Insulin Pump Therapy and Continuous Glucose Sensor Use in the Management of Diabetes Mellitus

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Faculty Disclosure

Dr. Louis Haenel IV has disclosed that he is a consultant and member of the Speakers Bureaus for sanofi-aventis, Novo Nordisk, AstraZeneca, Medtronic

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Overview

- Discuss the basics of insulin pump therapy
- Review the role and mechanisms of continuous glucose monitoring
- Discuss the use of CSII in patients with diabetes mellitus who are taking insulin

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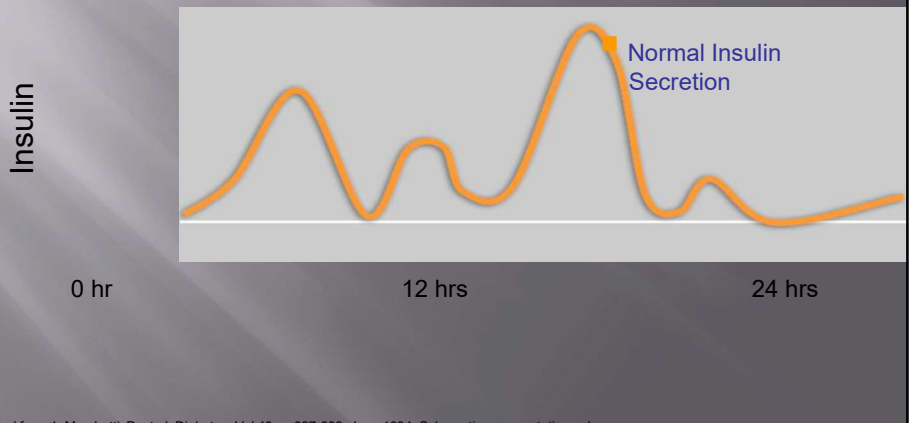
Normal Insulin Production:

The Pancreas

A healthy pancreas releases insulin automatically, on average, every 10-to 14-minutes[1], in amounts appropriate for your varying blood glucose levels.



Adapted from 1. Marchetti, P, et al. Diabetes, Vol 43, p. 827-839, June 1994. Schematic representation only

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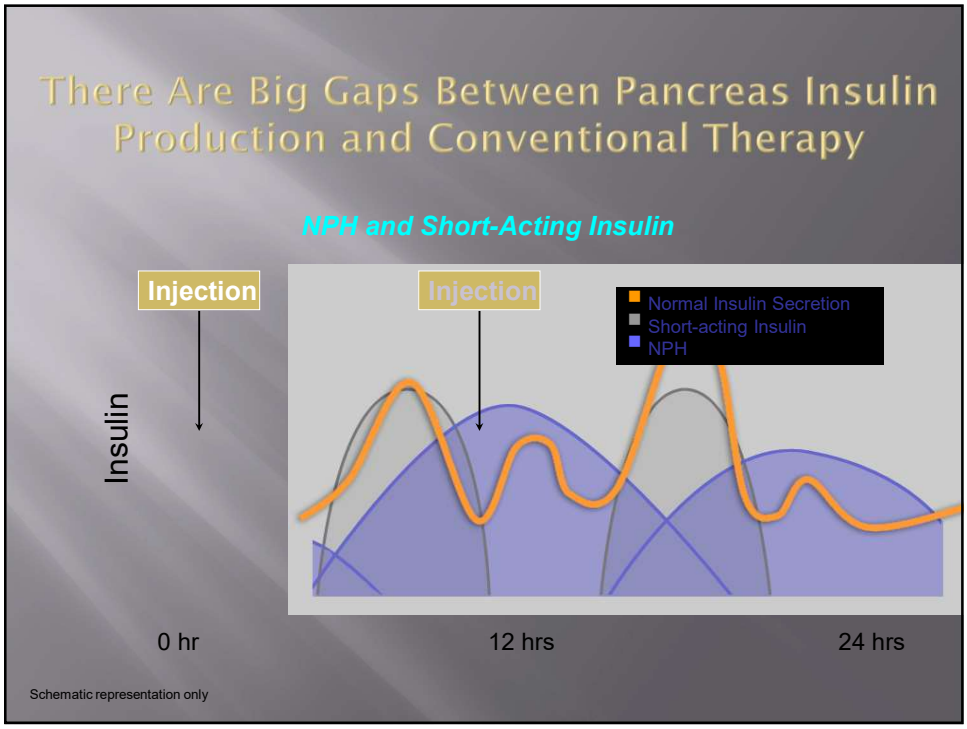
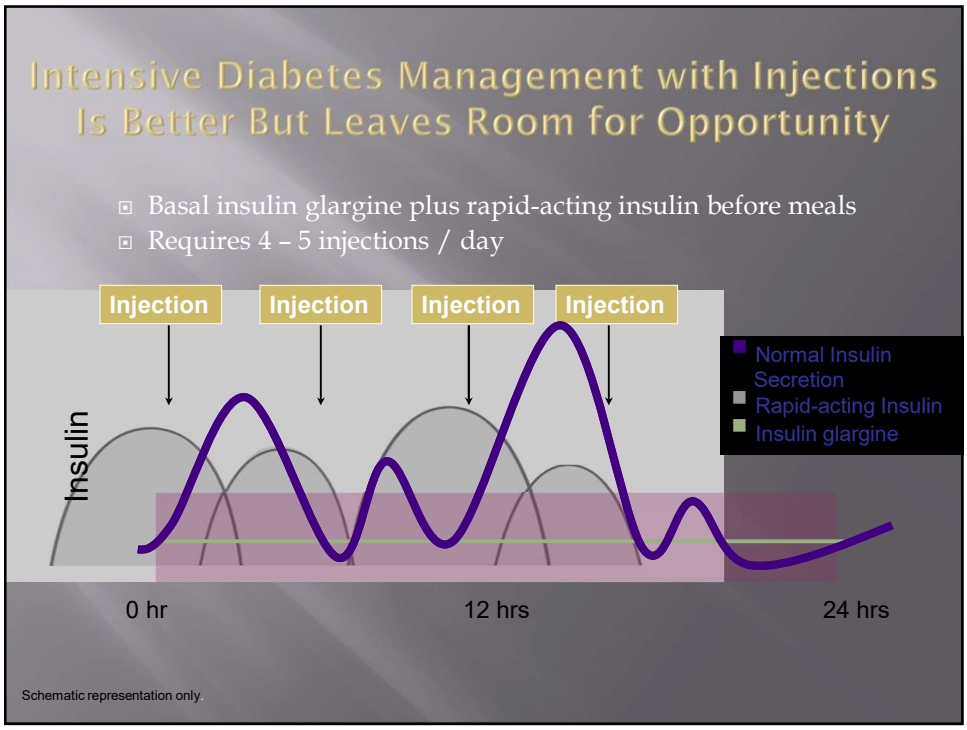
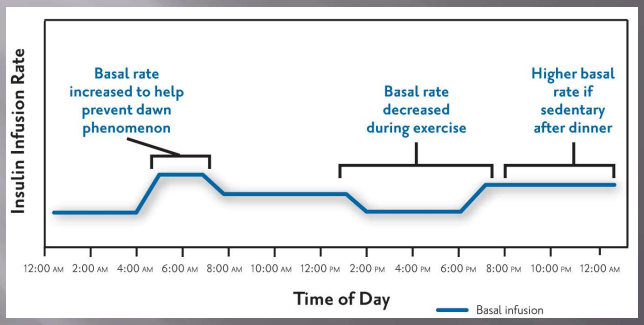

