The Current Approach to Type 1 Diabetes (T1D) in Children

Dina Panagiotopoulos, MD, FRCPC
Associate Professor, UBC
Endocrinologist, BC Children’s Hospital
Disclosures

- Consultant fees from Eli Lilly Canada Inc.
Diabetes Diagnosis

Usually children present with
• Polyuria, polydipsia, nocturia, enuresis, weight loss

Other presentations:
• School problems/declining athletic performance
• Genital rash/recurrent candidiasis
• “recurrent UTI’s”
• Tachypnea, respiratory distress with no chest findings or fever especially in toddlers
• Severe abdominal pain &/or recurrent vomiting
• Altered level of consciousness/coma
Diabetes Diagnosis

✓ Suspicion of diabetes in a child should lead to immediate confirmation of the diagnosis and initiation of treatment to reduce the likelihood of Diabetic Ketoacidosis (DKA).

✓ Management of pediatric DKA differs from DKA in adults because of the increased risk for cerebral edema. Pediatric protocols should be used.
0. Confirm DKA: plasma glucose (PG) ≥11 mmol/L, ketones, capillary pH ≤7.3, HCO₃⁻ ≤15 mmol/L.

1. Measure body weight (BW) in kilograms ................................................................. (1) ________ kg

2. Establish extent of dehydration (↓ BP, tears, skin turgor, capillary refill; ↑ hematocrit) in cc/kg.:
   - infants: |
     - mild: 5% = 50 cc/kg |
     - moderate: 10% = 100 cc/kg |
     - severe: 15% = 150 cc/kg |
   - children: |
     - mild: 3% = 30 cc/kg |
     - moderate: 6% = 60 cc/kg |
     - severe: 9% = 90 cc/kg .................................................... (2) ________ cc

3. Calculate total fluid deficit: multiply (1) x (2) ..................................................................... (3) ________ cc

4. Give normal saline (NS) resuscitation bolus only if patient is orthostatic or shocky:
   - recommended amount: 5–10 cc/kg BW over 1–2 hours, max <30 cc/kg ................................ (4) ________ cc

5. Calculate remainder of fluid deficit after fluid bolus: subtract (4) from (3) ...................... (5) ________ cc

6. Calculate maintenance fluid requirements for the next 48 hours:
   - 200 cc/kg for the first 10 kg BW
   + 100 cc/kg for the next 10 kg BW
   + 40 cc/kg for the rest of BW ................................................................. (6) ________ cc/48 h

7. Calculate total amount of fluid still to be given over 48 hours: add (5) and (6)............. (7) ________ cc/48 h

8. Calculate hourly rate of fluid replacement: divide (7) by 48 ............................................. (8) ________ cc/h

9. Use normal saline (NS) as initial replacement fluid, at rate determined in (8). Add KCl 20–40 mEq/L only if hypokalemic and patient has adequate urine output. Continue this for 1–2 hours.

10. After 1–2 hours, make up and start a piggyback insulin drip at 0.1 unit/kg BW/h.
    - 50 units Regular insulin (Humulin® R or Novolin® Toronto) in 500 cc NS or D10/NS
    - run at 1 cc/kg BW/h ....................................................................................... (10) ________ cc/h

11. Begin “2-bag method” to replace NS. Y together (a) NS with 40 mEq/L KCl and (b) D10–D12.5/NS with 40 mEq/L KCl. Decrease replacement fluid rate to adjust for insulin drip rate:
    - subtract (10) from (8) ....................................................................................... (11) ________ cc/h

12. Aim to keep PG ~10–15 mmol/L by titrating the rates of these two solutions, keeping the combined rate at (11) G. Continue this for the next 6–12 hours, monitoring as below in (15) and (16).

Rationale & Notes:

*Please note that this protocol is designed as an algorithm for treating the majority of cases of DKA in infants, children and adolescents. It cannot replace careful clinical observation and judgment in treating this potentially very serious condition. If you have questions or problems related to the management of DKA or diabetes, please feel free to contact the BCCH Pediatric Endocrinologist on call.

