Uncommon	Varies with population
Acanthosis nigricans	No	Common	No†	No†
Islet autoantibodies	Yes§	No	No	No

*MODY is maturity-onset diabetes in the young or monogenic diabetes (16). **Atypical diabetes is also referred to as Flatbush diabetes, type 1.5 diabetes, ketosis-prone diabetes, and idiopathic type 1 diabetes. ¶In North America, type 2 diabetes predominates in African American, Hispanic, Native American, and Canadian First Nations children and adolescents and is also more common in Asian and South Asian than in Caucasian individuals. †Mirrors rate in general population. §Diabetes-associated (islet) autoantibodies to insulin, islet cell cytoplasmic, glutamic acid decarboxylase, or tyrosine phosphatase (insulinoma-associated) antibody (IA-2, ICA512, ZnT8 antibodies in 85–95%) at diagnosis.

(www.diabetesgenes.org/content/mody-probability-calculator) can aid in the identification of individuals most likely to benefit from genetic testing, although the tool is still undergoing validation.

BLOOD GLUCOSE MANAGEMENT: MONITORING AND TREATMENT

Insulin

Recommendation

- Most children with type 1 diabetes should be treated with intensive insulin regimens via either multiple daily injections of prandial insulin and basal insulin or continuous subcutaneous insulin infusion. **A**

Insulin therapy is essential for survival in all people with type 1 diabetes. The goal of insulin replacement therapy is to mimic normal physiological insulin secretion patterns. Because plasma insulin levels normally vary widely throughout the day, with low levels in the fasting and overnight periods and rapid increases in the postprandial period, combinations of short- and long-acting insulin preparations are commonly used to replicate these patterns. Historically, children with type 1 diabetes were treated with combinations of short- and intermediate-acting insulins to minimize the number of daily injections. The Diabetes Control and Complications Trial (DCCT), which included teenagers, demonstrated that intensive insulin regimens achieved near-normal glycemic control and reduced the risk of development and progression of complications (28). New rapid- and long-acting insulin analogs with pharmacokinetic and pharmacodynamic properties that facilitate near-physiological insulin delivery are now available. Multiple daily injection basal-bolus regimens of 1–2 injections of long-acting insulin daily with rapid-acting insulin for meals and snacks are now the standard of care. Commercially available insulin preparations are shown in Table 5.

Continuous Subcutaneous Insulin Infusion

Once considered an alternative form of insulin delivery, continuous subcutaneous insulin infusion, or insulin pump therapy, is often used for children with type 1 diabetes (29). Meta-analyses of randomized controlled trials have shown modest differences between insulin pump therapy and injection regimens for improving glycemic control and reducing hypoglycemia (30–32). Results in children have thus far been equivocal (30,32,33). Large registries that track outcomes of type 1 diabetes treatment and long-term single-center observational studies do suggest children treated with continuous subcutaneous insulin infusion have lower A1C levels, lower hypoglycemia rates, improved diabetes-related quality of life, higher treatment satisfaction, and less fear of hypoglycemia (34). Insulin pump studies that incorporate continuous glucose monitoring (CGM) devices used continuously demonstrate significant improvement in both glycemic control and hypoglycemia reduction in pediatric patients with suboptimal blood glucose control at baseline (35).

Assessment of Glycemic Control

Recommendations

- A1C should be measured in all children and adolescents with type 1 diabetes at 3-month intervals to assess their overall glycemic control. **E**
- An A1C target of <7.5% should be considered in children and adolescents with type 1 diabetes but should be individualized based on the needs and situation of the patient and family. **E**
- With increasing use of CGM devices, outcomes other than A1C, such as time with glucose in target range and frequency of hypoglycemia, should be considered in the overall assessment of glycemic control. **E**

Table 5—Types of insulin preparations and approximate insulin action profiles

Insulin type	Onset of action (h)	Peak of action (h)	Duration of action (h)
Rapid-acting analogs			
Aspart (Novolog)	0.25–0.5	1–3	3–5
Lispro (Humalog)	0.25–0.5	1–3	3–5
Glulisine (Apidra)	0.25–0.5	1–3	3–5
Regular insulin	0.5–1	2–4	5–8
Intermediate-acting			
NPH	2–4	4–8	12–18
Long-acting analogs			
Detemir (Levemir)	2–4	none	12–24
Glargine (Lantus, Basaglar, Toujeo)	2–4	none	up to 24
Degludec (Tresiba)	2–4	none	>24

The DCCT showed that the severity and duration of hyperglycemia exposure are directly related to the risk of development and progression of microvascular complications in both adults and adolescents with type 1 diabetes (28,36). To assess average glycemia over the preceding 3 months, A1C levels should be routinely measured for all individuals with type 1 diabetes. Historically, recommended glycemic targets for children with type 1 diabetes were higher for younger children because of concern about severe hypoglycemia and its deleterious effects on cognitive development. Recently, recommended A1C targets have been adjusted to <7.5% owing to improved tools for diabetes management and a greater understanding and recognition of the adverse effects of chronic hyperglycemia on the developing brain (37), and a lower goal is reasonable if it can be achieved without excessive hypoglycemia. Individualization of glycemic targets, however, for considerations such as hypoglycemia unawareness, medical comorbidities, or other clinical, family, or environmental factors, is essential (see also 37 and 38).

Blood Glucose Monitoring

Recommendation

- All children and adolescents with type 1 diabetes should have blood glucose levels monitored multiple times daily (up to 6–10 times/day), including premeal and pre-bedtime, and as needed for safety in specific situations such as exercise, driving, illness, or the presence of symptoms of hypoglycemia. **B**

Self-monitoring of blood glucose levels (SMBG) is an essential component of treatment of type 1 diabetes in children. Routine SMBG is necessary for determination of immediate insulin needs (e.g., mealtime), assessment of safety (e.g., corrective action for or prevention of hyper- or hypoglycemia), and longer-term adjustment in insulin dosing regimens based on blood glucose patterns and trends. Studies have shown an association between the frequency of blood glucose tests per day and measures of glycemic control (39,40). Blood glucose should be measured before each meal (and snack, if using an intensive multiple daily injection or pump regimen), before bedtime, before (and often after) exercise, prior to and hourly while driving (unless using CGM), and when symptoms of hypoglycemia are present. Blood glucose targets should be individualized for patient age, insulin regimen, level of supervision, and other lifestyle issues, with the goal of achieving as many glucose values as close to target as possible without excessive hypoglycemia.