There Are Big Gaps Between Pancreas Insulin Production and Conventional Therapy
NPH and Short-Acting Insulin
Injection
Injection
Normal Insulin Secretion
Short-acting Insulin
NPH
Insulin
0 hr
12 hrs
24 hrs
Schematic representation only

5


Intensive Diabetes Management with Injections Is Better But Leaves Room for Opportunity
Basal insulin glargine plus rapid-acting insulin before meals
Requires 4 – 5 injections / day
Injection
Injection
Injection
Injection
Normal Insulin Secretion
Rapid-acting Insulin
Insulin glargine
Insulin
0 hr
12 hrs
24 hrs
Schematic representation only.

6

Insulin Pump Users Program Multiple Basal Rates According to Their Daily Routine



A typical profile of basal insulin rates in CSII. Many people are more active in the late afternoon, and more sedentary after dinner, necessitating adjustment to the basal rate. Note higher basal rate in pre-dawn hours

Lenhard MJ, Reeves GD. *Arch Intern Med.* 2001;161:2293-2300. Reused with permission.

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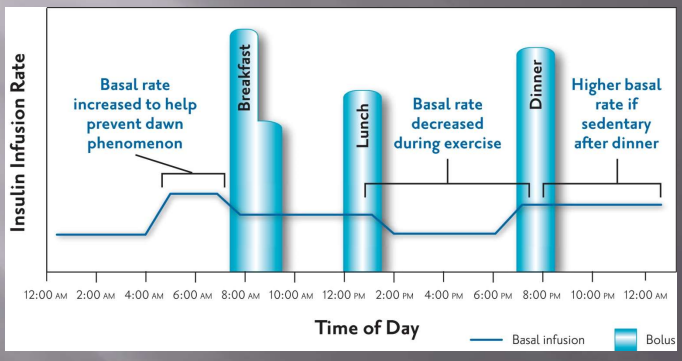
Insulin Pumps Also Deliver Customized Boluses for Different Types of Meals



Insulin pumps offer smart calculators to help determine how much bolus insulin is needed, and can deliver precise amounts of insulin based on the amount of carbs to be taken.

Lenhard MJ, Reeves GD. *Arch Intern Med.* 2001;161:2293-2300. Reused with permission.

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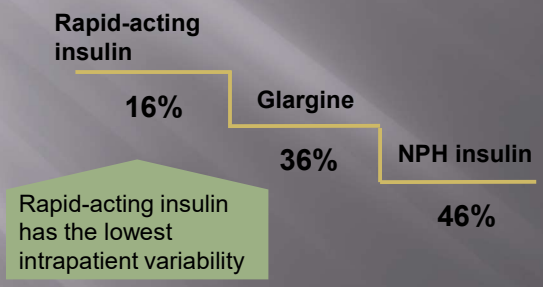
Insulin Pumps Use Only Rapid Acting Insulin which Has the Least Intrapatient Variability

Pharmacodynamic Variability in Insulin Action*

Pharmacodynamic Variability in Insulin Action*



*Percentages represent the coefficients of variation (CV) for insulin action as measured by the maximum glucose infusion rate in these euglycemic glucose clamp studies

Heinemann L, Weyer C, Rauhaus M, Heinrichs S, Heise T. *Diabetes Care.* 1998;21:1910–1914; Heise T, Nosek L, Rønn BB, et al. *Diabetes.* 2004; 53:1614-1620.

