Pediatric Diabetes: Diagnosis & Management Approaches

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Disclosures

No relevant disclosures
Learning objections

1. Be able to recognize presenting symptoms and diagnose diabetes in youth.
2. Appreciate that obese/overweight pediatric patients with dysglycemia warrant close follow-up and further pediatric endocrine evaluation/consultation.
3. Understand the role and indications for use of insulin in the management of type 2 diabetes (T2D) in youth.
4. Understand the role of intensive diabetes management in type 1 diabetes (T1D).
5. Approach management of diabetes in youth as chronic complex condition.
Outline

1. Case presentation
2. Presentation & Diagnosis
3. Management
   • Psychosocial aspects
   • ADA Standards of Care and Glycemic Targets
   • AAP Key Policy Statements
   • Glycemic control & monitoring: BG Monitoring & CGM
   • Insulin: management
   • Caveats of T2D

Disclaimer: lots of information- some additional slides for reference
For more information

CLINICAL PRACTICE GUIDELINE

Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children and Adolescents

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

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

Stanford University
Case Presentation

- 17 year 3 month old male admitted for management of uncontrolled diabetes and hyperglycemia.
- Initial labs/presentation: No distress. Glucose 213, pH 7.38, bicarb 16, trace ketones, HbA1c 14.2%
- Admission was his first pediatric endocrine evaluation after he was presumptively diagnosed with T2D at around the age of 13 years and started on Metformin by his PCP. HbA1c around that time was pre-diabetes range (~5.6 to 5.8%) and he was obese (BMI unknown).
- Over the past 1.5 years he has experienced ~90lb weight loss and HbA1c has increased to 14.2%. Current BMI now 21.1 (25-50th%).
- He has missed ~40 days of school because of fatigue and low energy level from his uncontrolled diabetes. Consequentially he failed some classes and had to repeat classes
DIABETES IN YOUTH
NOT JUST 1 TYPE
Diabetes in Obese Youth

Not Just 2 Type
Classification of Diabetes

- **Type 1 diabetes (T1D):** autoimmune β-cell destruction
- **Type 2 diabetes (T2D):** Progressive insulin secretory defect…that leads to β-cell destruction
- **Other specific types of diabetes**
  - Monogenic diabetes and inherited defects insulin production/secretion (ie, “MODY” forms)
  - Cystic Fibrosis related Diabetes (CFRD)
  - Drug- or chemical-induced
  - **Gestational diabetes mellitus (GDM)**

*For this lecture, we will focus on T1D vs. T2D*
When nearly 1/5 youth are obese, cannot assume that youth who are overweight/obese and have new onset diabetes have T2D.

If only assessing weight, youth who are overweight/obese have essentially same risk factor of having T1D as non-obese/overweight youth.
KEY CONCEPT: T2D is not insulin resistance...it is loss of beta cell function...and insulin resistance plays a role in progression towards T2D
Stages of T1D

<table>
<thead>
<tr>
<th></th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-cell autoimmunity</td>
<td>Present*</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>(with the presence of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>autoantibodies)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-cell loss</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Dysglycaemia</td>
<td>Absent</td>
<td>Hyperglycaemia</td>
<td>Hyperglycaemia</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>

Variable genetic and environmental risk for T1DM

Disease progression

Presymptomatic T1DM

Symptomatic T1DM

Katsarou, A. et al. (2017) Type 1 diabetes mellitus
DIABETES IN YOUTH
PRESENTATION & DIAGNOSIS
Criteria for the Diagnosis of Diabetes

A1C ≥6.5%  
(not established in pediatrics but used)

OR

Fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L)

OR

2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT

OR

A random plasma glucose ≥200 mg/dL (11.1 mmol/L)

