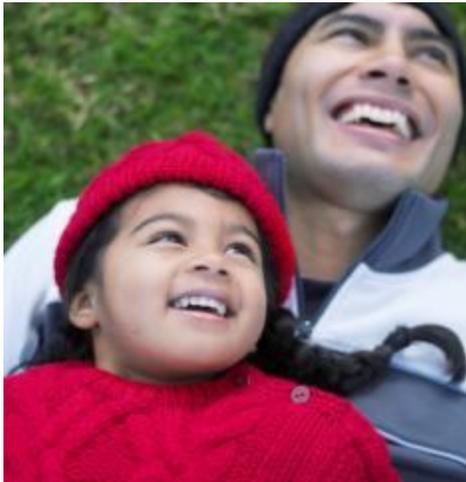


**JDRF**  
**typeone**  
**nationsummit**  
IMPROVING LIVES. CURING TYPE 1 DIABETES. **T1D**



# The Realities of Technology in Type 1 Diabetes

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May 6, 2017



# 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

# Plasma glucose: primary hormonal control

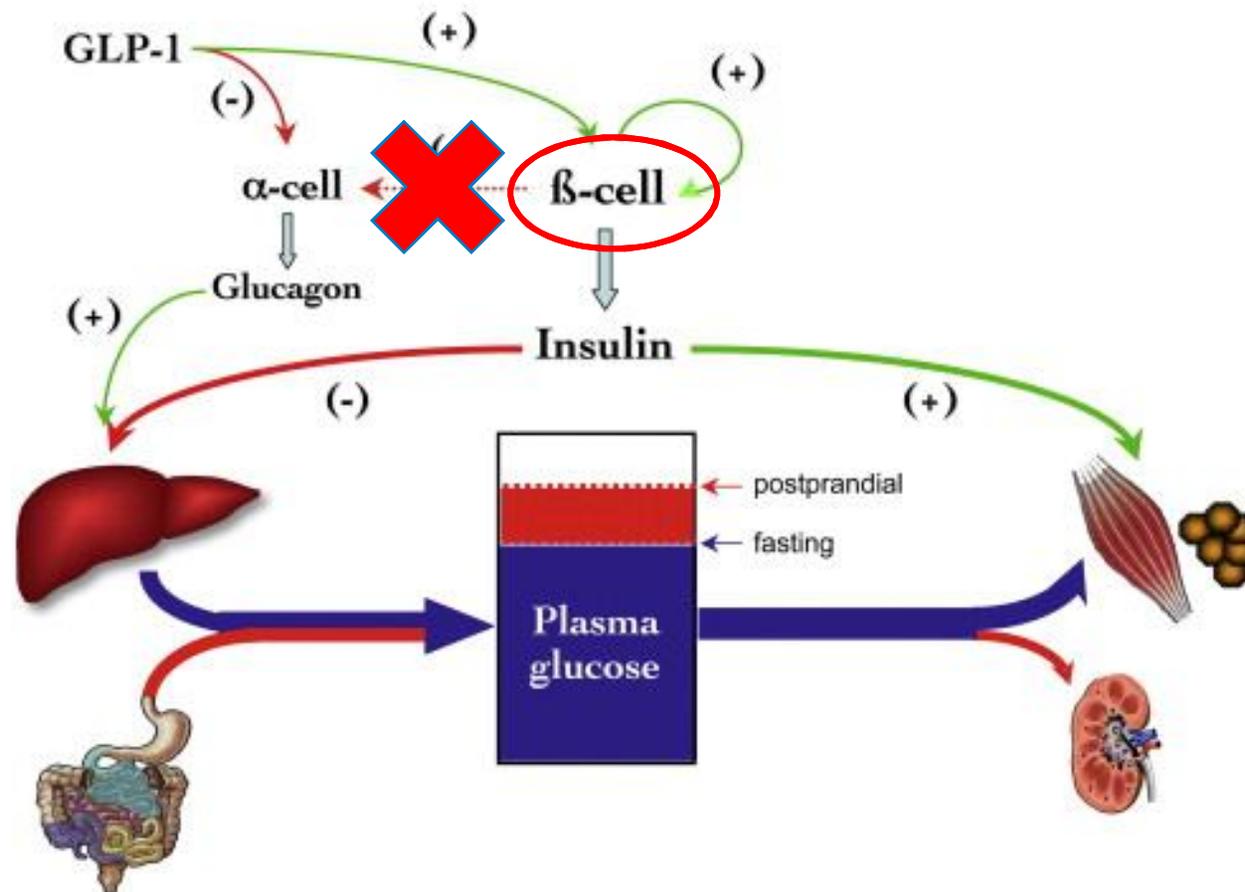
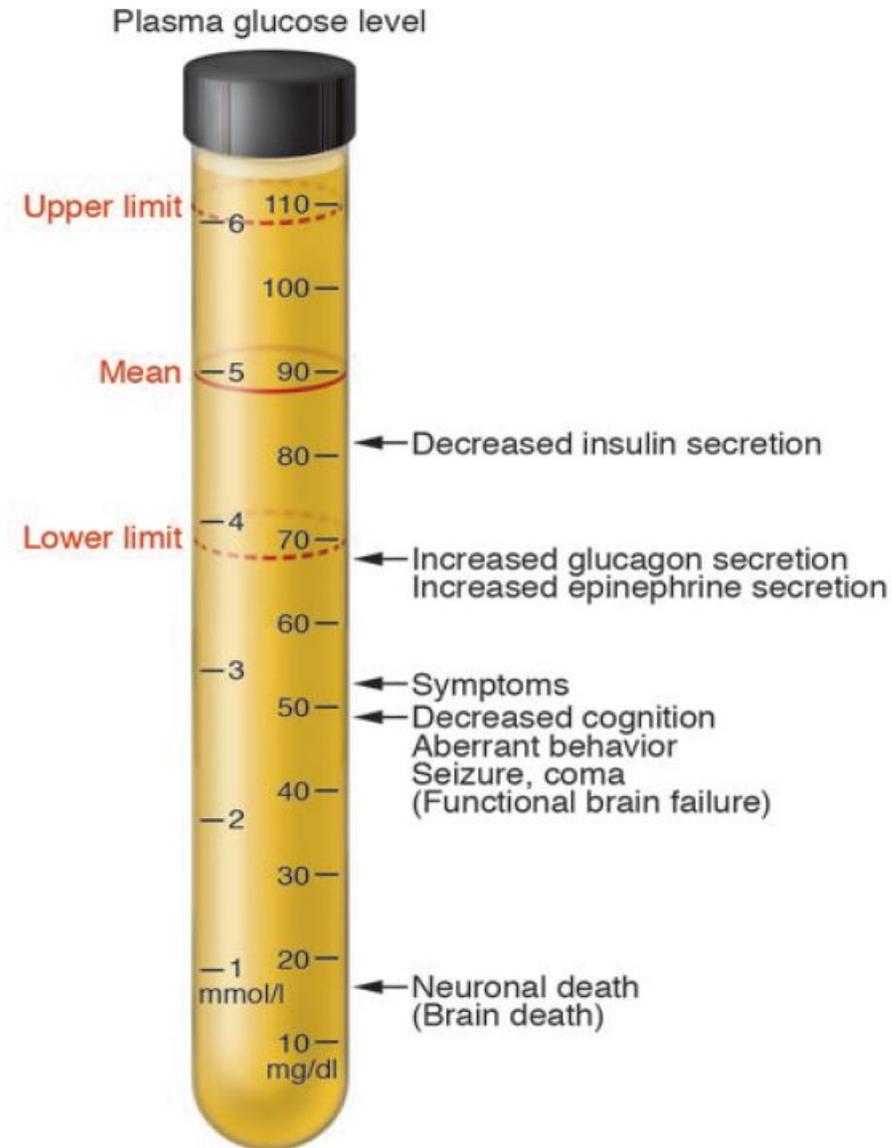


