



Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Association

Diabetes Care 2014;37:2034–2054 | DOI: 10.2337/dc14-1140

Jane L. Chiang,¹ M. Sue Kirkman,²
Lori M.B. Laffel,³ and Anne L. Peters,⁴ on
behalf of the Type 1 Diabetes Sourcebook
Authors*

Type 1 diabetes is characterized by an immune-mediated depletion of β -cells that results in lifelong dependence on exogenous insulin. While both type 1 and type 2 diabetes result in hyperglycemia, the pathophysiology and etiology of the diseases are distinct and require us to consider each type of diabetes independently. As such, this position statement summarizes available data specific to the comprehensive care of individuals with type 1 diabetes. The goal is to enhance our ability to recognize and manage type 1 diabetes, to prevent its associated complications, and to eventually cure and prevent this disease.

INCIDENCE AND PREVALENCE OF TYPE 1 DIABETES

The exact number of individuals with type 1 diabetes around the world is not known, but in the U.S., there are estimated to be up to 3 million (1). Although it has long been called “juvenile diabetes” due to the more frequent and relatively straightforward diagnosis in children, the majority of individuals with type 1 diabetes are adults.

Most children are referred and treated in tertiary centers, where clinical data are more readily captured. The SEARCH for Diabetes in Youth study estimated that, in 2009, 18,436 U.S. youth were newly diagnosed with type 1 diabetes (12,945 non-Hispanic white, 3,098 Hispanic, 2,070 non-Hispanic black, 276 Asian-Pacific Islander, and 47 American Indian) (2). Worldwide, ~78,000 youth are diagnosed with type 1 diabetes annually. Incidence varies tremendously among countries: East Asians and American Indians have the lowest incidence rates (0.1–8 per 100,000/year) as compared with the Finnish who have the highest rates (>64.2 per 100,000/year) (3). In the U.S., the number of youth with type 1 diabetes was estimated to be 166,984 (4).

The precise incidence of new-onset type 1 diabetes in those over 20 years of age is unknown. This may be due to the prolonged phase of onset and the subtleties in distinguishing the different types of diabetes. In one European study of adults aged 30–70 years, ~9% tested positive for GAD antibodies (GADA) within 5 years of a diabetes diagnosis, consistent with other studies (5).

Adults with type 1 diabetes often receive care in primary care settings rather than with an endocrinologist. Unlike the consolidated care seen in pediatric diabetes management, the lack of consolidated care in adults makes incidence and prevalence rates difficult to characterize, and therefore they are often underestimated. The number of adults living with type 1 diabetes is increasing due to two factors: 1) the rising number of new-onset cases of type 1 diabetes in adults, including those diagnosed with latent autoimmune diabetes in adults (LADA), and 2) individuals with childhood-onset diabetes are living longer (6,7).

CLASSIFICATION AND DIAGNOSIS

Type 1 diabetes has traditionally been diagnosed based on clinical catabolic symptoms suggestive of insulin deficiency: polyuria, polydipsia, weight loss, and marked hyperglycemia that is nonresponsive to oral agents. It is classified as an autoimmune disease with progressive β -cell destruction, resulting in a physiological dependence on exogenous insulin. Recent studies have broadened our understanding of the disease, but have made diagnosis more complex.

There is tremendous variability in the initial presentation of type 1 diabetes in both youth and adults. Children often present acutely, with severe symptoms of polyuria,

¹American Diabetes Association, Alexandria, VA

²Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

³Pediatric, Adolescent and Young Adult Section, Joslin Diabetes Center; Department of Pediatrics, Harvard Medical School, Boston, MA

⁴Division of Endocrinology, Keck School of Medicine of the University of Southern California, Los Angeles, CA

Corresponding author: Jane L. Chiang, jchiang@diabetes.org.

The position statement was reviewed and approved by the Professional Practice Committee in April 2014 and approved by the Executive Committee of the Board of Directors in April 2014.

*A list of authors of the American Diabetes Association/JDRF Type 1 Diabetes Sourcebook can be found in the ACKNOWLEDGMENTS.

© 2014 by the American Diabetes Association. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

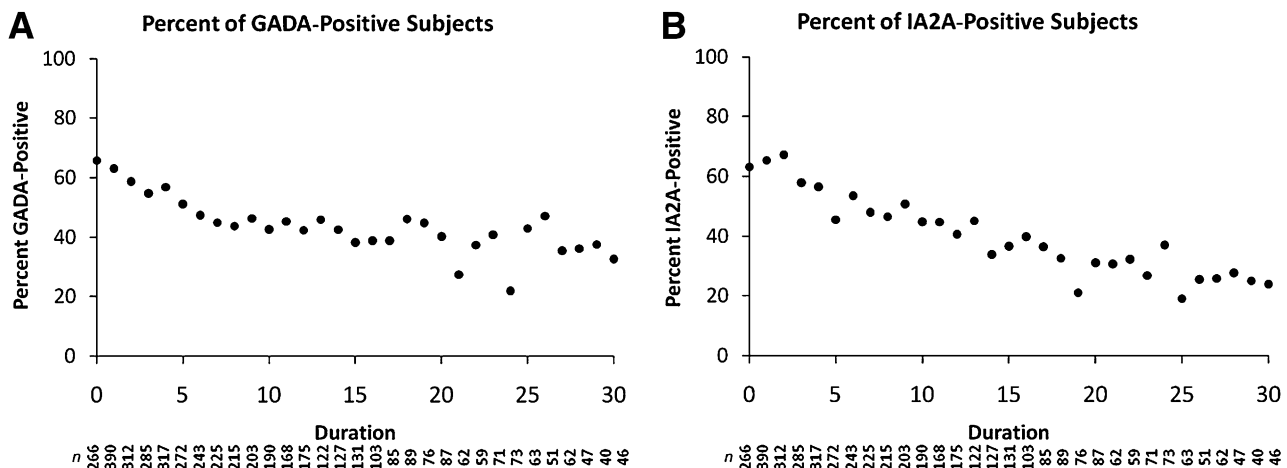


Figure 1—The percentage of antibody-positive subjects is affected by the duration of type 1 diabetes for GADA (A) and IA2A (B). Given an increase in the scatter (due to lower numbers of subjects), the x-axis is truncated at a duration of 30 years. Reproduced with permission from Tridgell et al. (16).

polydipsia, and ketonemia. However, in adults, type 1 diabetes presents with a more gradual onset, with a clinical presentation that may initially appear consistent with type 2 diabetes. Distinguishing between type 1 and type 2 diabetes presents diagnostic challenges. Traditionally, progressive β -cell destruction has been the hallmark of type 1 diabetes, but residual C-peptide (a surrogate marker for insulin secretion) may be detected over 40 years after initial diagnosis, regardless of whether the initial diagnosis was made in childhood or in adulthood (8).

Clinical Clues

Much of the diagnosis will depend on clinical clues, but the rising incidence of overweight/obesity has also confounded the diagnosis of type 1 diabetes. A lean individual presenting with clinical symptoms without a first-degree relative with diabetes (but often with a history of distant relatives with type 1 diabetes or other autoimmune disease) is generally suggestive of type 1 diabetes. An overweight individual (of any age) with metabolic syndrome and a strong family history of type 2 diabetes may be assessed only for the development of type 2 diabetes, even though type 1 diabetes is on the differential diagnosis. Obesity does not preclude that autoimmunity and hyperglycemia will occur even amid the relatively higher levels of endogenous insulin secretion observed in obesity. In young patients aged 10–17 years with phenotypic type 2 diabetes, 10% have evidence of islet autoimmunity suggesting that type 1 diabetes was the likely diagnosis (9). Thus, although leaner individuals are

more likely to be diagnosed as having type 1 diabetes, the potential for type 1 diabetes exists in those who phenotypically appear to have type 2 diabetes. If hyperglycemia persists after treatment with noninsulin agents, which is unusual in the treatment of newly diagnosed type 2 diabetes, then type 1 diabetes should be considered.

Pancreatic Autoantibodies

Pancreatic autoantibodies are characteristic of type 1 diabetes. Highly sensitive laboratory measurements capture ~98% of individuals with autoantibodies at diagnosis (10). Unfortunately, most commercial laboratories do not have reliably sensitive or specific assays that measure all five autoantibodies: GADA, islet cell antibodies (ICA), insulin autoantibodies (IAA), protein tyrosine phosphatase antibodies (ICA512 or IA2A), and zinc transporter protein (ZnT8). Thus, it may be inappropriate to report a patient as autoantibody negative. Another cause of “false-negative” autoantibodies is testing far out from diagnosis as antibody titers diminish over time (Fig. 1). It appears that there is an increased incidence of type 1 diabetes in ethnic populations where autoantibody markers may be of variable utility, such as in Asians where autoantibodies are often negative (11–15).

Family History

Type 1 diabetes has a genetic predilection and, in some cases, can be predicted in family members. The overall prevalence of type 1 diabetes in the U.S. is ~0.3%, but if a first-degree relative has diabetes,

the empiric risk of being affected is ~5% (17,18), representing a 15-fold increase among family members. Studies evaluating children at risk for developing type 1 diabetes have shown that the presence of more than two autoantibodies was associated with a nearly 70% risk for disease development within 10 years and 84% within 15 years (19). Evaluating at-risk individuals in the clinical setting is not yet recommended due to limited clinical interventions; however, ongoing research studies are identifying at-risk individuals through genetic testing in both the lower-risk general population and in the higher-risk population of relatives of people with type 1 diabetes.

Recommendations

Diagnosis

- The American Diabetes Association’s (ADA’s) diagnostic criteria for type 1 and type 2 diabetes are the same (Table 1). (A)
- Consider measurement of pancreatic autoantibodies to confirm the diagnosis of type 1 diabetes. (B)

Identification of At-Risk Relatives

- Inform type 1 diabetic patients of the opportunity to have their relatives tested for type 1 diabetes risk in the setting of a clinical research study. (B)

INITIAL EVALUATION AND FOLLOW-UP

General Considerations

All patients with type 1 diabetes need age-appropriate care, with an understanding of their specific needs and limitations. Infants and toddlers are approached quite differently from

Table 1—Criteria for the diagnosis of diabetes

A1C $\geq 6.5\%$. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

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

OR

Two-hour 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 containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

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

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

adolescents; the needs of young adults may vary from middle-aged or older adults. Regardless of age, the patient's needs are the same: an individualized care plan with ongoing education and support, ongoing assessment for acute and chronic complications, and access to medical providers with type 1 diabetes expertise. Just as patients change, the therapeutic approach should change and should be evaluated at each visit and modified as needed.

Type 1 diabetes care must be an iterative process, adapted as the needs of the individual evolve. Clinical assessments for type 1 diabetes in children and adults should incorporate age-appropriate and complication-focused evaluations, based on the likelihood that an abnormality will be present. For example, a young adult with low cardiovascular disease (CVD) risk and no complications may need more of an assessment of lifestyle adjustment as opposed to an older adult with longer duration of the disease who may need more evaluation of vascular and neurological issues.

Transition of Care From Pediatric to Adult Providers

As youth transition into emerging adulthood, the supportive infrastructure often abruptly disappears and glycemic control tends to deteriorate. The ADA recognizes that this is a challenging time and recommends a strong, practical transition plan to anticipate the upcoming changes. A successful transition plan should be initiated early (e.g., early teenage years) and include ongoing dialogue between the family and youth. The discussion should include finances, insurance, obtainment of supplies, identification of an adult care provider (ideally with communication between the

two providers), psychosocial issues (e.g., depression), and other issues identified by the family/youth. Health care providers, family, and youth should agree to an achievable diabetes management plan and provide resources for unanticipated issues. We refer the reader to the ADA's position statement on diabetes care for emerging adults (20).

Table 2 provides the childhood developmental phases and needs. Tables 3, 4, and 5 provide detailed elements of the initial and follow-up evaluation in individuals with type 1 diabetes.

Assessing the history of acute complications (e.g., severe hypoglycemia/hyperglycemia and diabetic ketoacidosis [DKA]) is important. Providers should provide continuing education for the patient/family to prevent ongoing recurrence. For example, it is important to review exercise management to reduce hypoglycemia risk and discuss sick-day management to reduce DKA risk.

Risk factor (e.g., cardiovascular) evaluation for prevention and screening for early evidence of micro- and macrovascular complications for early intervention should be implemented starting in adolescence and continue through adulthood. For children, risk factors should be assessed shortly after diagnosis based on family history and initial screening laboratory test results. Providers should manage risk factors, considering age-specific goals and targets (e.g., blood pressure, lipid, depression, and BMI assessment and management). The frequency of ongoing screening for complications should be based on age and disease duration.

