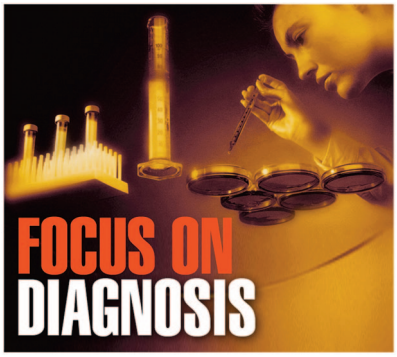
Focus on Diagnosis : Type 2 Diabetes Mellitus

Kristi M. Cowell

Pediatrics in Review 2008;29;289
DOI: 10.1542/pir.29-8-289



Author Disclosure
Dr Cowell has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Type 2 Diabetes Mellitus

Kristi M. Cowell, MD*

Introduction

Type 2 diabetes mellitus is a disease characterized by insulin resistance and a relative insulin deficiency leading to chronic hyperglycemia. With the increase in sedentary lifestyle and obesity among children and adolescents, the incidence of type 2 diabetes has risen dramatically in the last decade.

Diagnosis and management of type 2 diabetes in children can be particularly challenging. Unfortunately, few large, long-term studies of type 2 diabetes in children exist. Many of the current recommendations for children are extrapolated from adult studies. Additionally, type 2 diabetes often evolves from years of progressively increasing insulin resistance without hyperglycemia, which can make the distinction between type 2 diabetes and insulin resistance conditions difficult and somewhat arbitrary. Patients may meet diagnostic criteria for type 2 diabetes by one test method and yet have normal results or "prediabetes" by another test method performed during the same time period. Fortunately, this distinction does not affect management recommendations significantly, which are the same for children who have "diet-controlled" type 2 diabetes, have "prediabetes," or are "at high risk" for these conditions. Finally, children may have a form of diabetes mellitus that has features of both type 1 and type 2 disease, so-called "mixed diabetes" or "double diabetes."

*Resident in Medicine & Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, NY.

Clinical Presentation

Diabetes mellitus and hyperglycemia can present with polyuria, polydipsia, polyphagia, nocturia, enuresis, weight loss, or vaginal candidiasis, but many children who have type 2 diabetes are asymptomatic. Although most commonly associated with type 1 diabetes, diabetic ketoacidosis is the presenting symptom in 5% to 25% of adolescents who have type 2 diabetes.

Inherited and acquired risk factors predispose children to type 2 diabetes. Obesity (particularly abdominal obesity), family history of type 2 diabetes, racial/ethnic background, puberty, and the presence of a condition associated with insulin resistance should prompt the pediatrician to consider the child's risk for developing type 2 diabetes. Conditions associated with insulin resistance include hypertension, dyslipidemia, polycystic ovarian syndrome (PCOS), and acanthosis nigricans (Figure). Low-birthweight infants, especially those who later develop a high prepubertal weight, and infants born to mothers who have gestational diabetes also have a higher incidence of type 2 diabetes.

Screening

The American Diabetes Association recommends screening children who are at high risk for developing type 2 diabetes. High-risk children are overweight (body mass index ≥85th percentile for age and sex, weight-for-height >85th percentile, or weight >120% of ideal for height) and have at least two other risk factors for diabetes (Table 1). Screening, preferably by measuring a fasting blood glucose (FBG) concentration, should begin at age 10 years or at the onset of puberty, whichever comes first,