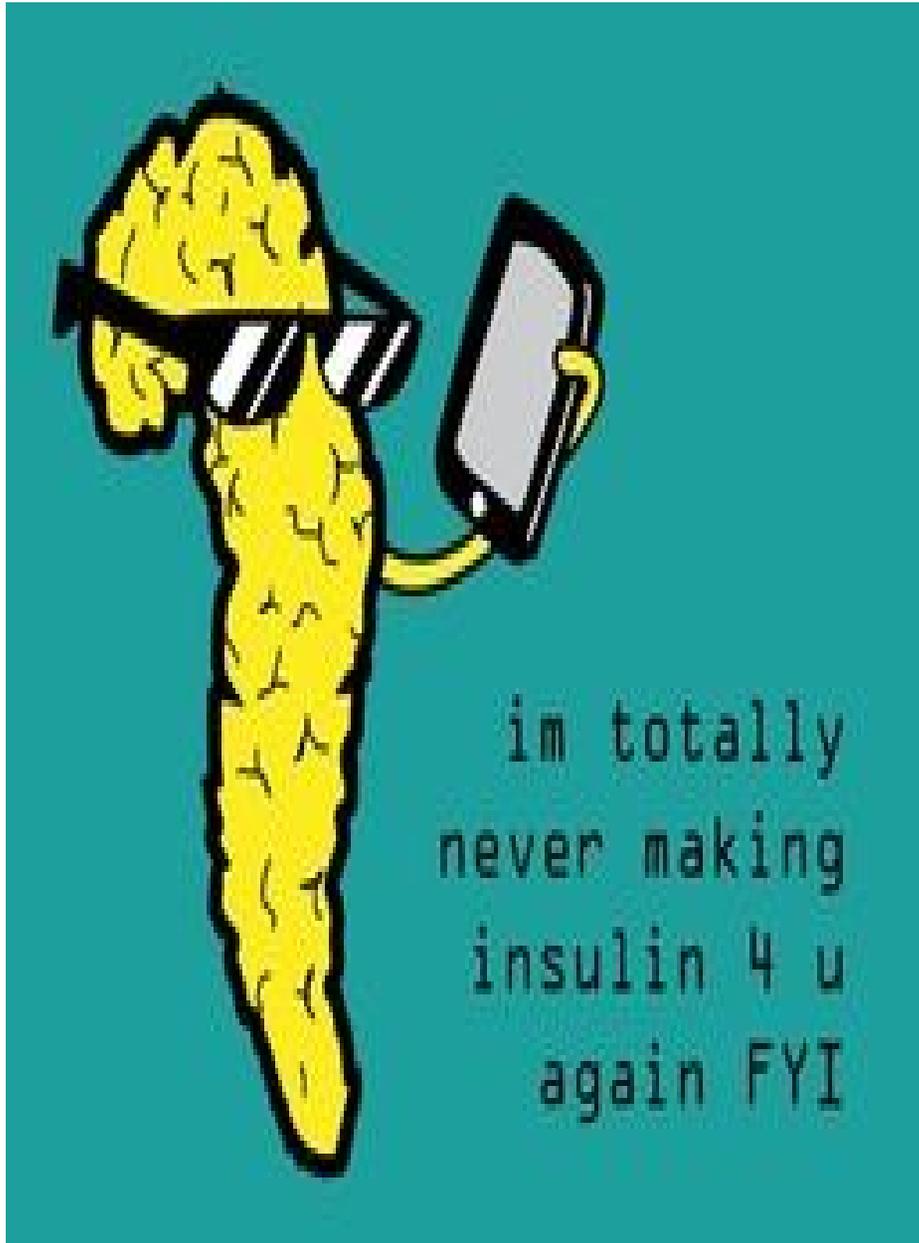
Diagram of the primary hormonal control of plasma glucose concentrations organized as an input-output system centered on plasma glucose level. (+) stimulation; (-) inhibition. GLP-1, glucagon-like peptide 1.

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

Copyright © 2012 Elsevier Inc.



Cryer, P. The Journal of Clinical Investigation. Volume 117 Number 4 April 2007



# B-cell insulin vs subcutaneous insulin

## Endogenous

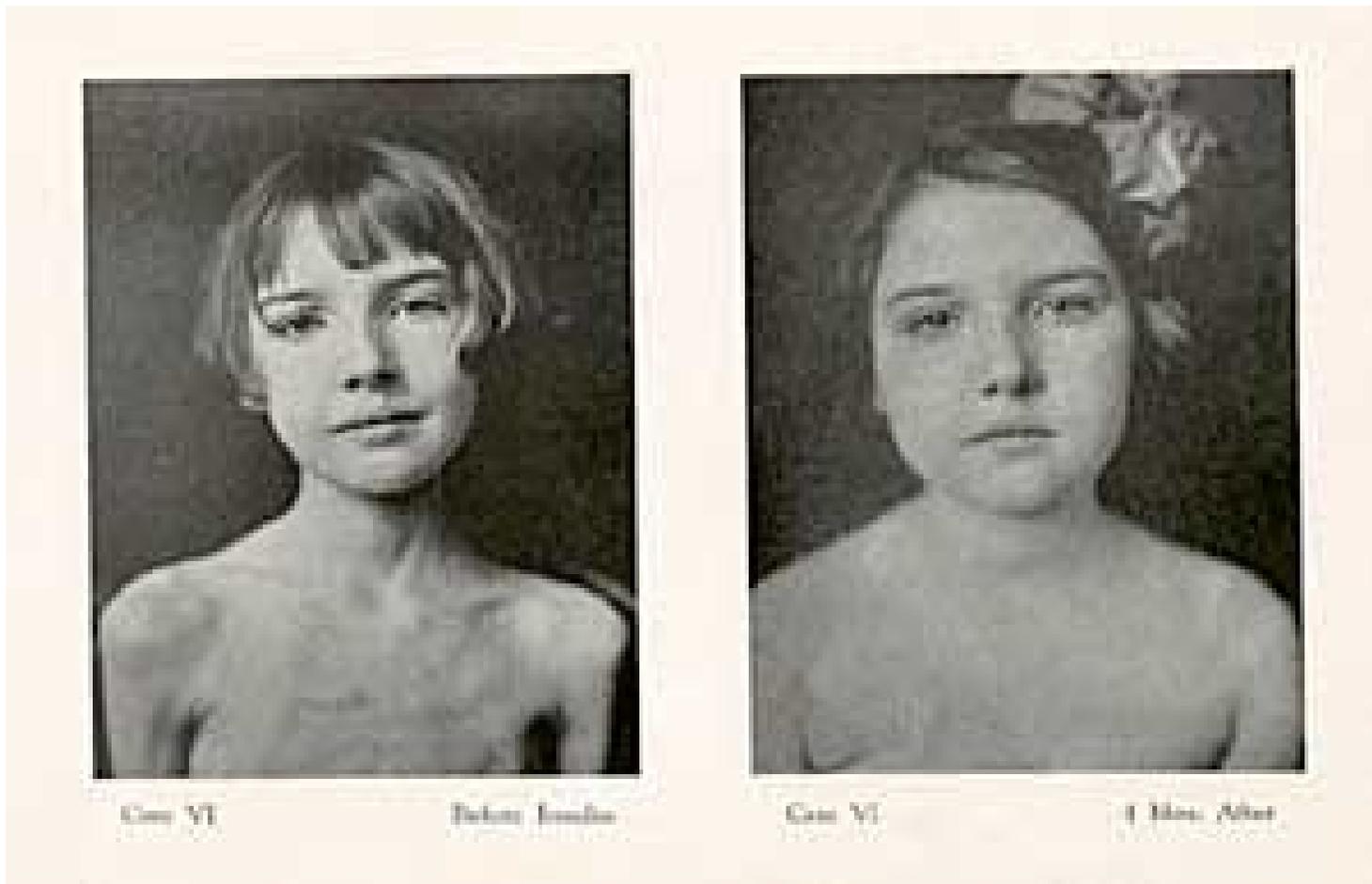
- Delivered directly into the portal vein
- Goes first to the liver to suppress glucose output during meals
- 50% of secreted insulin is metabolized by the liver before going into the systemic circulation
- Works instantly and it's cleared from the circulation in about 10 minutes