Coexistent Autoimmunity

Celiac Disease

Celiac disease is an immune-mediated disorder that occurs with increased

frequency in patients with type 1 diabetes (1–16% of individuals compared with 0.3–1% in the general population) (21,22). Symptoms of celiac disease include diarrhea, weight loss or poor weight gain, abdominal pain, bloating, chronic fatigue, malnutrition due to malabsorption, and unexplained hypoglycemia or erratic blood glucose levels. Screening for celiac disease with serum levels of tissue transglutaminase or antiendomysial antibodies should be considered soon after the diagnosis of diabetes and/or if symptoms develop. Individuals who test positive should be referred to a gastroenterologist for possible small-bowel biopsy to confirm the diagnosis, although this is not necessary in all cases. Symptomatic children with strongly positive antibodies and supportive genetic or HLA testing may not require a biopsy, but asymptomatic at-risk children should have a biopsy (23). In symptomatic individuals with type 1 diabetes and confirmed celiac disease, a gluten-free diet reduces symptoms and decreases rates of hypoglycemia (24).

Thyroid Disease

About one-quarter of children with type 1 diabetes have thyroid autoantibodies (thyroid peroxidase antibodies or antithyroglobulin antibodies) at the time of diagnosis (25,26). The presence of thyroid autoantibodies is predictive of thyroid dysfunction, generally hypothyroidism and less commonly hyperthyroidism (27). Thyroid dysfunction is more common in adults with type 1 diabetes, although the exact prevalence is unknown. Women are more commonly affected than men. Subclinical hypothyroidism, hyperthyroidism, or coexistent Addison disease (adrenal insufficiency) may also deteriorate metabolic control with increased risk of symptomatic hypoglycemia (28) and may reduce linear growth in children (29).

Additional Considerations for Pediatrics

All children require some level of adult supervision in managing their diabetes. Assessments of pediatric patients should address issues specific to infants/preschoolers, school-aged children, adolescents, and emerging adults (Table 2). Health care providers should do a thorough assessment of the developmental needs of the youth (and caregiver), focusing on physical and emotional development, family issues, and psychosocial needs. The diabetes treatment plan

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

Developmental stages (ages)	Normal developmental tasks	Type 1 diabetes management priorities	Family issues in type 1 diabetes management
Infancy (0–12 months)	Developing a trusting relationship or bond 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 (13–26 months)	Developing a sense of mastery and autonomy	Preventing hypoglycemia Avoiding extreme fluctuations in blood glucose levels due to irregular food intake	Establishing a schedule Managing the picky eater Limit-setting and coping with toddler's lack of cooperation with regimen Sharing the burden of care
Preschooler and early elementary school (3–7 years)	Developing initiative in activities and confidence in self	Preventing hypoglycemia Coping with unpredictable appetite and activity Positively reinforcing 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 (8–11 years)	Developing skills in athletic, cognitive, artistic, and social areas Consolidating self-esteem with respect to the peer group	Making diabetes regimen flexible to allow for participation in school or peer activities Child learning short- and long-term benefits of optimal control	Maintaining parental involvement in insulin and blood glucose management tasks while allowing for independent self-care for special occasions Continuing to educate school and other caregivers
Early adolescence (12–15 years)	Managing body changes Developing a strong sense of self-identity	Increasing insulin requirements during puberty Diabetes management and blood glucose control becoming more difficult Weight and body image concerns	Renegotiating parent and teenager's roles in diabetes management to be acceptable to both Learning coping skills to enhance ability to self-manage Preventing and intervening in diabetes-related family conflict Monitoring for signs of depression, eating disorders, and risky behaviors
Later adolescence (16–19 years)	Establishing a sense of identity after high school (decisions about location, social issues, work, and education)	Starting an ongoing discussion of transition to a new diabetes team (discussion may begin in earlier adolescent years) 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, and risky behaviors

should be individualized and tailored to the needs of individual patients and their families. Efforts to achieve target blood glucose and A1C levels should be balanced with preservation of quality of life and protect against excessive hypoglycemia.

Height and weight should be measured at each visit and tracked via appropriate height and weight growth charts. An age-adjusted BMI can be calculated starting at age 2 years. These tools can be found for children and teens at <http://apps.nccd.cdc.gov/dnpabmi>. Blood pressure measurements should be determined correctly,

using the appropriate size cuff and with the child seated and relaxed. Hypertension should be confirmed on at least 3 separate days. Normal blood pressure levels for age, sex, and height and appropriate methods for determinations are available online at www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.pdf.

Chronic Complications in Children

Retinopathy, nephropathy, and neuropathy rarely have been reported in prepubertal children and children with diabetes duration of only 1–2 years; however, they may occur after the onset

of puberty or after 5–10 years of diabetes (30). As screening recommendations are based on recent evidence, these periodically change. Therefore, we refer the reader to the ADA Standards of Care for the current screening recommendations for children. It is recommended that those with expertise in diabetes management should conduct the assessments. For example, ophthalmologic exams should be performed by those skilled in diabetic retinopathy management and experienced in counseling pediatric patients and parents on the importance of early prevention/intervention. Another example,

Table 3—Medical history

Age and characteristics of onset of diabetes (e.g., DKA, asymptomatic laboratory finding)
Eating patterns, physical activity habits, nutritional status, and weight history
Whether or not patient wears medical alert identification
Diabetes education history; health literacy assessment
Review of previous insulin treatment regimens and response to therapy (A1C records), treatment preferences, and prior difficulty with therapies
Current treatment of diabetes, including medications and medication adherence, meal plan, physical activity patterns, and readiness for behavior change
Use of insulin, insulin pumps, carbohydrate ratios, and corrections; knowledge of sick-day rules; ketone testing; pump troubleshooting (if applicable)
Results of glucose monitoring, including SMBG and CGM and patient's use of data
DKA frequency, severity, and cause
Hypoglycemic episodes
Hypoglycemia unawareness
Any severe hypoglycemia: frequency and cause
Whether or not patient has glucagon available and someone to administer it
History of diabetes-related complications
Microvascular: retinopathy, nephropathy, and neuropathy (sensory, including history of foot lesions; autonomic, including sexual dysfunction and gastroparesis)
Macrovascular: coronary heart disease, cerebrovascular disease, and peripheral artery disease
Other: dental disease
Psychosocial issues, including current or past history of depression, anxiety, eating disorders, and others; assess support systems and need for assistance
History of pregnancy and any diabetes-related complications; desire for future pregnancies
Contraception (if a woman is of childbearing age)
Smoking
Alcohol use, abuse, and impact on blood glucose levels
Illicit drug use
Driving

nephrologists with experience with diabetic nephropathy would be aware that intermittent elevations in urinary albumin excretion are common in pediatric patients, particularly in association with exercise.

Additional Considerations for Adults

Adults with type 1 diabetes now span a very large age spectrum—from 18 to 100 years of age and beyond. Unlike the well-characterized developmental stages of children, the life stages traversed through adulthood are often less well documented and underappreciated. However, an understanding of each individual's circumstances is vital. This is true for aging in general, but particularly true for those with significant comorbidities due to long-standing type 1 diabetes. Thus, it is important to assess the clinical needs of the patient, setting specific goals and expectations that may differ significantly between a healthy 26-year-old and a frail 84-year-old with CVD and retinopathy.

Recommendations

See 2014 ADA Standards of Medical Care for detailed screening information for CVD, nephropathy, retinopathy, neuropathy, and foot care.

- **Access to health care** should include clinicians with expertise in type 1 diabetes management, including (but not limited to) an endocrinologist (or other health care provider with expertise in type 1 diabetes management), a registered dietitian, a diabetes educator, a mental health professional, an exercise specialist/physiologist, and specialists required to treat diabetes complications. (E)
- **Routine follow-up** (generally quarterly) should include review of self-monitoring of blood glucose (SMBG), continuous glucose monitoring (CGM) and pump data (if applicable), A1C measurement, evidence for acute and/or chronic complications of diabetes (particularly episodes of DKA and mild and/or severe hypoglycemia),

measurement of blood pressure and weight (and height in children), foot exam, inspection of injection/insertion sites, and discussion of psychosocial and educational needs (Tables 4 and 5). (E)

- Providers should **routinely document** the patient's age and disease duration. When clinically indicated, laboratory measures such as lipids, renal function measurements, and antibodies for associated autoimmune disease (thyroid or celiac disease) should be documented. (E)
- **Parent/guardian involvement** in care is required throughout childhood, with a gradual shift in responsibility of care from the parent/guardian to the youth. (E)
- **Health care for adults** should be focused on the needs of the individual throughout the various stages of their life, with age-appropriate evaluation and treatment. (E)
- Evaluation and treatment of **CVD risk** should be individualized. (E)
- **Immunizations** should be given as recommended by the Centers for Disease Control and Prevention (CDC) for children/adults in general and people with diabetes specifically. (C)
- **Consider screening for celiac disease** by measuring IgA antitissue transglutaminase or antiendomysial antibodies, with documentation of normal total serum IgA levels, soon after the diagnosis of diabetes and/or if symptoms develop. Refer the patient to a gastroenterologist if the test is positive. (E)
- **Consider screening for thyroid** peroxidase and thyroglobulin antibodies soon after diagnosis. (E)
- Screen for thyroid dysfunction by measuring thyroid-stimulating hormone (TSH) concentrations soon after type 1 diabetes diagnosis (and after stable metabolic control). If normal, consider rechecking every 1–2 years or more frequently if the patient develops unusual glycemic variation or symptoms of thyroid dysfunction or thyromegaly. (E)
- Assess for the presence of **additional autoimmune conditions** at diagnosis and if symptoms develop. (E)
- **Ongoing nutrition and diabetes self-management education (DSME) and support (DSMS)** are needed to address changes in food preferences, access to food, daily schedules, activity patterns, and potential barriers to

Table 4—Children and adolescents*

Clinical evaluation	Initial	Annual	Quarterly follow-up
Height	X	X	X
Weight	X	X [†]	X [†]
BMI percentile	X	X	X
Blood pressure	X	X	X
General physical exam	X	X	
Thyroid exam	X	X	X
Injection/infusion sites	X (if already on insulin)	X	X
Comprehensive foot exam [‡]	If needed, based on age	Beginning with older teens with diabetes since childhood	
Visual foot exam		X	If needed, based on high-risk characteristics
Retinal exam by eye care specialist	X [§]	In some cases, may be done every 2 years (see ADA Standards of Care)	
Depression screen	X	X	X
Hypoglycemia assessment	X	X	X
Diabetes self-management skills	X	X	X
Physical activity assessment	X	X	X
Assess clinically relevant issues (e.g., alcohol, drug, and tobacco use; use of contraception; driving)	X	As needed for teens	As needed for teens
Nutritional knowledge	X	X	As needed
Query for evidence of other autoimmune disease	X	As needed	As needed
Immunizations as recommended by CDC	X	X	As needed
Laboratory assessments	Initial	Annual	Follow-up
A1C	X	X	Every 3 months
Creatinine clearance/estimated glomerular filtration rate	X	X	
Lipid panel	Once glycemia is stable	X	As needed based on treatment
TSH	X	X	As needed based on treatment
		Frequency of testing varies based on clinical symptoms, presence of antibodies, and/or if on treatment	
Antithyroid antibodies (antithyroid peroxidase and antithyroglobulin antibodies)	X	Repeat as clinically indicated	
	Frequency of testing is unknown; test if symptoms are present or for periodic screening		
Celiac antibody panel	X	Repeat as clinically indicated	
	Frequency of testing is unknown; test if symptoms are present or for periodic screening		
Urine albumin-to-creatinine ratio	Starting 5 years after diagnosis	X	As needed based on treatment
Islet cell antibodies: GADA/IA2A/IAA/ZnT8	X		
	May be needed in new-onset patients to establish diagnosis		
C-peptide levels	X		
	Occasionally needed to establish type 1 diabetes in a patient on insulin or to verify type 1 diabetes for insurance purposes—always measure a simultaneous blood glucose level		

*Assumes a patient has a health care provider to manage the nondiabetes-related health assessments and to perform annual evaluations. [†]Patient may opt out of measurement if psychologically distressing. [‡]Foot inspection should be done at each visit and self-exams taught if high-risk characteristics are present. Comprehensive foot exam includes inspection, palpation of dorsalis pedis and posterior tibial pulses, presence or absence of patellar and Achilles reflexes, and determination of proprioception, vibration, and monofilament sensation. [§]Within 5 years after diagnosis. || If triglycerides are elevated in a nonfasting specimen, measure a direct LDL cholesterol level.