*Mild hyperglycemia, even with ketones and mild acidosis, can often be managed without IV fluids or IV insulin. In particular in the older child or known diabetic who is not vomiting or seriously dehydrated.

*Rapid, deep mouth-breathing (Kussmaul respiration) often dries out the oral mucosa, making the child appear more dehydrated than she really is. The hematocrit and other clinical signs noted are more accurate.

*Large fluid boluses are potentially dangerous and should be administered slowly and with caution, unless the patient is truly shocky. Only very rarely will a larger (>20 cc/kg BW) fluid bolus be required to maintain perfusion.

*Since most patients develop DKA over days, slow metabolic repair is safest. Overhydration may contribute to cerebral edema.

*Nonetheless, DKA in children often resolves in less than 48 h.

*IV insulin boluses are always contra-indicated. Insulin given in the first 1–2 h of DKA repair is thought to increase mortality. This insulin rate fully inhibits ketogenesis and gluconeogenesis and should be maintained if possible. If unable to keep PG >10 mmol/L, drop the insulin rate by 25–50%.
Children with new-onset T1D and their families require intensive diabetes education by an interdisciplinary pediatric diabetes healthcare (DHC) team.

**Education topics should include:**

- Prevention, detection and treatment of hypoglycemia
- Insulin action and administration
- Dosage adjustment
- Blood glucose (BG) and ketone testing
- Sick-day management
- Prevention of DKA
- Nutrition and exercise
Anticipatory guidance and lifestyle counselling should be part of routine care during critical developmental transitions (e.g., school entry, beginning high school).

Healthcare providers should regularly initiate discussions with children and their families about

- School
- Diabetes camp
- Psychological issues
- Substance use
- Driving
- Career choices
Glycemic Targets

• Achieving adult targets for metabolic control is not always indicated and may be unsafe for some children

• Achieving targets may require much work on the part of family and care team to find the right insulin system
## Glycemic Targets: Graduate with Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Target A1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 years</td>
<td>&lt;8.0%</td>
</tr>
<tr>
<td>6 to 12 years</td>
<td>≤7.5%</td>
</tr>
<tr>
<td>Adolescents</td>
<td>≤7.0%</td>
</tr>
</tbody>
</table>
Chronic Poor Metabolic Control

- Diabetes control may worsen during adolescence, possibly due to the following factors:
  - Adolescent adjustment issues
  - Psychosocial distress
  - Intentional insulin omission
  - Physiologic insulin resistance
Insulin Therapy

• Insulin is the **mainstay** of medical management for type 1 diabetes

• The choice of insulin regimen depends on many factors:
  – Child’s age
  – Duration of diabetes
  – Family lifestyle
  – Socioeconomic factors
  – Family, patient, and physician preferences
Insulin Therapy – (Cont’d)

- It is reasonable to introduce a basic insulin regimen but a more intensive system is indicated if success not achieved despite good effort

- Starting regimen should comprise:
  - ≥2 daily bolus injections
  - ≥1 basal insulin injection
# Types of Insulin for Use in T1D

<table>
<thead>
<tr>
<th>Insulin Type (trade name)</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bolus (prandial) Insulins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid-acting insulin analogues (clear):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Insulin aspart (NovoRapid®)</td>
<td>10 - 15 min</td>
<td>1 - 1.5 h</td>
<td>3 - 5 h</td>
</tr>
<tr>
<td>• Insulin glulisine (Apidra™)</td>
<td>10 - 15 min</td>
<td>1 - 1.5 h</td>
<td>3 - 5 h</td>
</tr>
<tr>
<td>• Insulin lispro (Humalog®)</td>
<td>10 - 15 min</td>
<td>1 - 2 h</td>
<td>3.5 - 4.75 h</td>
</tr>
<tr>
<td>Short-acting insulins (clear):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Insulin regular (Humulin®-R)</td>
<td>30 min</td>
<td>2 - 3 h</td>
<td>6.5 h</td>
</tr>
<tr>
<td>• Insulin regular (Novolin®geToronto)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Basal Insulins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting insulins (cloudy):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Insulin NPH (Humulin®-N)</td>
<td>1 - 3 h</td>
<td>5 - 8 h</td>
<td>Up to 18 h</td>
</tr>
<tr>
<td>• Insulin NPH (Novolin®ge NPH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting basal insulin analogues (clear)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Insulin detemir (Levemir®)</td>
<td>90 min</td>
<td>Not applicable</td>
<td>Up to 24 h (glargine 24 h, detemir 16 - 24 h)</td>
</tr>
<tr>
<td>• Insulin glargine (Lantus®)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
If initial regimen fails to meet glycemic targets, more intensive management may be required.

