Taking Diabetes Back to School

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What is type 1 diabetes?

- Autoimmune destruction of pancreatic islet cells
- Insulin is unable to be produced = too much glucose!!!
- What does insulin do? Opens cells!

DCCT

Conventional/Control
- Goal: clinical well-being
- BG checks 1-2x/day
- Quarterly visits and HbA1c measurements

Intensive
- Goal: normalization of glucose
- BG checks 4x/day minimum
- Multiple Daily Injections or pump
- Monthly visits and HbA1c measurements

HbA1c / Blood Glucose Comparison

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>BG mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>4%</td>
<td>60</td>
</tr>
<tr>
<td>5%</td>
<td>90</td>
</tr>
<tr>
<td>6%</td>
<td>120</td>
</tr>
<tr>
<td>7% Target Goal</td>
<td>150</td>
</tr>
<tr>
<td>8%</td>
<td>180</td>
</tr>
<tr>
<td>9%</td>
<td>210</td>
</tr>
<tr>
<td>10%</td>
<td>240</td>
</tr>
<tr>
<td>11%</td>
<td>270</td>
</tr>
<tr>
<td>12%</td>
<td>300</td>
</tr>
<tr>
<td>13%</td>
<td>330</td>
</tr>
</tbody>
</table>

DCCT/EDIC Study Results*

Reduced Risk:
- Eye disease: 76%
- Kidney disease: 54%
- Nerve disease: 60%
- Cardiovascular disease: 42-57%

*DCCT/EDIC: New England Journal of Medicine, 353(25), December 22, 2005
Recommendations from DCCT/EDIC

Intensive therapy, with the goal of achieving glucose levels as close to normal as possible, should be employed in most patients.

Most recent goal for children (≤ 19 yrs) is an A1C less than 7.5%

**GOAL OF EVERY INSULIN REGIMEN:**
Mimic Insulin Delivery of Healthy Pancreas
Theoretical Representation of the Insulin Secretion of a Healthy Pancreas

**Insulin Available in the US**

<table>
<thead>
<tr>
<th></th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro (Humalog®)</td>
<td>10 mins.</td>
<td>30–60 mins.</td>
<td>2–4</td>
</tr>
<tr>
<td>Aspart (Novolog®)</td>
<td>10 mins.</td>
<td>30–60 mins.</td>
<td>2–4</td>
</tr>
<tr>
<td>Glulisine (Apidra®)</td>
<td>10 mins.</td>
<td>30–60 mins.</td>
<td>2–4</td>
</tr>
<tr>
<td>Regular</td>
<td>½–1</td>
<td>1–4</td>
<td>5–8</td>
</tr>
<tr>
<td>NPH</td>
<td>1–3</td>
<td>4–10</td>
<td>12–18</td>
</tr>
<tr>
<td>Glargine (Lantus®, Basalglar®)</td>
<td>1–2</td>
<td>peakless</td>
<td>&gt;24 hrs</td>
</tr>
<tr>
<td>Detemir (Levemir®)</td>
<td>1–2</td>
<td>peakless</td>
<td>&gt;24 hrs</td>
</tr>
</tbody>
</table>

**Action Profiles of Human Insulins and Insulin Analogues**

<table>
<thead>
<tr>
<th></th>
<th>Plasma insulin levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspart, lispro, glulisine 4–6 hours</td>
<td>regular 6–8 hours</td>
</tr>
<tr>
<td>NPH 12–20 hours</td>
<td>glargine, detemir, degludec 20–24 hrs</td>
</tr>
</tbody>
</table>

**Basal Bolus Regimen with Injections**

Glargine and Aspart

Injection Injection Injection

More physiological coverage of meals, exercise, & snacks
Think like a Pancreas

Basal Insulin

- Shot (MDI)
- Glargine, Detemir or Delgudec: Gives continuous background coverage
- Pump (CSII): Continuous delivery of rapid-aspart, lispro or glulisine- insulin to take place of Degludec, Glargine or Detemir

Bolus Insulin

- Insulin given with food. Based on: carbohydrates in food Carb ratio
- Supplemental insulin for blood sugars above target Sensitivity or Correction Factor