## Subcutaneous

- Absorbed from subcutaneous fat depot directly into the circulation, bypassing the liver
- Delayed absorption with delayed peak of action and delayed clearance from the blood
  - Rapid acting analog action can last for as long as 4-6 hours
  - Regular insulin can last 6-8 hours
- These differences result in increased risk for both hyperglycemia and hypoglycemia

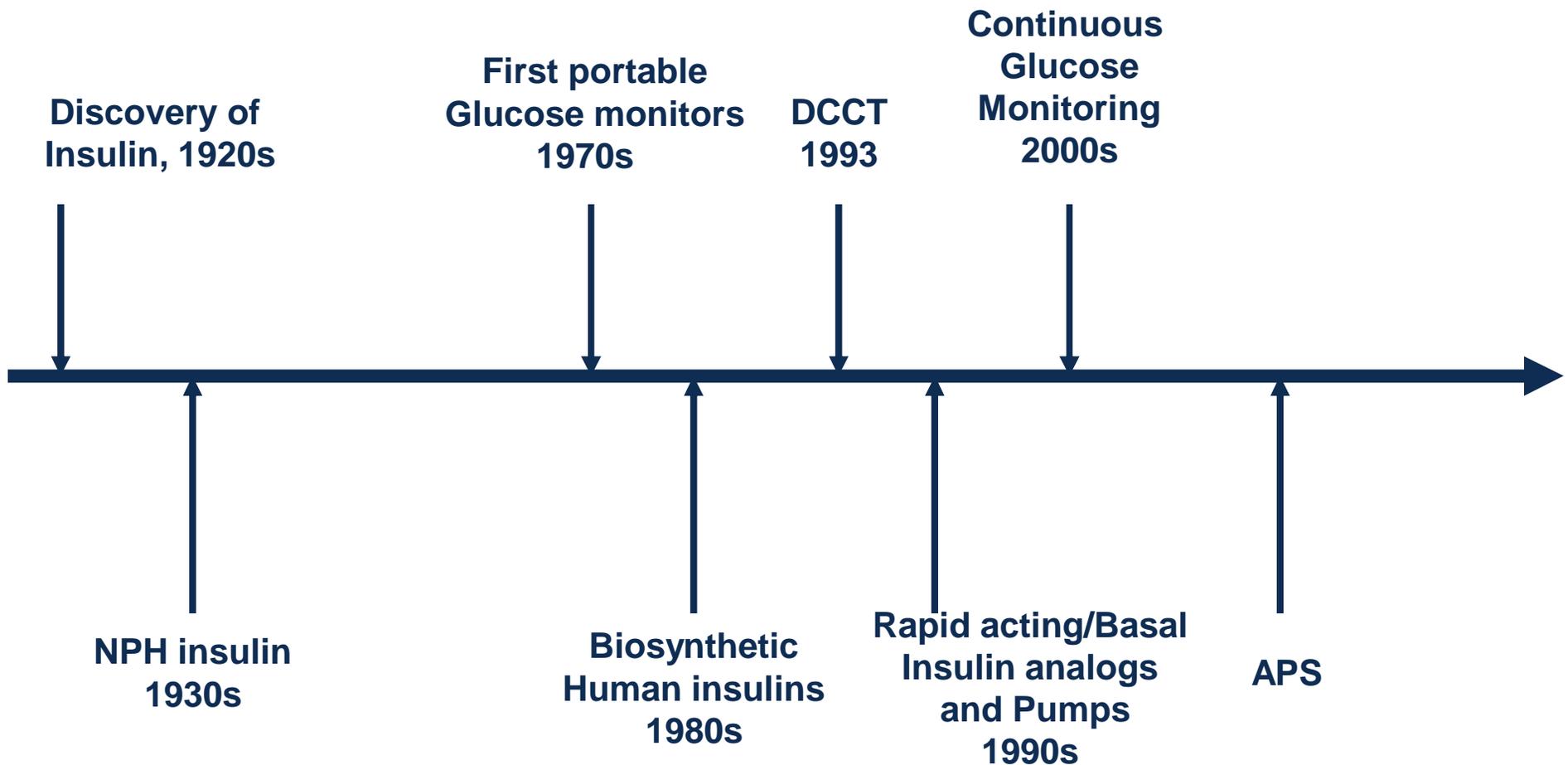
# Historical perspective

Evolution of type 1 diabetes management over the past century



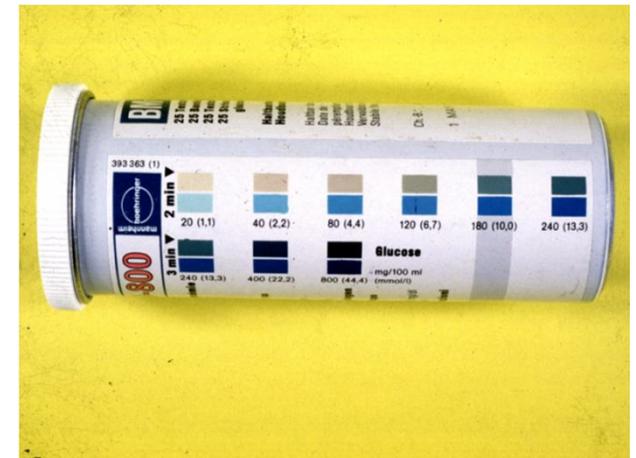
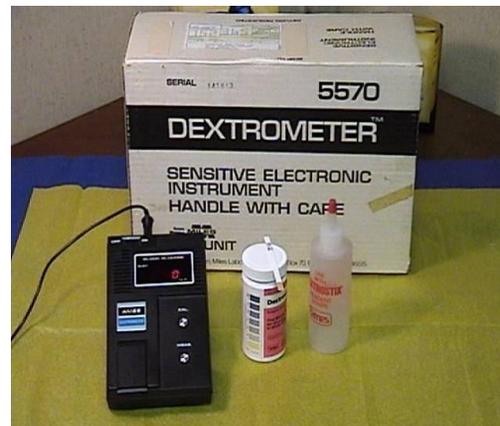
Typical patient with juvenile diabetes before and after treatment with insulin

# Progress in Diabetes Care



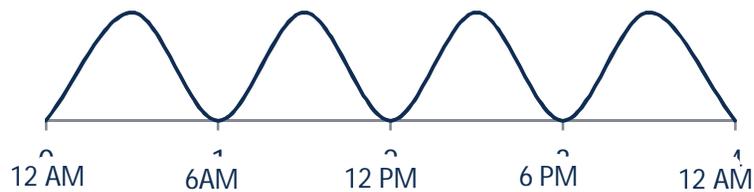
# Historical Perspective: Glucose testing

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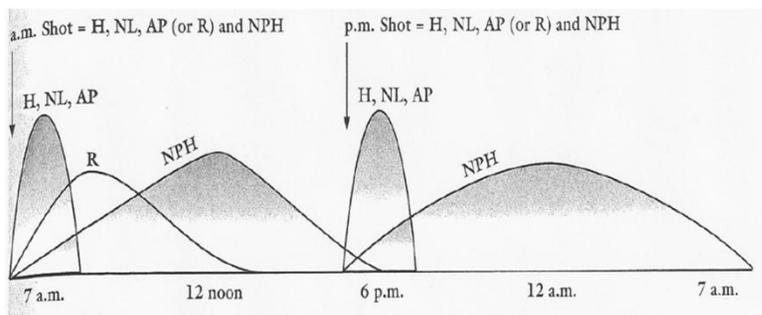


