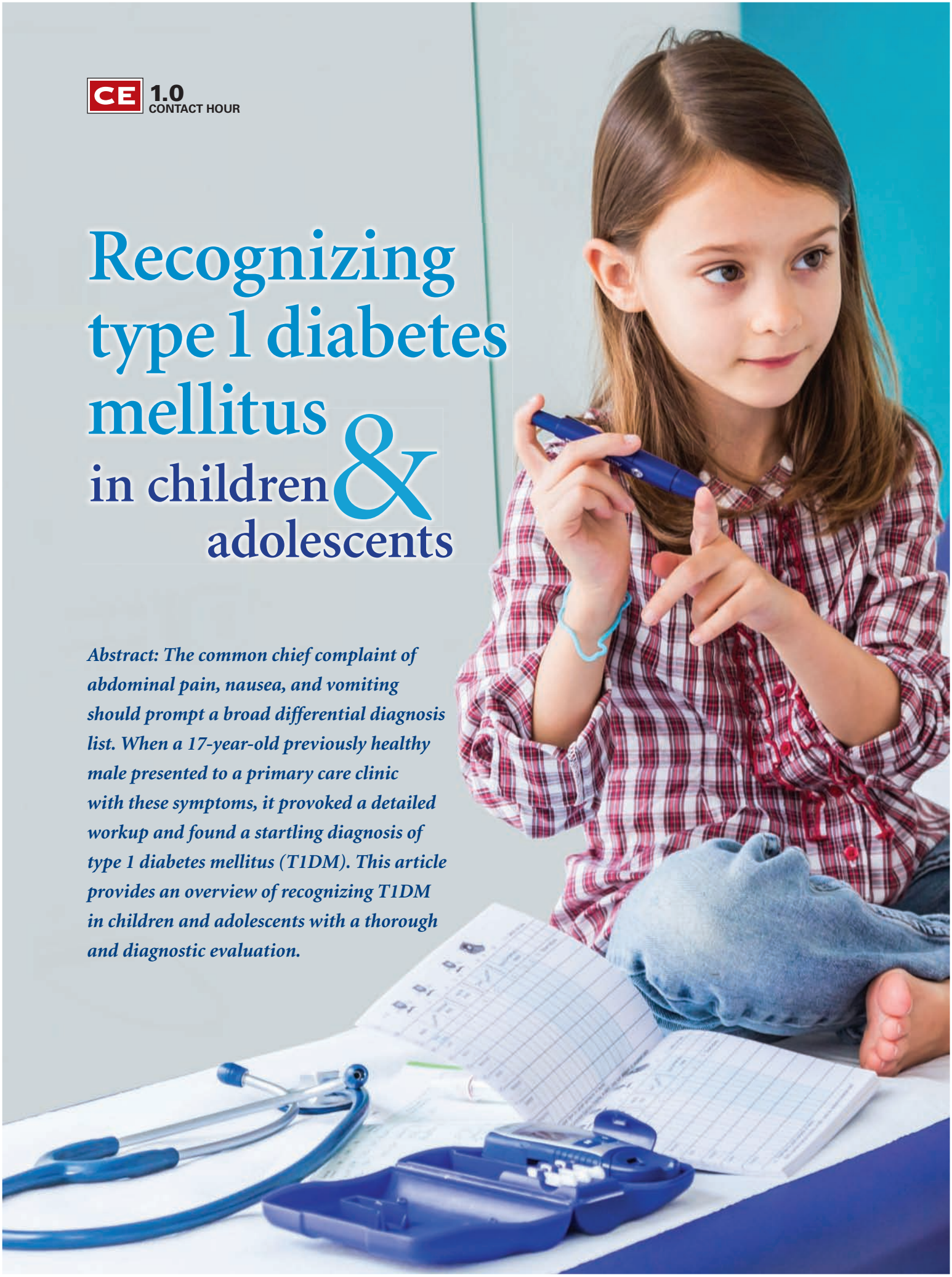