Blood/Urinary Ketone Monitoring

Recommendation

- Blood or urine ketone levels should be monitored in children with type 1 diabetes in the setting of prolonged/severe hyperglycemia or acute illness to determine if adjustment to treatment or referral to urgent care is needed. **B**

Routine testing of blood or urine ketones is recommended in the setting of prolonged hyperglycemia or acute illness (fever, nausea, vomiting, abdominal pain) to guide insulin therapy, prevent or reverse metabolic decompensation, and determine whether referral for urgent care is required. The availability of blood ketone meters that measure β-hydroxybutyrate in whole blood has practical and clinical advantages, including easier sampling when urine is difficult to obtain (e.g., young children) and potentially earlier and more accurate correlation with clinical status (41,42). It should be noted that fasting morning ketosis may occur in younger children with type 1 diabetes in the absence of illness or metabolic deterioration (43).

CGM

Recommendation

- CGM should be considered in all children and adolescents with type 1 diabetes, whether using injections or insulin pump therapy, as an additional tool to help improve glycemic control. Benefits of CGM correlate with adherence to ongoing use of the device. **B**

Real-time CGM is increasingly used for routine diabetes care in children and adolescents with type 1 diabetes. The first large-scale randomized controlled trial of CGM use as an adjunct to SMBG in type 1 diabetes demonstrated a positive impact on A1C reduction in adults, but not in the child or adolescent cohorts (44). A subsequent post hoc analysis, accounting for frequency of CGM use, showed that CGM lowered A1C levels in any age-group when the devices were used consistently. However, consistent CGM use fell below 50% overall in pediatric subjects, with 50% of 8–14-year-olds and only 30% of 15–24-year-olds demonstrating consistent CGM use over the study duration (45). Reduced CGM use in youth reflected challenges with device wear and the accuracy of early devices, although consistent CGM use, defined as 6 or more days per week for the 6-month duration of the trial, yielded better glycemic control (46). Similar studies in children under 10 years old demonstrated satisfaction with devices but no measurable impact on A1C or hypoglycemia reduction (47,48). In the pediatric cohort of the Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) trial, subjects aged 7–18 years using insulin pumps plus CGM had a 0.6%

reduction in A1C levels as well as significant reductions in glycemic variability compared with the group using injection therapy and no CGM; hypoglycemia exposure was not significantly different between groups (35).

Although it is still under 10%, recent reports from a U.S. diabetes registry estimate that CGM use in pediatric patients consistently increased between 2010–2012 and 2012–2014 (29) and sharply rose in 2014–2016 (49). The largest increase was in very young children (ages 2–5 years), in whom CGM use was approaching 40% (49). There have been improvements in CGM accuracy and performance (50). CGM is associated with lower mean A1C in youth for insulin pump users as well as patients using multiple daily injection regimens (51). For most CGM systems, confirmatory SMBG is required to make treatment decisions. However, the U.S. Food and Drug Administration (FDA) recently approved a CGM device (for ages 2 and older) for making treatment decisions without SMBG.

Automated Insulin Delivery

Recommendation

- Automated insulin delivery systems appear to improve glycemic control and reduce hypoglycemia in children and should be considered in pediatric patients with type 1 diabetes. **B**

The combination of continuous glucose sensors with insulin pumps has enabled the development of automated insulin delivery systems ("closed-loop" or "artificial pancreas" devices). A controller algorithm adjusts insulin delivery rates based on a continuous stream of glucose sensor data. Suspending basal insulin delivery for low sensor glucose levels has been shown to markedly reduce hypoglycemia without worsening glycemia (52). Sensor-augmented pumps that preemptively suspend insulin delivery when sensor glucose levels are predicted to be low show promise in minimizing hypoglycemia (53,54). The greatest potential for improved glycemic control is the dynamic regulation of insulin delivery for both high and low glucose levels. "Hybrid" closed-loop systems, which modulate basal insulin delivery based on sensor glucose levels, have increased time spent within target glucose ranges, reduced hyper- and hypoglycemia exposure, lowered A1C levels, and improved measures of quality of life in both adult and adolescent subjects (55–58). Translation of automated insulin delivery from research to clinical care will require patient and provider education to optimize outcomes (59). Users must still count carbohydrates and bolus manually before meals. Systems that reduce reliance on carbohydrate counting and systems that administer glucagon under automated control to mitigate the risk of hypoglycemia remain in development (60). A recent systematic review and meta-analysis of randomized controlled trials suggests that artificial pancreas systems uniformly improve glucose control in outpatient settings despite heterogenous technical and clinical factors (61).

Adjunctive Therapies

Recommendation

- There is insufficient evidence to support the routine use of adjunctive medical therapies in children with type 1 diabetes. **E**

Adjunctive therapies to treat type 1 diabetes, primarily targeting insulin resistance (during puberty and with obesity), have been investigated to assess potential benefit. However, clinical trials have failed to demonstrate a glycemic benefit of adding metformin (the only approved insulin sensitizer for use in the pediatric age range) to insulin in overweight and obese adolescents with type 1 diabetes, although some studies have shown weight loss and/or reductions in insulin requirements and cardiovascular disease (CVD) risk factors with adjunctive metformin (62,63).

Pramlintide, an analog of the pancreatic polypeptide amylin, has been shown to improve glycemic control when added to insulin in adults with type 1 diabetes, primarily through dampening glycemic excursions by suppressing glucagon secretion and delaying gastric emptying. Neither pramlintide nor other potentially useful adjuncts, such as glucagon-like peptide 1 receptor agonists (e.g., liraglutide, exenatide) or sodium–glucose cotransporter 2 inhibitors, have been thoroughly studied in the pediatric population with type 1 diabetes, and none have been approved for use in this population by the FDA at the time of this writing.

LIFESTYLE MANAGEMENT

Lifestyle management is important for pediatric patients with type 1 diabetes and enables health maintenance, CVD prevention, and glycemic control. Lifestyle management includes healthful approaches to nutrition and exercise. Training young patients and their families in medical nutrition therapy and approaches to mitigating both the hypo- and hyperglycemic effects of exercise is part of diabetes self-management education and support, which should be provided by a registered dietitian, a diabetes educator, an exercise specialist/physiologist, and a pediatric endocrinologist. Extensive training should occur at diagnosis, with annual updates by the registered dietitian. Quarterly visits with the diabetes educator and endocrinologist ensure ongoing training throughout childhood and adolescence.