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Pump therapy *vs* MDI: Consistently lower HbA1c in meta-analyses

Meta-analyses		HbA1c (CSII *vs* MDI)
Misso ML, et al. 2010 (Cochrane)[1]	↓	-0.3% (95% CI, -0.4, -0.1) improvement in HbA1c[1]
Fatourechi, et al. 2009[2]	↓	-0.2% (95% CI, -0.1 to -0.3)) improvement in HbA1c[2]
Pickup and Sutton 2008[3]	↓	-0.62% (95% CI, -0.47 to -0.78) improvement in HbA1c[3]
Jeitler, et al. 2008[4]	↓	-0.6 (95% CI, -0.87 to -0.22) improvement in HbA1c; with reduced insulin requirement[4]
Weissberg-Benchell, et al. 2003[5]	↓	-0.95 (95% CI, -0.8 to -1.1) improvement in HbA1c[5]

1. Meta-analysis of 23 randomized controlled trials in more than 976 patients with type 1 diabetes (T1D).
2. Meta-analysis of 15 studies, randomized controlled trials in patients with T1D.
3. Meta-analysis of 22 randomized controlled trials in patients with T1D.
4. Meta-analysis of 22 studies, with 12 studies reporting reductions in glucose in T1D.
5. Meta-analysis of 52 studies with 11 studies reporting reductions in glucose in patients with T1D.

MDI = multiple daily injections
CSII = continuous subcutaneous insulin infusion

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Pump therapy *vs* MDI: Fewer episodes of severe hypoglycemia[1,2]

- Pumps decrease risk of severe hypoglycemic episodes by 2.9-fold[1]
- Data from 15 trials suggest insulin pumps "may be better than MDI for reducing the incidence of severe hypoglycemic events"*†
- Severe hypoglycemic events significantly reduced following CSII introduction: from 37/year to 14/year; $p<0.05$[3]

Severe hypoglycemia

*Meta-analysis of 23 randomized controlled trials in more than 976 patients with type 1 diabetes (T1D)
†No difference in non-severe hypoglycemia
MDI = multiple daily injections
CSII = continuous subcutaneous insulin infusion

Pickup JC, Sutton AJ. *Diabet Med* 2008;25(7):765–774.
Misso ML, *et al. Cochrane Database Syst Rev* 2010;(1):CD005103.doi(1):CD005103.
Marmolin ES, *et al. Dan Med J* 2012;59(6):A4445.

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INSULIN PUMP THERAPY

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Insulin Pump Therapy Defined

- Insulin pump therapy
  - Also known as continuous subcutaneous insulin infusion (CSII)
  - Infuses rapid acting insulin in precise programmable doses to meet individual patient needs
  - Delivers insulin through a soft cannula under the skin
  - Replaces multiple injections

The insulin pump closely mimics normal pancreatic insulin delivery

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CSII – A Proven Therapy

Consensus statement:

"CSII is the most physiological method of insulin delivery currently available"[1]

American Diabetes Association. Cure • Care • Commitment

EASD

Why do you think more patients are not on insulin pump therapy?

1. Consensus statement on use of insulin pumps in pediatrics endorsed by the ADA and European Association for the Study of Diabetes (EASD)

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"Consider use of continuous subcutaneous insulin infusion in insulin-treated patients with type 2 diabetes mellitus"

2007 American Association of Clinical Endocrinologists Medical Guidelines For Clinical Practice for the Management of Diabetes Mellitus

"The efficacy and safety of CSII with an insulin pump are comparable to multiple daily injection insulin therapy for patients with type 2 diabetes mellitus"

2007 American Association of Clinical Endocrinologists Medical Guidelines For Clinical Practice for the Management of Diabetes Mellitus

AACE Diabetes Mellitus Guidelines. *Endocr Pract*. 2007;13(suppl 1):3-68.

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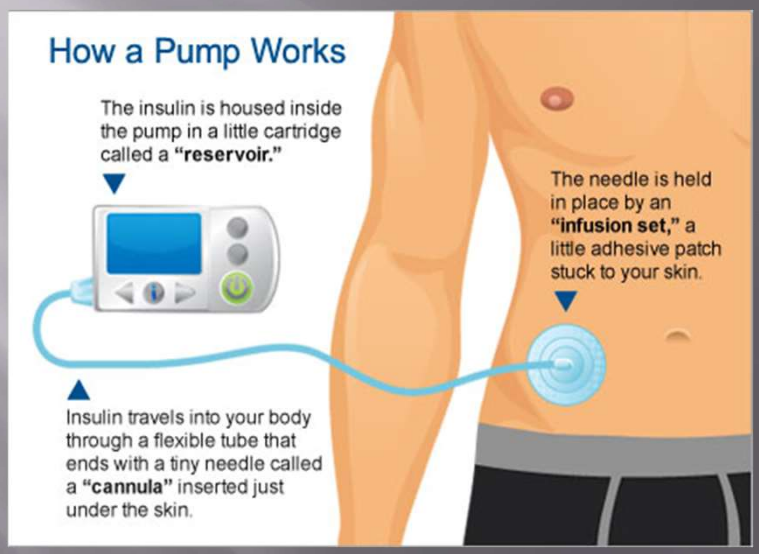

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How Does an Insulin Pump Work?

