The Latest on Pumps, CGMs, and Connectivity

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John Walsh, PA, CDTC
jwalsh@diabetesnet.com
(619) 497-0900
Advanced Metabolic Care + Research
700 West El Norte Pkwy
Escondido, CA 92126
(760) 743-1431

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Disclosure

- Book sales – all pump companies
- Advisory Boards – Companion Diabetes, Convatec, PicoLife Technologies
- Consultant – Bayer, Roche, BD, Abbott, Tandem Diabetes, Acon Laboratories, Companion Diabetes
- Speakers Bureau – Tandem Diabetes, Animas
- Sub-Investigator – Glaxo Smith Kline, Animas, Lilly, Sanofi-Aventis, Bayer, Medtronic, Biodel, Dexcom, Novo Nordisk, Halozyme
- Pump Trainer – Accu-Chek, Animas, Medtronic, Omnipod, Tandem
- Web Advertising – Sanofi-Aventis, Sooil, Tandem Diabetes Medtronic, Animas, Accu-Chek, Abbott, etc.

Advantages of an Insulin Pump

- Average A1c reduction = 0.2%[1]
- Convenience
- Software calculates doses
- Easier to match varying needs
- Less insulin stacking, less severe hypoglycemia, less BG variability [2]
- Freedom of lifestyle
- Better data (clinicians, pumpers, parents)

*

[1] Hsin-Chieh Y, et al: Ann Intern Med. 2012;157(5):336-347.
[2] Pickup JC, Sutton AJ: Diabet Med 2008 Jul;25(7):765-74.

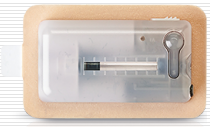
Line Pumps

Accu-Chek Combo

Animas Vibe
Ping

Medtronic 530G
(Revel)

Patch Pumps



Valeritas V-Go

Insulet
Omnipod

Calibra Finesse

Remote Controls

Accu-Chek
Combo

Animas Ping

Omnipod

- Integrated glucose meter for convenient testing
- Discreet carb and correction boluses
  (Omnipod remote must be present to give a bolus)
- Basal adjustments with Accu-Chek

Advantages of a CGM

- Average A1c reduction = 0.7%[1]
- Reads glucose every 5 min
- Gives alarms for lows and highs
- Security for wearer and family
- Trend line and arrows guide bolus doses
- Lower A1c, less severe hypoglycemia, less BG variability
- Better data (clinicians, pumpers, parents)

[1] Y Hsin-Chieh et al: Ann Intern Med. 2012;157(5):336-347.

Enlite Sensor – Medtronic 530G

- Low Glucose Suspend (LGS) – CGM suspends basal up to 2 hrs
- May reduce length of night lows
- 6 (5-9) day Enlite sensor
- Wearability, excess alarms, not hearing alarm are issues for some wearers
- Predictive glucose suspend in development

Dexcom G4 – Animas, Asante, Omnipod, Tandem

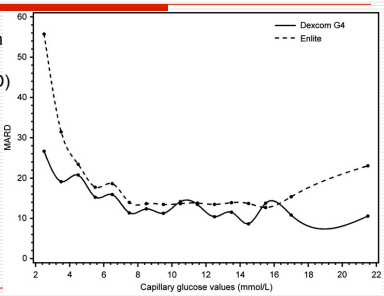
- High contrast color screens
- 1-2 week Dexcom G4 sensor
- Internet access via Diasend, t:connect, Tidepool, iHealth
- Nightscout remote readings
- Predictive glucose suspend in development

Dexcom G4 (ver 1) vs Enlite Accuracy

Continuous mean absolute relative difference (MARD)

Measures accuracy of each sensor

Lower is better



Matuleviciene V, Joseph J, Andelin M, Hirsch I, et al.: Diab Technol & Therapeut 2014 16(11), 759 -767

Dexcom G4 (ver 2) vs Enlite Accuracy

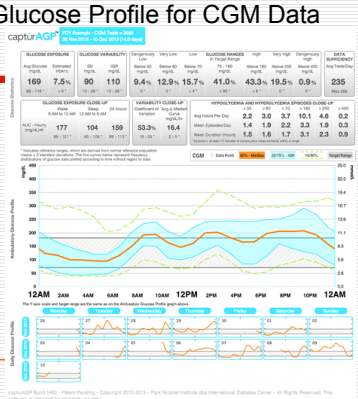
- MARD for 53 subjects wearing Dexcom G4 for 7 days = 9.0%[1] (Free software upgrade now available)
- For BGs <3.9 mmol/L (70 mg/dL), MARD was 0.36 mmol/L (6.4 mg/dL)
- 73% of sensors had MARD <10%
- 92.4% of readings were in Clarke error grid zone A
- MARD for Enlite sensor = 13.6%[2]