3 Roles of Insulin

- Basal
- Bolus
- Correction

Basal Insulin

- Background insulin
- Long-acting insulin to treat pre-meal glucose levels
- Necessary in type 1 diabetes because of absolute insulin deficiency
- Used in type 2 diabetes to suppress hepatic glucose output between meals and overnight
- 25-50% of total daily insulin needs (age dependent – younger children usually use less basal insulin)

Bolus Insulin

- Rapid-acting insulin to cover meals
- Given regardless of pre-meal BG
- Dose adjusted to match to carbohydrate content of the meal CHO:insulin ratio
- Held if the patient is not eating and blood sugar is in target
- 15% to 20% of total daily insulin requirement at each meal

Basal - Bolus Insulin

- Most closely mimics normal physiology
- Best achieved with insulin pump or Long acting background and rapid insulin with food and as needed.
- Pre- and post-meal BG testing to assess doses
- Difficult for patients who are not independent
  - Four injections per day
  - Timing of injections with meals
Individualized Insulin Treatment

- Select the appropriate type of insulin
- Select regimen for giving insulin
  - Multiple Daily Injections
  - Insulin Pump therapy
- Choose the appropriate starting dose of insulin
- Titrate doses to achieve the desired glucose control

Tips on Dosing

- Pre meal dosing
- Injection sites, rotation and absorption
- Pen preparation and dosing

Insulin Pump Therapy

Small computerized device that delivers insulin through an infusion set inserted into the fat tissue. The pump itself can be clipped to clothing or stored in a pocket.

Pumps deliver rapid-acting insulin, in a way that mimics the healthy pancreas by covering both basal and bolus insulin needs.

Infusion Sets

- Straight Set
- Angle Set

Important Definitions

- **Basal**: Maintains BG level during fasting state. Programmed to run automatically; can be changed, if needed, at any time. Small amount of insulin is automatically released every few minutes.
- **Bolus**: Insulin to cover carbohydrate intake. Insulin to cover high BG. Programmed and delivered by pump as needed; amounts will vary.

Pharmacokinetic Advantages

- Pump Therapy vs Multiple Daily Injections (MDI)
  - Uses only rapid acting
  - Uses only one injection site
  - Eliminates most of the SQ insulin depot
  - Better simulates normal pancreatic function
  - Day-to-day variability in absorption < 3% versus up to 52% for longer acting insulin injections
Advantages of pump therapy

- Dosing is very precise. You can accurately deliver 0.05 units of insulin for a bolus and 0.001 units as basal.
- Bolus when you want to eat vs. chasing insulin with food to prevent low blood sugars.
- "Tight Control" while minimizing the risk of low blood sugars.
- More flexible lifestyle. Improved quality of life!!!

Key Features of Pump Therapy

Bolus options:

- "Smart Pump" features assist with calculations
- Combination bolus
- Audio bolus
- One “needle stick” every 2-3 days
- May prevent “stacking” of bolus insulin by using Insulin on Board (IOB) feature

Challenges of Pump Therapy

- Risk of diabetic ketoacidosis (DKA)
- No long acting (basal) insulin
- Life threatening: pump malfunction or catheter failureS
- Possible site or skin problems
- Increased Glucose monitoring and continued need to count carbohydrates
- Adjustment/learning period
- Insurance coverage and costs

Watch out for Set failures
On to: carb counting and corrections

Continuous Glucose Monitoring (CGM)

What is CGM?
- Uses a tiny sensor or electrode inserted under the skin to continuously measure interstitial glucose.
- Stays in place from 6-7 days.
- Transmits the information to a receiver which displays in a graph and numerical format.
- CGM devices are not measuring blood glucose and there is a “lag” time between the blood glucose and the interstitial glucose.