Components and their functions:

- A small computerized, battery operated pump
  - Allows the user to control exactly how much insulin is delivered
- A pump reservoir
  - Similar to a regular syringe, holds 2 to 3 days worth of insulin
- A thin plastic tube called an infusion set
  - Has a soft cannula or needle at the end inserted just under the skin, usually on the abdomen

How does it work?

- Insulin passes from the pump reservoir through the tubing into the subcutaneous tissue

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An Infusion Set Is the Link Between the Insulin Pump and the Body

Center for Disease Control (CDC) Recommends Changing Infusion Sets Every 2-to-3 days

CDC. *MMWR Morb Mortal Wkly Rep.* 1983; 32(31):401-406,412.

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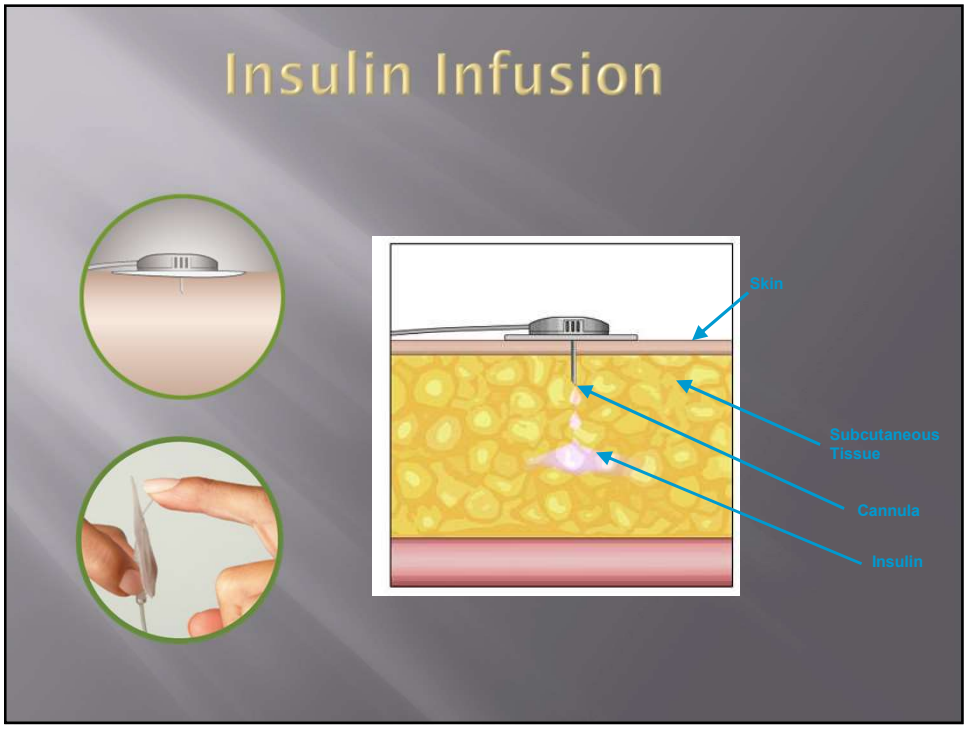
Insulin Infusion
Skin
Subcutaneous Tissue
Cannula
Insulin

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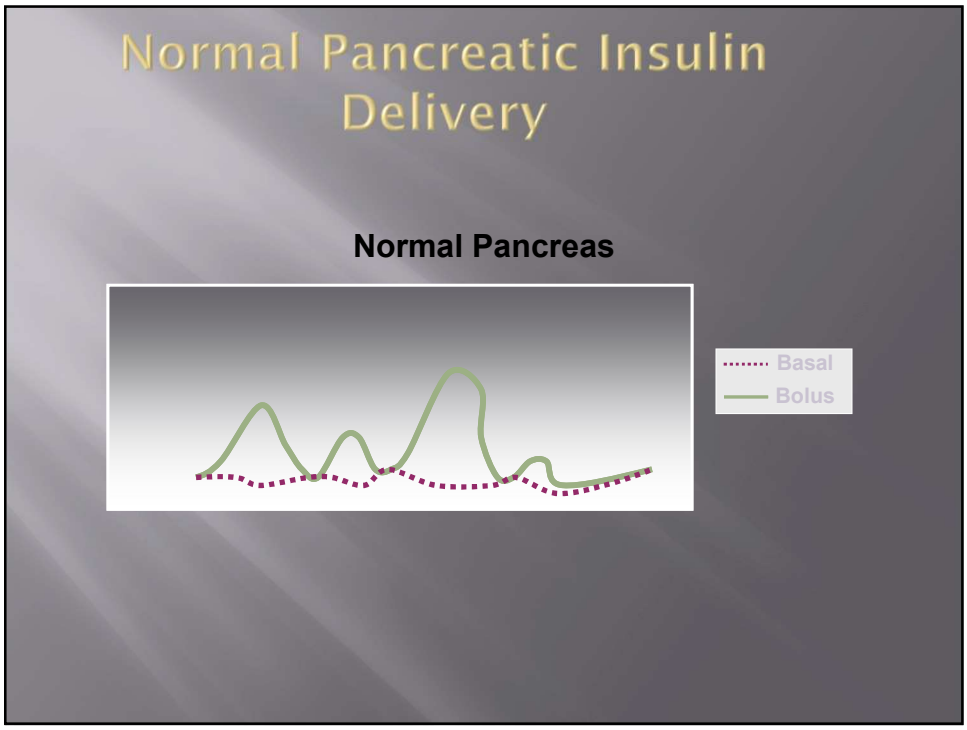
Normal Pancreatic Insulin Delivery
Normal Pancreas
Basal
Bolus