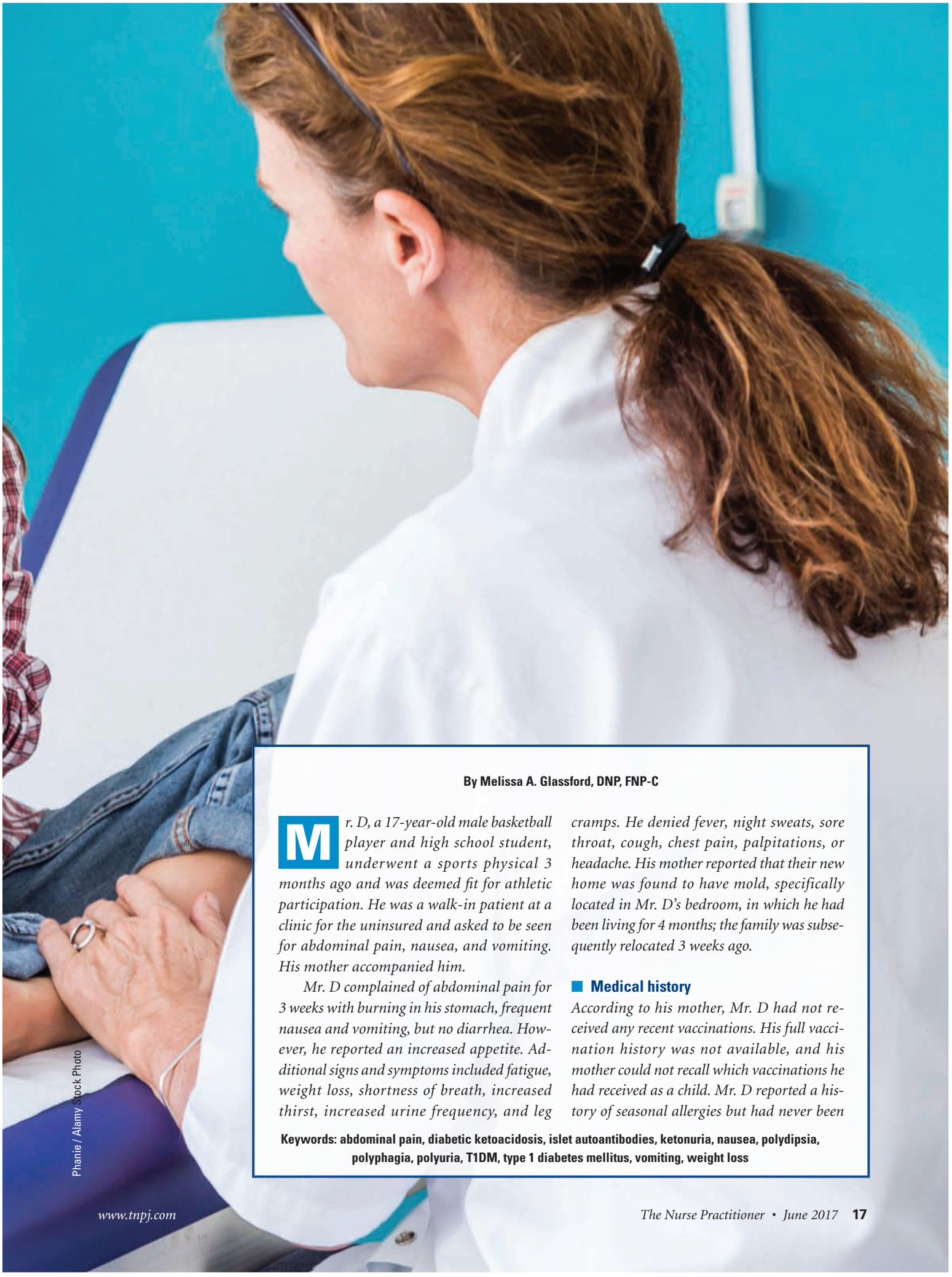
CE 1.0 CONTACT HOUR