Table 5—Adults*			
Clinical evaluation	Initial	Annual	Follow-up
Height	X		
Weight	X	X†	X†
BMI	X	X	
Blood pressure	X	X	X
General physical exam	X		
Thyroid exam	X	If indicated	
Injection/infusion sites	X	X	X
Comprehensive foot exam‡	X	X	
Visual foot exam			As needed—at each visit, if high-risk foot
Retinal exam by eye care specialist§	Starting 5 years after diagnosis; earlier if visual symptoms and/or true date of diagnosis is unknown	In some individuals, screening may be done every 2 years (see ADA Standards of Medical Care)	
Depression screen	X	X	
Hypoglycemia assessment	X	X	X
Diabetes self-management skills	X	X	X
Physical activity assessment	X	X	X
Assess clinically relevant issues (e.g., alcohol, drug, and tobacco use; use of contraception; driving)	X	As needed	As needed
Nutritional knowledge	X	X	As needed
Query for evidence of other autoimmune disease	X	As needed based on clinical scenario	As needed based on clinical scenario
Immunizations as recommended by CDC	X	X	As needed
Laboratory assessments	Initial	Annual	Follow-up
A1C	X	X	Every 3 months
Creatinine clearance/estimated glomerular filtration rate	X	X	
Fasting lipid panel	X	X	As needed based on treatment
TSH	X	X	As needed based on treatment
Antithyroid antibodies	X	Frequency of testing varies based on clinical symptoms, presence of antibodies, or if on treatment	
Celiac antibody panel	X	Frequency of testing is unknown; test if symptoms are present or for periodic screening	
Urine albumin-to-creatinine ratio	X	X	
GADA	X	May be needed in new-onset patients to establish diagnosis	
C-peptide levels	X	Occasionally needed to establish type 1 diabetes in a patient on insulin or to verify type 1 diabetes for insurance purposes—always measure a simultaneous blood glucose level	

*Assumes a patient has a health care provider to manage the nondiabetes-related health assessments and to perform annual evaluations. †Patient may opt out of measurement if psychologically distressing. ‡Foot inspection should be done at each visit and self-exams taught if high-risk characteristics are present. Comprehensive foot exam includes inspection, palpation of dorsalis pedis and posterior tibial pulses, determination of presence or absence of patellar and Achilles reflexes, and determination of proprioception, vibration, and monofilament sensation. §In some instances, the test may not need to be done yearly. || If a patient is unable to undertake a fasting test due to hypoglycemia, measure a direct LDL cholesterol level.

self-care, including the risk of an eating disorder. (E)

- Assess psychosocial status annually and more often as needed; treat and/or refer to a mental health professional as indicated. (E)

DSME AND DSMS

DSME and DSMS are the ongoing processes of facilitating the knowledge, skill, and ability necessary for diabetes self-care. These processes incorporate the needs, goals, and life experiences of the person with diabetes. The overall objectives of DSME and DSMS are to support informed decision making, self-care behaviors, problem solving, and active collaboration with the health care team to improve clinical outcomes, health status, and quality of life in a cost-effective manner (31). Because changes in both treatment and life circumstances occur across the life span, DSME and DSMS must be a continuous process adapted throughout the life of the person with type 1 diabetes so that self-management can be sustained.

No matter how sound the medical regimen, it can only be as successful as the ability of the individual and/or family to implement it. Family involvement remains an important component of optimal diabetes management throughout childhood and adolescence. Health care providers who care for children and adolescents must, therefore, be capable of evaluating the educational, behavioral, emotional, and psychosocial factors that impact implementation of a treatment plan and must assist the individual and family to overcome barriers or redefine goals as appropriate (Table 6). Diabetes education should occur at diagnosis and upon transition to adult diabetes care and should be an ongoing process. The information needs to be individualized and continually adapted to the patient's needs.

Recommendations

- Individuals with type 1 diabetes and parents/caregivers (for individuals aged <19 years) should receive culturally sensitive and developmentally appropriate individualized DSME and DSMS according to national standards for DSME and DSMS when their diabetes is diagnosed and routinely thereafter. (B)

Table 6—DSME content based on life stages

Infancy (birth–18 months)

Period of trust versus mistrust
Providing warmth and comfort measures after invasive procedures is important
Feeding and sleeping or nap routines
Vigilance for hypoglycemia

Play age (3–5 years)

Reassurance that body is intact, use of Band-Aids and kisses after procedures
Identification of hypoglycemic signs and symptoms (temper tantrums and nightmares are common)
Include child in choosing injection and finger-prick sites
Positive reinforcement for cooperation
Begin process for teaching child awareness of hypoglycemia

School age (6–12 years)

Integrate child into educational experience
Determine skill level
Identify self-care skills
Determine roles and responsibilities
Communication with peers and school staff—who and when to tell about diabetes

Adolescence (12–18 years)

Begin transition care planning
Personal meaning of diabetes
Determine roles and responsibilities in care
Social situations and dating
Who or when to tell about diabetes
Driving
Sex and preconception counseling
Alcohol and drugs
College and career planning

Young adults

Personal meaning of diabetes
Roles and responsibilities in care
Social situations and dating
Who or when to tell about diabetes
Genetic risks, conception, and preconception
Travel
Choosing or pursuing a career
Workplace rights
Health or life insurance
Involving friends and significant others in diabetes care
Safety
Creating a support network
Establishing or maintaining independence

Middle-aged adults

Personal meaning of diabetes
Roles and responsibilities in care
Involving spouse or significant other in care
Sexual functioning
Developing a support network
Travel
Pursuing a career
Workplace rights
Health or life insurance
Talking with children or other family members about diabetes
Balancing other responsibilities with diabetes care
Safety
Facing complications

Older adults

Personal meaning of diabetes
Roles and responsibilities in care
Maintaining independence
Obtaining assistance with diabetes care tasks
Involving spouse or significant other in care
Travel
Talking with adult children or other family members about diabetes
Safety
Assessing for declines in ability to perform self-care/activities of daily living
Caring for diabetes along with other chronic illnesses or comorbidities
Obtaining health care when living in multiple locations
Community resources
Care of type 1 diabetes in long-term or other care facilities

Additional Considerations for Pediatrics

- Education should be provided to appropriate school personnel as a significant portion of a child's day is spent in school. (E)
- The developing teenager must be educated about the transition to adult health care, beginning in early to mid-adolescence, with increasing efforts to establish self-reliance in diabetes care beginning at least 1 year prior to the transition. Even after the transition to adult care is made, support and reinforcement are recommended. (E)

Additional Considerations for Adults

- Adult learning theory can be used to tailor DSME and DSMS to the age, life stage, culture, literacy/numeracy, knowledge, experience, and cognitive ability of the patient. (C)

PSYCHOSOCIAL: ASSESSMENT AND TREATMENT OF PSYCHOSOCIAL ISSUES

Assessment and appropriate management of psychosocial issues are important throughout the life span of individuals with type 1 diabetes. In pediatrics, health care providers should assess the individual child and the child's family for their ability to function and behave appropriately regarding safe and responsible diabetes care. For adults, the individual is the focus of care. However, family involvement should be strongly encouraged when appropriate.

Depression screening and discussion about psychosocial issues are important components of the diabetes visit. Special attention should be paid to diabetes-related distress, fear of hypoglycemia (and hyperglycemia), eating disorders, insulin omission, subclinical depression, and clinical depression. These factors are significantly associated with poor diabetes self-management, a lower quality of life, and higher rates of diabetes complications. As individuals age, health care providers should evaluate issues related to self-care capacity, mobility, and autonomy. Such factors are to be promptly addressed, as they make the management of type 1 diabetes ever more problematic.

Recommendations

- Make age-appropriate screenings for psychosocial issues a component of most diabetes visits. Any concerns

should be pursued through treatment that may include referral to a mental health specialist. (E)

Additional Considerations for Pediatrics

- Ensure that there is developmentally appropriate parent/family involvement in the management of the child's/adolescent's diabetes care tasks, avoiding a premature transfer of sole responsibility for diabetes management to the developing child/teenager. (B)
- Directly ask about diabetes-related family conflict and stress and negotiate an acceptable resolution with the child/adolescent and parent(s). However, if family conflict is extremely entrenched and cannot be resolved by the diabetes team, referral should be made to a mental health specialist who is knowledgeable about type 1 diabetes in youth and family functioning. (C)

Additional Considerations for Adults

- Ongoing evaluation of patients' general and diabetes-related quality of life, emotional well-being, distress, depression, and resources is warranted, preferably by a team that includes a mental health specialist if such resources are available. (C)
- Health care providers should promptly address issues related to self-care capacity, mobility, and autonomy. (E)

NUTRITION THERAPY

Nutrition therapy is an important component of the treatment plan for all individuals with type 1 diabetes. Each patient should have an individualized food plan based on food preferences, schedule, and physical activity. Nutrition therapy aims to ensure that the patient and family understand the impact food has on blood glucose, how food interacts with exercise and insulin to prevent hypo- and hyperglycemia and to achieve glucose goals, and how to implement the food plan in a variety of situations. The food plan takes into consideration the patient's numeracy, literacy, engagement, and ability to adjust insulin.

General diabetes nutrition principles, as defined in the ADA Standards of Care, apply to people with type 1 diabetes, particularly in reference to normal growth and development in youth and the maintenance of a healthy body

weight at all ages. Specifically, with regards to individuals with type 1 diabetes, topics such as carbohydrate counting and meal composition should be addressed. For selected individuals who have mastered carbohydrate counting, education on the impact of protein and fat on glycemic excursions should be incorporated into diabetes management (32). Those who are overweight or obese may benefit from weight reduction counseling.

Recommendations

- Individualized medical nutrition therapy is recommended for all people with type 1 diabetes as an effective component of the overall treatment plan. (A)
- Monitoring carbohydrate intake, whether by carbohydrate counting or experience-based estimation, remains a key strategy in achieving glycemic control. (B)
- If adults with type 1 diabetes choose to drink alcohol, they should be advised to do so in moderation (one drink per day or less for adult women and two drinks per day or less for adult men). Discussion with a health care provider is advised to explore potential interactions with medications. Adults should be advised that alcohol can lower blood glucose levels and that driving after drinking alcohol is contraindicated. (E)

PHYSICAL ACTIVITY AND EXERCISE

Exercise has many positive health and psychological benefits including physical fitness, weight management, and enhanced insulin sensitivity. It also provides opportunities for social interactions and builds self-esteem. However, exercise creates challenges for people with type 1 diabetes due to the increased risk for both hypoglycemia and hyperglycemia. During exercise, multiple hormones (insulin, glucagon, catecholamines, growth hormone, and cortisol) control fuel metabolism and create a balance between glucose uptake by exercising muscles and hepatic glucose production (33,34). The equilibrium between insulin secretion and the counterregulatory hormones varies according to the exercise type, intensity, and duration (35).

Hyperglycemia results from counterregulatory hormone excess with insufficient insulin, leading to excessive hepatic glucose production and limiting

increased glucose uptake into skeletal muscle. Hyperglycemia can occur before, during, and after various types of exercise. If the patient feels well, with negative or minimal urine and/or blood ketones, and there is a clear reason for the elevated blood glucose level, such as underdosing insulin at the preceding meal, it is not necessary to postpone exercise based solely on hyperglycemia. However, when people with type 1 diabetes are deprived of insulin for 12–48 h and are ketotic, exercise can worsen hyperglycemia and ketosis. Therefore, vigorous activity should be avoided in the presence of severe hyperglycemia and ketosis, especially with known insulin omission.

Physical activity increases *hypoglycemia* risk during and immediately following exercise, and, again, about 7–11 h postexercise. This delayed susceptibility to hypoglycemia is referred to as the “lag effect” of exercise (36,37) and is caused by muscles replenishing glycogen stores postexercise. Hypoglycemia and fear of hypoglycemia can limit participation in exercise.

Strategies should be developed to prevent and treat hypoglycemia readily. Individualization is necessary, but clinical experience suggests that it is safest for most patients to have a blood glucose level of 100 mg/dL (5.6 mmol/L) or higher prior to starting exercise. This may be achieved by reducing the prandial insulin dose for the meal/snack preceding exercise and/or increasing food intake. Some patients can avoid hypoglycemia by reducing insulin (such as by lowering pump basal rates) (38) or by consuming additional carbohydrates during prolonged physical activity. One study in children on pumps suggested that a reduction in overnight basal insulin the night following exercise may reduce the risk of delayed exercise-induced hypoglycemia (39). Frequent SMBG and/or CGM use are key to exercising safely, as is ready access to carbohydrates.

Basic recommendations for physical activity are the same as those for all children and adults, independent of the diagnosis of diabetes: children should be encouraged to engage in at least 60 min of physical activity daily, and adults should be advised to perform at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate) or a lesser

amount (60–75 min/week) of vigorous-intensity activity (40,41). Exercise should also include resistance and flexibility training.

Individuals, particularly adults, should be assessed for cardiovascular risk and the presence of complications that might limit exercise as discussed more fully in the ADA Standards of Medical Care in Diabetes (42).