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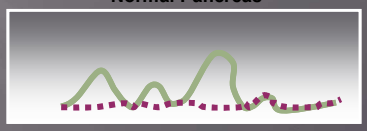
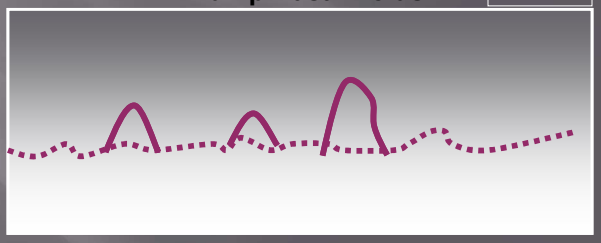
Similarity Between Insulin Pumps and a Normal Pancreas

- Delivery of basal rates
  - Programmed delivery of a constant background rate of insulin (basal rate)
  - Programmable to match the individual's needs
- Bolus delivery
  - Delivery of a dose of insulin (bolus) to meet the requirements of food intake
  - Calculated based on the amount of carbohydrates contained in the meal or snack
  - Can be used to correct high blood glucose readings

Normal Pancreas



Pump Basal/Bolus



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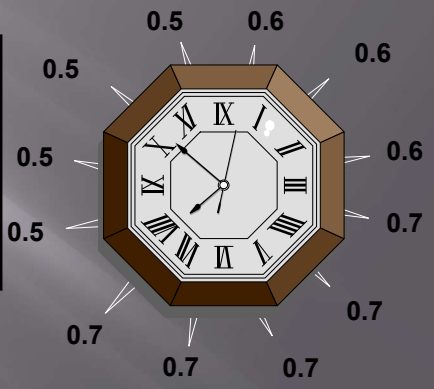
Basal Rate Delivery: Slow Continuous Infusion

- Delivers continuously/automatically
- Adjusted to match pt's hepatic glucose production *(i.e., fasting & nocturnal, & dawn)*
- Similar to a normal functioning pancreas – in maintaining BG stability



Example Basal Rate

1. 12 am @ 0.6 u / hr.
2. 3 am @ 0.7 u / hr.
3. 8 am @ 0.5 u / hr.

Advantages

1. Very precise delivery.
2. Eliminates large insulin depots.
3. Greatly reduces risk of lows.

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Advanced Basal Rate Features on Insulin Pumps

RC1

- Temporary Basal Rates
  - Used to increase or decrease basal insulin during physical activity or during illness
- Basal Rate Patterns
  - Allows for customized basal rates to be programmed in order to meet the patient's daily, weekly or monthly needs. This feature is useful in the following circumstances:
    - Changes in sleep times (weekends, shift work)
    - Different schedule during the week vs. weekends
    - High-activity or low-activity days vs. typical day
    - Monthly hormonal shift

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Bolus Insulin

- Insulin delivery 'on demand'
  - Meal Bolus: Given to cover rise in glucose from food
  - Correction Bolus: Given to correct a blood sugar over normal range
- Factors needed to calculate bolus

Meal Bolus	Correction Bolus
• Insulin-to-carbohydrate ratio • Carbohydrates in the Meal • Activity Level	• Insulin Sensitivity Factor • Blood Glucose Target • Pre-meal Blood Glucose • Active Insulin

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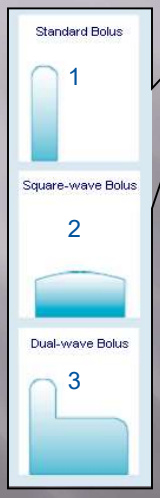
Slide 23

RC1 only true for medtronic pumps?
Reshma Carter, 3/23/2011

Bolus Types and How to Set Them

RC2



Bolus type

1. Normal—all at once
2. Square wave—gradually over time
3. Dual wave—a portion given immediately followed by the remainder over time

Note: All bolus types can be given through the Bolus Wizard calculator.

Ways to set a bolus

- Bolus Wizard® calculator—automatically calculates bolus dose based on carbohydrate content of food, glucose value, or active insulin. Keeps in memory all the given boluses to prevent stacking of insulin.
- Easy bolus—a pre-set normal bolus that can be increased by fixed amounts. Makes audible beeps to confirm the amount.
- Manual bolus—individual entry of each bolus dose

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Slide 25

RC2 Specific to one kind of pump?
Reshma Carter, 3/23/2011

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omnipod®
INSULIN MANAGEMENT SYSTEM

29

30

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The OmniPod system: just two simple parts

1. **Built-in BG meter** that automatically incorporates BG levels into suggested bolus calculations and history records

2. **Waterproof pod**

All-in-one

- Infusion set, insulin reservoir, automated inserter and batteries

Automated processes

- Cannula Insertion
- Priming

Intuitive user interface

- Full text navigation
- Set-up wizard
- Easy to teach, easy to learn

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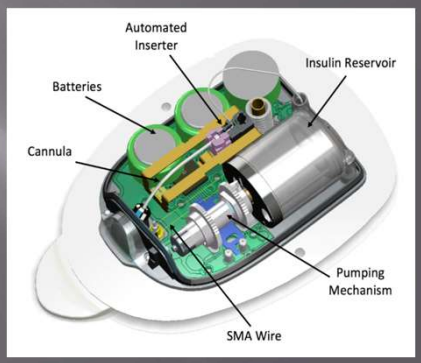
The OmniPod system is engineered for accuracy and reliability