Recognizing type 1 diabetes mellitus & in children adolescents

Abstract: The common chief complaint of abdominal pain, nausea, and vomiting should prompt a broad differential diagnosis list. When a 17-year-old previously healthy male presented to a primary care clinic with these symptoms, it provoked a detailed workup and found a startling diagnosis of type 1 diabetes mellitus (T1DM). This article provides an overview of recognizing T1DM in children and adolescents with a thorough and diagnostic evaluation.





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By Melissa A. Glassford, DNP, FNP-C

Mr. D, a 17-year-old male basketball player and high school student, underwent a sports physical 3 months ago and was deemed fit for athletic participation. He was a walk-in patient at a clinic for the uninsured and asked to be seen for abdominal pain, nausea, and vomiting. His mother accompanied him.

Mr. D complained of abdominal pain for 3 weeks with burning in his stomach, frequent nausea and vomiting, but no diarrhea. However, he reported an increased appetite. Additional signs and symptoms included fatigue, weight loss, shortness of breath, increased thirst, increased urine frequency, and leg cramps. He denied fever, night sweats, sore throat, cough, chest pain, palpitations, or headache. His mother reported that their new home was found to have mold, specifically located in Mr. D's bedroom, in which he had been living for 4 months; the family was subsequently relocated 3 weeks ago.

Medical history

According to his mother, Mr. D had not received any recent vaccinations. His full vaccination history was not available, and his mother could not recall which vaccinations he had received as a child. Mr. D reported a history of seasonal allergies but had never been

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clinically tested. He had not had any recent illnesses prior to his sudden onset of nausea and vomiting. Mr. D's exposure to mold occurred over a 4-month period. He denied any recent tick bite of which he was aware, smoking, or alcohol use. Family history included a paternal uncle with type 1 diabetes mellitus (T1DM).

Physical exam

Mr. D was a pleasant and engaging teen who appeared fatigued, pale, and thin. His vital signs were: temperature, 99.5° F (37.5° C); pulse, 98; respiratory rate, 16; BP, 115/68 mm Hg; and oxygen saturation, 99% on room air. Mr. D was 6 ft 4 in and weighed 129.1 lb (58.6 kg) with a body mass index (BMI) of 15.8. His ears were clear with a positive light reflex and his pupils were equal and reactive to light, both direct and consensual. Mr. D's sclera was white and conjunctiva clear, his fundi were normal with sharp disk margins, and he had no hemorrhages or papilledema.

Mr. D's oral mucosa was pink with dry mucous membranes, and his thyroid was barely palpable and without nodules. There were no palpable preauricular, postauricular, occipital, tonsillar, submandibular, cervical, or supraclavicular lymph nodes. His chest was symmetrical with a normal anterior/posterior diameter, and his respirations were nonlabored. Mr. D's lungs were clear to auscultation, and he had a regular heart rate and rhythm with a crisp S1 and S2 without murmurs or extra sounds.

The presence of DKA at onset is associated with poor long-term glycemic regulation and beta cell function.

Mr. D's apical pulse was at the 5th intercostal margin, midclavicular line. His abdomen was soft and nontender with normal active bowel sounds; no rebound tenderness or guarding was present. There was no palpable hepatosplenomegaly. Mr. D did not have any rashes or petechiae. Cranial nerves 2 to 12 were intact, and his patellar reflexes were 2+.

Assessment

Due to Mr. D's symptoms of weight loss, polyuria, and polydipsia, a capillary blood glucose level was obtained. Results revealed a blood glucose level of 285 mg/dL. He reported eating an energy bar and an apple for breakfast approximately 2 hours prior. Mr. D was sent for lab work and a urinalysis; a complete blood cell count and thyroid-stimulating hormone level were within normal limits.

