The evolution of diabetes management: Where we’ve been, where we are & where we are going

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2019

Conflict of Interest Disclosure
I am a certified pump trainer for Animas, Medtronic, Tandem and Omnipod

Objectives
1. The learner will be able to discuss the pros and cons of multiple daily injections versus continuous subcutaneous insulin infusion
2. The learner will be able to identify 2-3 ways that continuous glucose monitoring can help to prevent acute and chronic complications of diabetes
3. The learner will be able to name at least 2 of the newest insulin pumps on the market and discuss the pros and cons of each
4. The learner will be able to discuss at least 1 future diabetes treatment option under investigation
In the beginning

Ancient Egyptians first recognized diabetes around 1500 BC as a rare condition in which a person urinated excessively and lost weight.

Arataeus, a Greek physician, first used the term “diabetes,” which is derived from the Ionic and Latin terms meaning to pass through or to siphon. He described diabetes as a condition where “no essential part of the drink is absorbed by the body while great masses of the flesh are liquefied into urine.”

“Mellitus” means “honeyed,” referring to the sweet taste of the urine.

The first test for diabetes was the urine taste test.

Matthew Dobson, 1776, measured the concentration of glucose in the urine of patients with sweet-smelling and sweet-tasting urine and found it to be increased.

Paul Langerhans, 1869, discovered clusters of cells in the pancreas, later called “islets of Langerhans.”

von Mering & Minkowski, 1889, performed experiments on dogs to confirm diabetes.

Eugene Opie, 1901, discovered that the “islets of Langerhans” produce insulin.

Banting & Best/McLeod & Collip, 1921, developed insulin.

Evolution of diabetes management:

- **1900s**: Urine tasting
- **1922**: Saccharometer
- **1977**: Urine test strips
- **1999**: Glucose sensor

Integrated systems:

1977

1989

1999

Evolution of diabetes pump therapy and glucose sensor systems:

- Banting & Best/McLeod & Collip, 1921, developed insulin.
- Paul Langerhans, 1869, discovered clusters of cells in the pancreas.

Types of diabetes:

- Type 1: Insulin deficiency
- Type 2: Insulin resistance

Diabetes management:

- Insulin injections
- Urine testing
- Saccharometer
- BG meters
- Insulin pump therapy
- Glucose sensor
Evolution of insulin

Insulin

Diabetics

the only people that take drugs to avoid getting high.
Insulin

Sliding Scale

Bolus insulin – Sliding scale

Basal and Bolus

Newer Insulin

**Fiasp (Aspart) — 2017 Approved for adults only so far...**

2019: Novo asking FDA for approval for children with T1DM

- Fiasp can be dosed at mealtime or within 20 minutes after starting a meal.
- Fiasp enters the bloodstream in ~2.5 minutes
- Has 2 added excipients:
  - Niacinamide increases the rate of initial absorption
  - L-arginine helps to stabilize the formulation

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**The Future of Insulin**

- Glucose responsive insulin
- Smart insulin would work automatically in response to body's level of glucose. Ex: higher the BG the more insulin released
- Other smart insulins being researched with IDMF:
  - Eli Lilly-Glycostasis
  - Novo Nordisk-Ziylo
  - Sanofi-helping to fund 4 other teams working on smart insulin
  - University of Utah
  - Melbourne University in Australia
  - North Carolina State/UNC, developing a microneedle patch design
  - Sensulin
  - Biotechnology company, looking to partner
Keeping track of data

Home glucose monitoring
Glucometers and Bluetooth

Continuous Glucose Monitoring (CGM)

Continuous Glucose Monitors

A device that provides “real-time” glucose readings and data about trends in glucose levels
Reads the glucose levels under the skin every 1-5 minutes (10-15 minute delay)
Most provide alarms for high and low glucose levels and trend information
All CGM systems contain a sensor, a transmitter and a receiver
Continuous Glucose Monitors

**SHORT TERM BENEFITS**
- Minimize extremes in blood glucose levels
- Receive immediate feedback of the impact of food/exercise/stress on blood glucose levels
- Know the direction the blood glucose is trending
- Directional arrows add meaning to finger sticks

**LONG TERM BENEFITS**
- Reduces HbA1c
- Helps to identify patterns in blood glucose
- Allows us to better test and fine-tune basal rates, sensitivity factors and carbohydrate ratios
- Improves hypoglycemia unawareness

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**Why use a CGM?**

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**CGM-Dexcom**

**DEXCOM G5**
- Acetaminophen affects CGM readings
- Must calibrate at least every 12 hours
- 7 day wear

**DEXCOM G6**
- No interaction with Acetaminophen
- Do not need to calibrate
- 10 day wear
- Compatible with iOS 5 and up
- Urgent Low soon

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CGM-Guardian Connect (Medtronic)

Approved in patients on MDI ages 14-75
Real-time sensor glucose data, predictive alerts up to 60 minutes in advance.
Uses the Sugar.IQ app
Care providers (parents/significant others) use the CareLink Connect web app to track the patient’s glucose data in real time, can receive text message notifications for high and low glucose alerts (there is no “share” option people must have internet access).