Three methods of intensive diabetes management can be used at any age:

- Similar regimen with more frequent injections
- Basal bolus regimens using long and rapid acting insulin analogues
- Continuous subcutaneous insulin infusion (CSII; insulin pump therapy)
Glucose Monitoring

• Self-monitoring of blood glucose is an essential part of management of type 1 diabetes

• Subcutaneous continuous glucose sensors allow detection of asymptomatic hypoglycemia and hyperglycemia

• Subcutaneous continuous glucose sensors may have a beneficial role in children and adolescents but evidence is not as strong as in adults
Nutrition

- All children with type 1 diabetes should receive counselling from a registered dietitian experienced in pediatric diabetes

- Children with diabetes should follow a healthy diet as recommended for children without diabetes in *Eating Well with Canada’s Food Guide*

- There is no evidence that one form of nutrition therapy is superior to another in attaining age-appropriate glycemic targets.
Hypoglycemia

- Hypoglycaemia is a major obstacle for children with type 1 diabetes and can affect their ability to achieve glycemic targets.
- Significant risk of hypoglycemia often necessitates less stringent glycemic goals, particularly for younger children.
- There is no evidence in children that one insulin regimen or mode of administration is superior to another for reducing non-severe hypoglycemia.
Examples of Carbohydrate for Treatment of Mild to Moderate Hypoglycemia

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>&lt;15 kg</th>
<th>15 to 30 kg</th>
<th>&gt;30 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of carbohydrate</td>
<td>5g</td>
<td>10 g</td>
<td>15 g</td>
</tr>
<tr>
<td>Carbohydrate Source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose tablet (4 g)</td>
<td>1</td>
<td>2 or 3</td>
<td>4</td>
</tr>
<tr>
<td>Dextrose tablet (3 g)</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Apple or orange juice; regular soft drink; sweet beverage (cocktails)</td>
<td>40 ml</td>
<td>85 ml</td>
<td>125 ml</td>
</tr>
</tbody>
</table>
Hypoglycemia – Glucagon

- In children, the use of mini-doses of glucagon has been shown to be useful in the home management of mild or impending hypoglycemia associated with inability or refusal to take oral carbohydrate.
- Dose = 10 mcg x (years of age)
- Dose range 20 – 150 mcg
| Age ≤5 yrs | → | 0.5 mg glucagon SC or IM |
| Age >5 yrs | → | 1 mg glucagon SC or IM |

- Diabetes care team should be contacted following a severe hypoglycemic event
- Consider reducing insulin doses in short term to avoid repeat event
Illness Management

• As a general rule, **INSULIN SHOULD NEVER BE TOTALLY DISCONTINUED in children with type 1 diabetes**

• However, if child is vomiting or appetite markedly decreased, there is a potential for hypoglycemia.