A complete metabolic panel was normal except for the blood glucose, which was elevated with a value of 370 mg/dL; chloride was low at 95 mEq/L, and the anion gap was high at 16.5. Hemoglobin A1C was elevated at 17.3%, which indicated a 3-month average blood glucose of 450 mg/dL. Urinalysis revealed ketones of 40 mg/dL and glucose over 1,000 mg/dL (but negative for protein).

Diagnosis and treatment

Mr. D was diagnosed with T1DM based on his blood glucose level, hemoglobin A1C, and clinical presentation. Additional lab testing for pancreatic autoantibodies would further confirm the diagnosis.

After consultation with a pediatric endocrinologist, Mr. D was admitted to a local children's hospital through the ED. He was given I.V. fluids and started on insulin therapy (see Overview of insulin therapy*).*[1,2]

Prevalence of T1DM

T1DM is a chronic autoimmune disease that results in the destruction of insulin-producing beta cells from the pancreas.[3] It is one of the most common chronic conditions diagnosed in children.[4,5] Roughly 18,000 new diagnoses of T1DM are made annually.[6] Despite widespread knowledge of the typical clinical presentation, approximately 33% of patients are diagnosed in diabetic ketoacidosis (DKA).[7-9]

Younger children, those without medical insurance, and ethnic minorities are at greater risk for DKA with new-onset T1DM.[10] One study found that 50% of uninsured children presented with severe DKA compared with 30% of insured children.[11] The presence of DKA at onset is associated with poor long-term glycemic regulation and beta cell function, which makes prompt recognition of symptoms, early diagnosis, and referral to specialty care essential to improving disease outcomes.[12]

The prevalence of T1DM is increasing in the United States among all racial and ethnic groups.[6] The etiology of this increase is not known, but multiple hypotheses exist. Examples range from a viral illness triggering an autoimmune process that destroys beta cell function to the hygiene hypothesis or the synergistic effect of multiple factors.[13-15] The hygiene hypothesis postulates that the rise in allergic and autoimmune diseases in developed countries is a result of the decrease in infectious disease. Antibiotics, vaccination, and improved hygiene have all contributed to this. T1DM, along with other immune-mediated diseases such as Crohn and multiple sclerosis, is considered a part of this process.

Overview of insulin therapy[1,2]

Insulin preparations	Description	Types
Bolus insulins	• Given as premeal bolus • Based on carbohydrate count and blood glucose level	Rapid acting Short acting
Basal insulins	• Long duration of action • Given 1 to 2 times a day	Long acting

Insulin delivery	Advantages	Disadvantages
Needle and syringe	• NPH and rapid-acting insulins can be mixed, decreasing the number of injections	Needles are typically larger bore
Pen	• Ease of use and portability	Insulin pens are generally more expensive than needles, syringes and insulin vials
Pump	• Basal insulin provided through continuous infusion • Studies show insulin pump therapy improves glycemic control • Reduction in severe hypoglycemia	High cost

American Diabetes Association (ADA) recommendations:

- Most patients with T1DM should be treated with multiple daily injections of prandial insulin and basal insulin or continuous subcutaneous insulin infusion.
- Most patients with T1DM should use rapid-acting insulin analogues to reduce the risk of hypoglycemia.
- Educate patients with T1DM on matching prandial insulin doses to carbohydrate intake, premeal blood glucose levels, and their anticipated physical activity.
- Patients with T1DM who have been successfully using continuous subcutaneous insulin infusion should have continued access to this therapy after age 65.

The genetic susceptibility of T1DM has been confirmed by multiple studies. It is known as a polygenic disorder, with prior studies finding over 40 genes associated with susceptibility to developing the disease along with environmental triggers, such as viral infection.[16-18] A key gene variation associated with more than 50% of the genetic risk has been found on the major histocompatibility complex of chromosome 6.[3] Further research is emerging that will likely support screening high-risk individuals for islet autoantibodies and provide an opportunity for surveillance and earlier identification of symptoms, thereby reducing DKA at diagnosis.[18]