- Fully integrated design with **no assembly required**
  - Integrated insulin reservoir, infusion set, automated inserter, pumping mechanism, and power supply
- **Automated processes** including cannula insertion and priming:
  - **Automated and consistent insertion** alleviates potential for human error, and this unique design helps ensure that the cannula is inserted at the correct angle and depth
  - **Automated priming and tubing-free design** ensures consistent priming with no concern with bubbles in tubing

Omnipod utilizes an inexpensive, lightweight, reliable motor using Shape Memory Alloy (SMA) wire



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CONTINUOUS GLUCOSE MONITORING

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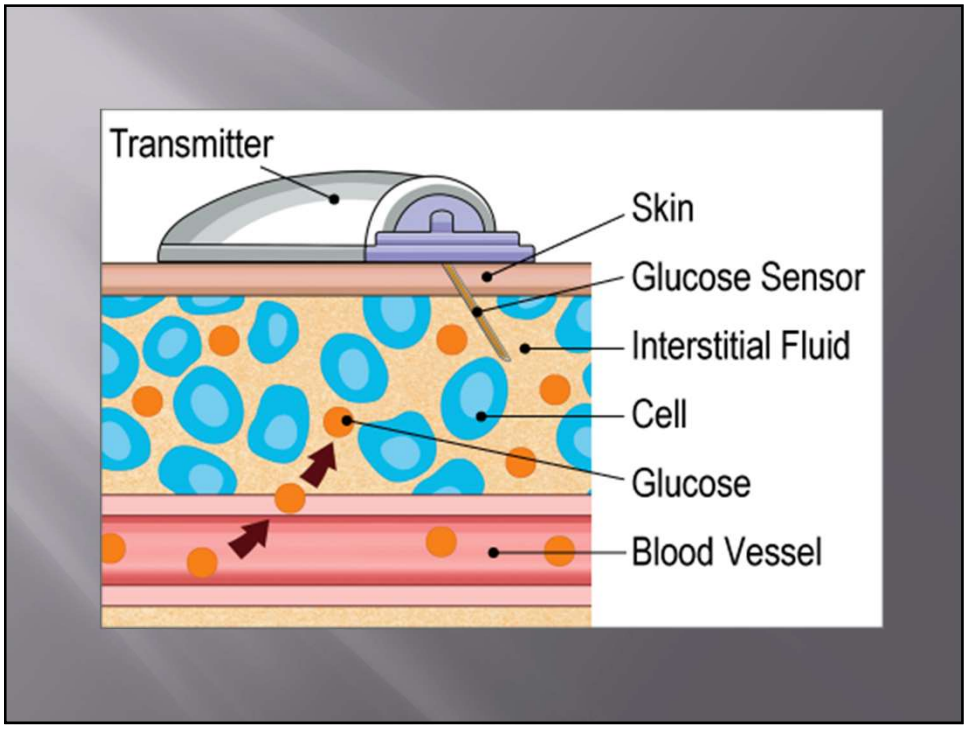
Transmitter
Skin
Glucose Sensor
Interstitial Fluid
Cell
Glucose
Blood Vessel

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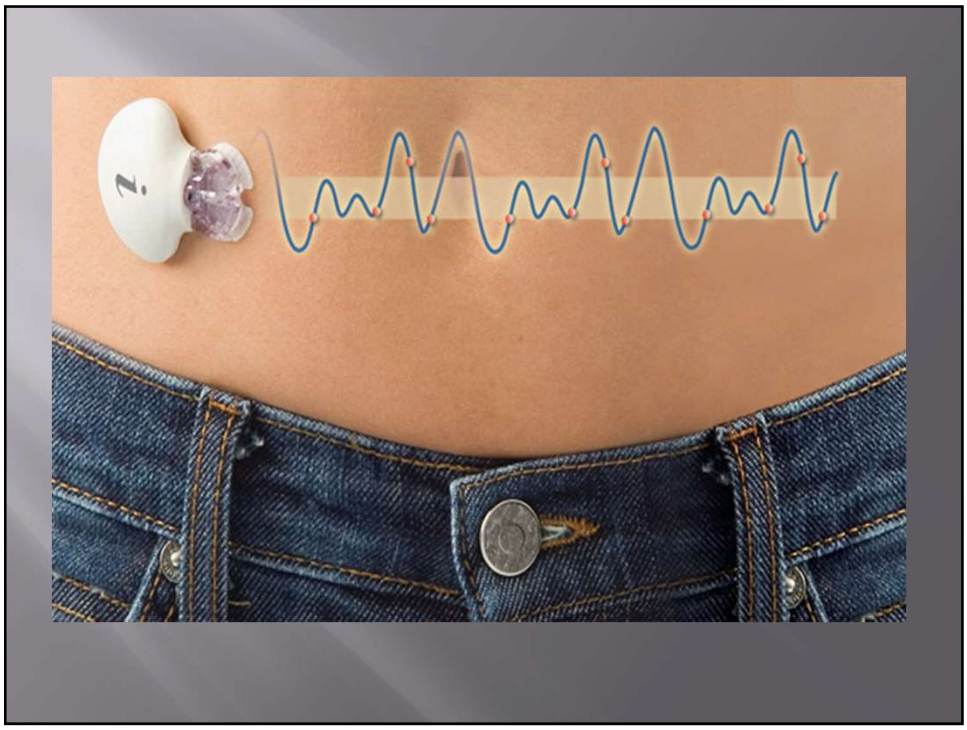