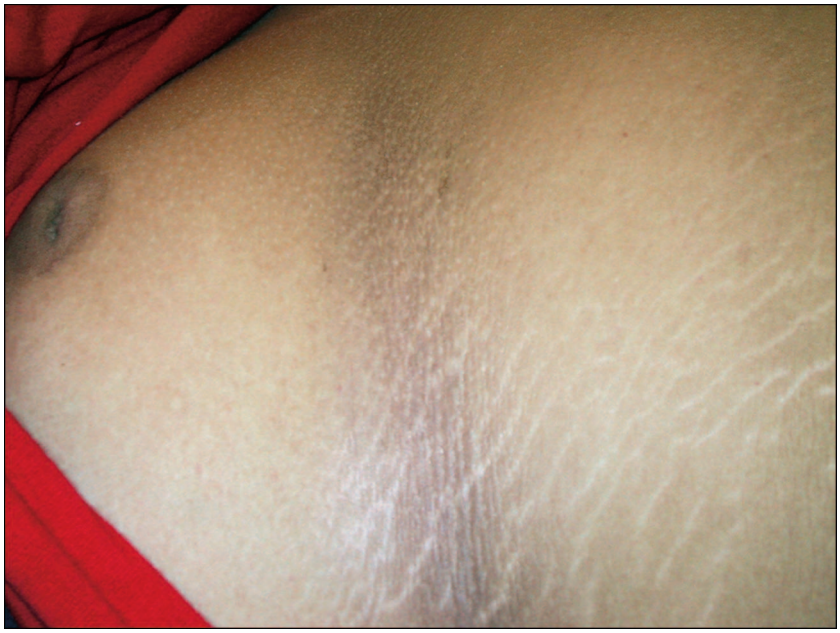


Figure. Acanthosis nigricans in the axilla. Other common sites for this pigmentation are the neck and the groin. Courtesy of Doernbecher Children's Hospital, Portland, Ore.

and should be repeated every 2 years thereafter.

Diabetes mellitus can be screened for and diagnosed by one of three methods: random blood glucose testing, measuring FBG concentration, or performing an oral glucose tolerance test (OGTT) (Table 2). An abnormal screening test result should prompt the clinician to repeat the same test or perform another test to confirm the diagnosis. The number of abnormal results required for diagnosis also hinges on the presence or absence of hyperglycemic symptoms.

During an OGTT, the patient should have at least 3 days of an unrestricted diet (usually more than 150 g/d carbohydrate for adults) and unlimited activity followed by an 8- to 14-hour overnight fast before the test. After the fasting period, the patient consumes 1.75 g/kg (maximum 75 g) of a glucose drink. Often, blood glucose is measured before the drink (fasting) and at 1 and 2 hours after drinking the glucose.

Patients who have no symptoms of hyperglycemia (ie, those being screened) and have an FBG result of 126.0 mg/dL (7.0 mmol/L) or greater or a 2-hour OGTT result of 200.0 mg/dL (11.1 mmol/L) or greater should have the test repeated to confirm the diagnosis of diabetes. An FBG value between 100.0 and 125.0 mg/dL (5.6 and 7.0 mmol/L) on two separate occasions indicates impaired fasting glucose (IFG). A 2-hour OGTT blood glucose value between 140.0 and 199.0 mg/dL (7.8 and 11.0 mmol/L) on two separate occasions indicates impaired glucose tolerance (IGT). IFG and IGT, also termed "prediabetes," indicate a higher risk for future type 2 diabetes in children and adults, especially if a child has a higher degree of obesity and if his or her body mass index increases.

Glycohemoglobin (also termed hemoglobin A1C) currently is not recommended for screening or diagnostic purposes due to lack of standardization between laboratories and inaccuracy when alterations in hemoglobin are present.

These test methods and criteria are not ideal. Although an FBG is the preferred diagnostic test because it is more convenient, less expensive, and less invasive than an OGTT, it is not as sensitive as an OGTT. In fact, 30% of adults diagnosed as having type 2 diabetes by OGTT have nondiagnostic FBG results. Another challenge is that the diagnostic cutoffs for FPG and OGTT are based on the risk of developing complications due to diabetes in adult studies; it is not clear that such cutoffs are applicable to children. The evidence for using

Table 1. Screening for Type 2 Diabetes in Children*

High-risk Criteria

Overweight (body mass index ≥85th percentile for age and sex, weight-for-height >85th percentile, or weight >120% of ideal for height) AND two other risk factors present:

- Family history of type 2 diabetes in a first- or second-degree relative
- High-risk racial/ethnic background (American Indian, Asian/Pacific Islander, African American, or Latino)
- Presence of a condition associated with insulin resistance (acanthosis nigricans, polycystic ovarian syndrome, hypertension, or dyslipidemia)
- Maternal history of gestational diabetes or diabetes

*Table constructed from data in American Diabetes Association. Standards of medical care in diabetes, 2008. *Diabetes Care*. 2008;31:S12-S54.