Diagnostic criteria is the same for T1D and T2D
<table>
<thead>
<tr>
<th></th>
<th>T1D</th>
<th>T2D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type diabetes</strong></td>
<td><strong>T1D</strong></td>
<td><strong>T2D</strong></td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Typically rapid (over weeks to months)</td>
<td>Typically indolent (over months to years)</td>
</tr>
<tr>
<td><strong>Overweight/obesity</strong></td>
<td>+/-</td>
<td>&gt;85%</td>
</tr>
<tr>
<td><strong>Presenting sx/sx/course</strong></td>
<td>More of a short/acute course</td>
<td>More indolent course</td>
</tr>
<tr>
<td><strong>DKA / Ketones</strong></td>
<td>~50% DKA</td>
<td>~50% ketonuria</td>
</tr>
<tr>
<td></td>
<td>&lt;25% DKA</td>
<td>&lt;25% DKA</td>
</tr>
<tr>
<td><strong>Family Hx</strong></td>
<td>~5% with T1D of 2nd degree relative with T1D</td>
<td>&gt;75% with 1st or 2nd degree relative with T2D</td>
</tr>
<tr>
<td></td>
<td>Familial autoimmune conditions</td>
<td></td>
</tr>
<tr>
<td><strong>Co-morbidities</strong></td>
<td>Autoimmunity: Thyroid (TPO, Tgb)</td>
<td>Acanthosis nigricans (almost 100%)</td>
</tr>
<tr>
<td></td>
<td>Celiac (celiac panel)</td>
<td>Hyperandrogenism and PCOS</td>
</tr>
<tr>
<td></td>
<td>Adrenal insufficiency (21OH'ase Abs)</td>
<td>Metabolic syndrome/overlap</td>
</tr>
<tr>
<td></td>
<td>Pernicious anemia (B12 deficiency)</td>
<td>OSA</td>
</tr>
<tr>
<td></td>
<td>Vit D deficiency (Vit D25OH level)</td>
<td>Microalbuminuria (~10% within 3 mo dx)</td>
</tr>
<tr>
<td></td>
<td>Vitiligo</td>
<td></td>
</tr>
<tr>
<td><strong>Insulin &amp; c-peptide</strong></td>
<td>Decrease insulin and c-peptide</td>
<td>Usually normal or increased (but can be low)</td>
</tr>
<tr>
<td></td>
<td>No increase levels with OGT</td>
<td>Inappropriate increase with OGT</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td>Caucasian most prevalent but effect ALL ethnicities</td>
<td>NA, AA, Latino, Pacific Islanders</td>
</tr>
<tr>
<td><strong>Puberty</strong></td>
<td>Any pubertal stage</td>
<td>More common Tanner Stage 4 to 5</td>
</tr>
</tbody>
</table>
Diagnosis of Pediatric T2D
ADA 2018 Standards of Care Recommendations:

• Given the obesity epidemic, distinguishing between T1D and T2D in children is difficult, but critical for determining the optimal treatment regimen

• Due to the significant comorbidities associated with T2D in youth, these tests are recommended at diagnosis:
  › Blood pressure measurement
  › fasting lipid panel
  › Albumin excretion assessment
  › Dilated eye examination

Thereafter, screening and treatment guidelines for in youth with T2D are similar to those with T1D.
Double diabetes?

Conventional wisdom:
Insulin resistance → T2D

Thinking critically:
Insulin resistance + T1D
T1D + insulin resistance
Screening Recommendations: Autoimmune Conditions (T1D) ADA 2018 Standards of Care Recommendations:

Screening

- Assess for the presence of additional autoimmune conditions at diagnosis and if symptoms develop

Example autoimmune screening newonset pediatric diabetes patients:

- Celiac panel: annual (1st five years after diagnosis)
- Autoimmune hypothyroidism: Antibodies (TPO and Tgb Abs) at diagnosis and TFTs (FT4 and TSH annually)
- Vit D Deficiency: VitD25OH annually
Major Pancreatic Islet Autoantigens

ICA

GAA

(ICA512BDC)

ZnT8

IA-2

IA

mIAA

Insulin autoantibodies

GAA (GAD65)

Negative antibodies do not rule out T1D
How to order T1D Antibodies

LABCORP

Diabetes Autoimmune Profile
Includes: GAD-65, ICA 512, insulin antibodies, and ZnT8 antibodies.

TEST: 504050 Test number copied
CPT: 86337(x1); 86341(x3)

Specimen Requirements
Serum, frozen
Volume 2.5 mL
Minimum Volume 1.0 mL
Red-top tube or gel-barrier tube

QUEST

GAD65, IA-2, and Insulin Autoantibody
Alternative Name(s)
IA-2 Antibody, Panel, Diabetes Antibody Panel, Glutamic Acid Decarboxylase-65 Antibody Panel, Insulin Autoantibody, Panel

CPT Code is informational only; obtain the Test Code for ordering.

CPT Code(s)**
86337, 86341 (x2)

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Diagnostic Approach Example: Determining Diabetes Type in Youth with BMI >85th%

New onset diabetes BMI > 85th percentile

- Positive
  - Type 1a

- Negative
  - Consider MODY

pancreatic autoantibodies

Negative

Likely Type 2

Monitor course

Insulin requirement

No

Type 2

Yes

- low c-peptide: Type 1b?
- Normal/elevated: Type 2
  - Poor adherence
  - Severe resistance
DIABETES IN YOUTH

MANAGEMENT
A Fine Balance of Goals

• Best blood sugars as possible

• As few uncomfortable lows as possible

• Have a life

This can be tough. Not impossible, but tough.

