The New Dawn of Technology in Type 1 Diabetes

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Pediatric Endocrinology and Diabetes
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The Division of Pediatric Endocrinology and Diabetes has multiple research projects with diabetes related technology companies. The institution receives grant funding from these companies to advance the field of diabetes technology.
T1D management before Insulin Therapy

• Patients life expectancy was 2-5 years after diagnosis of diabetes

• Patients were placed on a starvation diet
  – One week fast if there was glucose in the urine
  – Low calorie diet of 500 calories when no glucose in the urine

The Discovery of insulin, Bliss 1982
The Discovery of Insulin in 1921

• Dr. Frederick Banting, a surgeon, and Charles Best, a medical student, discovered insulin in 1921 in at the University of Toronto

• Dr. Banting removed pancreas of dogs, and then the dogs developed diabetes

• Banting and Best developed an extract of the removed dog pancreas and then injected back into the dogs.

• The extract made the symptoms of diabetes go away in dogs with no pancreas – “Insulin”

  • *The Discovery of insulin*, Bliss 1982
Insulin therapy first used in 1922
Early insulin treatment of diabetes

- Large reusable syringes
- Checked urine for glucose
- Insulin from pork and beef sources
- Strict diabetes exchange diet
Management until 1993

• Goals:
  – maintain normal body weight
  – Prevent symptoms of hyperglycemia, hypoglycemia and ketones

• 1-2 doses of a fixed mixture of intermediate and rapid acting
  – Ultralente, Lente, NPH and Regular insulin

• Monitor urine glucose levels and later blood glucose values

• People with type 1 diabetes at high risk of developing eye, kidney, neurologic and cardiovascular complications
  • N Engl J Med 1993; 329:977-986
The Diabetes Control and Complications Trial (DCCT) of 1983 to 1993

- The DCCT was randomized multicenter control trial with 1,441 patients with diabetes
  - Patients had diabetes from 1-15 years
  - No or mild diabetic retinopathy

- Goal of the study was to see if careful blood glucose control can reduce the rate of diabetes related complications

DCCT Study Arms

- **Conventional treatment arm**
  - Inject fixed amount of insulin 1-2 times a day
  - Goal of treatment was to avoid symptoms of hyperglycemia and hypoglycemia

- **Intensive treatment arm**
  - Inject insulin 3 or more times a day or use insulin pump
  - Daily adjustment of insulin doses
  - Goals of treatment
    - Have A1c of 6%
    - Premeal blood glucose of 70-120 mg/dL and post meal of 180 mg/dL

Results from the DCCT

• Significant decrease in complications of diabetes in intensive treatment arm
  – Reduction of retinopathy by 76%
  – Reduction in urine micro-albumin by 39%
  – Reduction of neuropathy by 60%
  – Increase of severe hypoglycemia by three times

• The study was stopped early in 1993, and all patients moved to “intensive diabetes treatment”

• Now intensive diabetes treatment is the standard of care for people with type 1 diabetes
Lessons from the DCCT

• Significant benefit to healthy A1c under 7%
  – Current guidelines in pediatrics is A1c under 7.5%

• Keeping blood glucose levels in near normal range is hard

• Tight diabetes control leads to increased risk of severe hypoglycemic reactions (seizures)

• Advances in technology and medications are needed to meet these goals
Other advance in T1D Therapy since 1993

• Changes in insulin activity allow for basal bolus insulin activity
  • Fast acting insulin: lispro or aspart or glulisine
  • Long acting insulin: glargine or detemir
Advances in Diabetes Technology

• Development of continuous subcutaneous insulin infusion or insulin pump therapy

• Continuous Glucose Monitoring Systems

• Development of Closed Loop Systems
Advances in Diabetes Technology

- Development of continuous subcutaneous insulin infusion or insulin pump therapy
- Continuous Glucose Monitoring Systems
- Development of Closed Loop Systems
Multiple Daily Injection or MDI