Recommendations

- Exercise should be a standard recommendation as it is for individuals without diabetes; however, recommendations may need modifications due to the presence of macro- and microvascular diabetes complications. (E)
- Patients of all ages (or caregivers of children) should be educated about the prevention and management of hypoglycemia that may occur during or after exercise. (E)
- Patients should be advised about safe preexercise blood glucose levels (typically 100 mg/dL or higher depending on the individual and type of physical activity). (E)
- Reducing the prandial insulin dose for the meal/snack preceding exercise and/or increasing food intake can be used to help raise the preexercise blood glucose level and reduce hypoglycemia. (E)
- A reduction in overnight basal insulin the night following exercise may reduce the risk for delayed exercise-induced hypoglycemia. (C)
- SMBG should be performed as frequently as needed (before, during, and after exercise) in order to prevent, detect, and treat hypoglycemia and hyperglycemia. (E)
- Source(s) of simple carbohydrate should be readily available before, during, and after exercise to prevent and treat hypoglycemia. (E)

TREATMENT TARGETS

General Considerations

Hyperglycemia defines diabetes and is directly related to the incidence of complications. Therefore, glycemic control is fundamental to diabetes management. The Diabetes Control and Complications Trial (DCCT) (43) was a prospective randomized controlled study comparing intensive versus standard glycemic control in patients diagnosed with type 1 diabetes relatively recently. The DCCT

demonstrated that achieving an A1C of <7% reduced the incidence of microvascular complications of type 1 diabetes compared with standard control, which achieved an A1C of ~9% during the period of the randomized trial. The Epidemiology of Diabetes Interventions and Complications (EDIC) study (44,45) was a follow-up of the DCCT cohorts. The EDIC study remarkably demonstrated persistent microvascular and cardiovascular benefits in subjects who had previously received intensive treatment, even though their glycemic control had deteriorated over time.

While A1C and blood glucose targets are needed, **the ADA emphasizes that glycemic targets should be individualized** with the goal of achieving the best possible control while minimizing the risk of severe hyperglycemia and hypoglycemia (Table 7). Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. More or less stringent glycemic goals may be appropriate for individual patients. Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals.

Recommendation

- Lifestyle, psychosocial, and medical circumstances should be considered when recommending glycemic goals for all age-groups. (E)

Glycemic Control Goals in Pediatrics

As the DCCT only included pediatric patients aged ≥ 13 years (195 adolescents aged 13–17 years at entry), treatment guidelines for pediatric patients have been based nearly exclusively on professional, expert advice. Furthermore,

Table 7—Summary of A1C recommendations for nonpregnant people with diabetes*

Youth (<18 years)	<7.5%
Adults	<7.0%
Older adults	
Healthy†	<7.5%
Complex/intermediate	<8.0%
Very complex/poor health	<8.5%

*Targets must be individualized based on a patient's circumstances. †No comorbidities, long life expectancy.

despite the overall A1C goal of <7% for adults with type 1 diabetes, pediatric patients, aged 13–19 years, had an A1C target of <7.5%. This slightly higher A1C target for adolescents with type 1 diabetes was based on expert recommendations and the clinical reality that optimizing glycemic control in adolescent patients with type 1 diabetes is especially challenging, given the physiological and behavioral challenges that confront this age-group.

The ADA's blood glucose and A1C goals traditionally have been developmentally or age based in the pediatric population, but it is now time to alter the traditional goals based on recent data. The traditional recommendations are an A1C goal of <8.5% for youth under the age of 6 years, <8% for those 6–12 years old, and <7.5% for those 13–19 years old. Lower blood glucose levels and lower A1C targets should be pursued as long as patients can avoid severe, recurrent hypoglycemia. Thus, the overall recommendation has included the goal to achieve as close to normal blood glucose and A1C levels as is possible without the occurrence of severe, recurrent hypoglycemia.

Historically, the ADA recommended higher A1C targets for young children. This recommendation arose from a combination of two lines of unsubstantiated evidence. First, an older body of literature, reflecting therapy in the pre-modern era, devoid of insulin analogs, easy-to-use blood glucose monitors, "smart pumps," and CGM devices, indicated that severe recurrent hypoglycemia with seizure and/or coma in young children was associated with neurocognitive compromise (46). The second line of evidence arose from literature that questioned what, if any, impact blood glucose and A1C levels prior to puberty have on the risk for the development of future long-term complications of diabetes (47,48). With the combination of these two independent lines of reports, it is not surprising that earlier recommendations regarding glycemic targets focused on the avoidance of severe hypoglycemia in order to reduce risk of neurocognitive dysfunction, especially in young children and even school-aged children.

Currently, treatment strategies for children recommend physiological insulin replacement with modern strategies and treatment tools. More recent investigation

and active ongoing research have dispelled concerns regarding hypoglycemia and neurocognitive dysfunction (49,50).

Studies assessing neurocognitive function have failed to identify adverse effects of a past history of hypoglycemia in the young child; however, as always, further research needs to be conducted.

There are also questions regarding the premise that the years prior to puberty do not impact the future risk of complications (51). Many investigators and clinicians believe in the importance of controlling blood glucose and A1C levels prior to puberty to reduce risk for both micro- and macrovascular complications. Additionally, there is burgeoning evidence that elevated blood glucose levels and glycemic variability in the very young child with diabetes may produce adverse outcomes in the short term on neurocognitive function and the central nervous system (52,53). These recent articles suggest that hyperglycemia and glycemic variability are associated with changes in the central nervous system white matter, as observed in MRI scans.

Taking into account the combination of spotty past evidence related to the adverse effects of hypoglycemia on the developing brain and increasing evidence from more recent investigations focused on the potential risks of hyperglycemia and glucose variability on the central nervous system, the ADA has decided to alter the recommendations for glycemic targets in pediatric patients with type 1 diabetes and harmonize with other organizations. The International Society for Pediatric and Adolescent Diabetes (ISPAD) uses a single A1C goal of <7.5% across all pediatric age-groups. This recommendation is based on clinical studies and expert opinion, as rigorous evidence does not currently exist. Specifically, the recommendation is derived from a combination of clinical experience and intensive management strategies that provide opportunities to achieve as near-normal glycemic control as possible without the occurrence of severe hypoglycemia.

In light of the above evidence, the ADA will harmonize its glycemic goals with those of ISPAD (as well as the Pediatric Endocrine Society and the International Diabetes Federation) by using a single A1C goal of <7.5% across all pediatric age-groups.

However, as mentioned previously, it must be emphasized that the ADA strongly believes that blood glucose and A1C targets should be individualized with the goal of achieving the best possible control while minimizing the risk of severe hyperglycemia and hypoglycemia and maintaining normal growth and development.

Recommendation

- An A1C goal of <7.5% is recommended across all pediatric age-groups. (E)

Glycemic Control Goals in Adults

Similar to in children, the care of older adults with diabetes is complicated by their clinical and functional heterogeneity. Unlike the large older adult population with type 2 diabetes, which includes patients with both long-standing and new-onset diabetes, most older adults with type 1 diabetes have long-standing disease. Even so, there is a wide spectrum of health across older individuals. They may have advanced complications, or they may have lived with diabetes for many years without the development of complications. Some older patients have multiple comorbid conditions and/or impairments of physical or cognitive functioning, while others have little comorbidity and high functional status. Life expectancy is highly variable and is defined by comorbidity and functional status more than it is by age.

Health care providers caring for older adults with diabetes must take this heterogeneity into consideration when setting and prioritizing treatment goals. The benefits of interventions such as stringent glycemic control may not apply to those with advanced complications of diabetes or to those with a life expectancy of less than the anticipated time frame of benefit. Conversely, the risks of interventions such as tight glycemic control (hypoglycemia, treatment burden) may be greater in older patients. Although individualization is critical, in general, older patients with long life expectancy and little comorbidity should have treatment targets similar to those of middle-aged or younger adults. In more frail patients, treatment targets might reasonably be relaxed, while symptomatic hyperglycemia or the risk of DKA should still be avoided (54).

Recommendations

- Lowering A1C to below or around 7% has been shown to reduce microvascular complications of diabetes, and, if achieved soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease. Therefore, a reasonable A1C goal for many nonpregnant adults with type 1 diabetes is <7%. (B)
- Providers might reasonably suggest more stringent A1C goals (such as <6.5%) for select individual patients, if this can be achieved without significant hypoglycemia or other adverse effects of treatment. Appropriate patients might include those with a short duration of diabetes, a long life expectancy, hypoglycemia awareness, and no significant CVD. (C)
- Less stringent A1C goals (such as <8.5%) may be appropriate for patients with a history of severe hypoglycemia, hypoglycemia unawareness, limited life expectancy, advanced microvascular/macrovascular complications, or extensive comorbid conditions. (B)
- Glycemic control for those of any age with type 1 diabetes should be assessed based on frequent SMBG levels (and CGM data, if available) in addition to A1C in order to direct changes in therapy. (B)

MONITORING

SMBG

The DCCT demonstrated the benefits of intensive glycemic control on diabetes complications with SMBG as part of a multifactorial intervention, suggesting that SMBG is a crucial component of effective therapy. SMBG allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being achieved. SMBG results are useful in preventing hypoglycemia, adjusting medications (particularly prandial insulin doses), and understanding the impact of appropriate nutrition therapy and physical activity. More frequent SMBG is correlated to lower A1C levels (55,56).

SMBG frequency and timing should be dictated by the patient's specific needs and goals. When prescribing SMBG, providers must ensure that patients receive ongoing instruction and regular evaluation of their SMBG technique and their ability to use SMBG data

to adjust therapy (insulin and/or food). Furthermore, SMBG results should be downloaded and reviewed at each visit.

SMBG is especially important for patients with type 1 diabetes to monitor for and prevent asymptomatic hypoglycemia and hyperglycemia. Type 1 diabetic patients should perform SMBG prior to, and sometimes after, meals and snacks, at bedtime, before and after exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. For many patients, this will require testing 6–10 times daily, although individual needs may vary. For example, sick children may require up to 10 SMBG tests per day or more.

A study of children and adolescents with type 1 diabetes showed that, after adjustment for multiple confounders, increased SMBG frequency was significantly associated with lower A1C. In the range of 0–5 tests per day, A1C decreased by 0.46% per additional test per day. Increased testing was associated with significantly less DKA and (probably due to reverse causality) significantly more hypoglycemia (55,56).

SMBG accuracy is dependent on both the instrument and the user (57), so it is important to evaluate each patient's monitoring technique, both initially and at regular intervals thereafter. Optimal use of SMBG requires a proper review and interpretation of the data by both the patient and the provider.

CGM

Real-time CGM through the measurement of interstitial glucose (which correlates well with plasma glucose) is available. These sensors require calibration with SMBG, and CGM users still require SMBG for making acute treatment decisions. CGM devices have alarms for hypo- and hyperglycemic excursions that include absolute level and rate-of-change alerts. A 26-week randomized trial of 322 type 1 diabetic patients showed that adults aged ≥ 25 years using intensive insulin therapy and CGM experienced a 0.5% reduction in A1C (from $\sim 7.6\%$ to 7.1%) compared with usual intensive insulin therapy with SMBG (58). Participants aged <25 years (children, teenagers, and young adults) randomized to sensor use did not achieve a significant A1C reduction.

However, these younger patients did not use CGM consistently. The greatest predictor of A1C lowering for all age-groups was frequency of sensor use, which was lowest in 15- to 24-year-old subjects. There was no significant difference in hypoglycemia in any age-group. In a smaller randomized controlled trial of 129 adults and children with baseline A1C <7.0%, outcomes combining A1C and hypoglycemia favored the group using CGM, suggesting that CGM is beneficial for pediatric patients and adults with type 1 diabetes who have already achieved excellent control (58).

Overall, meta-analyses suggest that, compared with SMBG, CGM use is associated with A1C lowering by $\sim 0.26\%$ (59) without an increase in hypoglycemia, although existing studies have small sample sizes and are of relatively short duration. The technology may be particularly useful in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes, although studies have not consistently shown significant reductions in the occurrence of severe hypoglycemia. A CGM device equipped with an automatic low threshold suspend feature was approved by the U.S. Food and Drug Administration (FDA) in 2013. The Automation to Simulate Pancreatic Insulin Response (ASPIRE) trial of 247 patients showed that sensor-augmented insulin pump therapy with a low glucose suspend feature significantly reduced nocturnal hypoglycemia without increasing A1C levels for those >16 years of age (60). These devices may offer the opportunity to reduce severe hypoglycemia for those with a history of nocturnal hypoglycemia, although more clinical trials are needed.

Recommendations

- Patients with type 1 diabetes should perform SMBG prior to meals and snacks, at a minimum, and at other times, including postprandially to assess insulin-to-carbohydrate ratios; at bedtime; midsleep; prior to, during, and/or after exercise; when they suspect low blood glucose; after treating low blood glucose until they have restored normoglycemia; when correcting a high blood glucose level; prior to critical tasks such as driving; and at more frequent intervals during illness or stress. (B)
- Individuals with type 1 diabetes need to have unimpeded access to glucose

test strips for blood glucose testing. Regardless of age, individuals may require 10 or more strips daily to monitor for hypoglycemia, assess insulin needs prior to eating, and determine if their blood glucose level is safe enough for overnight sleeping. (B)

- CGM is a useful tool to reduce A1C levels in adults without increasing hypoglycemia and can reduce glycemic excursions in children. Glycemic improvements are correlated with frequency of CGM use across all ages. (A)

Additional Considerations for Pediatrics

- Children should have additional blood glucose checks if the parent/caregiver is concerned that the child's behavior may be due to low/high blood glucose levels. (E)
- School employees and caregivers should be knowledgeable about SMBG and equipped with all necessary supplies. (E)
- Capable children should be permitted to self-manage their diabetes at school. (E)

A1C TESTING

A1C reflects average glycemia over 2–3 months (57) and strongly predicts diabetes complications (43,61). Thus, A1C testing should be performed routinely in all patients with diabetes at initial assessment and as part of continuing care. A1C is a convenient method to track diabetes control; however, there are disadvantages. Glycation rates, and thus A1C levels, may vary with patients' race/ethnicity. However, this is controversial. Additionally, anemias, hemoglobinopathies, and situations of abnormal red cell turnover affect A1C (42).