# Example of injection regimens

## Regular Insulin Regimen



## NPH and Regular insulin or Rapid acting Analog Basal and Rapid acting Analog insulin MDI regimen

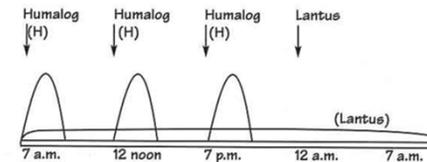


Chase HP, Understanding Diabetes, 10<sup>th</sup> Edition\*, p. 68

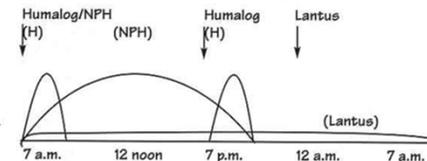
**Figure 1: Use of Lantus Insulin**

Two of the most common methods of using Lantus insulin:

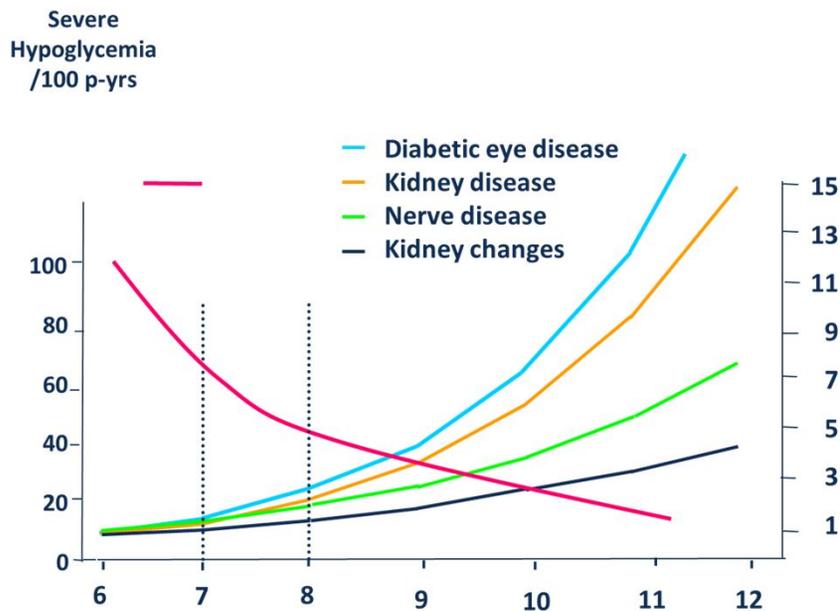
In the first example, Lantus is used as the basal insulin and Humalog (H) or NovoLog is taken prior to meals.



In this second example, NPH and Humalog (H) or NovoLog are taken in one syringe in the a.m. Humalog is taken alone at dinner. Lantus (alone in the syringe) is taken either at dinner, at bedtime or in the a.m.



# Risk of Long-term Complications vs. Hypoglycemia in DCCT



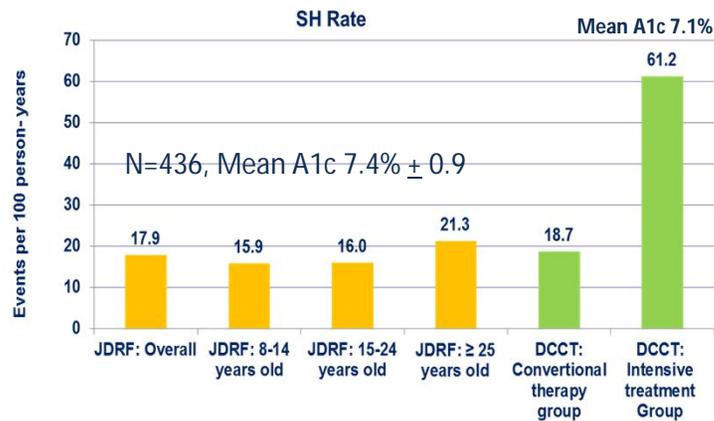
Skyler JF. *Endocrinol Metab Clin North Am.* 1996;25:243-54



How has technology helped?

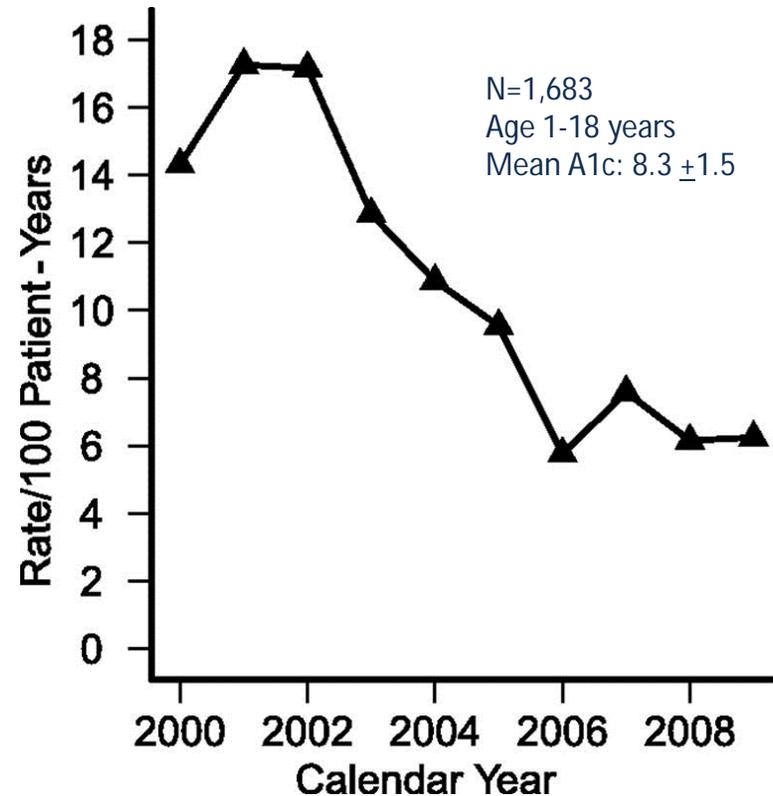
# Severe hypoglycemia and A1c since DCCT

## Rates of Severe hypoglycemia in JDRF CGM Study



Fiallo-Scharer R, JDRF study group . Diabetes Care. 2011 Mar; 34(3):586-90.