Nutrition Therapy

Recommendations

- Individualized medical nutrition therapy is recommended for children and adolescents with type 1 diabetes as an essential component of the overall treatment plan. **A**
- Monitoring carbohydrate intake, whether by carbohydrate counting or experience-based estimation, is key to achieving optimal glycemic control. **B**
- Comprehensive nutrition education at diagnosis, with annual updates, by an experienced registered dietitian is recommended to assess caloric and nutrition intake in relation to weight status and CVD risk factors and to inform macronutrient choices. **E**

Dietary management should be individualized: family habits, food preferences, religious or cultural needs, schedules, physical activity, and the patient's and family's abilities in numeracy, literacy, and self-management should be considered. Dietitian visits should include assessment for changes in food preferences over time, access to food, growth and development,

weight status, cardiovascular risk, and potential for eating disorders. Dietary adherence is associated with better glycemic control in youth with type 1 diabetes (64).

Pediatric nutrition management follows the ADA guidelines for dietary management (65). The best approach to healthful eating is within the context of the family, focusing on healthy eating for all members. There is no single ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with diabetes; therefore, macronutrient distribution should be individualized while keeping total calorie and metabolic goals in mind. Carbohydrate intake from vegetables, fruits, legumes, whole grains, and dairy products, with an emphasis on foods higher in fiber and lower in glycemic load, is preferred over other sources, especially those containing added sugars. Saturated fats should be limited. Caloric intake should fuel normal growth and development and avoid overweight and underweight, especially given the current trends, with at least one-third of pediatric patients with type 1 diabetes overweight or obese (21,66,67).

Nutrition education begins with carbohydrate counting, where consistency, rather than accuracy, results in optimal glycemic outcomes (68). Over- or undercalculating by up to 10 g or 15% of the carbohydrate amount is unlikely to yield substantial hypoglycemia or hyperglycemia, respectively (69,70). Persons lacking numeracy skills may use past experience to match insulin doses to carbohydrate intake.

Recent studies have shown that meals with protein, fat, and more complex carbohydrates delay glucose level increases and respond well to square-wave or dual-wave bolus doses or the splitting of bolus doses given by injection (71–74).

Physical Activity and Exercise

Recommendations

- Exercise is recommended for all youth with type 1 diabetes with the goal of 60 min of moderate- to vigorous-intensity aerobic activity daily, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days per week. **C**
- Education about prevention and management of potential hypoglycemia during and after exercise is essential, including pre-exercise glucose levels of 90–250 mg/dL (5–13 mmol/L) and accessible carbohydrates, individualized according to the type/intensity of the planned physical activity. **E**
- Strategies to prevent hypoglycemia during exercise, after exercise, and overnight following exercise include reducing prandial insulin dosing for the meal/snack preceding exercise, increasing carbohydrate intake, eating bedtime snacks, using CGM, and/or reducing basal insulin doses. **C**
- Frequent glucose monitoring before, during, and after exercise, with or without CGM use, is important to prevent, detect, and treat hypoglycemia and hyperglycemia with exercise. **C**

Exercise positively affects physical fitness, strength building, weight management, social interaction, self-esteem building, and creation of healthful habits for adulthood, but it also has the potential to cause both hypoglycemia and hyperglycemia.

The type, intensity, and duration of exercise trigger multiple hormones (insulin, glucagon, catecholamines, and glucocorticoids) that mediate fuel metabolism (75–77). Pancreatic islet cells achieve euglycemia by balancing peripheral glucose uptake and hepatic glucose production. In type 1 diabetes, this intrinsic balance does not exist. Exogenous insulin administration inhibits hepatic glucose production and promotes exercise-induced glucose uptake, both triggering hypoglycemia. Hyperglycemia may occur during high-intensity exercise such as sprints or resistance training when there is inadequate delivery of exogenous insulin and/or an excess of counterregulatory hormones that increase hepatic glucose production and inhibit glucose uptake into skeletal muscle.

Though the potential for hyperglycemia can frustrate patients and families, fear of exercise-induced hypoglycemia dominates clinical concerns. Intense exercise increases hypoglycemia risk during, immediately following, and 6–12 h after physical activity, the "lag effect" (78). This lag likely results from a combination of improved insulin sensitivity following exercise, blunted counterregulatory hormone release, and increased glucose uptake by the liver and skeletal muscles to replenish glycogen stores. Impaired counterregulatory hormone release in pediatric patients may include blunting during sleep, antecedent hypoglycemia, and autonomic failure (79–81). Delayed hypoglycemia often occurs at night following afternoon physical activities. Therefore, exercise-induced hypoglycemia and fear of hypoglycemia may limit desire to participate in exercise.

The following paragraphs outline strategies to mitigate hypoglycemia risk and minimize hyperglycemia with exercise. For in-depth discussions, see recently published reviews and guidelines (76,77,82).

Overall, it is recommended that youth with type 1 diabetes participate in 60 min or more of daily physical activity, including resistance and flexibility training (83). Although uncommon in the pediatric population, patients should be medically evaluated for comorbid conditions or diabetes complications that may restrict participation in an exercise program. As hyperglycemia can occur before, during, and after physical activity, it is important to ensure that the elevated glucose level is not related to insulin deficiency that would lead to worsening hyperglycemia with exercise and ketosis risk. Intense activity should be postponed with marked hyperglycemia (glucose $\geq$350 mg/dL [19.4 mmol/L]), moderate to large urine ketones, and/or β-hydroxybutyrate $>$1.5 mmol/L. Caution may be needed when β-hydroxybutyrate levels are $\geq$0.6 mmol/L (76,77).

The prevention and treatment of hypoglycemia associated with physical activity include decreasing the prandial insulin for the meal/snack before exercise and/or increasing food intake. Patients on insulin pumps can lower basal rates by $\sim$10–50% or more or suspend for 1–2 h during exercise (84). Decreasing basal rates or long-acting insulin doses by $\sim$20% after exercise may reduce delayed exercise-induced hypoglycemia (85). Accessible rapid-acting carbohydrates and frequent blood glucose monitoring before, during, and after exercise, with or without CGM, maximize safety with exercise.