A1C measurements approximately every 3 months determine whether a patient's glycemic targets have been reached and maintained. For any individual patient, the frequency of A1C testing should be dependent on the clinical situation, the treatment regimen used, and the clinician's judgment. Unstable or highly intensively managed patients (e.g., pregnant type 1 diabetic women) may require more frequent testing than every 3 months (62). In patients with hemoglobinopathies that interfere with the A1C assay or with hemolytic anemia or other conditions that shorten the red blood cell life span, the A1C may not accurately reflect

glycemic control or correlate well with SMBG testing results. In such conditions, fructosamine may be considered as a substitute measure of long-term (average over 2 weeks) glycemic control.

Recommendations

- Perform the A1C test quarterly in most patients with type 1 diabetes and more frequently as clinically indicated (i.e., pregnancy). (A)
- Point-of-care A1C testing, using a DCCT standardized assay, may provide an opportunity for more timely treatment changes. (E)

INSULIN THERAPY

The DCCT clearly showed that intensive insulin therapy, defined as three or more injections per day of insulin or continuous subcutaneous insulin infusion (CSII) (or insulin pump therapy), was a key part of improved glycemia and better outcomes (43,63). The study was carried out with short- and intermediate-acting human insulins. Despite better microvascular outcomes, intensive insulin therapy was associated with a high rate of severe hypoglycemia (62 episodes per 100 patient-years of therapy). Since the completion of the DCCT, a number of rapid-acting and long-acting insulin analogs have been developed. These analogs are associated with less hypoglycemia than human insulin while offering the same amount of A1C lowering in people with type 1 diabetes (64,65).

The Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) study was a large ($n = 485$) randomized clinical trial comparing insulin pump therapy and CGM with insulin injections in youth and adults with type 1 diabetes. The two study groups started with the same baseline A1C of 8.3%. After 1 year, the group using insulin pump therapy and CGM had lower A1C levels (7.5% vs. 8.1%, $P < 0.001$) without significant nocturnal hypoglycemia compared with the insulin injection cohort (66). Recently, a large randomized trial in patients with type 1 diabetes and nocturnal hypoglycemia reported that the use of sensor-augmented insulin pump therapy with the threshold-suspend feature reduced nocturnal hypoglycemia without increasing glycated hemoglobin values (60). In general, intensive management using pump therapy/CGM should be strongly encouraged, with

active patient/family participation enhancing successful outcomes (67–69).

Recommendations

- Most individuals with type 1 diabetes should be treated with multiple daily insulin injections (three or more injections per day of prandial insulin and one to two injections of basal insulin) or CSII. (A)
- Most individuals with type 1 diabetes should be educated in how to match prandial insulin dose to carbohydrate intake, premeal blood glucose, and anticipated activity. (E)
- Most individuals with type 1 diabetes should use insulin analogs to reduce hypoglycemia risk. (A)
- All individuals with type 1 diabetes should be taught how to manage blood glucose levels under varying circumstances, such as when ill or receiving glucocorticoids or for those on pumps, when pump problems arise. (E)
- Child caregivers and school personnel should be taught how to administer insulin based on provider orders when a child cannot self-manage and is out of the care and control of his or her parent/guardian. (E)

INTERDICTION

Therapy trials to prevent type 1 diabetes development (prevention), to preserve remaining β -cells (preservation), and to replace β -cells (transplantation) are ongoing. Although means are available to screen and predict family members at risk for developing type 1 diabetes, efforts to delay or prevent disease onset have been largely disappointing. A variety of different immunomodulatory and immune-suppressive agents have been evaluated in patients with recent-onset type 1 diabetes, and the effects have been modest at best: for the subset of drugs that appear to have an effect, not all patients respond; for those who do, the effects are generally transient. Many of the agents tested to date are FDA approved for other indications, but given the observations to date and potential toxicities, the recommendation is that patients should only receive these drugs after being enrolled in clinical research protocols with appropriate follow-up. Long-term safety and efficacy data are scarce, especially in children. Investigators continue to evaluate promising new agents and combinations of

drugs or cell-based therapies in an effort to safely and effectively modulate the autoimmune response (70).

β-CELL REPLACEMENT THERAPY

β-Cell replacement may be achieved through pancreas or islet transplantation in select candidates. Pancreas transplants are now accepted as a proven therapy, while islet transplants, though significantly improving, are still mostly done on an experimental basis.

Pancreas Transplants

Pancreas transplants are most often performed in combination with kidney transplantation, either as a simultaneous pancreas-kidney (SPK) transplant or as a pancreas-after-kidney (PAK) transplant (71). SPK and PAK transplants may be considered for individuals with late-stage kidney disease because the transplants can normalize glucose levels, which will prevent hypoglycemia and provide some protection for the transplanted kidney (72), and provide other benefits, including an improvement in quality of life (71). These recipients will already require immunosuppression for their renal transplants, which means the major additional risk is the operative procedure. SPK transplants function for an average of 9 years, compared with 6 years for PAK transplants (71).

There has been debate about pancreas transplant alone (PTA) in the absence of an indication for kidney transplantation because of the risks of mortality, morbidity, and immunosuppression. Outcomes have gradually improved (73), such that the procedure can be cautiously considered for individuals without renal failure who have unstable glucose control and hypoglycemia unawareness. Because of the risks of pancreas transplantation compared with traditional methods for controlling blood glucose levels, all available efforts to use exogenous insulin combined with technology, education, and glucose follow-up should be exhausted before PTA is performed. The durability of function averages 6 years, which is much better than islet transplantation but about the same as PAK and not as good as SPK (73).

Islet Transplantation

A major appeal of islet transplantation is that it does not require major surgery. Moreover, outcomes have improved

over the past decade such that normoglycemia without insulin is now maintained for an average of 3 years in specialized protocols (74). Even when insulin treatment is reinstated, residual insulin secretion can help recipients maintain good control with less hypoglycemia and a less complicated regimen for several more years.

At the present time, few islet transplants are being performed and most are experimental. However, they can be considered as a treatment option for those who are poor candidates for whole-organ transplants. Importantly, their current success has established a proof of principle for cellular transplantation. Great progress is being made in finding an abundant source of healthy insulin-producing cells and in developing better ways to protect transplanted cells from immune destruction (75,76). Potential solutions for the shortage of islets include embryonic stem cells, induced pluripotent stem cells, xenogeneic tissue, and various other potential sources—all the focus of ongoing research efforts. Another possible way to replenish the β-cell deficiency of diabetes is through regeneration of the endocrine pancreas; this too is being worked on intensively.

Recommendations

- Consider solid organ pancreas transplantation simultaneously with kidney transplantation in patients with type 1 diabetes who have an indication for kidney transplantation and are poorly controlled with large glycemic excursions. (B)
- Consider solid organ pancreas transplantation after kidney transplantation in adult patients with type 1 diabetes who have already received a kidney transplant. (C)
- Judiciously consider solid organ pancreas transplantation alone in adults with type 1 diabetes, unstable glucose control, hypoglycemia unawareness, and an increased risk of diabetes-related mortality, who have attempted all of the more traditional approaches to glycemic control and have remained unsuccessful, yet are judged responsible enough to manage the antirejection medication regimen, risks, and follow-up required with an organ transplant. (C)
- Consider referral to research centers for protocolized islet cell transplantation

in patients with type 1 diabetes and debilitating complications of diabetes who are interested in research possibilities and fit the criteria for the research protocol. (E)

ADJUNCTIVE THERAPIES

Pramlintide

Pramlintide, an amylin analog, is an agent that delays gastric emptying, blunts pancreatic secretion of glucagon, and enhances satiety. It is an FDA-approved therapy for use in type 1 diabetic patients and has been shown to reduce A1C, induce weight loss, and lower insulin dose. However, it is only indicated for adults. Two 52-week trials of pramlintide ($n = 1,131$; age >18 years) showed A1C reductions of ~0.3–0.4% (77,78). In both studies, a greater proportion of participants achieved an A1C target of <7% with the therapy than without the therapy. There are a few small, short-term studies of pramlintide use in children with type 1 diabetes, with outcomes similar to those in the adult studies. Clearly, larger, long-term studies are needed in pediatrics.

Incretin-Based Therapies

Injectable glucagon-like peptide-1 (GLP-1) agonists and oral dipeptidyl peptidase-4 (DPP-4) inhibitors are increasingly being studied in the type 1 diabetic population, but are not approved by the FDA for this indication. GLP-1 agonists delay gastric emptying, suppress the postprandial rise in glucagon secretion, and may increase satiety. Preliminary studies indicate that these agents may also facilitate weight loss. Further long-term clinical trials in type 1 diabetic patients are needed.

Sodium-Glucose Cotransporter 2 Inhibitors

Sodium-glucose cotransporter 2 (SGLT2) inhibitors work by inhibiting glucose reabsorption in the kidney and are also being tested in individuals with type 1 diabetes. These agents provide insulin-independent glucose lowering by blocking glucose reabsorption in the proximal renal tubule, leading to weight loss and A1C reduction in individuals with type 2 diabetes. However, insufficient data exist to recommend clinical use of these agents in type 1 diabetes at this time.

Metformin

Metformin is a biguanide that decreases hepatic gluconeogenesis and is used as first-line therapy in type 2 diabetes. It has been shown to have some benefit in reducing insulin doses and weight in small studies in patients with type 1 diabetes (79) and is now being evaluated more fully for use in patients with type 1 diabetes. Two randomized controlled trials are currently under way evaluating metformin in type 1 diabetic patients. The first study is in adults and is using carotid intima-medial thickness as an outcome measure (ClinicalTrials.gov identifier: NCT01483560). The second study is focusing on overweight or obese youths between the ages of 12 and 19 years who require ≥ 0.85 units/kg/day of insulin (ClinicalTrials.gov identifier: NCT01808690). Results are currently pending.

Recommendations

- Pramlintide may be considered for use as adjunctive therapy to prandial insulin in adults with type 1 diabetes failing to achieve glycemic goals. (B)
- Evidence suggests that adding metformin to insulin therapy may reduce insulin requirements and improve metabolic control in overweight/obese patients and poorly controlled adolescents with type 1 diabetes, but evidence from larger longitudinal studies is required. (C)
- Current type 2 diabetes medications (GLP-1 agonists, DPP-4 inhibitors, and SGLT2 inhibitors) may be potential therapies for type 1 diabetic patients, but require large clinical trials before use in type 1 diabetic patients. (E)

HYPOGLYCEMIA

Hypoglycemia risk is the limiting step in the treatment of type 1 diabetes at any age. Because current methods of blood glucose detection and insulin replacement are imperfect (though improved from prior eras), hypoglycemia risk is invariably present. Patient education (80), frequent SMBG, and CGM can help detect hypoglycemia and allow for adjustments in insulin dosing and carbohydrate intake. Severe hypoglycemia rates increase with antecedent episodes of hypoglycemia, age, and duration of diabetes; thus, this is an issue that must be reassessed frequently (81). Hypoglycemia unawareness is related to a

reduced sympathoadrenal response to hypoglycemia; it can occur in the setting of recurrent hypoglycemia or autonomic failure and can be reversed by scrupulous avoidance of hypoglycemia. Patients should be screened to determine the threshold at which hypoglycemia symptoms occur; if the threshold is suggestive of hypoglycemia unawareness, the treatment goals and regimen should be revisited and counseling regarding appropriate self-monitoring before critical tasks should be reinforced (82).

Oral carbohydrate is the treatment of choice for self-treatment or for the treatment of hypoglycemic adults and children who are alert and able to eat. Glucagon is used for severe hypoglycemia. In children, small studies have led to the concept of using age-based minidose glucagon if the child is alert but not able to eat (83).

