The Realities of Technology in Type 1 Diabetes

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Disclosures

- I have no conflicts of interest to disclose
- I will discuss some unapproved treatments
Overview

- Background: the beta cell and insulin
- Type 1 Diabetes: Historical Perspective
- Technology
- Meters
- Software
- Apps
- Pumps/SAP, CGM, and APS systems
Diagram of the primary hormonal control of plasma glucose concentrations organized as an input-output system centered on plasma glucose level. (+) stimulation; (−) inhibition. GLP-1, glucagon-like peptide 1.

Physiology of Glucose Homeostasis and Insulin Therapy in Type 1 and Type 2 Diabetes
Ferrannini, Ele, MD, Endocrinology and Metabolism Clinics, Volume 41, Issue 1, 25-39

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Plasma glucose level

- Upper limit
  - Decreased insulin secretion
  - Increased glucagon secretion
  - Increased epinephrine secretion

- Mean
  - Symptoms
    - Decreased cognition
    - Aberrant behavior
    - Seizure, coma
      (Functional brain failure)

- Lower limit
  - Neuronal death
    (Brain death)

im totally never making insulin 4 u again FYI
## B-cell insulin vs subcutaneous insulin

<table>
<thead>
<tr>
<th>Endogenous</th>
<th>Subcutaneous</th>
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<tbody>
<tr>
<td>Delivered directly into the portal vein</td>
<td>Absorbed from subcutaneous fat depot directly into the circulation, bypassing the liver</td>
</tr>
<tr>
<td>Goes first to the liver to suppress glucose output during meals</td>
<td>Delayed absorption with delayed peak of action and delayed clearance from the blood</td>
</tr>
<tr>
<td>50% of secreted insulin is metabolized by the liver before going into the systemic circulation</td>
<td>Rapid acting analog action can last for as long as 4-6 hours</td>
</tr>
<tr>
<td>Works instantly and it’s cleared from the circulation in about 10 minutes</td>
<td>Regular insulin can last 6-8 hours</td>
</tr>
<tr>
<td></td>
<td>These differences result in increased risk for both hyperglycemia and hypoglycemia</td>
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Historical perspective

Evolution of type 1 diabetes management over the past century
Typical patient with juvenile diabetes before and after treatment with insulin.
Progress in Diabetes Care

- Discovery of Insulin, 1920s
- NPH insulin, 1930s
- First portable Glucose monitors, 1970s
- DCCT 1993
- Continuous Glucose Monitoring, 2000s
- Rapid acting/Basal Insulin analogs and Pumps, 1990s
- Biosynthetic Human insulins, 1980s
- APS
Historical Perspective: Glucose testing
Example of injection regimens

Regular Insulin Regimen

12 AM 6 AM 12 PM 6 PM 12 AM

NPH and Regular insulin or Rapid acting Analog

Basal and Rapid acting Analog insulin MDI regimen

Chase HP, Understanding Diabetes, 10th Edition*, p. 68
Risk of Long-term Complications vs. Hypoglycemia in DCCT

How has technology helped?
Severe hypoglycemia and A1c since DCCT

Rates of Severe hypoglycemia in JDRF CGM Study


O’Connell S M et al. Dia Care 2011;34:2379-2380
Measuring glycemic control: Portable glucose meters and A1c

- HbA1c test was proposed for monitoring glucose control in the late 1970s
  - Allowed for more accurate assessment of overall control and risk of complications
  - Made DCCT study possible

- First portable glucose meter was developed in the 1970s
  - Allowed for more targeted insulin dosing

- Data storage/Downloading capabilities developed in the mid-late 1990s
  - Allowed for more accurate insulin adjustments
  - Currently available software provides information on BG pattern recognition and statistics to help with management
  - Future: software will provide pattern recognition assistance and advice on what adjustments to make
Increasing Risk for DKA
- Metabolic acidosis
- Ketonemia
- Hyperglycemia

Increasing Risk for Severe Hypoglycemia
- Assistance required
- Major Severe Hypoglycemia
  - Medical personnel assistance required (ambulance, ER, hospital)
  - Seizure, coma, death

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Diabetes Apps

- Blood Sugar Tracking
- Insulin Dose Calculators
- Carbohydrate Counters
- CGM & Pumps
Continuous glucose monitoring
CGM in diabetes management
Schematic Representation
Evolution of CGM

CGMS

Glucowatch Biographer
Three Parts to All CGMs:

A. Sensor

B. Transmitter

C. Receiver/Monitor
CGM uses and limitations

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provides many additional data points including trend information</td>
<td>Requires concomitant use of Fingersticks (minimum 2 FS per day</td>
</tr>
<tr>
<td>Can help “predict the future”</td>
<td>Only Dexcom G5 currently approved for using CGM results for insulin calculations</td>
</tr>
<tr>
<td>Alarms can alert user of out of range glucose excursions</td>
<td>Increased burden of daily management</td>
</tr>
<tr>
<td>Can help reduce A1c but only if used all the time</td>
<td>More devices on body, more thinking about blood sugars</td>
</tr>
<tr>
<td>Intermittent use can have some benefits</td>
<td>Alarms can be disruptive to daily activities/sleep</td>
</tr>
<tr>
<td></td>
<td>Teens frequently sleep through alarms</td>
</tr>
<tr>
<td></td>
<td>Requires frequent action from user to be effective</td>
</tr>
<tr>
<td></td>
<td>Only benefits highly motivated users</td>
</tr>
<tr>
<td></td>
<td>Increased cost</td>
</tr>
<tr>
<td></td>
<td>Sensor cost added to glucometer strip cost</td>
</tr>
<tr>
<td></td>
<td>Not covered by some payors</td>
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</tbody>
</table>
CGM reports