• In the event of above with normal or low blood sugars:
  • Dose of morning NPH should be decreased by approximately 30-50 % and no rapid acting insulin given
  • If child recovers quickly and eats at lunch then rapid-acting insulin can be given later
  • If BG ≥15 mmol/L and ketones, then additional rapid-acting will need to be given
Smoking

- Smoking prevention should be emphasized throughout childhood and adolescence.
Psychological / Psychiatric Risks

- Children and adolescents with diabetes have significant risks for psychological problems:
  - Depression
  - Anxiety
  - Eating disorders
  - Externalizing disorders

- The risks increase exponentially during adolescence
## Screening for Comorbid Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Indications for screening</th>
<th>Screening test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune thyroid disease</td>
<td>All children with type 1 diabetes</td>
<td>Serum TSH level + thyroperoxidase antibodies</td>
<td>At diagnosis and every 2 years thereafter</td>
</tr>
<tr>
<td></td>
<td>Positive thyroid antibodies, thyroid symptoms or goiter</td>
<td>Serum TSH level + thyroperoxidase antibodies</td>
<td>Every 6-12 months</td>
</tr>
<tr>
<td>Addison's disease</td>
<td>Unexplained recurrent hypoglycemia and decreasing insulin requirements</td>
<td>8 AM serum cortisol + serum sodium and potassium</td>
<td>As clinically indicated</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Recurrent gastrointestinal symptoms, poor linear growth, poor weight gain, fatigue, anemia, unexplained frequent hypoglycemia or poor metabolic control</td>
<td>Tissue transglutaminase + immunoglobulin A levels</td>
<td>As clinically indicated</td>
</tr>
</tbody>
</table>
Diabetes Complications – Key Messages

- Nephropathy, retinopathy, neuropathy and hypertension are relatively rare in pediatric diabetes

- Screening efforts should focus most attention on post-pubertal patients with longer duration and poorer control of their diabetes
Nephropathy

- Prepubertal children, and those in the first 5 years of diabetes, should be considered at very low risk for microalbuminuria.

- A first morning urine albumin to creatinine ratio (ACR) has high sensitivity and specificity for the detection of microalbuminuria (MAU).

- A random ACR may be compromised in adolescents due to their higher frequency of exercise-induced proteinuria and benign postural proteinuria.
Nephropathy

- Treatment is indicated only for those adolescents with persistent microalbuminuria

- There are no long-term intervention studies assessing the effectiveness of ACE inhibitors or angiotensin II receptor antagonists in delaying progression to overt nephropathy in adolescents with microalbuminuria

- Therefore, treatment guidelines are based on adult data
Retinopathy

- Retinopathy is rare in prepubertal children with type 1 diabetes and in postpubertal adolescents with good metabolic control.

- If the patient is between 5 and 10 years after diagnosis, with a normal eye exam and good glycemic control, screen every 2 years.

- If the patient is 15 years or older and has had diabetes for 5 years, begin annual screening.

- If the patient is between 5 and 10 years after diagnosis, with a normal eye exam and good glycemic control, screen every 2 years.
Neuropathy

- Neuropathy is mostly subclinical in children
- Prospective nerve conduction studies and autonomic neuropathy assessment studies have demonstrated increased prevalence of abnormalities over time
- Persistence of abnormalities is an inconsistent finding
- Vibration and monofilament testing have suboptimal sensitivity and specificity in adolescents
- The only treatment modality for children and adolescents is intensified diabetes management to achieve and maintain glycemic targets
<table>
<thead>
<tr>
<th>Complication</th>
<th>Indications &amp; intervals for screening</th>
<th>Screening method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephropathy</td>
<td>• Yearly screening commencing at 12 years of age in those with duration of type 1 diabetes ≥ 5 years</td>
<td>• First morning (preferred) or random ACR&lt;br&gt;• Abnormal ACR requires confirmation at least 1 month later with a first morning ACR, and if abnormal, followed by timed, overnight or 24-hour split urine collections for albumin excretion rate&lt;br&gt;• Repeated sampling should be done every 3-4 months over a 12-month period to demonstrate persistence</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>• Yearly screening commencing at 15 yrs of age with duration of DM ≥ 5 yrs&lt;br&gt;• Screening interval can increase to 2 yrs if good glycemic control, duration of diabetes &lt; 10 yrs, and no retinopathy at initial assessment</td>
<td>• 7-standard field, stereoscopic-colour fundus photography with interpretation by a trained reader (gold standard); or&lt;br&gt;• Direct ophthalmoscopy or indirect slit-lamp fundoscopy through dilated pupil; or&lt;br&gt;• Digital fundus photography</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>• Postpubertal adolescents with poor metabolic control should be screened yearly after 5 years’ duration of DM</td>
<td>• Question and examine for symptoms of numbness, pain, cramps and paresthesia, as well as sensation, vibration sense, light touch &amp; ankle reflexes</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>• Delay screening post-diabetes diagnosis until metabolic control has stabilized&lt;br&gt;• Screen at ≥12 years of age or &lt;12 years of age with BMI &gt; 95th percentile, family history of hyperlipidemia or premature CVD</td>
<td>• Fasting total cholesterol, high-density lipoprotein cholesterol, triglycerides, calculated low-density lipoprotein cholesterol</td>
</tr>
<tr>
<td>Hyper tension</td>
<td>• Screen all children with type 1 diabetes at least twice a year</td>
<td>• Use appropriate cuff size</td>
</tr>
</tbody>
</table>
Management of children and youth with T1D differs from those of adults in a number of ways:

- Less aggressive A1C target acceptable in younger children
- Less intensive screening for complications of diabetes in the younger years due to lower incidence
- Greater caution around DKA management given cerebral edema risk
- Greater awareness of unique psychosocial needs as children progress through developmental stages
Question 1:

Ricky, a 4 yo boy, is brought to your office by his mother because he has started wetting the bed again after he had stopped for 6 months. On questioning, he does appear to be more thirsty although mom thought it was just because it was getting hotter in the summer.

The recommended approach would be to:

1. Reassure the mom that it is normal for kids to start and stop wetting the bed at this age and no testing is required.

2. Give the mother a requisition to do a fasting blood sugar on Ricky in the next 1-2 weeks, when convenient.

3. Dip the urine for glucose and ketones and/or perform a random glucometer in the office immediately.
You ask the nurse to check Ricky’s urine and it is positive for glucose and ketones.

You would now advise mom:

1. To stop giving him any sugar to eat and come back in a week to recheck his urine.

2. Page the pediatric endocrinologist on call to advise them that you have made a new diagnosis of diabetes and are planning to send Ricky directly to the emergency room.

3. Give the mother a requisition to do a fasting blood sugar on Ricky in the next 1-2 weeks as you require confirmation first.
Ricky is now 15 years of age and prefers to be called “Rick” He wakes up feeling nauseated, with a low grade fever, and has a blood sugar of 17, 2+ urine ketones

His mom calls to say that he doesn’t feel like eating and asks what she should do?

You would recommend to hold his insulin and check his blood sugar in 2 hours.

1. True
2. False
Question 4

Joanne is a 13 year old girl who has had diabetes for the last 3 years, and her A1c has always ranged from 7.2% to 7.5%.

Her mother pulls out her logbook to show you and is pleased with how Joanne is doing.

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>AM</th>
<th>noon</th>
<th>PM</th>
<th>Bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>Monday</td>
<td>8.2</td>
<td>4.2</td>
<td>7.8</td>
<td>9.5</td>
</tr>
<tr>
<td>Tuesday</td>
<td>Tuesday</td>
<td>6.7</td>
<td>4.9</td>
<td>6.3</td>
<td>9.8</td>
</tr>
<tr>
<td>Wednesday</td>
<td>Wednesday</td>
<td>7.3</td>
<td>6.8</td>
<td>5.9</td>
<td>7.2</td>
</tr>
</tbody>
</table>

The nurse provides you with her A1c done in clinic and it is **11.2%** (N < 5.7%)
Question 4 (Continued)

The most **likely** cause of this discrepancy is:

1. There was a lab error with the A1c point of care testing because Joanne didn’t wash her hands.
2. Joanne is falsifying her blood sugar readings because she doesn’t want to take more insulin.
3. Joanne’s meter is no longer working