Table 2. Screening and Diagnostic Tests for Diabetes Mellitus (DM)*†

Random Blood Glucose
≥200 mg/dL (11.1 mmol/L)=DM
Fasting Blood Glucose (After 8 Hours of Fasting)
≥126 mg/dL (7.0 mmol/L)=DM
100 to 125 mg/dL (5.6 to 6.9 mmol/L)=Impaired Fasting Glucose (IFG)
Oral Glucose Tolerance Test (Blood Glucose Measurement 2 Hours After 1.75 g/kg [maximum, 75 g] Glucose Load)
≥200 mg/dL (11.1 mmol/L)=DM
140 to 199 mg/dL (7.8 to 11.0 mmol/L)=Impaired Glucose Tolerance (IGT)

*Any abnormal test result in the absence of hyperglycemic symptoms should be repeated before DM, IFG, or IGT is diagnosed.
†Table constructed from data in American Diabetes Association. Standards of medical care in diabetes, 2008. *Diabetes Care*. 2008;31:S12-S54.

1.75 g/kg glucose in an OGTT is not strong.

Differentiating Types of Diabetes

The most difficult challenge for pediatricians faced with a child who has hyperglycemia is differentiating between type 1 and type 2 diabetes. Some experts attempt to make the distinction based on the presence of risk factors for type 2 diabetes and clinical presentation (type 2 diabetes being less severe). Other experts suggest that even typical cases of type 2 diabetes be confirmed with an assessment of insulin resistance (fasting c-peptide, fasting insulin, or homeostasis model assessment of insulin resistance). Unfortunately, these measures have not been standardized to distinguish clearly between type 1 and type 2 diabetes and may give abnormal results for children whose pathophysiology is mixed. Even pancreatic (islet) autoantibodies, such as glutamic acid decarboxylase, insulin, islet cell cytoplasm, or tyrosine phosphatase autoantibodies, often found in type 1 diabetes, may be present in patients who have type 2 diabetes and, therefore, are not specific tests.

Types 1 and 2 are not the only forms of diabetes. Maturity-onset diabetes of youth, also called monogenic diabetes, is a type of diabetes associated with mutations of the glucokinase genes and hepatocyte nuclear factor-1-alpha and -4-alpha genes. This form of diabetes is more prevalent than type 2 diabetes (but less prevalent than type 1 diabetes) in non-Latino whites. Other forms and variants of diabetes occur in association with other conditions such as cystic fibrosis, hereditary hemochromatosis, chronic pancreatitis, Cushing syndrome, medication use (eg, glucocorticosteroids, human immunodeficiency virus protease inhibitors, cyclosporine), and mutations of mitochondrial DNA.

Treatment

The primary treatment for type 2 diabetes is education and lifestyle modification, specifically diet, exercise, and weight loss. Negotiating specific goals with the child and family as well as referring them for nutritional counseling are often helpful. If a trial of lifestyle modification is unsuccessful, metformin (the only oral hypoglycemic agent approved for use in children at this time) may be considered. Insulin also can be used for treatment, especially when children present with diabetic ketoacidosis. However, it is not used often as a first- or second-line agent because of the risk of hypoglycemia and weight gain. The thiazolidinedione class of oral hypoglycemic agents has not been approved for use in children and adolescents and should be prescribed with caution, given recent evidence of increased risks of cardiovascular disease with rosiglitazone in adults. Lifestyle modification is the cornerstone of treatment and should continue to be emphasized, even when other medical therapies are instituted.

Referral to a pediatric endocrinologist depends on the pediatrician's confidence with the diagnosis and management of this condition. Pediatricians should be able to treat the child who has clear type 2 diabetes and requires only education, lifestyle modification, and monitoring. Some pediatricians may refer a child if lifestyle modification alone is unsuccessful, but many are comfortable adding metformin to the treatment. A child should be referred to an endocrinologist if type 1 or "mixed" diabetes is considered or if hyperglycemia cannot be controlled.