- **glargine**
- **lispro**
### Sample Insulin Sheet

**Lucile Salter Packard Children’s Hospital**  
STANFORD UNIVERSITY MEDICAL CENTER  
Toland Way, Palo Alto, CA 94304  

**Medical Record Number**  
Patient Name  
Address or Label  

**Packard Pediatric Diabetes Center**  
Diabetes Educator Line: (650) 498-7353  

**Insulin Scale for:**  
Standard Insulin Dose  
High dose version: 11/1/2007  

**Breakfast**  
NPH:  
Lantus:  
Humalog:  

**Lunch**  
NPH:  
Lantus:  
Humalog:  

**Dinner**  
NPH:  
Lantus:  
Humalog:  

**Insulin to Carbohydrate Ratio**  
- Carb Ratio= Amount of grams of carbs covered by 1 unit of Humalog  

<table>
<thead>
<tr>
<th>Breakfast Carb Ratio: 8</th>
<th>Lunch Carb Ratio: 10</th>
<th>Dinner Carb Ratio: 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Grains of Carbs</td>
<td>10 Grains of Carbs</td>
<td>10 Grains of Carbs</td>
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<tr>
<td>10</td>
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<tr>
<td>60</td>
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<td>5</td>
</tr>
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</table>

**Correction insulin**  
- Correction Factor= How many points 1 unit of Humalog lowers blood glucose  
- Target BG= Correction factor tries to bring BG to this desired number  
- Do not use correction scale if your last shot was less than 2 hours ago  

<table>
<thead>
<tr>
<th>Breakfast Correction</th>
<th>Target BG: 120</th>
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<tbody>
<tr>
<td>70 to 100 = subtract 1H</td>
<td>10</td>
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<tr>
<td>101 to 120 = no extra</td>
<td>10</td>
</tr>
<tr>
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Insulin Pumps

• Device that delivers insulin
  – Tube or patch

• Only short acting insulin in the pump
  – Adjustable basal rate
  – Increased flexibility in dosing, schedule, and snacking
  – Insulin on board feature
  – Deliver small amounts of insulin (as little as 0.05 units)
  – Dose calculations
Insulin Pump Evolution

1920s
Insulin Injections

1978
First Insulin Pump

1983
First Minimed Pump-502

1999
First Animas Pump-R1000

2005
First Omnipod pump

2006
Medtronic combine Pump and CGM

2013
Suspend on low pump

2016
Hybrid artificial pancreas

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Insulin Delivery with an Insulin Pump

Continuous basal delivery

Bolus doses

Insulin release with insulin pump therapy mimics normal pancreatic function

\[ \text{pump bolus} \]
• Must still check blood sugar and count carbohydrates

• Pumps do fail and can cause DKA

• Pumps can decrease HbA1c if used consistently and appropriately  
Advances in Diabetes Technology

- Development of continuous subcutaneous insulin infusion or insulin pump therapy
- Continuous Glucose Monitoring Systems
- Development of Closed Loop Systems
Meters over the years:

• Smaller
• Lighter
• More accurate

www.diabeteshealth.com
Continuous Glucose Monitoring

— A system that consists of:
  • A thin wire inserted under the skin (sensor)
  • A device taped over the skin (transmitter)
  • A device to show you the data (receiver)

— What does it do?
  • Monitors your glucose level every 5 minutes
  • Has arrows to show which way your glucose is going
  • Can set alerts to tell you if your number is too high or too low
  • Ability to share data with up to 5 people (Dexcom G4 with Share, Dexcom G5)

— Does it replace my fingersticks?
  • Still need to calibrate twice a day
  • Can dose off of CGM reading (Dexcom G5)
Evolution of Blood Glucose Self Monitoring

Glucose Monitoring

- Urine Testing
- 1977 Blood Glucose Meter
- 2000 First CGM system
- 2005-2007 Real-time CGM
- 2006 1st Dexcom
- 2016 Dexcom G5 treatment decisions

- Discreet measures
- Continuous measures
- Real Time Continuous Measures

Diabetes Mellitus History of Blood Glucose Self Monitoring Br J of Biomedical Science, 2012
Dexcom G5 Continuous Glucose Monitor (CGM)
Dexcom Trend Arrows
On iPhone

Where You Are Going

To know where you are going, look at your trend arrows. Remember it is not all about the number. Pay attention to the direction and speed of your glucose change.

| Steady: Not increasing/decreasing more than 1 mg/dL each minute. |
| Slowly falling: Glucose could decrease up to 30 mg/dL in 15 minutes. |
| Falling: Glucose could decrease up to 45 mg/dL in 15 minutes. |
| Rapidly falling: Glucose could decrease more than 45 mg/dL in 15 minutes. |
| Slowly rising: Glucose could increase up to 30 mg/dL in 15 minutes. |
| Rising: Glucose could increase up to 45 mg/dL in 15 minutes. |
| Rapidly rising: Glucose could increase more than 45 mg/dL in 15 minutes. |

CGM measures the mg/dL per minute, this chart calculates what that could mean per 15 minutes.