## Rates of severe hypoglycemia by calendar year.



O'Connell S M et al. Dia Care 2011;34:2379-2380

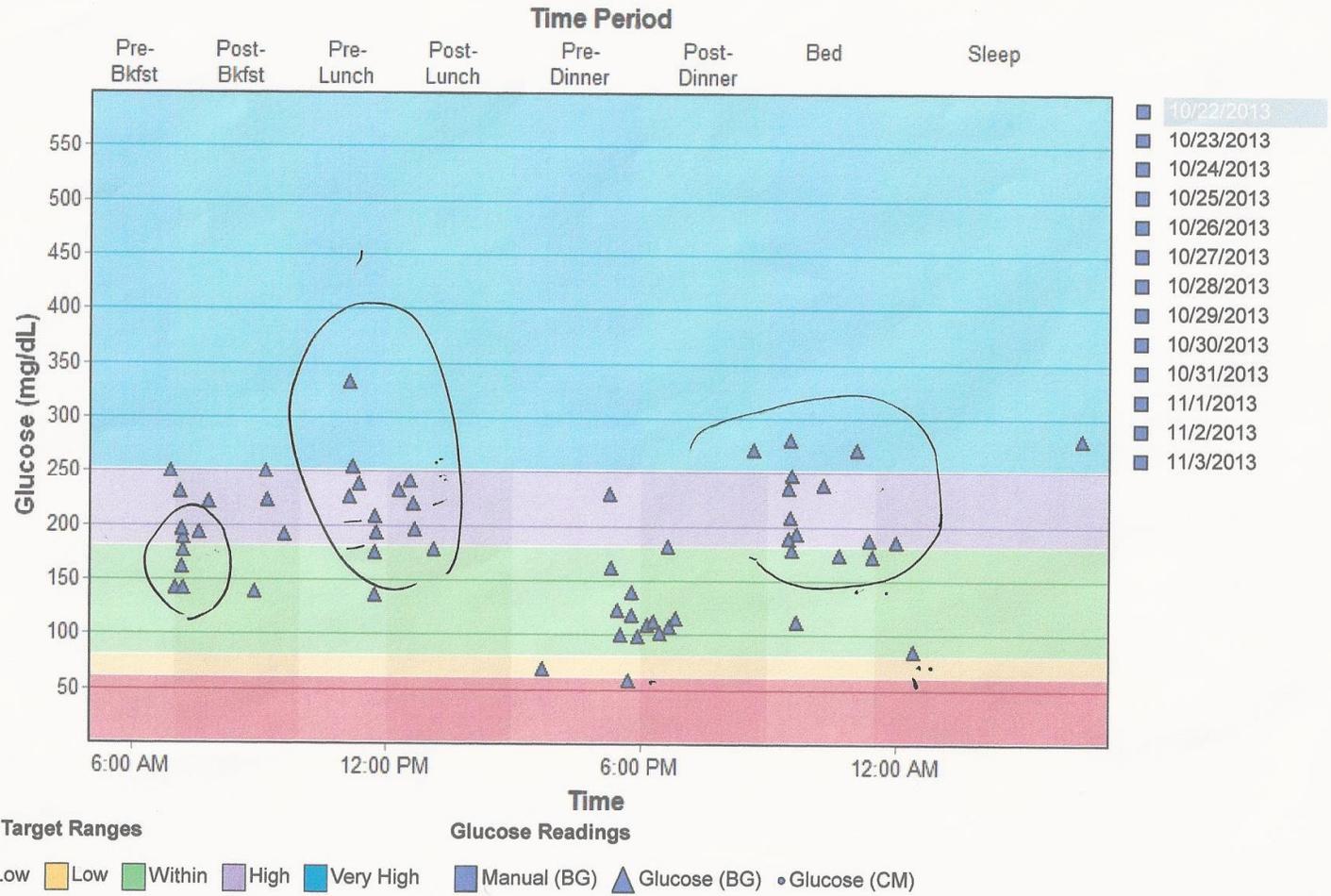
# Measuring glycemic control: Portable glucose meters and A1c

- 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

Date of Birth: Not Specified

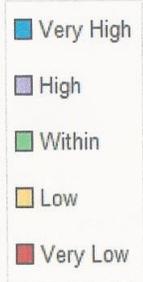
Date Range: 10/22/2013 - 11/4/2013

### Glucose Modal Day Report

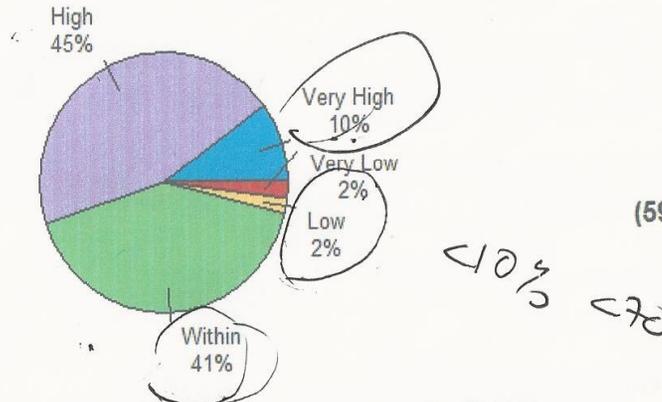


Date of Birth: Not Specified

### Glucose Pie Chart

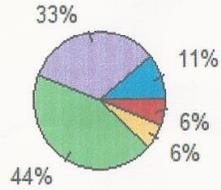


70-180

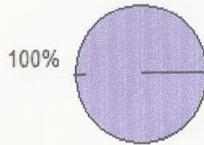


Total (59 Readings)

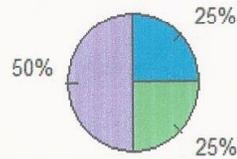
All Pre (18 Readings)



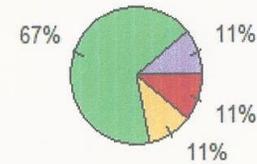
Pre-Bkfst (1 Reading)



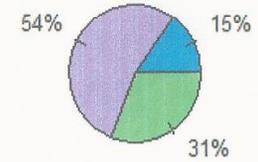
Pre-Lunch (8 Readings)



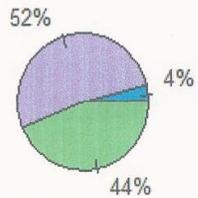
Pre-Dinner (9 Readings)



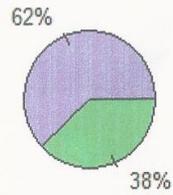
Bed (13 Readings)



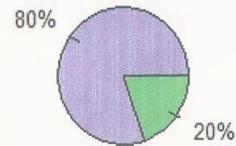
All Post (25 Readings)



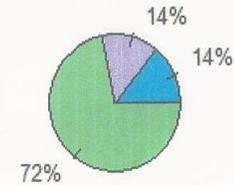
Post-Bkfst (13 Readings)



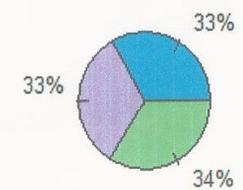
Post-Lunch (5 Readings)