CGM-Guardian Connect

- CGM consists of
  - Guardian sensor 3-wear for 7 days on abdomen or arm
  - Guardian Transmitter—1 yr
- Calibrations
  - 2 hours after inserting sensor
  - Within 6 hours
  - At least every 12 hours
- Cannot make treatment decisions based on CGM data alone, must check finger stick

CGM-Freestyle Libre (Abbott)

- Indicated for ages 18+
- 10 day or 14 day wear only on the back of the upper arm
- 1 hour warm up period but must check FS during the first 12 hours of use
- Sensor must be scanned at least every 8 hours with the phone App or reader
- Each scan provides a current glucose reading, a trend arrow and an 8 hour history
- Compatible with the freestyle Libre link app with iOS7 and later versions
- Integrates with LibreView cloud based diabetes management system
CGM-Freestyle Libre

Freestyle Libre
- There are no alerts or alarms unless the sensor is scanned
- You must check blood glucose with a fingerstick:
  - During the first 12 hours of wearing a FreeStyle Libre 14 day Sensor

CGM-Eversense (Senseonics)

- Fluorescence technology to measure glucose with a tiny sensor implanted completely under the skin.
- 3 month wear
- A smart transmitter is worn over the sensor on the arm and the adhesive is changed daily
- The smart transmitter can be removed and replaced without ending the sensor session.
- The smart transmitter wirelessly powers the sensor, collects the glucose data and wirelessly powers the Eversense Mobile App every 5 minutes

CGM-Eversense

- 24 hour warm up
- Initialization- 4 BG calibrations 2-12 hours apart
- Calibrate every day, 10-14 hours apart
- Finger stick needed before treatment decisions
Future of home glucose monitoring

- Non-invasive blood glucose monitor
  - A hybrid technique combining Near Infrared (NIR) absorption and bio-impedance measurements
  - Electromagnetic wave-based technologies for non-invasive glucose measurement, including infrared (IR) spectroscopy, photoacoustic (PA) spectroscopy, Raman spectroscopy, fluorescence, optical coherence tomography (OCT), terahertz (THz) spectroscopy, and microwave sensing.

- Glucowise
  - Non-invasive device that uses high frequency radio waves
  - Gently squeeze the skin between the thumb and forefinger or earlobe
  - Mobile app and cloud based data management

- K'Track Glucose Watch
  - Biosensors under watch face: “K’apsul”
  - Tiny microneedles penetrate the top layer of skin and analyze interstitial fluid
  - Monitors sugar every time a button is pressed on the watch

- Google contact lens
  - Smart contact lenses that also monitor blood sugar levels by analyzing tears
  - This research has been stopped
INSULIN DELIVERY

Two TT's walk into a bar, and first one says "The first shot is on me..."
The second one says "I don't do injections. I'm on the pump!"

NPH & rapid acting insulin

[Graph showing insulin levels at different times of the day]
Breakfast Lunch Dinner

Basal & bolus insulin dosing

Plasma insulin

Time

2:00  7:00  12:00  16:00  20:00  24:00  7:00  12:00  7:00

Basal

Multiple Daily Injections vs Continuous Subcutaneous Insulin Infusion

It is a personal (& provider) choice

Neither method will improve control without:
- Frequent glucose monitoring
- Assessing basal and bolus needs
- Carbohydrate counting
- Giving correction doses

Continuous Subcutaneous Insulin Infusion (CSII=Pumps)

ADVANTAGES
- Can fine tune basal insulin, especially overnight
- Ease of giving multiple insulin boluses
- Can be integrated with meters & CGMs
- Bolus calculations
  - Carbohydrates
  - Correction doses
  - Basal cover
- Alarm
- Ability to Download and Review Results

DISADVANTAGES
- Always wearing a device
- If infusion is interrupted, can develop ketosis or DKA
- Local scarring at infusion set sites
- Pain of infusion set insertion
Multiple Daily Injections (MDI)

**ADVANTAGES**
- Not wearing a device
- No skin scarring from subcutaneous catheters
- Basal insulin is always onboard – less chance of DKA