Blood glucose targets prior to exercise should be 90–250 mg/dL (5.0–13.9 mmol/L). Consider additional carbohydrate intake during and/or after exercise, depending on the duration and intensity of physical activity, to prevent hypoglycemia. For low- to moderate-intensity aerobic activities

(30−60 min), and if the patient is fasting, 10−15 g of carbohydrate may prevent hypoglycemia (86). After insulin boluses (relative hyperinsulinemia), consider 0.5–1.0 g of carbohydrates/kg per hour of exercise (~30−60 g), which is similar to carbohydrate requirements to optimize performance in athletes without type 1 diabetes (87–89).

BEHAVIORAL ASPECTS OF SELF-MANAGEMENT

Recommendations

- At diagnosis and during routine follow-up care, assess psychosocial issues and family stresses that could impact diabetes management and provide appropriate referrals to trained mental health professionals, preferably experienced in childhood diabetes. **E**
- Providers should consider asking youth and their parents about social adjustment (peer relationships) and school performance to determine whether further evaluation is needed. **B**
- Assess youth with diabetes for generic and diabetes-related distress, generally starting at 7–8 years of age. **B**
- Providers should encourage developmentally appropriate family involvement in diabetes management tasks for children and adolescents, recognizing that premature transfer of diabetes care to the child may result in poor self-management behaviors and deterioration in glycemic control. **A**
- Consider including children in consent processes as early as cognitive development indicates understanding of health consequences of behavior. **E**
- Offer adolescents time by themselves with their care provider(s) starting at age 12 years, or when developmentally appropriate. **E**
- Consider screening for disordered or disrupted eating behaviors using validated screening measures when hyperglycemia and/or weight loss are unexplained based on self-reported behaviors related to medication dosing, meal plan, and physical activity. In addition, a review of the medical regimen is recommended to identify potential treatment-related effects on hunger/caloric intake. **B**

Youth with type 1 diabetes are part of a larger ecosystem of family, community, and peer influences that impact health and quality-of-life outcomes. Thus, a family-centered diabetes care approach for youth with type 1 diabetes is essential to ensure that all psychosocial influences are addressed. For background information, please refer to the ADA Position Statement on the psychosocial care of people with diabetes (90) and to "Standards of Medical Care in Diabetes" for current general recommendations (65). The sections below offer specific considerations applicable to providing care to youth with type 1 diabetes.

Age-Groups

Table 6 illustrates typical development and diabetes demands and priorities across childhood, updated from the original version (1). The responsibility for and supervision of type 1 diabetes management falls largely to the primary caregiver during the early years of childhood, with a gradual transition to other caregivers and school personnel as the child ages. However, the primary caregiver will remain a major part of type 1 diabetes management through adolescence.

Unique Challenges of Adolescence

The adolescent years may disrupt diabetes care and communication between family members, youth, and providers. Hallmarks of normal adolescence are increased independence in decision making and reliance on the peer group for validation of self-concept and self-worth. Wishing to "fit in" may contribute to youth hiding or minimizing diabetes care behaviors, thereby compromising management in the school setting (91). Cognitive development and medical decision-making skills will impact a wide variety of risk-taking behaviors and acceptance of self-management behaviors into daily life (92,93). Suboptimal glycemic management should not automatically be attributed to adolescent rebellion or lack of concern for health. A thorough, age-appropriate psychosocial evaluation and review of the medical regimen will suggest targets for modification to facilitate self-management and well-being. If the adolescent is resistant to accepting support from clinicians, family, and friends, the possibility of a more serious psychological issue must be considered and evaluated.

For these reasons, adolescents should be offered time by themselves with their care provider(s) starting at age 12 years. Care should be taken to respect the privacy of teens/young adults, especially regarding behaviors that are considered taboo or risky (94). Discussions with adolescents should include questions about well-being in general, diabetes distress, and risk behaviors (e.g., substance use and sexual activity) (95,96). It is recommended that prior to or shortly after puberty, girls with type 1 diabetes should be counseled about the importance of good metabolic control prior to conception and should be made aware that safe and effective family planning methods are available should they become sexually active and not desire pregnancy.

Screening, Prevention, and Treatment

Given the rapid and dynamic nature of cognitive, developmental, and emotional changes in youth, early detection of depression, anxiety disorders, disordered eating (97), and learning disabilities enhances the range and effectiveness of potential treatment options and may help to minimize adverse effects on diabetes management and disease outcomes. Although rates of psychological distress and disorders in children with type 1 diabetes may not differ from the general population, adolescents with type 1 diabetes do tend to show 2–3 times the rate of psychological distress as their peers without diabetes (98–101). Distinguishing between frank depressive or anxiety disorders and diabetes-related distress should be left to mental health providers so that appropriate treatment options can be determined.

Because youth depend on social support systems (family and care providers) and must eventually transition to independent diabetes self-management as adults, their families and related social networks should be included in psychosocial assessment and treatment (102–104). Teaching family members effective problem-solving and conflict-resolution skills can improve diabetes management and facilitate better glycemic control, with the potential to reduce diabetes distress and improve quality of life (102,105,106). Parents of children with type 1 diabetes are prone to high rates of depression, especially around the time of diagnosis (107,108). Persistence of parental depression is