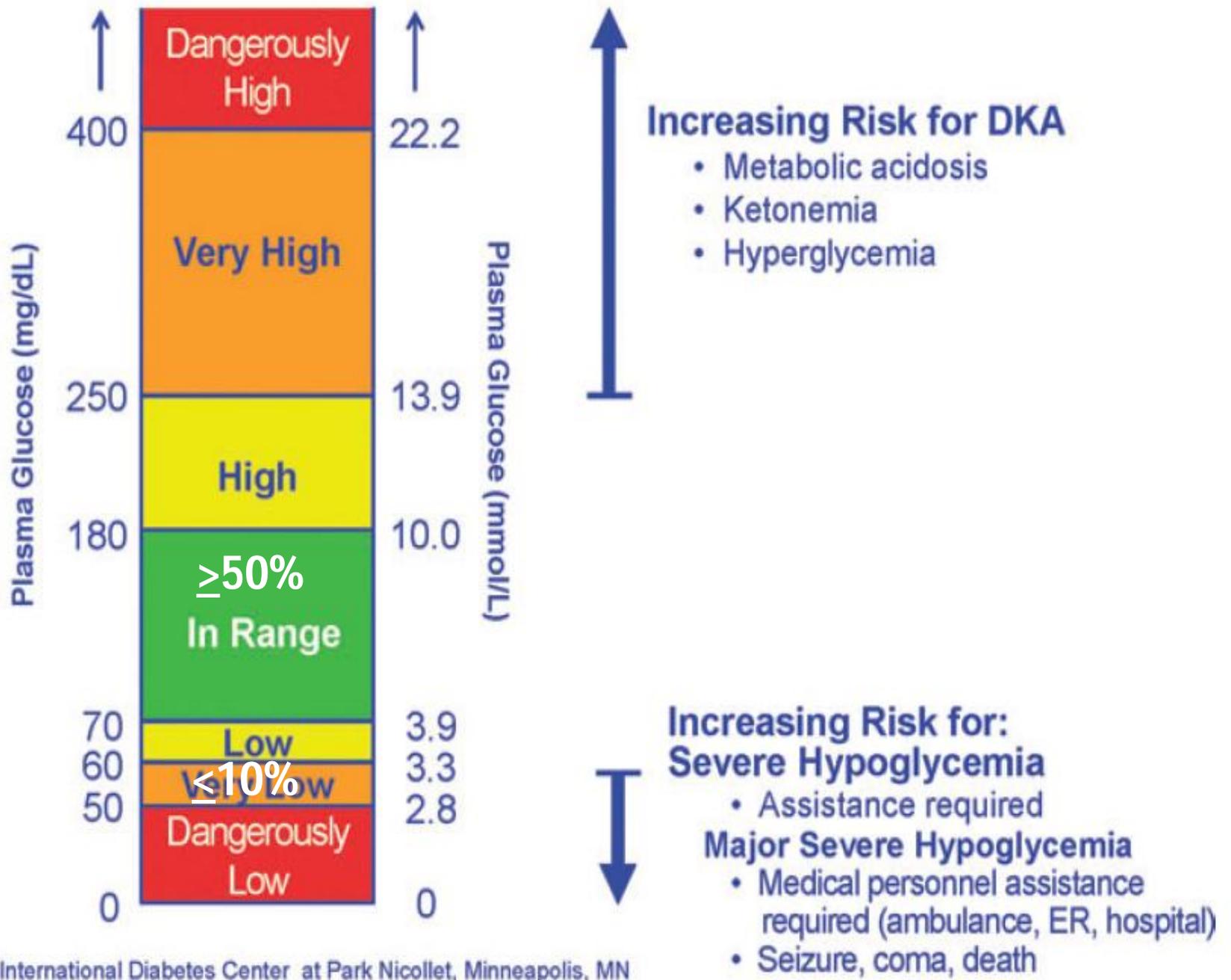


Post-Dinner (7 Readings)



Sleep (3 Readings)



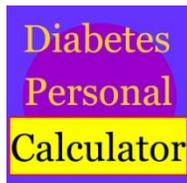


# Diabetes Apps

## ■ Blood Sugar Tracking



## ■ Insulin Dose Calculators



## ■ Carbohydrate Counters



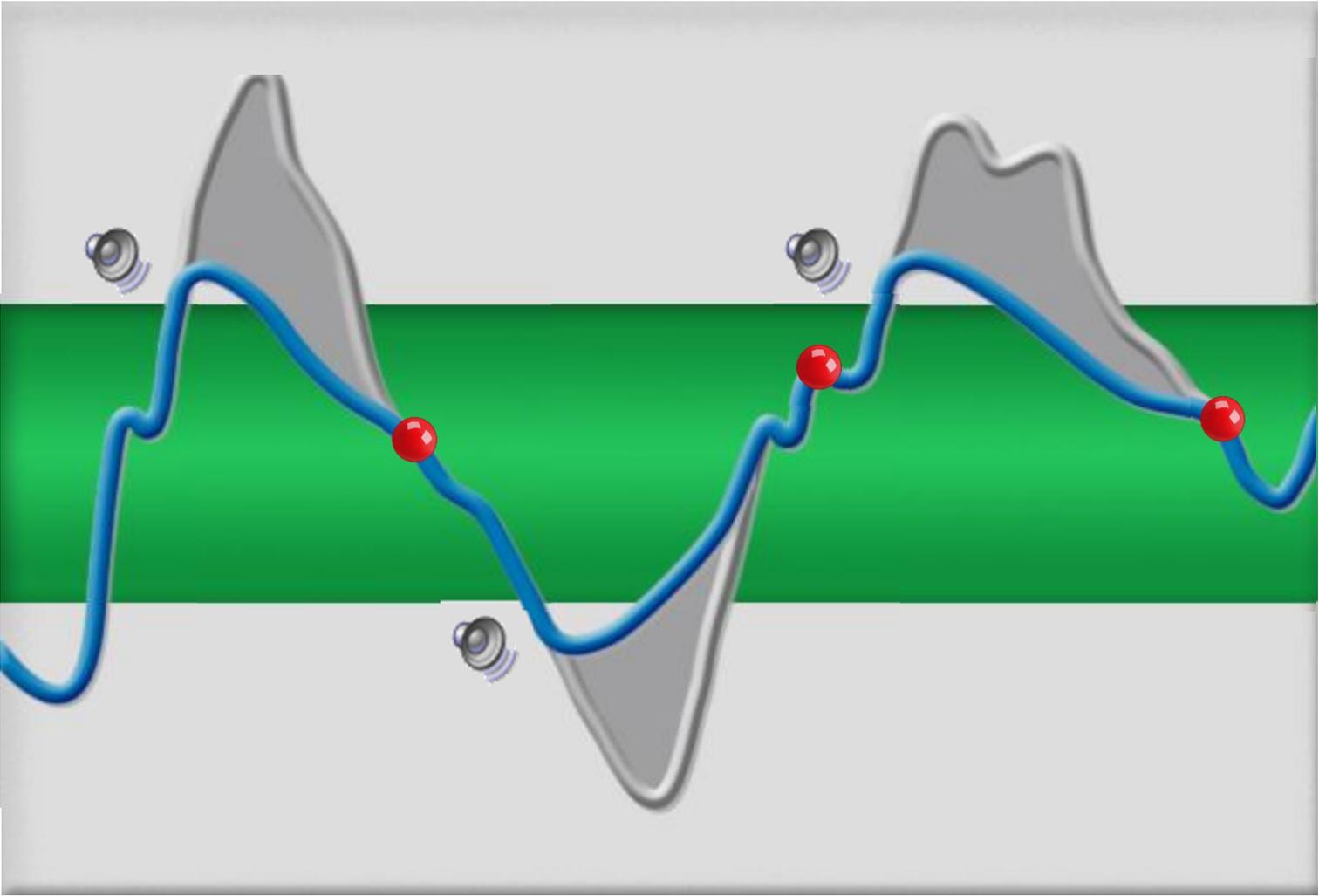
## ■ CGM & Pumps



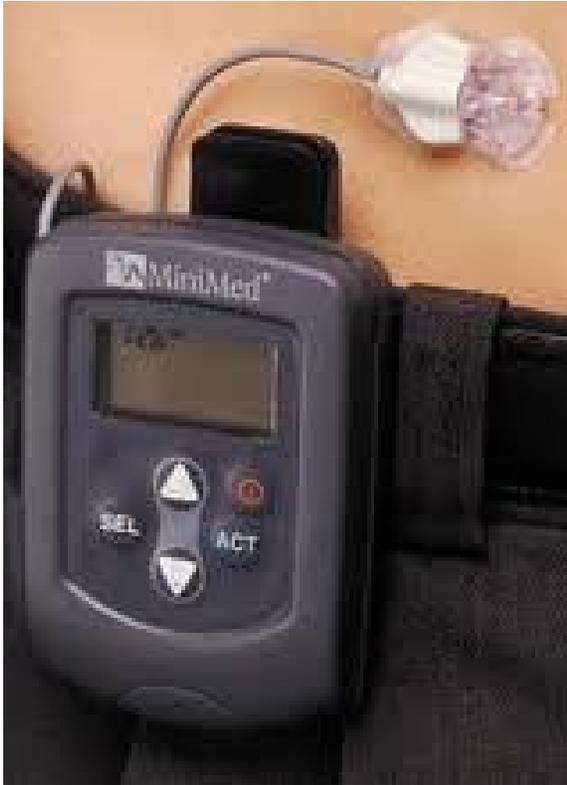
# Continuous glucose monitoring

# 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

## Advantages

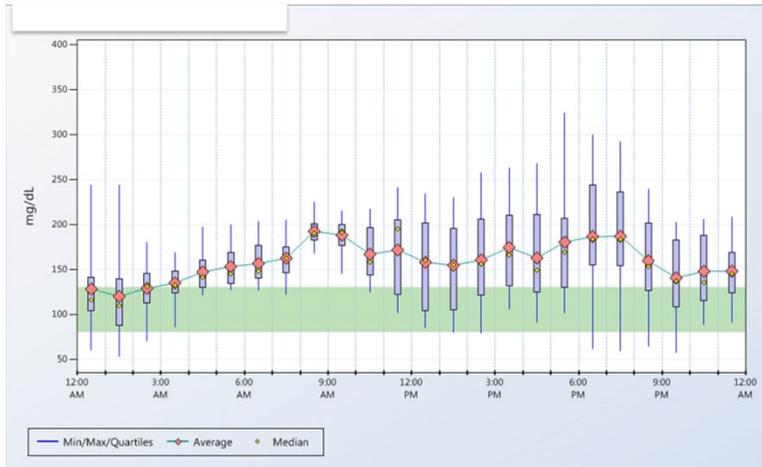
- Provides many additional data points including trend information
  - Can help “predict the future”
- Alarms can alert user of out of range glucose excursions
- Can help reduce A1c but only if used all the time
- Intermittent use can have some benefits