Adapted as presented by Dr. William Polonsky, AYUDA VTP E-Course (April 2014)
We do NOT say disease
We say condition or lifestyle

- Although a medical dictionary might describe diabetes as a disease, it is not an accurate description as it denotes illness/sickness.

- Diabetes is more similar to a “condition” than a disease as diabetes requires you to make multiple daily decisions about your diabetes every day of the week, every day of your life.
Kids WITH diabetes are so much more than “diabetics.”
THEY ARE PEOPLE WHO ARE... AND who have diabetes!!!

Although this is a subtle difference, “people first” language actually makes a big difference. Children realize that they are more than just their diabetes.
Pediatric Psychosocial Issues
ADA 2018 Standards of Care Recommendations:

- At diagnosis and during routine follow-up care, assess psychosocial issues and family stresses that could impact adherence with diabetes management. Provide appropriate referrals to trained mental health professions, preferably experienced in childhood diabetes.

- Encourage developmentally appropriate family involvement in diabetes management tasks for children and adolescents, recognizing that premature transfer of diabetes care to the child can result in nonadherence and deterioration in glycemic control.

- Assess youth with diabetes for psychosocial and diabetes-related distress, generally starting at 7–8 years of age.
Transition from Pediatric to Adult Care
ADA 2018 Standards of Care Recommendations:

• As teens transition into emerging adulthood, health care providers and families must recognize their many vulnerabilities and prepare the developing teen, beginning in early to mid adolescence and at least 1 year prior to the transition.

• Both pediatricians and adult health care providers should assist in providing support and links to resources for the teen and emerging adult.
Diabetes Self-management Education and Support (DSME/DSMS)
ADA 2018 Standards of Care Recommendations:

- Youth with T1D and parents/caregivers (for patients aged <18 years) should receive diabetes self-management education and support at diagnosis and routinely thereafter that is B
  - Culturally sensitive
  - Developmentally appropriate
  - Individualized
### Glycemic Goal

**ADA 2018 Standards of Care Recommendations:**

<table>
<thead>
<tr>
<th>Plasma blood glucose goal range</th>
<th>A1C</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before meals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90–130 mg/dL (5.0–7.2 mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bedtime/overnight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90–150 mg/dL (5.0–8.3 mmol/L)</td>
<td>&lt;7.5%</td>
<td>A lower goal (&lt;7.0%) is reasonable if it can be achieved without excessive hypoglycemia</td>
</tr>
</tbody>
</table>
We do not say “good” or “bad” blood sugars

- In target, above target (high), or below target (low)
- Only ”bad” blood sugar is when we don’t use our brains to think why BG is above or below target- and sometimes we cannot figure out why and that is ok!

Targets should be **individualized**, and lower targets may be reasonable based on benefit-risk assessment.

Patients with higher A1cs who are accustomed to being above target are most likely going to have *relative symptoms of hypoglycemia* when in a standard “normal” target range.
Pediatric Glycemic Control
ADA 2018 Standards of Care Recommendations:

• All children and adolescents with T1D should **self-monitor blood glucose (SMBG)** levels multiple times daily, including pre-meal, pre-bedtime, and as needed for safety in specific clinical situations such as exercise, driving, or for symptoms of hypoglycemia.  

  • **Continuous glucose monitoring (CGM)** should be considered in children and adolescents with T1D, whether using injections or continuous subcutaneous insulin infusion.  

• The majority of children and adolescents with T1D should be treated with intensive insulin regimens, either via **multiple daily injections or continuous subcutaneous insulin infusion**.  

• **Automated insulin delivery systems** improve glycemic control and reduce hypoglycemia in adolescents and should be considered in adolescents with T1D.
Original Article

A contrast between children and adolescents with excellent and poor control: the T1D exchange clinic registry experience


Objectives: Optimizing glycemic control in pediatric type 1 diabetes (T1D) is essential to minimizing long-term risk of complications. We used the T1D Exchange database from 58 US diabetes clinics to identify differences in diabetes management characteristics among children categorized as having excellent vs. poor glycemic control.

Methods: Among registry participants 6–17 yr old with diabetes duration...
Average HbA1c by frequency SMBG (self blood glucose monitoring)- excluding CGM (continuous glucose monitoring)

Child (< 18 Years)

Adult (≥ 18 Years)

Beck R W et al. JCEM 2012;97:4383-4389
Relative Risk/Benefit Analysis

More SMBG checks (think CGM) =

More opportunities =

Lower HbA1c =

(?) Lower risk complications
Representation of benefits of reduction HbA1c (T1D+T2D)

Relative Risk of Complications

Reduction Risk of Complications

Hemoglobin A1c

Average Glucose

Slide adapted from Kendall D, International Diabetes Center, Minneapolis.
Review of glucose monitoring

Traditional “fingerstick” glucose testing

Continuous glucose monitoring (CGM)

1) Sensor
2) Transmitter
3) Receiver
Available CGM Devices

Dexcom
Medtronic
FreeStyle Libre ("Flash" CGM)
How CGM is used

- Real time glucose updates + trend allows timely intervention
- Alerts: low, high, rate of change, predictive
- Behavioral modification tool
- Provides robust data to better understand patterns
What to Do?

