Guidelines for Monitoring and Education in Pre-Symptomatic T1D: Monitoring of Children

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Case

Mom of Kennedy, a 9-year-old female, recently watched an ad campaign suggesting that she screen herself and her family for T1D. There is autoimmune disease in the family, so mom ordered a T1D antibody test. Kennedy came back positive for two antibodies. Mom called the PCP, and PCP referred Kennedy to a pediatric endocrinologist. The endocrinology office gave Kennedy an appointment in 4 months. Mom is anxious and doesn’t want to wait 4 months. She did a web-dive and called EXPERTS for help determining next steps.
Evidence Based Monitoring Guidance

• There is a lack of published guidance on monitoring patients in early stages of T1D.
What are the steps we need to take to identify and care for individuals with Early Stages of T1D?

- Especially important in cases where only 1 antibody is positive
- Should not limit initiation of monitoring
- May be waived if testing in CLIA certified, high quality (IASP participant) lab with low false positives
Rule Out Clinical T1D

Assess Symptoms

- Excessive thirst
- Frequent urination
- Weight loss
- Bed wetting
- Lack of energy
- In late stages, vomiting, dehydration, rapid deep breathing, or coma (ketoacidosis) can occur - consider diabetes in any severely ill child or young adult

Check blood or urine glucose.

Check HbA1c when possible.

#TestOneDrop
Confirms + AND Hyperglycemia: Stage 3

- Evaluate for symptoms of hyperglycemia and diabetic ketoacidosis
- Referral to pediatric endocrinologist (if managed by PCP to this point)
Confirms + AND Absence of Hyperglycemia

Random blood glucose <140 mg/dl and HbA1c <5.7%

Random blood glucose 140-199 mg/dl and/or HbA1c 5.7-6.4%

Now what?
What are the steps we need to take to identify and care for individuals with Early Stages of T1D?
for progression of T1D (dysglycemia or hyperglycemia)
Goals of Follow-Up with IA Positive Patients

- **Safety**
  - Symptom awareness
  - Home blood glucose testing

- **Monitoring for Progression**
  - **OGTT**
  - **CGM**
  - **HbA1c + Blood Glucose**

Pay attention to growth
- Appropriate weight gain
- Healthy diet

Complete when healthy, without illness

Simmons et al., *DTT*, 2023
Clinical Visit

- Educate
- Stage (Monitor) for Dysglycemia/Hyperglycemia
- Provide Psychosocial Support
- Discuss Early Treatment Options
Engagement is Important for Medical Safety

- DKA Prevention
- Facilitate smooth transition to clinical T1D
  - Initiation of insulin
  - Psychological needs addressed
  - Social needs addressed

DKA occurrence at onset in study participants undergoing routine metabolic monitoring is 10X lower than in community patients.

unpublished data courtesy of Morgan Sooy, CDCES, RN, BSN
Engagement is Important for Monitoring T1D Progression

- Stage using ADA criteria
- Determine risk of progression (metabolic risk scores)

Offer approved early treatment options to delay clinical T1D (in US, Tzield® if ≥ age 8)

figures from https://www.niaid.nih.gov
Islet Autoantibody (IA) Status Alone is Not Enough to Monitor for Progression

• Multiple IA+ more likely to progress to clinical T1D if younger, more T1D related IA, HLA DR3/DR4-DQ8 or IA-2A present.

• Single IA+ more likely to progress if 2nd IA develops sooner.

Risk of progression from time of seroconversion, in high-risk individuals with antibodies done at gold standard laboratories

Ziegler et al., 2013
Home Blood Glucose Testing

SMBG meters and strips should be provided to all IA+ children and their families to be used during illness or when symptoms may be present.

Home Glucose Testing Reminders

- A HIGH blood glucose (BG) on home testing is not sufficient to diagnose diabetes; it should be confirmed by a health care provider.
- If your child has a HIGH BG level, wash the child’s hands with soap and water again and retest.
- If the BG is still HIGH, follow the instructions in this chart (see reverse).

Remember to Monitor for Symptoms of T1D

Most common symptoms include:
- Excessive thirst
- Frequent urination or getting up at night to urinate
- Wetting the bed in a child who was previously dry
- Unexplained weight loss or poor weight gain
- Change in appetite

Additional symptoms people experience include:
- low energy
- blurred vision, yeast infections, mood changes, behavior changes

Symptoms that require urgent attention include:
- heavy breathing, vomiting and confusion
Test blood glucose once biweekly and with any illness or T1D symptoms.
Frequency of Metabolic Monitoring Depends on Age and Stage