## Limitations

- Requires concomitant use of Fingersticks (minimum 2 FS per day)
  - Only Dexcom G5 currently approved for using CGM results for insulin calculations)
- Increased burden of daily management
  - More devices on body, more thinking about blood sugars
- Alarms can be disruptive to daily activities/sleep
- Teens frequently sleep through alarms
- Requires frequent action from user to be effective
  - Only benefits highly motivated users
- Increased cost
  - Sensor cost added to glucometer strip cost
  - Not covered by some payors

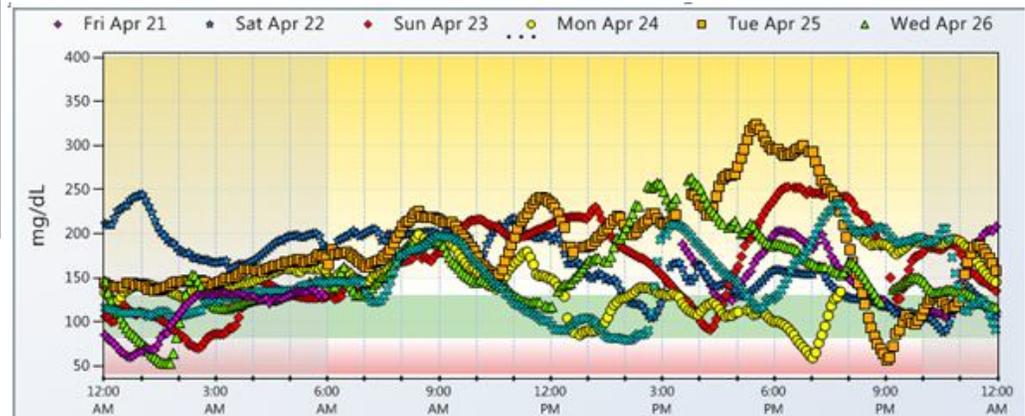
# CGM reports

**A1c: 7.5%**  
**N=1866**



Statistics		
Average Glucose	158 mg/dL	
Sensor Usage	8 of 10 Days	
Calibrations / day	1.9	
Standard Deviation	± 45 mg/dL	
	72 % High	26
	26 % Target	73%
	3 % Low	1
Target Range	80 - 130 mg/dL	
Nighttime	10:00 PM - 6:00 AM	

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 1<sup>st</sup> 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

I love you like a brother.



I'm a girl.



Omnipod



Medtronic



T-Slim



Accucheck Combo



# Current status of pump therapy

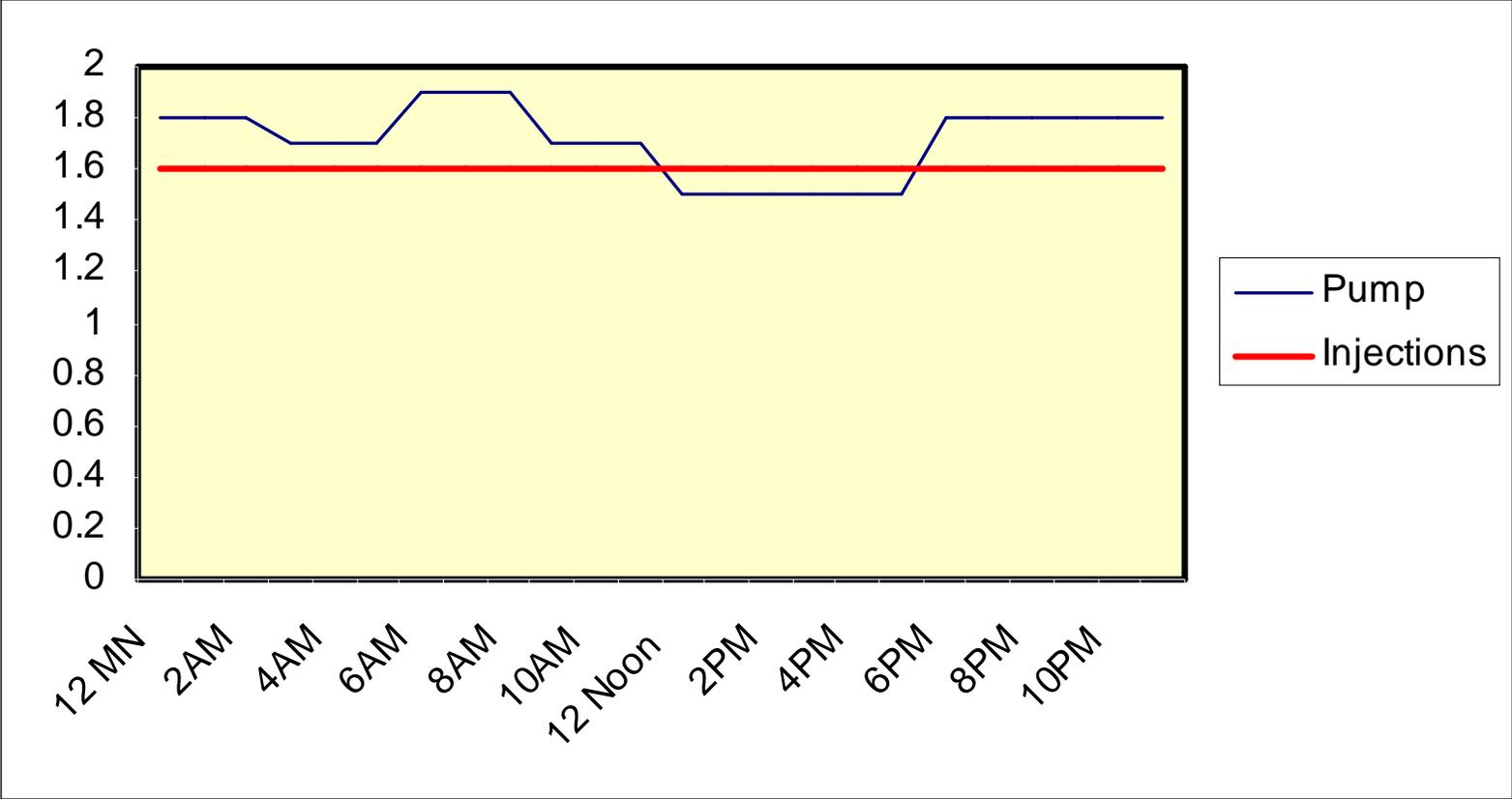
- All have bolus calculator
  - ICR
  - ISF
  - Target range
  - IOB with reverse correction option protects against insulin stacking and hypoglycemia
  - Two pumps have option to pre-program bolus adjustments for specific events
- Most have integrated or linked glucose meter
- Small dose increments suitable for small children (0.001-0.1 unit increments)
- Alternative basal patterns and temporary basal rate options