Where You Were

Stanford
Children’s Health
Lucile Packard
Children’s Hospital
Stanford
FDA News Release

FDA expands indication for continuous glucose monitoring system, first to replace fingerstick testing for diabetes treatment decisions

For Immediate Release

December 20, 2016

Release

The U.S. Food and Drug Administration today expanded the approved use of Dexcom’s G5 Mobile Continuous Glucose Monitoring System to allow for replacement of fingerstick blood glucose (sugar) testing for diabetes treatment decisions in people 2 years of age and older with diabetes. This is the first FDA-approved continuous glucose monitoring system that can be used to make diabetes treatment decisions without confirmation with a traditional fingerstick test. The system was previously approved to complement, not replace, fingerstick testing for diabetes treatment decisions.
Current Work Flow between Families and Providers is inefficient
Blood Glucose Meter
Data collection

Apple
Data consolidation
Data are conveyed on mobile device to Health app via HealthKit

Epic
Data analysis and communication
Data are conveyed on mobile device to Epic MyChart app
Data are available for analytics/review within the EHR
Data are visualized and assessed by diabetes provider

Provider communicates with patient/parent securely via Epic MyChart
Where are we with diabetes technology use in the United States?
Type 1 Diabetes treatment in 2015
Data From Type 1 Diabetes Exchange

• Many use an insulin pump
  – 65% of kids 6-12 yrs
  – 58% kids 13-17 years

• Increased number of blood glucose readings a day
  – 6-12 years old, 89% checking 3 or more times a day
  – 13-17 years old, 61% checking 3 or more times a day

Diabetes Care 2015;38:971–978
Type 1 Diabetes Mellitus Therapy in 2015

Continuous glucose monitor (CGM) use
– Children 6-12 years old, 8% use CGM
– Children 13-17, 5% use CGM

Children not successful in reaching A1c target for their age
– Children 6-12 years old, only 20% have A1c under 7.5%
– Children 13-17 years old, only 16% under 7.5%
– Young adults 18-25 years old, 25% have A1c under 7.5%

• Diabetes Care 2015;38:971–978
Advances in Diabetes Technology

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Steps to a Closed-Loop System

Urine Testing

Glucose Monitoring

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2013 Suspend on low pump

2016 Dexcom G5 treatment decisions

2016 Commercial Hybrid artificial pancreas

Artificial Pancreas

Insulin Delivery

1920s First Insulin Pump

1977 Urine Testing

1977 Blood Glucose Meter
FDA approves first automated insulin delivery device for type 1 diabetes

For Immediate Release  September 28, 2016

Release

The U.S. Food and Drug Administration today approved Medtronic's MiniMed 670G hybrid closed looped system, the first FDA-approved device that is intended to automatically monitor glucose (sugar) and provide appropriate basal insulin doses in people 14 years of age and older with type 1 diabetes.
Medtronic 670G Hybrid Closed Loop System

- Much of the sentinel work was done by Dr. Bruce Buckingham’s team
- Insulin pump and CGM system
- Algorithm in pump determines how much basal insulin is needed
- Basal rate regulator
  - Patients still need to count carbs and bolus for meals
  - Still need to check BGs several times a day to calibrate CGM
- Approved for children 14 years or older
What we learned from the 670G Study

• In 12,000 patient days, no severe hypoglycemia or DKA

• Teens used system 75% of the time

• Average A1c went from 7.7% to 7.1%

• Teens time in target glucose (71-180 mg/dL) went from 60% of time to 67% of the time in target


• All patients report dislike for amount of alerts and alarms

  • Almost all patients liked overnight glucose control, some burden by system during the day

  • Most patients not willing to return device at end of study
Glucose Sensor Data before and after
What does the future of diabetes hold?

• Other insulin pump companies will be coming to market with their own Artificial Pancreas Systems
  – iLet System (Bionic Pancreas: insulin and glucagon pump)
  – OmniPod, Animas, Tandem, BigFoot etc.

• Factory calibrated CGM, Freestyle Libre (not yet FDA approved)
  – Do not have to check blood glucose and enter into system

• Full closed loop
  – No need to carb count or correct high BGs
Some patients might be on their own artificial pancreas
Thank you and Questions?