Assessment of T1DM

The most common presenting signs and symptoms in T1DM include polyuria, polydipsia, and weight loss.[19] Common complaints seen in primary care (such as abdominal pain or nausea) can also be symptoms of hyperglycemia. In children under age 6 years, particularly prior to toilet training, symptoms of diabetes mellitus can be subtle. Providers should pay close attention to the presence of candidiasis as an early symptom of new-onset diabetes mellitus.[20]

Enuresis is another age-dependent symptom that is often the earliest symptom of school-age children with new-onset T1DM.[20] In addition, young children are often in critical condition at the time of diagnosis, highlighting the importance of early recognition of hyperglycemia.[21] Some research has found that age at presentation is a main risk factor for delayed diagnosis, with children under age 2 years being most vulnerable.[10,22] Furthermore, nonspecific symptoms such as constipation, recurrent infections, or fatigue can be attributed to other etiologies, so the connection to hyperglycemia is often overlooked.

Differential diagnoses with a clinical presentation of nausea and vomiting would likely begin with evaluating possible gastrointestinal causes. For any female patient of childbearing age with symptoms of nausea and vomiting, pregnancy should be considered first. Common inflammatory or infectious etiologies include gastroesophageal reflux, appendicitis, foodborne illness, cholecystitis, pancreatitis, peptic ulcer disease, and irritable bowel syndrome.[23,24] Additional differentials could include overdoses or withdrawal, psychogenic vomiting, eating disorders, celiac

disease, cyclic vomiting syndrome, migraines, thyroid dysfunction, and malignancy.[24,25]

Diagnostic tests and referrals

A diabetes diagnosis can be made based on hemoglobin A1C measurement or plasma glucose criteria.[26] Distinguishing T1DM and type 2 diabetes (T2DM) is initially based on the clinical features of body habitus, age, and family history. In patients with T1DM, 35% to 50% are overweight or obese.[6] This compares with roughly 80% of children and adolescents with T2DM who are overweight or obese.[27]

However, children and adolescents who appear more phenotypically associated with T2DM may still have islet autoantibodies suggesting T1DM.[28] These findings suggest that weight and BMI alone cannot be used to accurately differentiate T1DM versus T2DM diabetes in children and adolescents. Age can lead the clinician to suspect T1DM because it represents the majority of cases diagnosed in childhood; however, T2DM is steadily on the rise.[6]

The etiologic classification of diabetes mellitus can be further elucidated with discovering autoimmunity. Cell-mediated autoimmune destruction of pancreatic islet beta cells can be detected through autoantibody testing. A panel of serum biomarkers can identify the majority of T1DM cases. The five main markers for T1DM are islet cell autoantibodies, antibodies to insulin, glutamic acid decarboxylase, protein tyrosine phosphatase, and zinc transporter 8.[29]

The ADA defines T1DM as the presence of one or more autoantibodies.[26] However, approximately 2% to 5% of children with T1DM will not carry detectable islet autoantibodies. In one study, children (prior to diagnosis) with the presence of two or more islet autoantibodies were found to have a conversion rate to T1DM of 69.7%, whereas children with one autoantibody had a conversion rate of 14.5%.[30] This highlights some of the current challenges in the diagnosis of T1DM.

Population-based screening to detect individuals with a susceptibility to T1DM in the presymptomatic stage is a current area of study. This allows for early intervention and monitoring with an end goal of more favorable long-term outcomes, beta cell preservation, and a decrease in ketoacidosis. Raab and colleagues conducted a screening for the presence of islet autoantibodies in Bavaria, Germany.[31] Of the 26,760 children screened, only 105 (0.39%) had two or more islet autoantibodies indicative of pre-T1DM. None of the children diagnosed with T1DM had gone on to develop DKA, which is associated with increased mortality and longer hospitalization.[31]

A diagnosis of T1DM

The initial period after diagnosis is a critical time for the patient and family to absorb and comprehend the complexity of the chronic disease. Intensive outpatient management versus hospitalization does not appear to be unfavorable to

Key management points for children and adolescents with T1DM[28,33]

Care should be provided by a multidisciplinary team of specialists trained in pediatric diabetes.