Recommendations

- Individuals with type 1 diabetes, or their caregivers, should be asked about symptomatic and asymptomatic hypoglycemia at each encounter. (E)
- Glucose (15–20 g) is the preferred treatment for the conscious individual with hypoglycemia, 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 consume a meal or snack to prevent recurrence of hypoglycemia. (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 strictly avoid further hypoglycemia for at least several weeks to partially reverse hypoglycemia unawareness and reduce the risk of future episodes. (B)

DKA

DKA (see ref. 70 for definition) is an acute complication of diabetes that can be

associated with new-onset type 1 diabetes, insulin omission, and increased levels of counterregulatory hormones/cytokines associated with stress, such as an infection. Mild cases can be safely and effectively treated in an acute care setting with appropriate resources and may not require hospitalization. Education must be provided to individuals with type 1 diabetes in order to help prevent DKA, which can have serious sequelae, particularly in children under 5 years of age. Although DKA and hyperglycemic hyperosmolar state (HHS) may overlap, especially when dehydration is severe, DKA must be distinguished from HHS (serum glucose >600 mg/dL, serum osmolality >330 mOsm/kg, and no significant ketosis and acidosis) because patients with HHS typically are severely dehydrated and require more aggressive fluid management. There are multiple guidelines available for the management of DKA (84).

Recommendations

- Individuals and caregivers of individuals with type 1 diabetes should be educated and reminded annually how to prevent DKA, including a review of sick-day rules and the critical importance of always administering insulin and monitoring both glucose and ketone levels. (B)
- Insulin omission is the major cause of DKA; therefore, individuals with type 1 diabetes must have access to an uninterrupted supply of insulin. (E)
- Patients with type 1 diabetes and their families should have around-the-clock access to medical advice and support to assist with sick-day management. (C)
- Standard protocols for DKA treatment should be available in emergency departments and hospitals. (E)

CVD SCREENING AND TREATMENT

Much of the existing data on the risk of CVD in individuals with diabetes is based on people with type 2 diabetes who often have additional CVD risk factors, such as metabolic syndrome, hypertension, and dyslipidemia. How much is applicable to people with type 1 diabetes is unknown. However, people with type 1 diabetes are at increased risk for CVD, particularly those with additional risk factors.

In type 1 diabetes, standard risk factors apply, such as hyperlipidemia, hypertension, age, family history, smoking, weight, and presence of albuminuria. As such,

these should be considered when determining the need for evaluation and treatment for CVD. However, even in the absence of classic risk factors, there may be high CVD risk. An adult with childhood-onset type 1 diabetes of 20-year duration has a substantially increased risk of coronary artery disease of 1% per year (83), thus meriting high-intensity statin therapy according to the new joint American College of Cardiology/American Heart Association guidelines ($\geq 7.5\%$ 10-year risk) (85). In some cases, measurement of coronary artery calcification may be a helpful method for determining CVD risk (86). Here, as with all management issues for people with type 1 diabetes, providers need to individualize assessment and treatment options.

With regard to treatment, statin therapy is the preferred treatment for lipid lowering/CVD risk reduction (85). The Heart Protection Study (HPS) did include type 1 diabetic participants who appeared to experience the same degree of benefit from statins as others in the study, though the finding was not statistically significant due to low numbers (87). Unfortunately, there are no blood pressure intervention trials with CVD end points in type 1 diabetes and only one LDL cholesterol-lowering trial (85). Statin and aspirin therapy (if not contraindicated) should be considered and used as is individually indicated.

Recommendations

- Therapy for those under age 40 years with less than a 20-year diabetes duration (or over age 75 years) should be considered on an individual basis, though, depending on overall risk, an LDL cholesterol < 100 mg/dL has been suggested as an appropriate goal with statin intervention for those with LDL cholesterol levels of 130–160 mg/dL. (E)
- Individuals with type 1 diabetes aged 40–75 years may benefit from moderate-to-intensive statin therapy with consideration of diabetes duration and CVD risk factors. If 10-year risk is estimated to be $\geq 7.5\%$, then intensive statin therapy should be considered. (B)

SPECIFIC SETTINGS AND POPULATIONS

Pregnancy

Preconception Counseling and Care

To minimize risks associated with pregnancy and type 1 diabetes, preconception

counseling and care are critical. Preconception care with tight glycemic control improves outcomes including lower cesarean rates (88), decreased perinatal mortality (89–91), and decreased congenital malformations (89–97). Although there is some evidence that childbearing may be reduced (98–100), in general, fertility should be assumed to be normal, and all young women with type 1 diabetes should receive preconception counseling covering diabetes and general topics, including use of prenatal vitamin, discontinuation of potentially teratogenic medications, and the importance of glycemic control to reduce the risk of congenital malformations.

Pregnancy

Type 1 diabetes affects approximately 0.1–0.2% of all pregnancies (101). During pregnancy, there are substantial changes in maternal insulin sensitivity that may cause profound changes in insulin requirements. Whereas insulin resistance increases markedly during the second and third trimesters, a greater proportion of total daily insulin dose must be given prandially and a lower proportion used to cover basal metabolic requirements (102). Pregnant women with type 1 diabetes require meticulous glycemic management by experts trained in obstetrics, endocrinology, and maternal-fetal medicine. Women who are planning pregnancy or who are pregnant may need to test blood glucose levels frequently (often 10 or more times daily) to reach and maintain a near-normal A1C level without excessive hypoglycemia.

Severe hypoglycemia may occur early during pregnancy (102). This is followed by periods of insulin resistance and subsequent hyperglycemia if the increased insulin needs are not met. Therefore,

health care providers must be vigilant and frequently adjust insulin dosing throughout gestation.

In a pregnancy complicated by diabetes and chronic hypertension, target blood pressure goals of systolic blood pressure 110–129 mmHg and diastolic blood pressure 65–79 mmHg are reasonable. Lower blood pressure levels may be associated with impaired fetal growth (Table 8). ACE inhibitors and angiotensin receptor blockers are contraindicated during pregnancy because they may have adverse effects on the fetus. Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, diltiazem, clonidine, and prazosin.

Eye examinations should occur in the first trimester with close follow-up throughout pregnancy and for 1 year postpartum because of the risk of rapid retinopathy progression during pregnancy. Those with progressive retinopathy should have more frequent screening by an ophthalmologist experienced in retinopathy management. See the *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook* (70) for a summary of pregnancy recommendations. The prevalence of Hashimoto thyroiditis may be as high as 31% in women with type 1 diabetes (105). Therefore, all pregnant women with type 1 diabetes should be screened for thyroid disease early in pregnancy.

Recommendations

- Starting at puberty, preconception counseling should be incorporated into routine diabetes clinic visits for all adolescents and women of childbearing potential, and appropriate birth control techniques should be discussed with women who do not desire pregnancy. (C)

Table 8—ADA Standards of Care optimal targets in pregnancy*

Target maternal glucose†	
Fasting	60–99 mg/dL
Peak postprandial	100–129 mg/dL
Mean	< 100 mg/dL
Labor and delivery	80–110 mg/dL (mean < 100)
A1C	Insulin drips + D10 50 cc/h Preconception $< 7\%$ and as close to normal as possible without significant hypoglycemia During pregnancy $< 6\%$

*See refs. 70, 103, and 104. †These represent the mean + 2 SD for normal. They are targets, but not everyone can achieve them. There is certainly marked variability, which explains why there is greater incidence of large-for-gestational-age infants in patients with type 1 diabetes.

- As most pregnancies are unplanned, consider the potential risks and benefits of medications that are contraindicated in pregnancy in all adolescents and women of childbearing potential and counsel women using such medications accordingly. (E)
- Such medications should be evaluated prior to conception, as drugs commonly used to treat diabetes and its complications may be contraindicated or not recommended in pregnancy, including statins, ACE inhibitors, angiotensin receptor blockers, and most noninsulin therapies. (B)
- Prenatal vitamins with folate should be started with preconception planning to reduce the risk for birth defects. (B)
- All pregnant women with type 1 diabetes should be screened for thyroid disease early in pregnancy. (B)
- Women contemplating pregnancy should be evaluated and, if indicated, treated for diabetic retinopathy, nephropathy, neuropathy, and CVD. (B)
- A1C levels should be as close to normal as possible (<7%) before conception is attempted. (B)
- Nutritional intake should be optimized and included in preconception planning according to general pregnancy guidelines. (E)

Inpatient Management and Outpatient Procedures

Management of individuals with type 1 diabetes in the hospital and in preparation for scheduled outpatient procedures often differs from that of individuals with type 2 diabetes. The challenges include difficulties associated with fasting, maintaining a consistent source of carbohydrate, and facilitating inpatient blood glucose management while modifying scheduled insulin therapy. Outpatient procedures should be performed with the awareness that individuals with type 1 diabetes may have difficulty fasting for long periods of time (more than 10 h) prior to a procedure. Patients with type 1 diabetes should be prepared with a treatment plan for insulin dose adjustments and oral glucose intake prior to any procedure that requires alterations in dietary intake and/or fasting.

It is imperative that the entire health care team, including anesthesiologists

and surgeons as well as other specialists who perform procedures, understands type 1 diabetes and how it factors into the comprehensive delivery of care. From a practical perspective, this means that people with type 1 diabetes will be at high risk for hypoglycemia during prolonged fasting and are at risk for ketosis if insulin is inappropriately withheld. Once under anesthesia, individuals with type 1 diabetes must be carefully monitored for hypoglycemia and hyperglycemia.

For some individuals, once the most acute phase of an illness has resolved or improved, patients may be able to self-administer their prior multiple-dose or CSII insulin regimen under the guidance of hospital personnel who are knowledgeable in glycemic management. Individuals managed with insulin pumps and/or multiple-dose regimens with carbohydrate counting and correction dosing may be allowed to manage their own diabetes if this is what they desire, once they are capable of doing so.

Recommendations

- All patients admitted to the hospital should have type 1 diabetes clearly identified in the medical record. (E)
- SMBG should be ordered to fit the patient's usual insulin regimen with modifications as needed based on clinical status. (E)
- Goals for blood glucose levels are the same as for people with type 2 diabetes or hospital-related hyperglycemia. (E)
- A plan for preventing and treating hypoglycemia should be established for each patient. (E)
- Insulin dosing adjustments should be made in the perioperative period and inpatient setting with consideration of changes in oral intake, recent blood glucose trends, and the need for uninterrupted basal insulin to prevent hyperglycemia and ketoacidosis, with adjustment of the long-acting insulin or basal insulin requirement to reflect true basal requirements, insofar as they may be anticipated. (B)

Child Care and Schools

Because a large portion of a child's day may be spent in school and/or in the child care setting, close communication with and cooperation of the school or day

care personnel is essential for optimal diabetes management, safety, and maximal academic opportunities. Child care personnel and school staff should receive training to provide diabetes care in the absence of a school nurse or licensed health care professional. Able and willing school staff members should be taught the principles of diabetes management and trained to provide needed care for the child according to the ADA's Safe at School program (see the ADA position statement on diabetes care in the school and day care setting [106] for further discussion). Young children often lack the motor, cognitive, and communication skills and abilities to manage their diabetes and completely depend on adult caregivers. The management priority for younger children is the prevention, recognition, and treatment of hypoglycemia and marked hyperglycemia.

Students with diabetes should receive proper diabetes management in school, with as little disruption to the school and child's routine as possible. Whenever possible, the student should have the opportunity to self-manage by performing blood glucose monitoring, using CGM (if utilized), administering insulin, having access to meals/snacks, managing hypoglycemia (with trained personnel prepared to provide glucagon treatment, if required) and hyperglycemia, and participating fully in all school-sponsored activities (Table 9).

Camps

A diabetes camp is an ideal place for children and youth to have an enjoyable camp experience and receive peer support from other children with diabetes under close medical oversight. The goals for campers are to learn to cope more effectively with diabetes, learn self-management skills to gain more independence, and share experiences with other young people with diabetes.

The camp medical director is responsible for the diabetes management of the children. A registered dietitian oversees dietary planning at camp. Medical directors and staff should have expertise in managing type 1 diabetes and must receive training concerning routine diabetes management and treatment of diabetes-related emergencies at camp. Staff must follow universal precautions including Occupational Safety

Table 9—Diabetes care tasks for school personnel

Diabetes care tasks	Signs*	Treatment	Outcome if not treated
Hypoglycemia recognition and treatment	Catecholamine effect (sweating, jitteriness, tachycardia, and palpitations) or neuroglycopenia (behavior change)	Glucose, wait 15 min, recheck, give food if blood glucose is adequate (based on DMMP) Know when and how to give glucagon Know when to contact parents or emergency medical services Have all contact information available on emergency plan	Seizure or coma
Hyperglycemia recognition and treatment	Polyuria, polydipsia (most common), difficulty concentrating, headache, or irritability	Rapid- or short-acting insulin Dose and frequency should be clearly elucidated on emergency plan to avoid “insulin stacking” and consequent hypoglycemia (DMMP) Insulin dosing technique (syringe/vial, pens, pumps) Insulin required (DMMP) Ketone checks and when to call parents Correction factor calculations and insulin for hyperglycemia and ketones	Check for ketones. Follow directions for ketones if positive to avoid ketoacidosis

DMMP, Diabetes Medical Management Plan. *Varies among individuals but consistent within a given child.

and Health Administration (OSHA) regulations, Clinical Laboratory Improvement Amendments (CLIA) standards, and state regulations (107).