Why Use CGM
- Record dangerously low overnight blood sugar levels, which often go undetected
- Track high levels between meals
- Show early morning spikes in blood sugar
- Evaluate how diet and exercise affects control
- Determine if treatment plan works on a day-to-day basis
- Use as a substitution for Fingerstick BG testing

Understanding glucose “lag” times
- Physiologic “lag” time
  - Glucose → blood → interstitial fluid → cells
  - Meters test blood glucose; sensors test interstitial fluid
  - The glucose levels in these fluids may differ at any given time
- Technology “lag” time
  - Glucose and oxygen diffuse across membrane of glucose sensor
  - System updates display glucose every 5 minutes
  - Sensor will not match up directly with BG meter, especially when glucose levels are rapidly changing

- Acetaminophen may falsely raise sensor readings
- Insulin infusion must be at least 3” away
- No alternate site glucose testing for calibration
Using Dexcom G6 CGM data to make insulin delivery decisions.

- The Dexcom G6 Continuous Glucose Monitoring System (Dexcom G6 System) is a real-time, continuous glucose monitoring device indicated for the management of diabetes in persons age 2 years and older.
- The Dexcom G6 System is intended to replace fingerstick blood glucose testing for diabetes treatment decisions. Interpretation of the Dexcom G6 System results should be based on the glucose trends and several sequential readings over time. The Dexcom G6 System also aids in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long-term therapy adjustments.
- The Dexcom G6 System is also intended to autonomously communicate with digitally connected devices, including automated insulin dosing (AID) systems. The Dexcom G6 System can be used alone or in conjunction with these digitally connected medical devices for the purpose of managing diabetes.

Setting Expectations

- Two different types of body fluids: interstitial fluid (Dexcom G6) and blood (meter)
- Readings can be different and still be considered accurate

Overview

- Receiver: Shows glucose information
- Applicator with Sensor: Sensor applicator inserts sensor under your skin, sensor gets glucose information, wear for 10 days
- Transmitter: Sends glucose information from sensor to receiver, use for 3 months

Viewing the Receiver Trend Screen

- Bluetooth
- Current Glucose: 150
- High Glucose Alert Level
- Low Glucose Alert Level
- Tap for Ideas Options
- Trend Arrow
- Battery
- Current Glucose: 150
- High Glucose Alert Level
- Low Glucose Alert Level
- Tap to enter Events
Sensor Augmented Pump Therapy

- Currently
  - Medtronic 670G
  - Tandem x2
  - In development
    - Insulet
    - Bionic Pancreas
    - Home grown

**STAR 3 2010: Effectiveness of Sensor-Augmented Insulin-Pump Therapy in Type 1 Diabetes**

- **485 Type 1 Patients**
- **60-120 mg/dL goal**
- **45% achieved goal**
- **No severe hypoglycemia**
- **A1C 7.4% to 9.5%**
- **Two Arms:**
  - Sensor augmented pump (SAP) therapy
  - Multiple daily injections
- **Primary Outcome:**
  - Change in A1C levels at 12 months

1. dQ&A Connections Survey Q4 2015.
2. 38% smaller than MiniMed 630G and 670G and 25% smaller than MiniMed 530G, Animas Vibe and Omnipod System.

- Up to 38% smaller than other pumps.1
- Milled from a solid piece of aluminum.
- Watertight to 3 feet for 30 minutes (IPX7)
- Holds 300 units of insulin
- Green technology with rechargeable battery
- Advanced Bluetooth radio allows 2-way communication with multiple devices.

How does Basal-IQ™ Technology work?
When the Basal-IQ feature is on, the system predicts glucose levels 30 minutes ahead and suspends insulin if levels are predicted to drop below 80 mg/dL to help reduce the frequency and duration of low glucose events.

FDA APPROVED!
Now with Dexcom G6® CGM Integration
EXCEPTIONAL ACCURACY & PERFORMANCE
- The only CGM approved for treatment decisions with zero fingersticks*
- The #1-preferred CGM brand†
- Transmits real-time glucose data to your smart device and up to 5 followers†
- 10-day wear and acetaminophen blocking*

Linear Regression Algorithm
- CGM values are sent every 5 minutes.
- Linear regression needs at least the last 3 of 4 data points to project a future glucose value 30 minutes into the future.
- Insulin will suspend when predicted to be below 80mg/dL or below 70mg/dL in real-time

Tandem x2
- Basal-IQ Technology
- Predicts and helps prevent lows
- Basal-IQ™ Technology
- Predicts glucose 30 minutes ahead
- Suspends insulin to help avoid the low
- Resumes insulin once glucose rises

• The only CGM approved for treatment decisions with zero fingersticks*
• The #1-preferred CGM brand†
• Transmits real-time glucose data to your smart device and up to 5 followers†
• 10-day wear and acetaminophen blocking*
MINIMED 670G SYSTEM HIGHLIGHTS.