Table 6—Typical development and diabetes demands and priorities across childhood

Ages and corresponding developmental level	Typical developmental tasks	T1D management priorities (and person responsible)	Family considerations due to presence of T1D
0–2 years; infancy and start of toddlerhood	Attachment and development of trusting bond with caregivers	Reduction of wide fluctuations in glucose levels (caregiver)	Vigilance in identifying child symptoms of hypo- and hyperglycemia
	Physical development and reaching milestones of first words and walking	Prevention of hypoglycemia (caregiver)	Coping with stress associated with management and additional responsibilities
2–6 years; end of toddlerhood through early childhood	Often begin formal schooling—preschool to elementary school	Reduction of wide fluctuations in glucose levels (caregiver, school personnel)	Continued vigilance in identifying child symptoms
	Separating from caregivers for activities	Prevention of hypoglycemia (caregivers, school personnel)	Communicating and planning for monitoring when not with child; coping with stress
	Physical growth with interests in exploring new challenges and activities	Trusting others to help with diabetes management (child)	Close monitoring of food intake and adjustments for variable appetites
7–11 years; late childhood	Developing skills in physical, social, and academic areas	Sharing in the identification of symptoms of hypo- and hyperglycemia (child and caregiver)	Teaching child symptoms of hyperglycemia and hypoglycemia
	Gaining more autonomy from primary caregivers, yet still very reliant on caregiver supervision and planning	Treating hypoglycemia and carrying supplies (child with planning/ supervision from adults)	Teaching basics of diabetes management and treatment
	Often engaging in team activities that promote sharing and understanding views of others	Developing sense of problem solving and flexibility with regimen if plans or activities change (child with guidance/ modeling from caregiver)	Praising conduct of management tasks
			Modeling problem solving when new diabetes problems arise
			Helping teach child to disclose to others about diabetes
			Coping with stress and new challenges of complex schedules and eating patterns
12–15 years; early adolescence	Managing changes with body	More decision making about diabetes management and regimen changes (teen)	Coping with common increase in conflict about diabetes management
	Attempts at "fitting in" with peer groups; peers becoming larger influence on behavior	Expectation to monitor and be vigilant about glucose excursions when away from primary caregivers (teen)	Developing new forms of monitoring and communicating about diabetes
	Developing stronger sense of self and identity	Disclose to others about diabetes for safety (teen)	Supervising enough but attempting to support growing autonomy in teen
	Desiring less guidance and supervision from caregivers, yet still needing it		
16–19 years; late adolescence	Expansion of networks and activities	Increasing autonomy for many management tasks (teen)	Balancing need for supervision and guidance with less face-to-face time with teen and more teen autonomy
	Increased thinking and worries about what is next	Diminishing seeking of guidance and supervision from caregivers (teens)	Modeling positive decision making about diabetes and life choices
	Expectation to make decisions based on interests and opportunities	Discussions about transition to different diabetes care providers (teens, care team, and caregivers)	Creating scaffolding for transition with diabetes and next phase of life

T1D, type 1 diabetes.

associated with poorer child adjustment and diabetes management, especially in younger children (109).

Emerging technologies, like phone and computer transmission of glucose and insulin management data, can be useful in maintaining communication of information through nonconfrontational channels and may provide a means for youth

to communicate directly with care providers as they transition to more independent self-management (110). Remote monitoring of glucose levels should be discussed with the child and family to determine "rules of engagement" about acceptable times and situations to monitor.

Anticipatory Guidance

Immunization

Children with diabetes should receive all immunizations in accordance with the recommendations of the Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention, including annual vaccination against influenza for children with diabetes who are at least 6 months of age. The child and adolescent vaccination schedule is available at www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html. Large studies have shown no causal relationship between childhood vaccination and type 1 diabetes (111).

Growth

Normal linear growth and appropriate weight gain throughout childhood and adolescence are excellent indexes of general health and reasonable markers of metabolic control. Height and weight should be measured at each visit and tracked via appropriate height and weight growth charts (www.cdc.gov/growthcharts/clinical_charts.htm). Overweight and obesity are emerging issues in youth with type 1 diabetes (21,66,67) and should be considered as part of dietary counseling.

COMPLICATIONS AND COMORBIDITIES

Acute Complications

DKA

Recommendations

- Individuals and caregivers of individuals with type 1 diabetes should be educated annually on DKA prevention, including sick-day management, the importance of insulin administration, and glucose and ketone level monitoring. **B**
- All individuals with type 1 diabetes should have access to an uninterrupted supply of insulin. Lack of access and insulin omissions are major causes of DKA. **A**
- Patients and families with type 1 diabetes should have continual access to medical support to assist with sick-day management. **C**
- Standard pediatric-specific protocols for DKA treatment should be available in emergency departments and hospitals. **E**

DKA is an acute complication usually associated with new-onset type 1 diabetes, insulin omission, and increased levels of stress-related counterregulatory hormones/cytokines (e.g., infection) (112). Mild cases may be safely and effectively treated in an acute care setting with appropriate resources and may not require hospitalization. Education must be provided to families to prevent DKA, which may have serious sequelae, particularly in young children. Refer to guidelines for DKA management (112).

Hypoglycemia

Recommendations

- Individuals with type 1 diabetes, or their caregivers, should be asked about symptomatic and asymptomatic hypoglycemia at each encounter. **E**
- Glucose (15 g) is the preferred treatment for the conscious individual with hypoglycemia (blood glucose $<$70 mg/dL [3.9 mmol/L]), although any form of carbohydrate may be used. If the SMBG result 15 min after treatment shows continued hypoglycemia, the treatment should be repeated. Once blood glucose concentration returns to normal, the individual should consider a meal or snack and/or reduce insulin to prevent hypoglycemia recurrence. **E**
- Glucagon should be prescribed for all individuals with type 1 diabetes. Caregivers or family members of these individuals should be instructed in its administration. **E**
- Hypoglycemia unawareness or one or more episodes of severe hypoglycemia should trigger reevaluation of the treatment regimen. **E**
- Insulin-treated patients with hypoglycemia unawareness or an episode of severe hypoglycemia should be advised to raise their glycemic targets to avoid further hypoglycemia for at least several weeks to partially reverse hypoglycemia unawareness and reduce the risk of future episodes. **B**

The risk of hypoglycemia limits optimal treatment of type 1 diabetes. Because current methods of blood glucose monitoring and insulin replacement are imperfect, hypoglycemia risk is invariably present. Registry data suggest that severe hypoglycemia has decreased with advances in care since the DCCT (113). Patient education, frequent SMBG, and CGM may detect hypoglycemia and help adjust insulin dosing and carbohydrate intake. Closed-loop systems with predicted low glucose suspend reduce hypoglycemia in children and adolescents in research studies (57).

Clinicians should ask patients about their symptoms of hypoglycemia and at what threshold of glycemia these occur; if the threshold is suggestive of hypoglycemia unawareness, then the treatment regimen and glycemia goals should be adjusted upwards (114). Oral carbohydrate (15 g) is the preferred treatment for patients with blood glucose $<$70 mg/dL (3.9 mmol/L) or those with symptoms of hypoglycemia who are alert and able to eat. Glucagon is used for severe hypoglycemia. In children, small studies have led to age-based minidoses of glucagon (0.02–0.15 mg) if the child is alert but not able to eat (115). Alternate delivery methods for glucagon are in development (116).

Microvascular Complications

Retinopathy, diabetic kidney disease (DKD) (previously referred to as "nephropathy"), and neuropathy are rarely reported in prepubertal children and children with diabetes duration of only 1–2 years; however, complications may occur after the onset of puberty or after 5–10 years of diabetes (117). It is recommended that clinicians with expertise in diabetes management should counsel the pediatric patient and family on the importance of early prevention and intervention.