Diabetes in the Workplace

There are practical and legal issues related to diabetes in the workplace. Employers and employees with diabetes should work together to find solutions and educate themselves about the rights of individuals with diabetes. Individuals with diabetes are responsible for having all necessary diabetes supplies, eating properly, and being aware of safety issues and regulations at work. The Americans with Disabilities Act states that most employers must provide “reasonable accommodations” to allow an individual with diabetes to safely and successfully perform a job, unless doing so would place an “undue burden” on the employer. We refer the reader to ADA position statement on diabetes and employment for additional information (108) and to the relevant section of the *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook* (70).

Older Adults

Older individuals with type 1 diabetes are unique in that they have lived for many years with a complex disease.

Not all older adults are alike: some may continue a rigorous regimen, with tighter control, while others may require less stringent targets. Along with age-related conditions, older adults may develop diabetes-related complications, which make managing type 1 diabetes more challenging. Providers should be aware that insulin dosing errors, meal planning, and physical activities must be properly managed in older adults. Severe hyperglycemia can lead to symptoms of dehydration and hyperglycemic crises. While chronic hyperglycemia is detrimental, hypoglycemia may be more of a concern in some older adults. Declining cognition may contribute to hypoglycemia unawareness or the inability to safely manage hypoglycemia when it occurs. An individualized approach that includes the reassessment of prior targets may be warranted. We refer the reader to the ADA consensus report “Diabetes in Older Adults” (54). Even though this report focuses primarily on the type 2 diabetic population, there is significant overlap in the comorbidities and complications experienced by the older type 1 and type 2 diabetic populations.

Special Population Groups

Although type 1 diabetes is increasing in several ethnic and racial groups, it

remains less common in people of non-European descent. A better understanding of the unique pathophysiology of type 1 diabetes is needed. In addition, multidisciplinary diabetes teams should receive training to properly address the diverse cultural needs of these populations and to optimize health care delivery, improve glycemic control, and prevent complications. Additionally, there is a need for approaches to reduce health disparities and improve outcomes in racial/ethnic minorities and in the underserved population with type 1 diabetes (70).

Developing Countries: The Global Epidemic

Type 1 diabetes is an increasing global public health burden. The demands of daily management, chronicity of the disease, potential complications, paucity of diabetes specialists, and rising incidence are challenging in the U.S., but these issues, including the considerable cost of management, are crippling for those in the developing world. International organizations play a major role in improving care for individuals with type 1 diabetes in the developing world, but implementable, cost-saving, and sustainable strategies are needed to make such programs successful (70).

Acknowledgments. The authors thank the following contributors to the *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook*: Nora Algothani, Pamela Allweiss, Barbara J. Anderson, Florence M. Brown, H. Peter Chase, William L. Clarke, Sheri R. Colberg, Kathleen Dungan, Steven Edelman, Martha M. Funnell, Stephen E. Gitelman, Ann E. Goebel-Fabbri, Jeffrey S. Gonzalez, Carla J. Greenbaum, Michael J. Haller, Kara Hawkins, Laurie A. Higgins, Irl B. Hirsch, William C. Hsu, Heba Ismail, Crystal Crismond Jackson, Tamarra James-Todd, Georgeanna J. Klingensmith, David C. Klonoff, Mary Korytkowski, David Maahs, Hussain Mahmud, Medha N. Munshi, Trevor Orchard, Bruce A. Perkins, Jeremy Hodson Pettus, Andrew M. Posselt, Michael C. Riddell, Elizabeth R. Seaquist, Janet Silverstein, Linda M. Siminerio, Peter Stock, William V. Tamborlane, Guillermo E. Umpierrez, Raynard Washington, Joseph I. Wolfsdorf, Howard Wolpert, Jennifer Ann Wyckoff, and Mary Ziotas Zacharatos. The authors acknowledge Gordon Weir and the Steering Committee members: Belinda Childs, Richard A. Insel, Margaret A. Powers, Richard Rubin, Desmond Schatz, and Linda M. Siminerio.

The authors also thank Erika Gebel Berg (American Diabetes Association) for her invaluable editorial contribution.

Duality of Interest. M.S.K. received research support from Novo Nordisk (to the University of North Carolina) for a study of an investigational drug for type 1 diabetes. In 2013–2014, L.M.B.L. received grant support from Bayer Diabetes Care; served as a consultant/advisory board member for Bristol-Myers Squibb/AstraZeneca, Sanofi, Novo Nordisk, and Boehringer Ingelheim; and served as a consultant for Johnson & Johnson, LifeScan/Animas, Lilly, Menarini, and Dexcom. In the past year, A.L.P. consulted with Abbott Diabetes Care, BD, Janssen, Lilly, Medscape, Medtronic MiniMed, Novo Nordisk, Sanofi, and Takeda; has been on the speaker's bureau for Bristol-Myers Squibb/AstraZeneca and Novo Nordisk; and received grant funding from the Medtronic MiniMed Foundation. No other potential conflicts of interest relevant to this article were reported.

References

1. Prime Group for JDRF. *Type 1 Diabetes*, 2010. JDRF, 2011
2. Lawrence JM, Imperatore G, Pettitt DJ, et al.; SEARCH for Diabetes in Youth Study Group. Incidence of diabetes in U.S. youth by type, race/ethnicity, and age, 2008–2009. *Diabetes* 2014; 63(Suppl. 1):A407
3. Harjutsalo V, Sjöberg L, Tuomilehto J. Time trends in the incidence of type 1 diabetes in Finnish children: a cohort study. *Lancet* 2008; 371:1777–1782
4. Pettitt DJ, Talton J, Dabelea D, et al.; SEARCH for Diabetes in Youth Study Group. Prevalence of diabetes in U.S. youth in 2009: the SEARCH for Diabetes in Youth study. *Diabetes Care* 2014; 37:402–408
5. Hawa MI, Kolb H, Schloot N, et al.; Action LADA consortium. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7. *Diabetes Care* 2013;36:908–913
6. Miller RG, Secrest AM, Sharma RK, Songer TJ, Orchard TJ. Improvements in the life expectancy of type 1 diabetes: the Pittsburgh Epidemiology of Diabetes Complications study cohort. *Diabetes* 2012;61:2987–2992
7. Scottish Diabetes Research Network Epidemiology Group. Life expectancy in type 1 diabetes: a Scottish Registry Linkage Study [Internet], 2013. Available from <http://www.easdvirtualmeeting.org/resources/3906>. Accessed 9 April 2014
8. Davis A, Haller MJ, Miller K, et al. Residual C-peptide in patients 3–81 years from diagnosis of T1D: A T1D Exchange Study. *Diabetes* 2013; 62(Suppl. 1):A422
9. Klingensmith GJ, Pyle L, Arslanian S, et al.; TODAY Study Group. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study. *Diabetes Care* 2010;33:1970–1975
10. Wenzlau JM, Juhl K, Yu L, et al. The cation efflux transporter ZnT8 (Slc30A8) is a major autoantigen in human type 1 diabetes. *Proc Natl Acad Sci USA* 2007;104:17040–17045
11. Todd AL, Ng WY, Lui KF, Thai AC. Low prevalence of autoimmune diabetes markers in a mixed ethnic population of Singaporean diabetics. *Intern Med J* 2004;34:24–30
12. Thai AC, Ng WY, Loke KY, Lee WR, Lui KF, Cheah JS. Anti-GAD antibodies in Chinese patients with youth and adult-onset IDDM and NIDDM. *Diabetologia* 1997;40:1425–1430
13. Ly LD, Twigg SM, Tran DT, Nguyen KT. Most type 1 diabetes presenting as diabetic ketoacidosis in Vietnamese people is negative for pancreatic islet cell autoantibodies. *Diabetes Res Clin Pract* 2012;96:e63–e65
14. Tuomi T, Zimmet P, Rowley MJ, et al. Differing frequency of autoantibodies to glutamic acid decarboxylase among Koreans, Thais, and Australians with diabetes mellitus. *Clin Immunol Immunopathol* 1995;74:202–206
15. Chan JC, Yeung VT, Chow CC, et al. Pancreatic beta cell function and antibodies to glutamic acid decarboxylase (anti-GAD) in Chinese patients with clinical diagnosis of insulin-dependent diabetes mellitus. *Diabetes Res Clin Pract* 1996;32:27–34
16. Tridgell DM, Spiekerman C, Wang RS, Greenbaum CJ. Interaction of onset and duration of diabetes on the percent of GAD and IA-2 antibody-positive subjects in the Type 1 Diabetes Genetics Consortium Database. *Diabetes Care* 2011;34:988–993
17. Bonifacio E, Ziegler AG. Advances in the prediction and natural history of type 1 diabetes. *Endocrinol Metab Clin North Am* 2010;39:513–525
18. Tuomilehto J. The emerging global epidemic of type 1 diabetes. *Curr Diab Rep* 2013; 13:795–804
19. Ziegler AG, Rewers M, Simell O, et al. Seroprevalence to multiple islet autoantibodies and risk of progression to diabetes in children. *JAMA* 2013;309:2473–2479
20. Peters A, Laffel L; American Diabetes Association Transitions Working Group. Diabetes care for emerging adults: recommendations for transition from pediatric to adult diabetes care systems: a position statement of the American Diabetes Association, with representation by the American College of Osteopathic Family Physicians, the American Academy of Pediatrics, the American Association of Clinical Endocrinologists, the American Osteopathic Association, the Centers for Disease Control and Prevention, Children with Diabetes, The Endocrine Society, the International Society for Pediatric and Adolescent Diabetes, Juvenile Diabetes Research Foundation International, the National Diabetes Education Program, and the Pediatric Endocrine Society (formerly Lawson Wilkins Pediatric Endocrine Society). *Diabetes Care* 2011;34:2477–2485
21. Holmes GK. Coeliac disease and type 1 diabetes mellitus - the case for screening. *Diabet Med* 2001;18:169–177
22. Rewers M, Liu E, Simmons J, Redondo MJ, Hoffenberg EJ. Celiac disease associated with type 1 diabetes mellitus. *Endocrinol Metab Clin North Am* 2004;33:197–214
23. Husby S, Koletzko S, Korponay-Szabó IR, et al.; ESPGHAN Working Group on Coeliac Disease Diagnosis; ESPGHAN Gastroenterology Committee; European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr* 2012;54:136–160
24. Abid N, McGlone O, Cardwell C, McCallion W, Carson D. Clinical and metabolic effects of gluten free diet in children with type 1 diabetes and coeliac disease. *Pediatr Diabetes* 2011;12:322–325
25. Roldán MB, Alonso M, Barrio R. Thyroid autoimmunity in children and adolescents with type 1 diabetes mellitus. *Diabetes Nutr Metab* 1999;12:27–31
26. Triolo TM, Armstrong TK, McFann K, et al. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. *Diabetes Care* 2011;34:1211–1213
27. Kordonouri O, Deiss D, Danne T, Dorow A, Bassir C, Grüters-Kieslich A. Predictivity of thyroid autoantibodies for the development of thyroid disorders in children and adolescents with type 1 diabetes. *Diabet Med* 2002;19:518–521
28. Mohn A, Di Michele S, Di Luzio R, Tumini S, Chiarelli F. The effect of subclinical hypothyroidism on metabolic control in children and adolescents with type 1 diabetes mellitus. *Diabet Med* 2002;19:70–73
29. Chase HP, Garg SK, Cockerham RS, Wilcox WD, Walravens PA. Thyroid hormone replacement and growth of children with subclinical hypothyroidism and diabetes. *Diabet Med* 1990;7:299–303
30. Cho YH, Craig ME, Hing S, et al. Microvascular complications assessment in adolescents with 2- to 5-yr duration of type 1 diabetes from 1990 to 2006. *Pediatr Diabetes* 2011;12:682–689
31. Haas L, Maryniuk M, Beck J, et al. National Standards for Diabetes Self-Management Education and Support. *Diabetes Care* 2014;37(Suppl.1):S144–S153
32. Wolpert HA, Atakov-Castillo A, Smith SA, Steil GM. Dietary fat acutely increases glucose concentrations and insulin requirements in patients with type 1 diabetes: implications for carbohydrate-based bolus dose calculation and intensive diabetes management. *Diabetes Care* 2013;36:810–816
33. Riddell MC, Perkins BA. Type 1 diabetes and vigorous exercise: applications of exercise