**DISADVANTAGES**
- Multiple injections
- Need to always carry an insulin pen or syringe and vial
- Can have days of variable basal insulin absorption
- No electronic record of insulin administration and no integration with glucose test results (usually)

Insulin Pens

- **NovoPen Echo**
- **Insulin pens-InPen (companion medical)**
  - Smart Insulin Pen-InPen – Companion Medical
  - Bluetooth chip in the pen connects to an app
  - App will calculate insulin dose, monitor insulin temperature, track injections, offer reminders
  - Can be used with most smart devices
  - Dose is dialed manually using app recommendation
  - Uses Novolog or Humalog Cartridges
  - Tracking and reporting to health care provider
  - Can pair some meters and the Dexcom with app through Apple Health
  - Does not have a “sharing” feature
Insulin Pumps--NOW

- Omnipod DASH
- Medtronic Revel, Medtronic 530 G
- Animas OneTouch Ping
- Medtronic 630G & 670G
- Tium, Tflex, Tium X2

Insulin pumps-Omnipod

Tubeless insulin pump

- 2 parts
  - Pod
  - PDM (Personal Diabetes Manager)

PDM has an integrated blood glucose meter and uses freestyle test strips

Pod and PDM must be within 5 feet of each other when delivering a bolus or making changes to the pump settings

Pod holds 200 units of insulin and can be worn for 72 hours

Insulin pumps-Omnipod Dash

- Personal Diabetes Manager (PDM) with a color, touch-screen interface-Android platform
- Contour next one Blood Glucose Meter
- CalorieKing food library
- Mobile applications on their iOS smartphone (coming soon)
  - Omnipod VIEW lets parents/caregivers view the PDM data on their smart-phones
  - Omnigod DISPLAY lets users see their PDM data on their own smartphone and also has a “Find my PDM” feature
  - Today View Widget lets users see their insulin and CGM data on one smartphone screen, with one swipe
Insulin pumps-Omnipod Dash

- Menu icon
- Touchscreen
- Bolus button
- Back
- Micro-B USB Port
- Non-functional

Settings icon
- Status bar
- Tab labels
- Tab area
- Value and time of most recent blood glucose reading
- Amount and time of most recent bolus

Integrated Systems

- Minimed 530G with Enlite CGM and threshold suspend
- Animas Vibe with Dexcom G4 CGM
- Minimed 670G with Guardian 3 CGM and smartguard technology and meter remote
- T:slim X2 with Dexcom G6
- Minimed 630G with Guardian 3 CGM and smartguard technology and meter remote
Integrated Pumps and CGMs

MINIMED 530G
- MiniLink Transmitter with Enlite Sensor
- Threshold Suspend: automatically stops insulin delivery when sensor glucose values reach a preset low threshold
- 6 day wear
- Minimed Connect for android and iphone

MINIMED 630G
- CGM with Guardian Sensor 3 and Guardian Link 3 transmitter
- SmartGuard Technology
  - Takes action for you if your sensor glucose values go below a preset level. If you don’t respond in 2 hours, it can pause insulin delivery for up to 2 hours
- Predictive Alerts
  - The pump lets you know up to 30 minutes ahead if you’re trending high or low
- Contour Next Link 2.4 meter
  - Can give remote boluses
  - Cannot use Minimed connect app

MINIMED 670G
- 670G with Auto Mode
- Medtronic

670G with Auto Mode

630G with Guardian CGM
Integrated Pumps & CGMs-670G

**MiniMed 670G**
- Hybrid closed loop system that uses glucose data obtained from a CGM to adjust basal insulin delivery via pump.
- The system targets a blood glucose level of 120 mg/dl and uses the Guardian 3 sensor.
- Not fully automated or hands-off—still requires carb counting, manual bolus corrections, infusion set changes, sensor wear, and calibrations.
- Contour next link 2.4 meter and remote meter bolusing.
- Approved ages 7 and older.

**SmartGuard features**
- **Automode**
  - Automatically adjusts your basal (background) insulin every five minutes based on your CGM readings.
  - Helps keep your sugar levels in your target range for fewer lows and highs.
  - Can compensate for reasonable over or underestimation of carbs intake.
- **Suspend before low**
  - Stops insulin up to 30 minutes before reaching your preset low limits.
  - Automatically restarts insulin when your levels recover without alerts.
  - Helps you avoid lows and rebound highs.