Conclusion

The incidence of type 2 diabetes in adolescents is increasing. Clinicians caring for children should consider screening high-risk youth and know how to interpret different screening and diagnostic test results. In doing so, they can monitor and provide education on changes in diet, exercise, and weight to reduce the risk of complications associated with type 2 diabetes.

ACKNOWLEDGMENTS. The author wishes to thank Drs Craig Or-

lowski, John Chamberlain, and Steve Cook for their input.

Suggested Reading

Alberti G, Zimmet P, Shaw J, Bloomgarden Z, Kaufman F, Silink M. Type 2 diabetes in the young: the evolving epidemic. *Diabetes Care*. 2004;27:1798–1811

American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2008;31:S55–S60

American Diabetes Association. Standards of medical care in diabetes—2008. *Diabetes Care*. 2008;31:S12–S54

American Diabetes Association. Type 2 diabetes in children and adolescents (consensus statement). *Diabetes Care*. 2000; 23:381–389

Aye T, Levitsky LL. Type 2 diabetes: an epidemic disease in childhood. *Curr Opin Pediatr*. 2003;15:411–415

Gungor N, Hannon T, Libman I, Bacha F, Arslanian S. Type 2 diabetes mellitus in youth: the complete picture to date. *Pediatr Clin North Am*. 2005;52: 1579–1609

Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG. Prevalence and determinants of insulin resistance among US adolescents. *Diabetes Care*. 2006;29: 2427–2432

The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care*. 2003; 26:3160–3167

The Writing Group for the SEARCH for Diabetes in Youth Study Group. Incidence of diabetes in youth in the United States. *JAMA*. 2007;297:2716–2724

In Brief

International Adoption

Fatimah Dawood, MD
Johns Hopkins University School of Medicine
Baltimore, Md.

Author Disclosure

Drs Dawood and Serwint have disclosed no financial relationships relevant to this In Brief. This commentary does not contain a discussion of an unapproved/ investigative use of a commercial product/device.

Medical Evaluation of Internationally Adopted Children for Infectious Diseases. American Academy of Pediatrics. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, Ill: American Academy of Pediatrics; 2006:182–183

Health Care in the First Year after International Adoption. Schulte EE, Springer SH. *Pediatr Clin North Am.* 2005;52:1331–1350

Immediate Behavioral and Developmentally Adopted Children Transitioning to Families. Miller LC. *Pediatr Clin North Am.* 2005;52:1311–1330

Preadoption Opportunities for Pediatric Providers. Chambers J. *Pediatr Clin North Am.* 2005;52:1247–1270

The number of children adopted from foreign countries into the United States has tripled over the last 15 years, with approximately 7,000 and 21,000 adoptees entering the United States in 1990 and 2006, respectively. The demographics of international adoptions during this time also have shifted. In 1990, Korea sent the largest number of children to the United States. Most of these Korean children were born to single, young mothers and put up for adoption, accompanied by at least some information about family and prenatal health. In addition, many of these children were cared for in American-style foster homes prior to adoption. By 2006, most international adoptees came from China, Russia, and Guatemala. In contrast to the Korean adoptees of the early 1990s, children adopted from China and Russia are more likely to have been abandoned or removed from the home. In China, the adoptees more commonly are girls because of the one-child policy and cultural preference for males. Russian adoptees are more likely to have been removed from the home because of concerns about child abuse and neglect, maternal mental illness, or maternal substance abuse. In instances of abandonment, often little is known about the child's pre- and postnatal health history or family health history.

The circumstances leading to international adoption suggest some of the unique challenges facing pediatricians who care for this patient population. Some children may be adopted with little or no information about their medical histories, including their immunization status. When medical records are available, they may be written in a foreign language; when translated, they still may contain medical terminology that has no clear analogous English term or may be used in a context that is unfamiliar to American clinicians.

The circumstances under which international adoptees are born as well as the conditions in which they live prior to their adoption may place them at risk for certain medical problems. In

Focus on Diagnosis : Type 2 Diabetes Mellitus

Kristi M. Cowell

Pediatrics in Review 2008;29;289
DOI: 10.1542/pir.29-8-289