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Ohio Cardiovascular and Diabetes Health Collaborative

Youth-Onset Type 2 Diabetes:
How to Identify, Screen, and Treat

Contributing authors on behalf of Team Best Practices:
Anuradha Viswanathan, MD, Case Western Reserve University
Ryan Farrell, MD, Case Western Reserve University
Rose Gubitosi-Klug, MD, PhD, Case Western Reserve University

The recognition of youth-onset type 2 diabetes (T2D) parallels the rise in obesity among children.[1,2]

Youth-onset T2D has distinct features from both type 1 diabetes (T1D) in youth and T2D in adults (Table 1).[3,4] Identifying those children at highest risk for T2D may allow for better screening and earlier diagnosis and treatment.

This document highlights distinguishing characteristics of youth-onset T2D and identifies the most vulnerable patients that need to be screened. Also included is a review of treatment options, how to identify those patients at highest risk of requiring insulin, and discussion of the rapid development of complications in this population.

Youth-onset T2D leads to more rapid development of diabetes complications and requires early recognition and aggressive treatment from the time of diagnosis.

Table 1. Features of Type 1 Diabetes Compared to Youth-Onset Type 2 Diabetes

Features	Type 1 Diabetes	Youth-Onset Type 2 Diabetes
Race/Ethnicity	More common in Caucasians	80% of youth-onset T2D are racial and ethnic minorities
Sex	Equally common in females and males	More common in females
Body Habitus	Normal/underweight; no features of insulin resistance	Overweight or obese; features suggestive of insulin resistance such as acanthosis nigricans
Screening: (Symptoms: polyuria, polydipsia, nocturia, weight loss)	Symptomatic	Symptomatic, or at time of puberty or age 10 years, whichever is sooner, for at-risk racial and ethnic minorities
Diagnostic Testing	American Diabetes Association criteria: Fasting glucose (> 126 mg/dL), or two-hour glucose during an oral glucose tolerance test (> 200 mg/dL), or A1C (≥ 6.5%)	American Diabetes Association criteria, or presence of symptoms and random glucose > 200mg/dL A1C of 6.5% may not identify all youth with early T2D
Symptom-Onset	Rapid onset of symptoms; often present in ketoacidosis	Gradual onset of symptoms; occasional ketoacidosis
Pathophysiology: Autoimmunity	Autoimmunity present	Autoimmunity absent; should exclude type 1 diabetes with antibody testing
Pancreatic function	Insulin deficiency	Insulin resistance due to puberty as well as increased adiposity and stress; decreased exercise and sleep; and rapid beta cell failure
Family History	Family association with other autoimmune disorders, but may be only individual with type 1 diabetes in family	Strong family history of type 2 diabetes; in utero exposure to maternal gestational diabetes
Treatment Options	Managed with insulin	Lifestyle plus pharmacotherapy; rapidly progress to requiring insulin (> 50% by 2-5 years after diagnosis)[1]

Screening for Youth-Onset Type 2 Diabetes[4]

Identifying youth with T2D and starting treatment early is critical to prevent complications. By 2060, the relative rates of increase in T2D in children are projected to approach a near-equal distribution of T1D versus T2D in children over 20 years old. Much of this increase will disparately affect minority populations.[5] Consider screening with symptoms or high-risk features as described below:

- Symptomatic individuals with polyuria, polydipsia, nocturia, or enuresis should be screened.
- Overweight or obese individuals at the time of puberty or > 10 years of age with one or more additional risk factor:
  - Racial and ethnic minorities (Native American, African American, Latino/Latina, Asian American, Pacific Islander).
  - T2D in first- or second-degree relative.
  - Maternal history of gestational diabetes.
  - Physical exam or lab findings associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, small-for-gestational-age birth weight).

The Importance of Treatment

Several clinical trials of youth-onset T2D uncover an aggressive decline in beta cell function and early treatment failure of oral medications, which correlate with elevated glucose levels and rapid progression to complications including diabetic retinopathy, diabetic kidney disease, diabetic peripheral neuropathy, cardiovascular disease, and stroke while only in their mid-20s.[3] When treating youth-onset T2D, consider screening for obstructive sleep apnea, depression and anxiety, eating disorders, cognitive delays, and polycystic ovary syndrome.

Treatment begins at the time of diagnosis with lifestyle, psychosocial, and pharmacologic interventions.

Lifestyle Changes.

Diet and physical activity must play a role in treating T2D:

- Diet modifications include avoiding sugar-sweetened beverages, limiting portion sizes, minimizing processed carbohydrates, and increasing servings of vegetables and fruit.[6]
- Cardiovascular exercise should include 60 minutes of activity daily, with half at moderate to vigorous levels.[4]
  - One-fourth of females and one-third of males are successful in achieving better cardiovascular fitness, which is associated with better glycemic control.[6]

Psychosocial and Social Determinants of Health Assessment.

High rates of depression (~15%) and disordered eating (25% for both males and females), lower socioeconomic status, higher unemployment, food insecurity, and housing instability all negatively impact glycemic control.[4] Perform the following to assess psychosocial factors:

- Assess social barriers at each visit, and integrate social workers into care early as indicated.
- Screen for diabetes distress and assess mental health frequently and make a psychology/psychiatry referral as appropriate.
- Discuss preconception counseling given that 10% of females became pregnant over an average of 3.8 years in longitudinal studies.

Pharmacologic Interventions.