DKD

Recommendations

- Annual screening for albuminuria with a random (morning sample preferred to avoid effects of exercise) spot urine sample for albumin-to-creatinine ratio should be considered at puberty or at age $>$10 years, whichever is earlier,

once the child has had diabetes for 5 years. **B**

- An ACE inhibitor or an angiotensin receptor blocker (ARB), titrated to normalization of albumin excretion, may be considered when elevated urinary albumin-to-creatinine ratio (>30 mg/g) is documented (two of three urine samples obtained over a 6-month interval following efforts to improve glycemic control and normalize blood pressure). **E**

Screening provides an opportunity to detect albuminuria early, initiate ACE inhibitor or ARB therapy, particularly in the presence of hypertension, and encourage meticulous attention to achieving glycemic goals, especially during the reversible phase of DKD (118). Evaluation for possible nondiabetic kidney disease should be considered as part of the clinical evaluation. If females are prescribed ACE inhibitors/ARBs, they should be counseled on the teratogenic risks associated with pregnancy (refer to "Standards of Medical Care in Diabetes" for additional guidance on pharmacologic treatment of hypertension [119]). Hypertension, or even a rise in blood pressure within the normal range, may accompany progression to albuminuria (120) or its persistence (121). Risk factors for DKD include poor glycemic control, smoking, a parent with essential hypertension, and a family history of DKD or CVD (122). Even in the absence of hypertension, an ACE inhibitor or ARB may reverse increased albumin excretion or delay the progression to albuminuria (123–125). In adults with diabetes, treatment of elevated albumin excretion in the absence of hypertension is not recommended (126). Data on the long-term benefit of these therapies are needed to support the benefit on long-term vascular disease risk reduction (127,128). The Adolescent type 1 Diabetes cardio-renal Intervention Trial (AdDIT) in adolescents with type 1 diabetes demonstrated safety of ACE inhibitor treatment but did not change the albumin-to-creatinine ratio over the course of the study (129). The T1D Exchange clinic registry reported only 36% of those diagnosed with albuminuria or greater were treated (130). An estimation of glomerular filtration rate (eGFR) (131) can be approximated based on measurement of serum creatinine concentration along with consideration of clinical status, age, diabetes duration, and therapies. Improved methods are needed to screen for early GFR loss since eGFR is inaccurate at GFR >60 mL/min/1.73 m^2 (132).

Retinopathy

Recommendations

- An initial dilated and comprehensive eye examination is recommended at age 10 years or after puberty has started, whichever is earlier, once the youth has had diabetes for 3–5 years. **B**
- After the initial examination, annual routine follow-up is generally recommended. Less frequent examinations, every 2 years, may be acceptable on the advice of an eye care professional and based on risk factor assessment. **E**

In children and adolescents, most patients with retinopathy have either nonproliferative or preproliferative retinopathy. Retinopathy (like albuminuria) most commonly occurs after the onset of puberty and after 5–10 years of diabetes duration (117,133). Hypertension, poor metabolic control, albuminuria, hyperlipidemia, smoking, diabetes duration, and pregnancy all confer increased retinopathy risk (122, 134). ACE inhibitors slow retinopathy progression, even in normotensive patients (135).

Early referrals establish appropriate follow-up patterns for ophthalmologic examinations by eye care professionals with expertise in diabetic retinopathy, particularly in the pediatric patient, and engage and educate the pediatric patient and family about diabetes management and its comorbidities. Fundus photography, including nonmydriatic modalities, may be an additional helpful educational tool for the adolescent. A recent report of a large study ($n = 5,453$) indicated that only 64.9% of youth with type 1 diabetes and 42.2% of youth with type 2 diabetes received retinal screening by 6 years postdiagnosis and that getting screened was particularly challenging for racial minorities and less affluent families (136). More data on best screening practices and cost-effectiveness are needed (137).

Neuropathy

Recommendation

- Consider an annual comprehensive foot exam for the adolescent at the start of puberty or at age 10 years, whichever is earlier, once the youth has had type 1 diabetes for 5 years. **B**

Neuropathy rarely occurs in prepubertal children or after only 1–2 years of diabetes (117). A comprehensive foot exam, including inspection, palpation of dorsalis pedis and posterior tibial pulses, assessment of the patellar and Achilles reflexes, and determination of proprioception, vibration, and monofilament sensation, should be performed annually along with assessment of symptoms of neuropathic pain. The SEARCH study reported a 7% prevalence of diabetic peripheral neuropathy with poorer glucose control, older age, longer diabetes duration, smoking, increased diastolic blood pressure, obesity, increased LDL cholesterol and triglycerides, and lower HDL cholesterol as risk factors (138). The ADA has published clinical practice recommendations for preventive foot care in adults with diabetes (122) and for diabetic neuropathy (139); for future updates to these recommendations, see the ADA's "Standards of Medical Care in Diabetes" (professional.diabetes.org/SOC).

Macrovascular Complications

CVD, cerebrovascular disease, and peripheral vascular disease resulting from atherosclerosis are leading causes of morbidity and mortality in adults with type 1 diabetes (140–142). Factors contributing to atherosclerosis and elevated plasma lipid concentrations in children and youth include smoking, hypertension, obesity, family history of heart disease, and diabetes (143,144). Diabetes is an independent risk factor for CVD in adults, conferring a two- to fourfold increased incidence of CVD. There is unequivocal evidence that the atherosclerotic process begins in childhood (145–147), and although CVD events are not expected to occur during childhood, various methodologies show that youth with type 1 diabetes may have subclinical CVD abnormalities within the

first decade of diagnosis (148–150). Population-based studies estimate that 14–45% of children with type 1 diabetes have two or more CVD risk factors (151–153). The American Heart Association published a joint statement with the ADA on CVD in type 1 diabetes (143) and a scientific statement on CVD risk factors in youth with diabetes (144).