Care should be developmentally appropriate and culturally sensitive.

- Incorporate a model of shared decision-making to promote self-efficacy and increase adherence.
- Pay attention to weight and body image concerns.
- Negotiate parent/family roles in the adolescent's diabetes management.
- Provide education for the adolescent and parents to recognize signs of depression, eating disorders, and risky behaviors.

Screen for psychosocial distress and mental health problems.

- Provide appropriate referrals.
- Integrate mental health professionals into the treatment team.
- Assess the adolescent's distress, peer relationships, and school performance.
- Provide preconception counseling for all females of childbearing age.

Set a goal hemoglobin A1C level of <7.5% across all pediatric age groups.

- In setting glycemic targets, long-term health benefits must be weighed against risks of hypoglycemia and developmental burdens of children and adolescents.

Manage cardiovascular risk factors.

- Provide routine BP screening.
- Begin fasting lipid panel at age 10 years and then every 3 to 5 years (if normal).
- Assess smoking history (discourage smoking or offer smoking cessation guidance).
- Conduct an annual albuminuria screening beginning 5 years after diagnosis.
- Refer the patient for an annual dilated eye exam beginning at age 10 years or after puberty has started (whichever is earlier), once the child or adolescent has had T1DM for 3 to 5 years.
- Conduct an annual comprehensive foot exam beginning at age 10 years or at the start of puberty (whichever is sooner) and 5 years after diagnosis.

Consider screening for additional autoimmune conditions such as thyroid and celiac disease.

metabolic control, and hospital-based home care has been shown repeatedly to be an equally safe choice.[32] Regular follow-up, comprehensive patient and parent education, and referrals for nutrition therapy are key elements of disease management (see *Key management points for children and adolescents with T1DM*).[33] Age-appropriate interventions are essential for young patients to adjust to the complexities of the new diagnosis and need for comprehensive disease management strategies.[28]

Screening guidelines

Widespread screening for T1DM in asymptomatic individuals has not been recommended, as it would be of low yield.[26] In the absence of population-based screening, identifying individuals in the early stage of the disease process could have significant implications for preservation of beta cell function and subsequent complications. Multiple studies have referred relatives of individuals with T1DM for islet cell autoantibody testing to diagnose T1DM prior to symptom onset.

Participation in a prevention trial could identify patients with T1DM even prior to elevations in hemoglobin A1C level, allowing for a targeted surveillance and earlier intervention.[34] The ADA suggests referring relatives of individuals with T1DM to a prevention trial for islet cell autoantibody testing, diabetes education, and prevention of DKA.[26]

The NP's role

NPs in the primary care setting are well positioned to screen for and detect T1DM before patients become critically ill. This role has become far more important with the increasing demand for primary care providers and the shortage of primary care physicians. In light of this, NPs will be performing more annual wellness exams, sports physicals, and seeing children for acute complaints.

Obtaining a thorough family history can identify individuals who have a relative with T1DM and are at greater risk for developing the disease. The clinical clues for detecting T1DM can be subtle, with parents often attributing them to an alternate explanation.[35] Referring high-risk individuals with a positive family history for T1DM for islet cell autoantibody testing could help facilitate the early identification of T1DM symptoms and prompt quick interventions to prevent ketoacidosis. However, the ADA currently recommends this only in the setting of a clinical research study.[28]

This case study illustrates the importance of a thorough diagnostic evaluation. Rather than yielding to the obvious diagnosis of gastroenteritis, the associated symptoms of weight loss and fatigue led the examiner to think about the possibility of T1DM. Every effort should be made to detect the symptoms of hyperglycemia in children and adolescents and initiate prompt evaluation and referral when a diagnosis of T1DM is confirmed. NP

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Melissa A. Glassford is an instructor of nursing at the Nursing Family Nurse Practitioner Program at Vanderbilt University, Nashville, Tenn.

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Recognizing type 1 diabetes mellitus in children & adolescents

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