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Monitoring Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 years</td>
<td>Q3 months</td>
</tr>
<tr>
<td>4-5 years</td>
<td>Q3-6 months</td>
</tr>
<tr>
<td>&gt;6 years</td>
<td>Q6 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 1 T1D</th>
<th>Stage 2 T1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Islet autoantibodies</td>
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</tr>
<tr>
<td>● Normal glucose (FPG &lt; 100 mg/dL; 2h-PG &lt; 140 mg/dL; HbA1c &lt; 5.7%)</td>
<td>● Normal glucose (FPG 100-125 mg/dL; 2h-PG 140-199 mg/dL; HbA1c 5.7-6.4%)</td>
</tr>
<tr>
<td>● No symptoms</td>
<td>● No symptoms</td>
</tr>
</tbody>
</table>
Consider Stage of T1D When Deciding Tool(s) for Metabolic Monitoring

CGM
- Blinded to the individual wearing it.
- Applied and interpreted by trained HCP, with education for the user and their family.

OGTT

HbA1c

CGM

Stage 1 T1D
- Islet autoantibodies
- Normal glucose (FPG < 100 mg/dL; 2h-PG < 140 mg/dL; HbA1c < 5.7%)
- No symptoms

Stage 2 T1D
- Islet autoantibodies
- Abnormal glucose (FPG 100-125 mg/dL; 2h-PG 140-199 mg/dL; HbA1c 5.7-6.4%)
- No symptoms

Stage 3 T1D
- Islet autoantibodies
- High glucose (FPG > 126 mg/dL; 2h-PG or RPG > 200 mg/dL; HbA1c > 6.5%)
- Symptoms

FPG = fasting plasma glucose / 2h-PG = 2-hour plasma glucose / RPG = random plasma glucose

* ADA Standards of Medical Care in Diabetes: In absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal test results from same or separate samples
HbA1c

Classify Stage of T1D

- Highly specific for T1D
- Can use capillary finger poke sample
- POC testing widely available

<5.7%

5.7-6.4% or >10% increase

>6.5%

- Not sensitive for T1D
- Late indicator, often normal or mildly dysglycemia in patients with early stage 3 by another glycemic indicator
Oral Glucose Tolerance Test

Classify Stage of T1D

2-hour BG
<140 mg/dl

2-hour BG
140-199 mg/dl

2-hour BG
>200 mg/dl

• Gold standard
• Calculate metabolic risk scores (DPTRS, DPTRS60, Index60, M60, M120), which can help estimate the risk of prediction to clinical diagnosis of T1D
• Identify people eligible for early treatment options through clinic or research

• Requires glucose load, which isn't always well tolerated
• Preceding diet and activity can impact results
• Risk scores not used clinically and time points needed for BG and c-peptide vary among scores (60, 90, 120 minutes)
Continuous Glucose Monitor (CGM)

- Collects glucose every 5 minutes at home
- Collects glucose data during normal daily activities
- Finger pokes limited to confirming abnormal glucose levels
- Helpful in detecting glucose impairments earlier than HbA1c and random blood glucose
- Wearing of device may increase burden
- If unblinded, numbers may increase psychological distress/anxiety
- Low glucose alarms common
- Requires HCP expertise to interpret results for a person without diabetes diagnosis
- Payor coverage unpredictable (R73.03)

*If placing a CGM on a person without diabetes, the recommendation is for it to be worn blinded. If an unblinded CGM is preferred, then adequate provider support should be made available to the individual.
The risk of progression to T1D in 1 year was 80% in those with time above 140 mg/dl >10%.

Steck et al., 2022
Learning Opportunities

Do recommendations for frequency of antibody and metabolic testing apply to general population individuals?

What biomarkers can be developed to monitor disease progression?

How do we engage patients in active follow-up to derive benefits associated with screening?
Case

Kennedy confirmed to be positive for multiple antibodies (GADA and ZnT8A). A random blood glucose was 103 mg/dl. HbA1c was 5.4%.

What stage of T1D does Kennedy have?

Kennedy is seen in clinic every 6 months. She refuses to do an OGTT and is followed with HbA1c and CGM wear. At her most recent visit, HbA1c was 5.9%, fasting blood glucose was 112 mg/dl and the percentage of CGM glucoses >140 mg/dl was 35%.

What stage of T1D does Kennedy have?
Key Messages

• After a positive screen, confirm antibody status and rule out clinical type 1 diabetes with a random blood glucose and HbA1c.

• Engagement of antibody positive individuals results in reduced DKA at onset.

• Metabolic monitoring is important for staging of type 1 diabetes and determining available treatment options.

• HbA1c, OGTT and CGM can be used to monitor for disease progression.

• Monitoring should occur every 3-6 months in children and adolescents depending on age and stage of type 1 diabetes.
Thank You!

Evidence Based Guidance Will be Updated as Available on www.AsktheEXPERTS.org.
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Ask the Experts