- Medtronic 670G system offers SmartGuard technology for better control of blood glucose levels, helping you manage type 1 diabetes more effectively.
- Includes SmartGuard settings for optimal glucose control.
- AUTO MODE: Automatically adjusts insulin delivery based on glucose levels.
- Suspend before low: Stops insulin delivery if glucose levels fall below a set limit.
- Helps avoid hypoglycemia and hyperglycemia.

MANUAL MODE

PROTOCOLS SAME AS STANDARD PUMP / CGM THERAPY

Manual Mode with or without CGM

Pump
- Calculate initial pump settings
- Adjust pump settings

CGM
- SmartGuard HCL features:
  - Suspended by sensor
  - Suspended on low
  - Suspended before low
  - Resume basal by CGM

SUSPEND BEFORE LOW

AUTOMATED INSULIN SUSPENSION BY SENSOR GLUCOSE

Suspend before low: Insulin delivery stops IF...
- Glucose level is < 70 mg/dL at the set low limit AND
- Predicted glucose will be 20 mg/dL below low limit in less than 30 minutes

In this example: Low limit is set at 65mg/dL; low alarm would suspend insulin when glucose reached 138mg/dL; AND was predicted to reach 80 mg/dL within 30 minutes

Note: Must choose between ‘Suspend on low’ and ‘Suspend before low’

Recommendation: Use ‘Suspend before low’

AUTO BASAL

Dynamic and always adjusting

Goal:
- Adjust basal insulin to address glucose fluctuations, dawn phenomenon, illness, activity, stress, moderate post-meal excursions
- Increase / decrease as needed to drive 90 to 120 mg/dL target

Adjustments are conservative and not intended to correct a single meal in carb or missed bolus

Temp Target: A temporary target of 150 mg/dL can be set from 30 minutes to 12 hours

Key Concept: Auto basal is adjusted by the dosing algorithm.
Clinician does not fine-tune Auto Basal
The Bionic Pancreas

Approaches to Normal Glycemia

Biologic
- Replace Beta cells
  - Organ transplant
  - Islet cell transplant
- Limitations
  - Immunosuppression
  - Procedure risk
  - Availability of transplant
  - Limited survival

Mechanical
- Intensive Therapy
  - IAD or pump
  - Frequent glucose monitoring
  - Decision making related to food, activity and illness
- Limiting factor: Hypoglycemia

Biologic
- Artificial Pancreas
  - Insulin only
  - Insulin and Glucagon

Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes

Variation in the Mean Glucose Level among Adults and Adolescents.
Distributions of Mean Glucose Levels and Hypoglycemia among Adults and Adolescents.

Histogram Distributions of Mean Glucose Levels and Insulin Doses among Adults and Adolescents.

Conclusions
• As compared with an insulin pump, a wearable, automated, bihormonal, bionic pancreas improved mean glycemic levels, with less frequent hypoglycemic episodes, among both adults and adolescents with type 1 diabetes mellitus.

Limitations of Current Therapy
- Risk of hypoglycemia with acetaminophen (DexCom G6 ok with < 1000 mg/6 hrs)
- Currently available rapid acting insulin has relatively slow absorption
- No currently available stable glucagon formulations
- Device currently does not integrate all components and relies on wireless connectivity to insulin and glucagon pumps (reliability)

Insulet
Genesys
Genesis

NIDDK
Helping the Student with Diabetes Succeed: A Guide for School Personnel
https://www.niddk.nih.gov/health-information/health-communication-programs/health-care-professionals/school-guide/Pages/publicationdetail.aspx

This comprehensive resource guide helps students with diabetes, their health care teams, school staff, and parents work together to provide optimal diabetes management in the school setting. View or download promotional tools.
The End!!