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**Integrated Pumps and CGMs-T:slim X2**

- Approved for use with the Dexcom G6 2018.
- Predictive Low Glucose Suspend (PLGS) with Basal IQ will suspend insulin delivery up to half an hour before the predicted low BG.
- Can pair the pump, CGM and a smart device but cannot see data on both the pump and Dexcom receiver at the same time.
- Remains the slimmest pump on the market.
- Only pump with a rechargeable battery.
- Waterproof—3 feet of water for up to 30 minutes.
- Optimized for use with the Tandem Device Updater for remote software and feature updates from a personal computer “Plug and play.”
Integrated pump and CGM’s—T:Slim X2 with Basal IQ and PLGS

What’s coming with pumps & CGM’s???

Omnipod future technology

Omnipod Horizon Automated glucose control system

Insulet’s automated insulin delivery

The on-body pod and Dexcom CGM will communicate with one another directly, meaning that users won’t need to have the handheld Dash PDM with them to remain in closed loop.

To partner with Tidepool Loop—automated insulin delivery app.

Omnipod future technology

Lilly U500 and U200 Omnipod System –
Insulet has partnered with Lilly to develop Omnipod systems for more concentrated U200 and U500.
Omnipod U200 will be applicable for users with a total daily dose of greater than 70 units of insulin; the U500 will be applicable for people with type 2 diabetes and a total daily dose of greater than 200 units of insulin.
The big change is the addition of different software on the handheld PDM that is compatible with concentrated insulins.

Tandem’s pipeline

-Tandem, Dexcom and TypeZero are working together on the integration of their technologies into the NIH-funded International Diabetes Closed Loop (IDCL) trial. Tandem is working on development of an insulin pump that integrates the data from a Dexcom G6 sensor and TypeZero’s inControl algorithm directly into the pump’s touchscreen interface.

-T:slim X2 Mobile app: T: connect
-Control IQ is an algorithm built into the T:slim X2 pump that automatically adjusts basal insulin; the system is also built to automatically deliver correction boluses to bring down very high blood sugars.

-T:Sport Insulin patch pump with hybrid wear
   Users will be able to wear the t:sport pump like a patch (very short infusion set) or in a pocket like a traditional tubed pump (longer infusion set). t:Sport will be about half the size of the current t:slim X2, is expected to hold 200 units of insulin, and will include an on-pump bolus button. t:Sport will integrate the Control IQ hybrid closed loop algorithm

MiniMed’s pipeline
- Blue tooth enabled MiniMed 670G pump and mobile app display to enable remote monitoring for caregivers
- Project Harmony CGM sensor - next generation CGM sensor. Approval for insulin dosing
- Sensor with 1 time per day calibration
- Advanced hybrid closed loop with automatic correction blousing. Using a new Unity CGM (1)
- A combo CGM-insulin set with extended wear. The single patch would house the Harmony CGM sensor and a cannula for insulin infusion – one place on the body.

Beta Bionics-iLet
ILET
- Led by Ed Damiano
- Bihormonal bionic pancreas
- Dual-chamber bionic pancreas is designed to use blood glucose data to autonomously adjust insulin and glucagon starts with patient’s weight
- No need for carb counting
- Fiasp, lispro, aspart studies
- Beta Bionics’ device can dose insulin, glucagon or both as needed. The iLet system calculates and doses insulin or glucagon based on data from a continuous glucose monitor.
- Beta Bionics and Senseonics plan to work together to combine the two systems in the hopes of driving insulin and glucagon dosing with real-time data from the Eversense monitor.

https://www.drugdeliverybusiness.com/beta-bionics-58m-for-iLet-bionic-pancreas/
Bigfoot Biomedical
A disposable Asante pump connected to a Bigfoot reusable closed-loop controller (with no screen or buttons)
Bluetooth connected to a Dexcom G5 CGM, but more recently trying Freestyle Libre CGM
Bluetooth connected to a smartphone app that functions as the system’s user interface
A paired Bluetooth glucose meter for CGM calibration.
The key difference from other closed-loop devices is that users will only interact with the smartphone app, which will function as a “window” to the automated insulin delivery system.
Also working on smart pens

https://www.bigfootbiomedical.com/abbott-bigfoot-collaboration
Glucagon!

2 new glucagon formulations are at the FDA
- Eli Lilly—Nasal glucagon
  - If approved, it will be the first dry powder nasal spray on market to treat severe hypoglycemia.
- Xeris Pharmaceuticals- Ready to use glucagon emergency pen
  - first ready-to-use, liquid-stable glucagon in an auto-injector to treat severe hypoglycemia.

Take home points

- Diabetes management is an art
- There is no single right way to manage diabetes
- Patient’s should have choice
- Diabetes management options are changing fast, so keep yourself educated!

THANK YOU!!!

Questions???
references

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