My pump always gives me the same answer.

Take a larger than usual dose.

No insulin and maybe eat carbs.
BEYOND HbA1c Goals to Consider

- Minimize lows
- Maximize time in range
- Minimize the roller coaster of hi-low s (ie glucose variability)
  p.s. have a life!
WAYS TO GIVE INSULIN PEDIATRIC DIABETES

Injections

Syringes/Pens: think about ½ units and needle length/Gauge (4mm, 32G)

Insulin Pump
Continuous Subcutaneous Insulin Infusion (CSII)

Different brands: think tubing vs non-tubing, CGM integration
Insulin Dosage Schedules

Conventional (Old): 1 to 2 shots/day

Conventional (Current/out-dated): 3 shots/day

Intensive Insulin Therapy (current): Basal/Bolus

✓ Continuous Subcutaneous Insulin Infusion (CSII, ie. “Pump” therapy)
✓ Basal Insulin + Bolus (fast-acting) insulin analog
   › Basal usually given in evening before bed
   › Sometimes Basal insulin is split between morning and bed
✓ Basal insulin + pump analog

Pre-Mixed insulins (ie, 70/30) should not be used in the pediatric population
Clinicians must ensure that insulin therapy is initiated for children and adolescents with T2DM:

1. who are ketotic or in diabetic ketoacidosis and who have venous or plasma blood glucose level > 250 mg/dl
2. whose Hemoglobin A1c is > 9% or
3. In whom the distinction between T1D and T2D is unclear.

In all other instances, clinicians should **start metformin** as first-line therapy for children and adolescents at the time of diagnosis with T2DM, and initiate a **lifestyle modification** program including **nutrition** and **physical activity**.

## T2D Diabetes Management Approach

Based on initial symptoms, BG, and ketones

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Blood Glucose</th>
<th>Ketones</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>&lt; 250</td>
<td>Negative</td>
<td>Metformin +/- Insulin +/- lifestyle changes +/- underlying co-morbidities</td>
</tr>
<tr>
<td>No</td>
<td>&gt; 250</td>
<td>Negative</td>
<td>Insulin +/- metformin +/- lifestyle changes +/- underlying co-morbidities</td>
</tr>
<tr>
<td>Yes</td>
<td>&lt; 250</td>
<td>Negative</td>
<td>Insulin +/- metformin +/- lifestyle changes +/- underlying co-morbidities</td>
</tr>
<tr>
<td>Yes</td>
<td>&lt;250</td>
<td>Positive</td>
<td>Insulin +/- metformin +/- lifestyle changes +/- underlying co-morbidities</td>
</tr>
</tbody>
</table>
ADDITIONAL INFORMATION

Advances in diabetes management
Insulin Pumps
Remote Monitoring

THIS IS THE NIGHTSCOUT PROJECT

You’ll Always Know with the World’s First CCM on the Phone

FOLLOW
Currently on Market
Medtronic 670G
Open APS
Introducing the iLet
Future of closed-loop
Healthy life styles & food choices
Physical Activity Guidelines For Children & AAP KEY ACTION STATEMENT

Children and adolescents should do 60 minutes (1 hour) or more of physical activity daily.

**Aerobic:** Most of the 60 or more minutes a day should be either moderate- or vigorous-intensity aerobic physical activity, and should include **vigorous-intensity physical activity** at least 3 days a week.

**Muscle-strengthening:** As part of their 60 or more minutes of daily physical activity, children and adolescents should include muscle-strengthening physical activity on at least 3 days of the week.

**Bone-strengthening:** As part of their 60 or more minutes of daily physical activity, children and adolescents should include bone-strengthening physical activity on at least 3 days of the week.

It is important to encourage young people to participate in physical activities that are **appropriate for their age**, that are **enjoyable**, and that offer variety.
But any exercise is better than none!
EAT REAL FOOD
If your food can go bad, it’s good for you.

If your food can’t go bad, it’s not good for you.
Pediatric Diabetes HbA1c Goals

All ages

HbA1c < 7.5
Recognizing the facts: on average, the current system of deliver for T1D in the US is failing patients.

HbA1c Target < 18 year old: < 7.5%
HbA1c Target > 18 years old: <7%

Bottom line:
System failure for patients with T1D of all ages

Discussion and Thank You!

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