# Benefits of pump vs injections

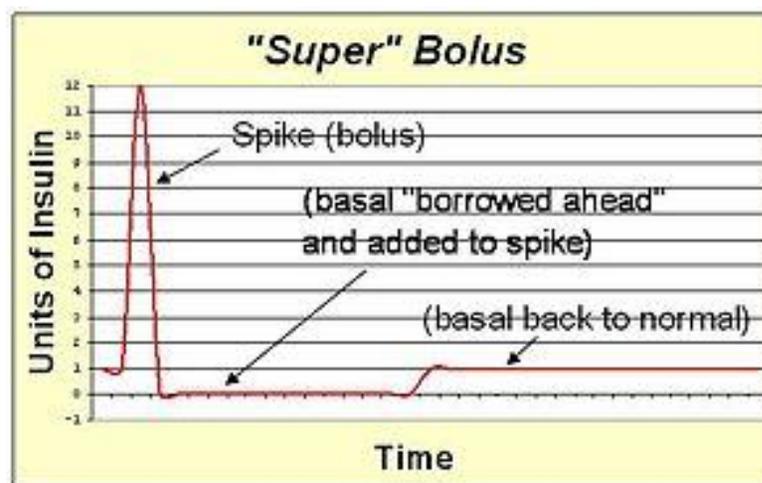
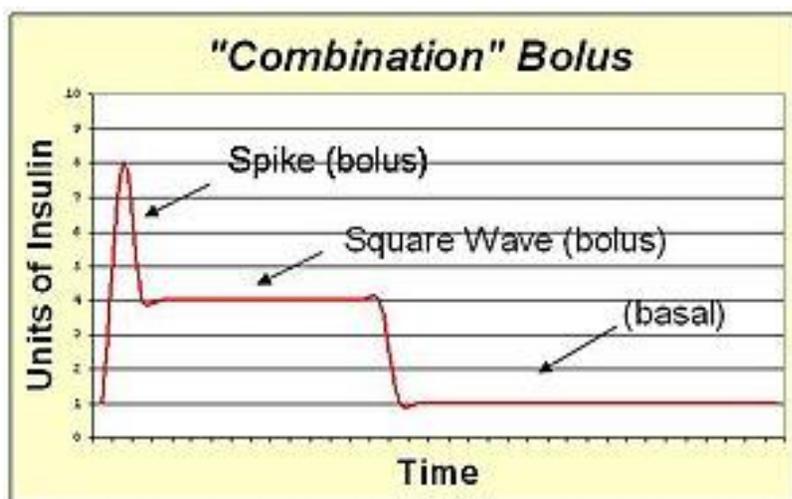
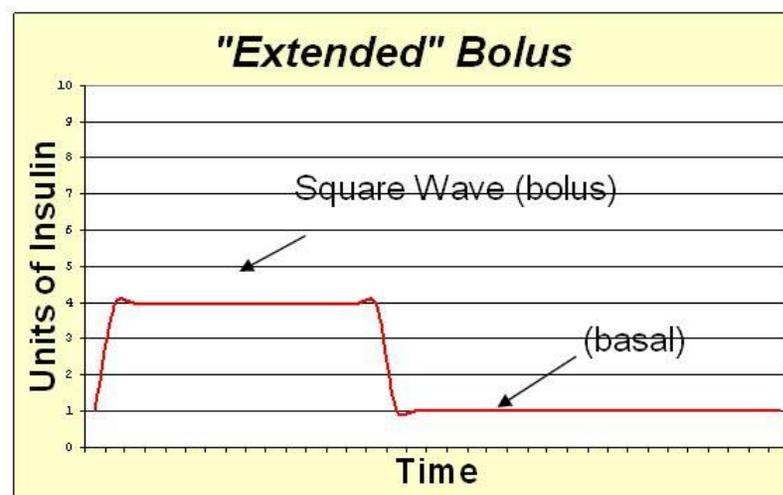
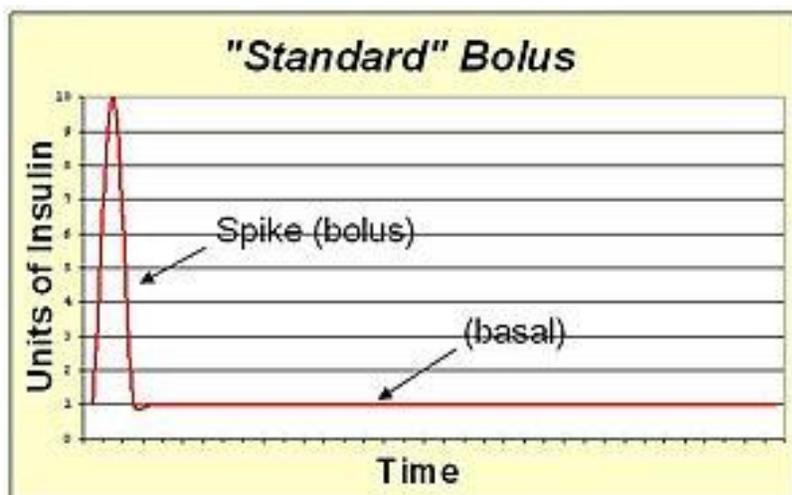
## Basal rate

- 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



# Pump Advanced Bolus Options



# 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

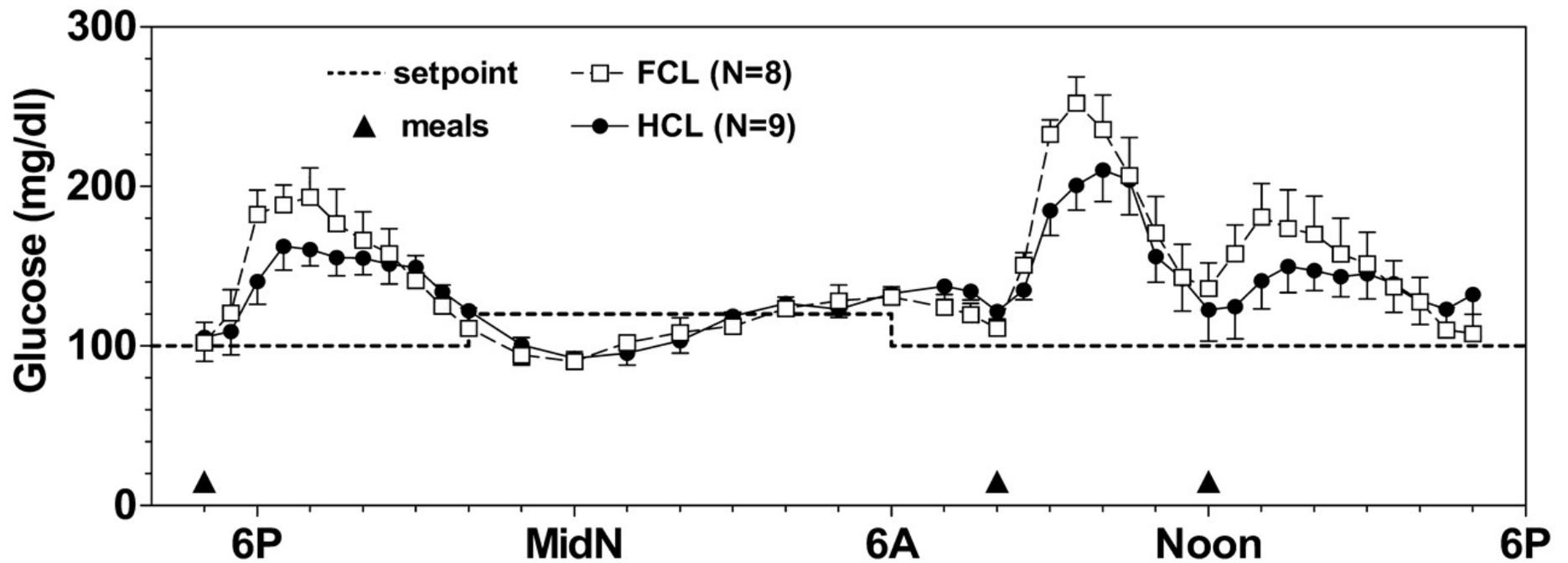
# Artificial Pancreas Systems

Closed loop vs open loop

# Components of the 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





Weinzimer et al. Diabetes care 2008 May;31(5):934-9.

# 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
- MMPPC (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