- physiology to patient management. *Can J Diabetes* 2006;30:63–71
34. Robertson K, Adolfsson P, Scheiner G, Hanas R, Riddell MC. Exercise in children and adolescents with diabetes. *Pediatr Diabetes* 2009;10(Suppl. 12):154–168
35. Galassetti P, Riddell MC. Exercise and type 1 diabetes (T1DM). In *Comprehensive Physiology*, John Wiley & Sons, Inc., 2013. Available from <http://onlinelibrary.wiley.com/doi/10.1002/cphy.c110040/abstract>. Accessed 27 March 2014
36. McMahan SK, Ferreira LD, Ratnam N, et al. Glucose requirements to maintain euglycemia after moderate-intensity afternoon exercise in adolescents with type 1 diabetes are increased in a biphasic manner. *J Clin Endocrinol Metab* 2007;92:963–968
37. Tsalikian E, Mauras N, Beck RW, et al.; Diabetes Research in Children Network DirecNet Study Group. Impact of exercise on overnight glycemic control in children with type 1 diabetes mellitus. *J Pediatr* 2005;147:528–534
38. Tsalikian E, Kollman C, Tamborlane WB, et al.; Diabetes Research in Children Network (DirecNet) Study Group. Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. *Diabetes Care* 2006;29:2200–2204
39. Taplin CE, Cobry E, Messer L, McFann K, Chase HP, Fiallo-Scharer R. Preventing post-exercise nocturnal hypoglycemia in children with type 1 diabetes. *J Pediatr* 2010;157:784–788.e1
40. U.S. Department of Health and Human Services. 2008 Physical Activity Guidelines for Americans [Internet], 2008. Available from <http://www.health.gov/PAGuidelines/guidelines>. Accessed 8 April 2014
41. Garber CE, Blissmer B, Deschenes MR, et al.; American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;43:1334–1359
42. American Diabetes Association. Standards of Medical Care in Diabetes—2014. *Diabetes Care* 2014;37(Suppl. 1):S14–S80
43. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–986
44. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *N Engl J Med* 2000;342:381–389
45. Martin CL, Albers J, Herman WH, et al.; DCCT/EDIC Research Group. Neuropathy among the diabetes control and complications trial cohort 8 years after trial completion. *Diabetes Care* 2006;29:340–344
46. Rovet JF, Ehrlich RM. The effect of hypoglycemic seizures on cognitive function in children with diabetes: a 7-year prospective study. *J Pediatr* 1999;134:503–506
47. Krolewski AS, Warram JH, Christlieb AR, Busick EJ, Kahn CR. The changing natural history of nephropathy in type 1 diabetes. *Am J Med* 1985;78:785–794
48. Kostraba JN, Dorman JS, Orchard TJ, et al. Contribution of diabetes duration before puberty to development of microvascular complications in IDDM subjects. *Diabetes Care* 1989;12:686–693
49. Cato MA, Mauras N, Ambrosino J, et al.; Diabetes Research in Children Network (DirecNet). Cognitive functioning in young children with type 1 diabetes. *J Int Neuropsychol Soc* 2014;20:238–247
50. Marzelli MJ, Mazaika PK, Barnea-Goraly N, et al.; Diabetes Research in Children Network (DirecNet). Neuroanatomical correlates of dysglycemia in young children with type 1 diabetes. *Diabetes* 2014;63:343–353
51. Donaghue KC, Fairchild JM, Craig ME, et al. Do all prepubertal years of diabetes duration contribute equally to diabetes complications? *Diabetes Care* 2003;26:1224–1229
52. Kirchoff BA, Lugar HM, Smith SE, et al. Hypoglycaemia-induced changes in regional brain volume and memory function. *Diabet Med* 2013;30:e151–e156
53. Barnea-Goraly N, Raman M, Mazaika P, et al.; Diabetes Research in Children Network (DirecNet). Alterations in white matter structure in young children with type 1 diabetes. *Diabetes Care* 2014;37:332–340
54. Kirkman MS, Briscoe VJ, Clark N, et al. Diabetes in older adults. *Diabetes Care* 2012;35:2650–2664
55. Miller KM, Beck RW, Bergenstal RM, et al.; T1D Exchange Clinic Network. Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D Exchange clinic registry participants. *Diabetes Care* 2013;36:2009–2014
56. Ziegler R, Heidtmann B, Hilgard D, Hofer S, Rosenbauer J, Holl R; DPV-Wiss-Initiative. Frequency of SMBG correlates with HbA1c and acute complications in children and adolescents with type 1 diabetes. *Pediatr Diabetes* 2011;12:11–17
57. Sacks DB, Arnold M, Bakris GL, et al.; National Academy of Clinical Biochemistry; Evidence-Based Laboratory Medicine Committee of the American Association for Clinical Chemistry. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Diabetes Care* 2011;34:e61–e99
58. Tamborlane WV, Beck RW, Bode BW, et al.; Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 2008;359:1464–1476
59. Yeh H-C, Brown TT, Maruthur N, et al. Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: a systematic review and meta-analysis. *Ann Intern Med* 2012;157:336–347
60. Bergenstal RM, Klonoff DC, Garg SK, et al.; ASPIRE In-Home Study Group. Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med* 2013;369:224–232
61. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405–412
62. Jovanović L, Savas H, Mehta M, Trujillo A, Pettitt DJ. Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy. *Diabetes Care* 2011;34:53–54
63. Nathan DM, Cleary PA, Backlund JY, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005;353:2643–2653
64. Rosenstock J, Dailey G, Massi-Benedetti M, Fritsche A, Lin Z, Salzman A. Reduced hypoglycemia risk with insulin glargine: a meta-analysis comparing insulin glargine with human NPH insulin in type 2 diabetes. *Diabetes Care* 2005;28:950–955
65. DeWitt DE, Dugdale DC. Using new insulin strategies in the outpatient treatment of diabetes: clinical applications. *JAMA* 2003;289:2265–2269
66. Bergenstal RM, Tamborlane WV, Ahmann A, et al.; STAR 3 Study Group. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med* 2010;363:311–320
67. Wood JR, Miller KM, Maahs DM, et al.; T1D Exchange Clinic Network. Most youth with type 1 diabetes in the T1D Exchange clinic registry do not meet American Diabetes Association or International Society for Pediatric and Adolescent Diabetes clinical guidelines. *Diabetes Care* 2013;36:2035–2037
68. Kmiotowicz Z. Insulin pumps improve control and reduce complications in children with type 1 diabetes. *BMJ* 2013;347:f5154
69. Phillip M, Battelino T, Atlas E, et al. Nocturnal glucose control with an artificial pancreas at a diabetes camp. *N Engl J Med* 2013;368:824–833
70. Peters AL, Laffel L (Eds.). *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook*. Alexandria, VA, American Diabetes Association, 2013
71. Gruessner AC. 2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Transplant Registry (IPTR). *Rev Diabet Stud* 2011;8:6–16
72. Fioretto P, Steffes MW, Sutherland DER, Goetz FC, Mauer M. Reversal of lesions of diabetic nephropathy after pancreas transplantation. *N Engl J Med* 1998;339:69–75
73. Gruessner RWG, Gruessner AC. Pancreas transplant alone: a procedure coming of age. *Diabetes Care* 2013;36:2440–2447
74. Barton FB, Rickels MR, Alejandro R, et al. Improvement in outcomes of clinical islet transplantation: 1999–2010. *Diabetes Care* 2012;35:1436–1445
75. Pagliuca FW, Melton DA. How to make a functional β -cell. *Development* 2013;140:2472–2483
76. Pepper AR, Gala-Lopez B, Ziff O, Shapiro AJ. Current status of clinical islet transplantation. *World J Transplant* 2013;3:48–53
77. Whitehouse F, Kruger DF, Fineman M, et al. A randomized study and open-label extension evaluating the long-term efficacy of pramlintide as an adjunct to insulin therapy

- in type 1 diabetes. *Diabetes Care* 2002;25:724–730
78. Ratner RE, Dickey R, Fineman M, et al. Amylin replacement with pramlintide as an adjunct to insulin therapy improves long-term glycaemic and weight control in type 1 diabetes mellitus: a 1-year, randomized controlled trial. *Diabet Med* 2004;21:1204–1212
79. Vella S, Buetow L, Royle P, Livingstone S, Colhoun HM, Petrie JR. The use of metformin in type 1 diabetes: a systematic review of efficacy. *Diabetologia* 2010;53:809–820
80. Hopkins D, Lawrence I, Mansell P, et al. Improved biomedical and psychological outcomes 1 year after structured education in flexible insulin therapy for people with type 1 diabetes: the U.K. DAFNE experience. *Diabetes Care* 2012;35:1638–1642
81. Seaquist ER, Anderson J, Childs B, et al. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and The Endocrine Society. *Diabetes Care* 2013;36:1384–1395
82. Cryer PE, Davis SN, Shamooh H. Hypoglycemia in diabetes. *Diabetes Care* 2003;26:1902–1912
83. Orchard TJ, Costacou T, Kretowski A, Nesto RW. Type 1 diabetes and coronary artery disease. *Diabetes Care* 2006;29:2528–2538
84. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 2009;32:1335–1343
85. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 7 November 2013 [Epub ahead of print]
86. Cleary PA, Orchard TJ, Genuth S, et al.; DCCT/EDIC Research Group. The effect of intensive glycaemic treatment on coronary artery calcification in type 1 diabetic participants of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study. *Diabetes* 2006;55:3556–3565
87. Collins R, Armitage J, Parish S, Sleight P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 2003;361:2005–2016
88. Gunton JE, Morris J, Boyce S, Kelso I, McElduff A. Outcome of pregnancy complicated by pre-gestational diabetes—improvement in outcomes. *Aust N Z J Obstet Gynaecol* 2002;42:478–481
89. Jensen DM, Damm P, Moelsted-Pedersen L, et al. Outcomes in type 1 diabetic pregnancies: a nationwide, population-based study. *Diabetes Care* 2004;27:2819–2823
90. Steel JM, Johnstone FD, Hepburn DA, Smith AF. Can prepregnancy care of diabetic women reduce the risk of abnormal babies? *BMJ* 1990;301:1070–1074
91. Willhoite MB, Bennert HW Jr, Palomaki GE, et al. The impact of preconception counseling on pregnancy outcomes. The experience of the Maine Diabetes in Pregnancy Program. *Diabetes Care* 1993;16:450–455
92. Kitzmiller JL, Gavin LA, Gin GD, Jovanovic-Peterson L, Main EK, Zigrang WD. Preconception care of diabetes: glycemic control prevents congenital anomalies. *JAMA* 1991;265:731–736
93. McElvy SS, Miodovnik M, Rosenn B, et al. A focused preconceptional and early pregnancy program in women with type 1 diabetes reduces perinatal mortality and malformation rates to general population levels. *J Matern Fetal Med* 2000;9:14–20
94. Ray JG, O'Brien TE, Chan WS. Preconception care and the risk of congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis. *QJM* 2001;94:435–444
95. Evers IM, de Valk HW, Visser GHA. Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in the Netherlands. *BMJ* 2004;328:915
96. Wahabi HA, Alzeidan RA, Bawazeer GA, Alansari LA, Esmaeil SA. Preconception care for diabetic women for improving maternal and fetal outcomes: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2010;10:63
97. Murphy HR, Roland JM, Skinner TC, et al. Effectiveness of a regional prepregnancy care program in women with type 1 and type 2 diabetes: benefits beyond glycaemic control. *Diabetes Care* 2010;33:2514–2520
98. Jonasson JM, Brismar K, Sparén P, et al. Fertility in women with type 1 diabetes: a population-based cohort study in Sweden. *Diabetes Care* 2007;30:2271–2276
99. Snell-Bergeon JK, Dabelea D, Ogden LG, et al. Reproductive history and hormonal birth control use are associated with coronary calcium progression in women with type 1 diabetes mellitus. *J Clin Endocrinol Metab* 2008;93:2142–2148
100. Whitworth KW, Baird DD, Stene LC, Skjaerven R, Longnecker MP. Fecundability among women with type 1 and type 2 diabetes in the Norwegian Mother and Child Cohort Study. *Diabetologia* 2011;54:516–522
101. American Diabetes Association. *Medical Management of Type 1 Diabetes*. Alexandria, VA, American Diabetes Association, 2008
102. Garcia-Patterson A, Gich I, Amini SB, Catalano PM, de Leiva A, Corcoy R. Insulin requirements throughout pregnancy in women with type 1 diabetes mellitus: three changes of direction. *Diabetologia* 2010;53:446–451
103. Kitzmiller JL, Jovanovic L, Brown F, Coustan D, Reader DM (Eds.). *Managing Preexisting Diabetes and Pregnancy: Technical Reviews and Consensus Recommendations for Care*. Alexandria, VA, American Diabetes Association, 2008
104. Kitzmiller JL, Block JM, Brown FM, et al. Managing preexisting diabetes for pregnancy: summary of evidence and consensus recommendations for care. *Diabetes Care* 2008;31:1060–1079
105. Perros P, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. *Diabet Med* 1995;12:622–627
106. American Diabetes Association. Diabetes care in the school and day care setting. *Diabetes Care* 2006;29(Suppl. 1):S49–S55
107. American Diabetes Association. Diabetes management at camps for children with diabetes. *Diabetes Care* 2012;35(Suppl. 1):S72–S75
108. American Diabetes Association. Diabetes and employment. *Diabetes Care* 2011;34(Suppl. 1):S82–S86