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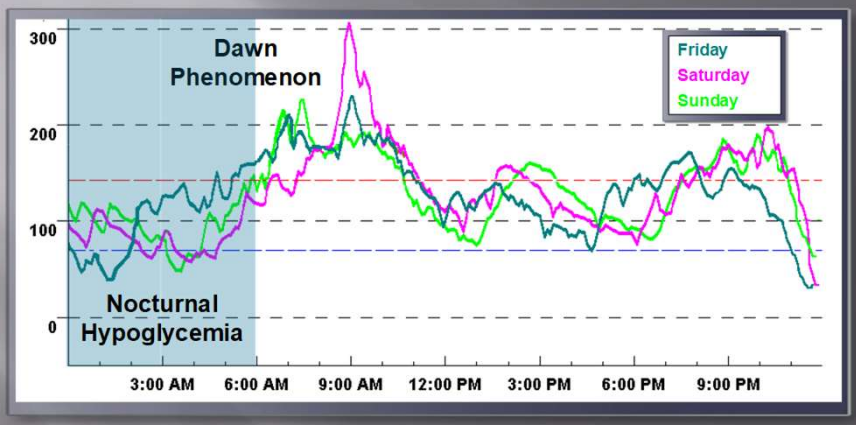
Modal Day Summary Report: Case Study



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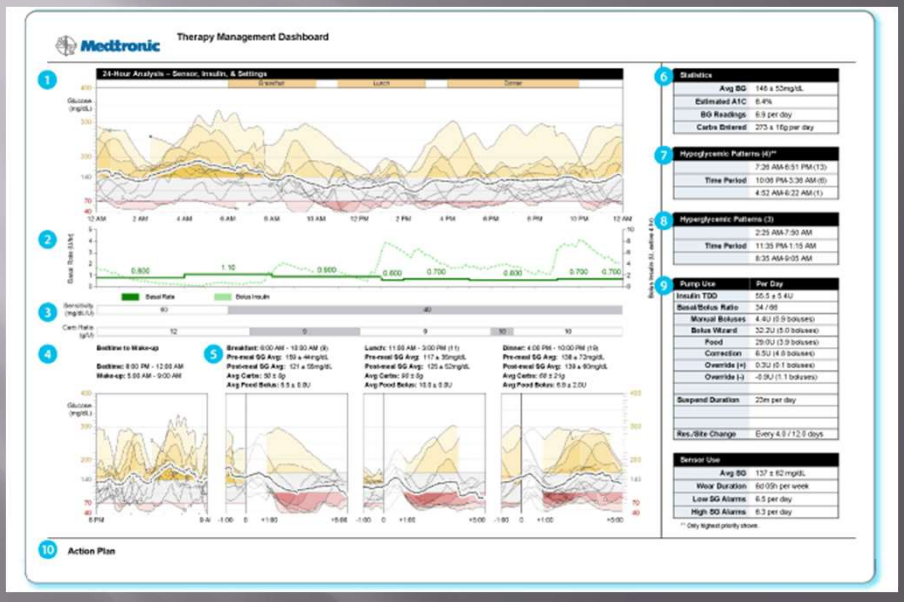

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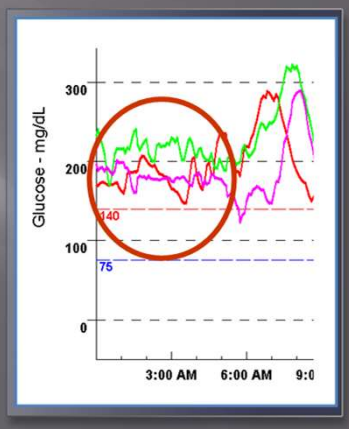
Step 1: Look at the Overnight Period

First: Look for Hypo

- For glucose levels BELOW low limit
  - Problem: basal rate is probably too high
  - Solution: decrease basal rate?

Second: Look for Hyper

- For glucose levels ABOVE high limit
  - Problem: basal rate is probably too low
  - Solution: increase basal rate?



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Step 2: Look at Pre-prandial Periods

First: Look for Hypo

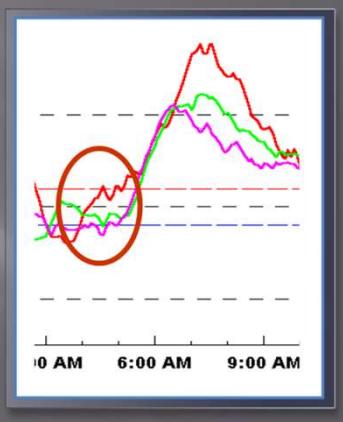
Consider:

- Influence of bolus, previous meal, active insulin
- Exercise and activity
- Food: Timing, Quantity, Composition

Second: Look for Hyper

Consider:

- Same considerations as hypo
- Plus breakfast related dawn phenomenon



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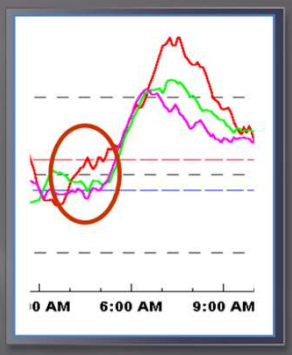
Step 3: Look at Post-prandial Periods