- ***Metformin.*** This is a first-line treatment due to cost, safety, and efficacy, indicated for children with newly diagnosed T2D based on American Diabetes Association (ADA) criteria, along with lifestyle changes. However, it does have limitations, and is important to consider the following:
  - High treatment failure rates (almost half within three years of starting treatment) are likely due to increased insulin resistance of puberty.
  - Lactic acidosis is incredibly rare in children. Hold in the situation of vomiting or IV contrast.
  - Half of the patients treated experience significant gastrointestinal adverse effects. Titrate the dose as tolerated (start with 500 mg daily and increase by 500 mg per day weekly until at 2,000 mg per day or the maximum tolerated dose).
  - A1C > 6.3% shortly after starting metformin predicts higher rates of treatment failure in youth on metformin monotherapy.[7] Rises in A1C beyond 6.5-7% may indicate the need for treatment escalation.
- ***Weekly Glucagon-Like Peptide 1 Agonists (GLP1a):***
  - *Exenatide (Bydureon).* In 2021, the FDA approved once-weekly exenatide for youth-onset T2D (ages 10 and up).[9]
    - A reduced A1C of -0.36% was seen (+0.49% in placebo) with trends of modest weight reduction (less than 1 kg).
    - Adverse effects were similar in frequency to placebo.
    - Gastrointestinal side effects were most common but did not lead to discontinuation in clinical trials.
  - *Dulaglutide (Trulicity).* In 2022, the FDA approved once-weekly dulaglutide for the treatment of youth-onset T2D (ages 10 and up).[10]
    - At 26 weeks of therapy, A1C was reduced by 0.6% and 0.9% for the 0.75 mg and 1.5 mg doses respectively. The placebo group had an increase in A1C of 0.6%.
    - Over half of patients had an A1C below 7% (compared to 14% in the placebo group).
    - The weight loss benefit is minimal (mean < 0.2 kg).
    - May cause vomiting (seen more often than placebo in clinical trials).

- ***Daily Glucagon-Like Peptide 1 Agonists (GLP1a):***
  - ***Liraglutide.*** In 2019, the U.S. Food and Drug Administration (FDA) approved liraglutide for youth with T2D (ages 10 and up).[8] It may serve as next-line therapy, demonstrating a mean A1C reduction of 0.64%. Nearly two-thirds of patients achieve A1C < 7%.

    Additional benefits and drawbacks include:
    - May preserve insulin production.
    - May help with weight loss.
    - Higher cost.
    - Injection may negatively affect adherence.
- ***Sodium-Glucose Transport Protein 2 Inhibitors (SGLT2i):***
  - ***Empagliflozin (Jardiance).*** In 2023, the FDA approved daily empagliflozin for youth-onset T2D (ages 10 and up).[11]
    - By 26 weeks on treatment, A1C dropped at least 0.5% or to < 7% in over half of individuals. By one year, this benefit was maintained in 40% of patients.
    - Patients should monitor for normoglycemic ketoacidosis and risk of dehydration.
    - Should be considered as early treatment option in those with coexisting diabetic kidney disease or in individuals at higher risk for kidney or cardiovascular disease.
- ***Insulin.*** Use as a rescue treatment if A1C rises to > 8-9% or fasting glucose is > 200-250 mg/dL.
  - May be able to start with basal insulin only (0.25-0.5 u/kg) but may require mealtime insulin if there is decompensation.
  - Youth presenting with decompensation/diabetic ketoacidosis may require insulin initially, with the chance to wean off it rapidly once the condition is stabilized and metformin is initiated.

Other medications (e.g., sulfonylureas and dipeptidyl peptidase 4 inhibitors [DPP4i]) are not FDA-approved for youth-onset T2D. Ongoing studies will likely result in the approval of additional treatments in the future.

Patient Monitoring: Frequency and Referral

Youth with T2D require frequent clinic follow-up and recommended monitoring for comorbidities and complications.

	At Diagnosis	Quarterly	Annually
A1C (with target less than 7%)		X	
Blood Pressure		X	
Liver Function Test			X
Lipid Profile			X
Urine Albumin			X
Glomerular Filtration Rate (hyperfiltration followed by rapidly declining filtration)			X
Eye Exam	X		X
Foot Exam			X
Psych Comorbidities	X	X	X
Social Determinants of Health	X	X	X

If the patient is unable to reach target A1C < 7% within the first six months of care, referral to an endocrinologist is appropriate. Care may require additional support by a multi-disciplinary team that includes a certified diabetes care and education specialist, psychologist, dietitian, and social worker.

Also Consider and Exclude Maturity-Onset Diabetes of the Young

(Monogenic Diabetes)

Maturity-onset diabetes of the young (MODY) requires genetic testing to confirm the diagnosis based on clinical suspicion. Treatment and surveillance of MODY is specific to MODY type. Referral to a pediatric endocrinologist is recommended.

MODY has the following features:

- Heterogeneous group of disorders.
- Autosomal dominant inheritance (e.g., two and preferably three consecutive affected generations).
- More prevalent in Caucasians.
- Mostly normal body mass index – rising obesity rates may obscure the suspicion.
- Usually diagnosed before 25 years of age.
- 2-5% of individuals with youth-onset diabetes may have MODY.
- 65% of MODY cases are MODY 3.
- MODY 5 is associated with renal cysts or other renopelvic anomalies.
- MODY 2 may present with stable mild hyperglycemia that may not require aggressive treatment.

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