A1c: 7.5%
N=1866

Statistics
- Average Glucose: 155 mg/dL
- Sensor Usage: 6 of 10 Days
- Calibrations / day: 1.9
- Standard Deviation: ± 45 mg/dL
- 72% High
- 26% Target
- 3% Low
- Target Range: 80 - 130 mg/dL
- Nighttime: 10:00 PM - 6:00 AM

Target Range: 70-180
Freestyle Libre Flash Glucose monitor (FGM)

- Hybrid between glucose meter and CGM
- Does not require calibration fingersticks
- Each sensor lasts for 2 weeks
- Approved in Europe in September 2014
- Currently under review by the FDA
- Only professional version approved in USA
Insulin pumps
Evolution of pumps

- The 1st insulin pump was developed in 1963
- Compact pumps on 1990s
- Smart pumps in early 2000s
- Sensor augmented pumps
  - Medtronic, Animas vibe
- 530 G, 630G -Automatic basal rate shutoff
- 670G-hybrid APS
Evolution of pumps

First portable insulin pump (1970s)

The first insulin pump (1963)
Insulin pump Therapy

Animas One touch ping

Omnipod

Medtronic

T-Slim

Accucheck Combo

I love you like a brother.

I'm a girl.
Current status of pump therapy

- All have bolus calculator
  - ICR
  - ISF
  - Target range
  - IOB with reverse correction option protects against insulin stacking and hypoglycemia
  - Two pumps have option to pre-program bolus adjustments for specific events

- Most have integrated or linked glucose meter

- Small dose increments suitable for small children (0.001-0.1 unit increments)

- Alternative basal patterns and temporary basal rate options
Benefits of pump vs injections

Basal rate

- The use of rapid acting insulin in a continuous infusion allows for a more targeted delivery of basal insulin to match the circadian variations in hormones that affect insulin sensitivity
  - Higher basal delivery at dawn can offset “Dawn effect”
  - Can adjust/suspend basal rate delivery during/after exercise to reduce hypoglycemia
  - Temporary basal rate feature can be useful during sick days, menstrual days, sports, steroids, etc.
  - Option to program alternative basal rate patterns that can be used to match specific changing needs for activity, menses, etc.
Basal rate: Pump vs. injection

![Graph comparing basal rates of pump and injections across different times of the day.]
Pump Advanced Bolus Options

"Standard" Bolus

Units of Insulin

Time

Spike (bolus)

(basal)

"Extended" Bolus

Units of Insulin

Time

Square Wave (bolus)

(basal)

"Combination" Bolus

Units of Insulin

Time

Spike (bolus)

Square Wave (bolus)

(basal)

"Super" Bolus

Units of Insulin

Time

Spike (bolus)

(basal "borrowed ahead" and added to spike)

(basal back to normal)
Does the pump improve A1c levels?

- Short term studies show that most patients have an A1c improvement in the first 3 months after starting on the pump.
- Long term studies show that only patients who routinely use the pump’s Advanced features achieve sustained A1c in target.
- Success with the pump still relies heavily on the motivation of the patient.
- Pump users report improved quality of life.
Artificial Pancreas Systems

Closed loop vs open loop
Components of the Closed Loop Pancreas

1. A CGM device
2. A control algorithm to compute the amount of insulin delivered
3. An insulin pump to deliver the insulin subcutaneously
Glucose control in fully automated vs. hybrid closed loop

Medtronic 670G

- Only APS currently approved in the US
- Hybrid system
- Currently approved only for ages 14 years and up
- Controller automatically adjusts the basal rate in the background to maintain BG at a target 120
- Sensor requires at least 2 calibrations per day, but 3 are recommended for best accuracy
- Patient required to bolus before meals and snacks
Other AP systems currently in pediatric trials

- Study of 670G in kids 7-13 years old currently ongoing
- Study of 670G for kids 2-6 years old in planning stages
  - Must take at least 8 units per day
- Dual hormone APS
  - Glucagon
  - Pramlintide
- Insulet
- Tandem
- BigFoot
- MMPCC (fully closed loop system)
New insulins

- Several companies are developing ultra rapid acting insulins that will have faster absorption and shorter duration than currently available insulin analogs
  - Will likely be needed for a fully automated APS without required “meal announcements”
  - Insulin Fiasp from Novo Nordisk already approved in Europe and Canada

- Smart insulin that can be released from blood “Depot” based on blood glucose level is also in development-Not expected to be available before 2021
Progress in diabetes care

- Discovery of insulin
- Home blood glucose testing
- DCCT
- Insulin analogs
- CGM and SAP
- Artificial pancreas
- Diabetes prevention
- Diabetes prevention

Thank You