Hypertension

Recommendations

- Blood pressure should be measured at each routine visit. Children found to have high-normal blood pressure (systolic blood pressure or diastolic blood pressure at the 90th percentile for age, sex, and height) or hypertension (systolic blood pressure or diastolic blood pressure at the 95th percentile for age, sex, and height) should have blood pressure confirmed on three separate days. **B**
- Initial treatment of high-normal blood pressure (systolic blood pressure or diastolic blood pressure consistently at the 90th percentile for age, sex, and height) includes dietary modification and increased exercise, if appropriate, aimed at weight control. If target blood pressure is not reached with 3–6 months of initiating lifestyle intervention, pharmacologic treatment should be considered. **E**
- In addition to lifestyle modification, pharmacologic treatment of hypertension (systolic blood pressure or diastolic blood pressure consistently at the 95th percentile for age, sex, and height) should be considered as soon as hypertension is confirmed. **E**
- ACE inhibitors or ARBs should be considered for the initial pharmacologic treatment of hypertension, following reproductive counseling because of the potential teratogenic effects of both drug classes. **E**
- Treatment goal is blood pressure consistently <90th percentile for age, sex, and height. **E**

Blood pressure measurements should be determined using the appropriate size cuff with the child seated and relaxed. Parental hypertension is a major risk factor for elevated blood pressure in childhood and should be evaluated. Normal blood pressure levels for age, sex, and height and appropriate methods for measurement are available online at www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf. Treatment for hypertension is generally an ACE inhibitor, but an ARB may be used if the ACE inhibitor is not tolerated. Hypertension diagnosis in children with diabetes is often delayed and undertreated (154). If hypertension is documented, pathological causes other than DKD 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).

Dyslipidemia

Recommendations

- Obtain a fasting lipid profile in children 10 years of age or older as soon as convenient after the diagnosis of diabetes (once glycemic control has been established). **E**
- If LDL cholesterol values are within the accepted risk level (<100 mg/dL [2.6 mmol/L]), a lipid profile repeated every 3–5 years is reasonable. **E**
- If lipids are abnormal, initial therapy should consist of optimizing glucose control and medical nutrition therapy using a Step 2 American Heart Association diet that restricts saturated fat to 7% of total calories and dietary cholesterol to 200 mg/day, which is safe and does not interfere with normal growth and development. **B**
- After 10 years of age, consider adding a statin in patients who, despite medical nutrition therapy and lifestyle changes for 6 months, continue to have LDL cholesterol >160 mg/dL (4.1 mmol/L) or LDL cholesterol >130 mg/dL (3.4 mmol/L) and one or more CVD risk factors, following reproductive counseling because of the potential teratogenic effects of statins. **E**
- Therapy goal is an LDL cholesterol value <100 mg/dL (2.6 mmol/L). **E**

For children with a significant family history of CVD, the National Heart, Lung, and Blood Institute recommends obtaining a fasting lipid panel beginning at 2 years of age (155). Abnormal results from a random lipid panel should be confirmed with a fasting lipid panel. SEARCH study data show that improved glucose control over a 2-year period is associated with a more favorable lipid profile; however, improved glycemic control alone is unlikely to normalize lipids in youth with type 1 diabetes and dyslipidemia (156,157). Initial treatment should include medical nutrition therapy and a diet restricting saturated fats (158).

Neither long-term safety nor cardiovascular outcome efficacy of statin therapy has been established for adolescents; however, studies have shown short-term safety equivalent to that seen in adults and efficacy in lowering LDL cholesterol levels in familial hypercholesterolemia or severe hyperlipidemia, improving endothelial function, and causing regression of carotid intimal thickening (129,159,160). The AdDIT study demonstrated the safety of statin use over 2–4 years in adolescents with type 1 diabetes. This study showed significant reductions in total, LDL, and non-HDL cholesterol levels, in triglyceride levels, and in ratios of apolipoprotein B to apolipoprotein A1. However, statin use had no significant effects on carotid intima-media thickness, other cardiovascular markers, the GFR, or retinopathy progression (129). Statins are not approved for patients aged <10 years, and statin treatment should generally not be used in children with type 1 diabetes before this age. Statins are contraindicated in pregnancy; therefore, pregnancy prevention is of paramount importance for postpubertal girls.

Smoking

Recommendation

- Elicit a smoking history at initial and follow-up diabetes visits, and discourage smoking in youth who do not smoke and encourage smoking cessation in those who do smoke. **A**

The adverse health effects of smoking are well recognized with respect to future cancer and risk of vascular disease (161). Cigarette smoking cessation, including e-cigarettes, is an important part

of routine diabetes care, as is assessment of exposure to secondhand smoke.

Autoimmune Conditions

Recommendation

- Assess for additional autoimmune conditions soon after the diagnosis of type 1 diabetes and if symptoms develop. **E**

Screening for thyroid dysfunction and celiac disease is recommended because of increased risk for additional autoimmune disorders. Periodic screening in asymptomatic individuals has been recommended, but the optimal frequency and benefit of screening are unclear. Although much less common than celiac disease and thyroid dysfunction, other autoimmune conditions, such as Addison disease (primary adrenal insufficiency), autoimmune hepatitis, autoimmune gastritis, dermatomyositis, and myasthenia gravis, occur more commonly with patients with type 1 diabetes than in the general pediatric population and should be assessed and monitored as clinically indicated.

Thyroid Disease

Recommendations

- Consider testing children with type 1 diabetes for antithyroid peroxidase and antithyroglobulin antibodies soon after the diagnosis. **B**
- Measure thyroid-stimulating hormone concentrations at diagnosis when clinically stable or soon after glycemic control has been established. If normal, suggest rechecking every 1–2 years or sooner if the patient develops symptoms or signs suggestive of thyroid dysfunction, thyromegaly, an abnormal growth rate, or unexplained glycemic variability. **E**

Autoimmune thyroid disease is the most common autoimmune disorder associated with diabetes, occurring in 17–30% of patients with type 1 diabetes (162). At diagnosis, about 25% of children (more females than males) with type 1 diabetes have thyroid autoantibodies (163); their presence predicts thyroid dysfunction—most commonly hypothyroidism, although hyperthyroidism occurs in ~0.5% of cases (164,165). For thyroid antibodies, a recent study from Sweden indicated TPOAb was more predictive than TGAb in multivariate analysis (166). Thyroid function tests may be misleading (euthyroid sick syndrome) if performed at diagnosis. Therefore, if thyroid function tests are slightly abnormal after diagnosis, they should be repeated upon metabolic stability and achievement of glycemic targets. Subclinical hypothyroidism may be associated with increased risk of symptomatic hypoglycemia (167) and reduced linear growth rate.