First: Look for Hypo

- If hypoglycemia is observed in the PP period (2–3 hours after meal):
  - Suggests issue with the bolus for that meal
  - Consider timing, type, accuracy of bolus
  - Consider influence of exercise



Second: Look for Hyper

- If Hyperglycemia peaks above 180 mg/dl (<10.0mmol/l) post meal:
  - Consider timing, type, accuracy of bolus
  - Consider food intake, food quantity and meal composition

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ZERO
Fingersticks!*
DexcomG6®
Welcome to the world of real-time CGM
*If your glucose alerts and readings from the G6 do not match symptoms or expectations, use a blood glucose meter to make diabetes treatment decisions.
LBL016304 Rev00

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DexcomG6®
G6 at a Glance
No fingersticks*
No calibration required
Urgent Low Soon alert
Overall MARD†‡ of 9.0%
Acetaminophen blocking*
Custom alert schedules
10-day wear sensor
Slimmer wearable profile
Indicated for treatment decisions/dosing
Simple, one-touch sensor insertion‡
*If your glucose alerts and readings from the G6 do not match symptoms or expectations or you're taking over the recommended maximum dosage amount of 1000mg of acetaminophen every 6 hours, use a blood glucose meter to make diabetes treatment decisions. †MARD is a statistical measure of accuracy; the lower the number, the better. ‡Dexcom G6 CGM System User Guide, 2018

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dexcomG6
The ALL NEW and Improved Dexcom G6
Applicator
Less Painful[1]
Push Button Sensor Applicator
Tiny Insertion Needle (26Ga)[1]
Sensor + Algorithm
No Calibration Required
10 Day Session Duration
Acetaminophen Blocking*[2]
Transmitter
28% Thinner
3 Month Life
20 Foot Range
Direct Transmission of CGM data to Receiver or Mobile Device
Receiver
Touchscreen Receiver
NEW Urgent Low Soon Alert
Firmwear upgradable
Apps
New G6 apps
NEW Urgent Low Soon Alert
CLARITY app
*G6 readings can be used to make diabetes treatment decisions when taking up to a maximum acetaminophen dose of 1,000 mg every 6 hours. Taking a higher dose may affect the G6 readings.
[1]Dexcom G6 CGM System User Guide, 2018.
[2]Calhoun P, Johnson TK, Hughes J, Price D, Balo AK. Resistance to Acetaminophen Interference in a Novel Continuous Glucose Monitoring System. J Diabetes Sci Technol. 2018:1932296818755797.

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CLARITY Reports
Browse summaries, dive into details, identify patterns and trends
Print, save and view interactive reports.
Allows for on-demand CGM interpretation and billing - (CPT handout available)
dexcom CLARITY
For Patients Too!
Patients can review their Dexcom data in the Dexcom CLARITY app's weekly summary emails and notifications.

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FreeStyle
Libre
6.2
FreeStyle Libre

51

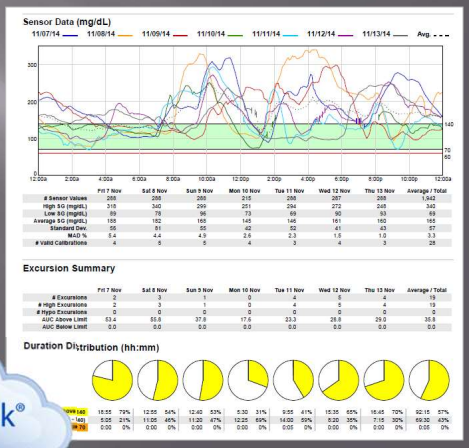

RISING QUICKLY
RISING
CHANGING SLOWLY
FALLING
FALLING QUICKLY
1
2
3
6.2
FreeStyle Libre

52

For Healthcare Providers

Convenient access to patient diabetes data

- Automatic uploads of pump and sensor glucose data to CareLink Personal every 24 hours
- Minimizes manual data uploads during office visits
- Easier follow-up and tracking of patients who may need more help
- Information can be displayed in CareLink Professional after syncing with CareLink Personal



CareLink®

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Integrated Technology

- Artificial Pancreas Platform
- Threshold Suspend Feature
- Predictive Alerts
- Audible alarms/Vibration alarms

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Insulin Pumps
Omnipod 400
Omnipod DASH
Tandem t:slim X2 Insulin Pump with Dexcom G6 (Basal IQ Technology)
Medtronic Insulin Pump with the Guardian CGM

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Animas®
CORPORATION
a Johnson & Johnson company
dexcom
THE GLUCOSE SENSOR COMPANY

57


7:35 AM
14 Nov
100%
235 u
400
350
300
250
200
150
100
50
162
mg/dL
3
HRS
INSULIN ON BOARD
3.4 u
BOLUS
Control-IQ: 0.80 u
dexcomG6

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Smart Contact Lens | Google X
ROGUE VALLEY MICRODEVICES
Tiny wireless chip and miniaturized glucose sensor embedded between two layers of soft contact lens material
Accurate glucose monitoring for diabetics using bodily fluids, i.e. tears
Prototypes can generate one reading per second
Experimenting with LEDs to serve as early warning for the wearer
Soft Contact lens
Encapsulates electronics
Sensor
Detects glucose in tears
Chip and antenna
Receives power and sends info
Source: Google X
www.roguevalleymicro.com
2

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