Celiac Disease

Recommendations

- Screen children with type 1 diabetes for celiac disease by measuring IgA tissue transglutaminase (tTG) antibodies, with documentation of normal total serum IgA levels, soon after the diagnosis of diabetes, or IgG to tTG and deamidated gliadin antibodies if IgA deficient. **E**
- Repeat screening within 2 years of initial screening and then again 5 years thereafter and consider more frequent screening in children who have symptoms or a first-degree relative with celiac disease. **B**
- Children with biopsy-confirmed celiac disease should be placed on a gluten-free diet and have a consultation with a dietitian experienced in managing both diabetes and celiac disease. **B**

Celiac disease is an immune-mediated disorder that occurs with increased frequency in patients with type 1 diabetes (1–16% vs. 0.3–1% in the general population) (168–171). Classic symptoms of celiac disease include diarrhea, weight loss or poor weight gain, growth failure, abdominal pain, chronic fatigue, irritability, inability to concentrate, malnutrition due to malabsorption, other gastrointestinal problems, and occasional skin conditions (dermatitis herpetiformis). Unpredictable blood glucose levels, unexplained hypoglycemia, and glycemic deterioration may occur in patients with diabetes and celiac disease (172–174). Occasionally, one may see excessive weight, for example, in older female teens and young adults, associated with gastrointestinal distress leading to overeating. In symptomatic children with type 1 diabetes and confirmed celiac disease, a gluten-free diet reduces symptoms and hypoglycemia (175). The challenging dietary restrictions associated with having both type 1 diabetes and celiac disease are a significant burden. Therefore, a biopsy to confirm the diagnosis of celiac disease is recommended, especially in asymptomatic children, before prescribing significant dietary changes (176). Some patients and providers may choose to start a gluten-free diet without a biopsy in the presence of a high antibody titer and symptoms of celiac disease. Genetic screening (HLA-DQ2 and HLA-DQ8) confirms high risk for celiac disease (177).

TRANSITION FROM PEDIATRIC TO ADULT CARE

Recommendations

- Pediatric diabetes providers should begin to prepare youth for transition in early adolescence and, at the latest, at least 1 year before the transition to adult health care. **E**
- Both pediatric and adult diabetes care providers should provide support and resources for transitioning young adults. **E**

The developmental stage of emerging adulthood is characterized by competing educational, social, vocational, and financial priorities (178). During this phase, youth experience decreasing parental support and become fully responsible for their diabetes care, which may trigger a decline in medication-taking behavior and difficulty achieving blood glucose targets (179). Consequently, young adults with type 1 diabetes are at risk for acute diabetes complications, chronic macrovascular and microvascular complications, psychosocial challenges, and early mortality (180–182).

An ineffective transition from pediatric to adult diabetes care may contribute to fragmentation of health care and increased risk for adverse outcomes. Prior research has highlighted challenges in the transition process, including gaps between pediatric and adult care (183,184), suboptimal transition preparation (184), deterioration of glycemic control (185,186), and increased hospitalizations (187).

Available data suggest that many young adults in the U.S. do not transition to adult care until their early to

mid-twenties (186,188), but timing is highly variable. There is no clear optimal transition age, and the overriding priority is to ensure consistent follow-up. An individualized approach to transition timing is recommended, prioritizing the developmental needs and preferences of the patient.

The ADA and numerous professional societies recommend that pediatric diabetes providers begin transition preparation during the early adolescent years but, at the latest, at least 1 year prior to transfer (94). Preparation should include patient counseling on diabetes self-management, the differences between pediatric and adult care systems, the coordination of transfer, direct communication with receiving adult providers, and a written care summary.

Please refer to ADA's Position Statement (94) for a comprehensive discussion regarding the challenges of emerging adulthood and specific transition care recommendations. Organizations including Got Transition (189) and the Endocrine Society (190) have developed transition tools for clinicians, patients, and families. Clinical trials to study interventional approaches to transition preparation and transfer coordination, in order to optimize biomedical and psychosocial outcomes, are still needed.

CONCLUSIONS

Multicenter collaborative research and technological advances have increased type 1 diabetes disease understanding and led to advances in treatment. However, management of type 1 diabetes in youth remains imperfect, requiring unending vigilance and behavioral intervention. While it is burdensome to all affected individuals and their families, it is particularly challenging to those with limited resources and skills. Interdiction studies have yet to accomplish their goals of preventing and preserving β-cell function.

Type 1 diabetes requires youth to conform their lifestyle and behavior to a diabetes care regimen to control disease outcomes. In young children (under 6 years old), sick-day management, hypoglycemia unawareness, and caregiver issues are common but are manageable with education and attentiveness (191). When adolescents seek independence, caregivers must carefully balance autonomy with supervision. Caregivers should not delegate all diabetes care to the youth, as adolescents often need more, not less, support during this challenging developmental period. There is a dearth of quality research on high-risk behaviors (e.g., illicit drug use, alcohol and tobacco use, unprotected sexual activity, and disordered eating) in youth with type 1 diabetes, although the few studies suggest that rates are similar to the general population (96). However, in youth with type 1 diabetes, the combination of high-risk behaviors and dysglycemia are potentially disastrous. Health care providers should meet with youth alone and conduct a comprehensive HEADSS (home, education, eating, activities, drugs, sexuality, suicide/depression, and safety) assessment, incorporating diabetes as appropriate.

Engaging youth in highly supervised and supportive environments, such as diabetes camps, provides real-time education and reinforces the concept that they are not alone. A recent study in emerging adults with type 1 diabetes showed that young adults with diabetes fared comparably to their peers without diabetes in life path decisions, health behaviors, and psychological well-being (192). Psychosocial research studies that evaluate quality-of-life measures and effective behavioral interventions in youth with type 1 diabetes are critically important.

Technological advances have revolutionized diabetes management with novel hardware, software, and the ability to capture endless streams of data. Improved data quality, including improving current methods to translate data from diabetes devices to patient, family, and provider use, are needed to transform clinical care. Future clinical studies should evaluate how best to leverage the technology tools and efficiently analyze and translate the data generated into diabetes management. Patients would benefit from device manufacturers enabling data interoperability, regulatory agencies expediting and harmonizing approvals, and payors reimbursing the numerous supplies needed to optimize type 1 diabetes management in a timely manner, especially for the pediatric population. All patients with type 1 diabetes should have access to appropriate insulin therapy and advanced diabetes technologies.

Parallel to the technological advances, ongoing research is required to better understand the complexities involving epidemiology, pathophysiology, complications, and quality of life and to improve long-term outcomes associated with the disease in pediatrics. Adult diabetes research trials often do not include youth, and it is unclear how many, if any, of the findings apply to the pediatric population; therefore, inclusion of a diverse pediatric population is needed. Preserving β-cell function and ultimately preventing type 1 diabetes is the aim.

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