1. Bailey TS, Chang A, Mark Christiansen M: *J Diabetes Sci Technol November 3, 2014*
2. Bailey TS, Ahmann A, Mark Christiansen M, et al.: Diabetes Tech Therap. 2014, 16(5): 277-283

Ambulatory Glucose Profile for CGM Data

Internat. Diab. Center

- Time in range
- Shaded modal day with median, IQ range, and 10/90% range
- Dashboard



Bergenstal et al: DT&T 2013

Size Up the Glucose Problem

- If it ain't broke, don't fix it!
- **Severe** – Reset the TDD to an improved TDD (iTDD) to correct problem and select new settings from this iTDD.
- **Moderate** – With pattern, use pattern management or reset TDD
- **Mild** – tweak pump settings

APP Study Background

- 396 pumps had >95% of BGs entered from an attached meter; >73 days of data and >300 BG tests per pump
- 92.7% of pump wearers used BC to cover carbs (>2 meals a day) and 96.5% used BC to correct high readings
- Pumps were divided into tertiles by avg. BG
- Basal %, CarbF and CorrF formulas were derived from the tertile with the lowest avg. BG

1. Walsh J, Roberts R, Bailey T: J Diab Science & Technology 2010, Vol 4, #5, Sept 2010
2. Walsh J, Roberts R, Bailey T. Guidelines for Optimal Bolus Calculator Settings in Adults. J Diabetes Sci Technol 5(1): 1711-1717, 2011.

APP Study – BGs, Basal Rates, and TDDs

Glucose, Insulin and Carb Data

Group:	All 396 Pumps	Low Third	Mid Third	High Third
Avg. Meter BG	184 mg/10.2 mmol	144 mg/dL (8.0)	181 mg/dL (10.0)	227mg/dL (12.6)
BG Tests/Day	4.38	4.73	4.41	4.01
TDD	49.4	47.9	49.1	51.1
Basal %	47.6%	47.6%	47.2%	47.8%

1. J Walsh, R Roberts, T Bailey: J Diab Science & Technology 2010, Vol 4, #5, Sept 2010

The Total Daily Dose (TDD)

- Major factor that controls A1c and the frequency of lows
- Great guide to correct pump settings
- Adjust TDD to fix major control problems

Find Initial TDD – Jim's Starting TDD

Wt = 184 lbs A1c = 7.0%

① Current TDD (injections) = _65_ u/day

② TDD by weight lbs/4 = _46_ u/day

③ Sum of 1 + 2 = _111_ units

④ Times 0.45 x 0.45

⑤ Starting TDD = _50_ u/day

Use TDD to Find Initial Settings[1]

Basal = *~ 48% of TDD (0.02 x TDD = avg. U/hr)*

CarbF = $5.7 \times \frac{Wt(kg)}{TDD}$ or $2.6 \times \frac{Wt(lbs)}{TDD}$

Corr. Factor = *110/TDD (mmol/L)* *(85 to 120)*

Poor control = need for smaller CorrF (larger correction doses)

Or use Pump Settings Tool at
www.diabetesnet.com/diabetes_tools/pumpsettings/

[1] *J Walsh, R Roberts, T Bailey: J Diab Science & Technology 2010, Vol 4, #5, Sept 2010*

Jim's Starting Pump Settings

Wt = 184 lbs TDD = 50 u A1c = 7.0%

Basal = *50 u x 0.02 = 1.0 u/hr*

CarbF = *2.6 x* $\frac{184\ lbs}{50}$ *= 9.6 grams/unit*

CorrF = *110/50 = 2.2 mmol/L per unit*

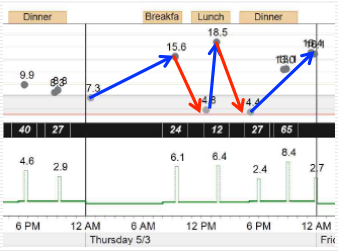
[1]J Walsh, R Roberts, T Bailey: J Diab Science & Technology 2010, Vol 4, #5, Sept 2010

Stop Frequent Lows First

- **You cannot tell how much excess insulin there is!**
- Start with a 5% or 10% reduction in TDD
- Compare the current TDD to an "ideal" TDD for weight.
  - Divide weight(lbs) by 4 to see what TDD would be used with an average sensitivity to insulin

Example: Someone who weighs 160 lbs would be expected to have a TDD of 40 units (160/4 = 40).

Example – Frequent Lows



41 yo female with A1c = 6.9%

TDD = 50.5 u/d

152 lb/4 = 38.0 u/d

Be Careful of Hidden Lows

This person felt low and ate, but never tested with a meter. There's no record of these lows without a CGM!

Then Stop Frequent Highs

Raise TDD by 3% for each 1 mmol/L you want to lower the average BG (or 5% for each 1% in A1c)

Current BG – Target BG x 3 = % rise in TDD

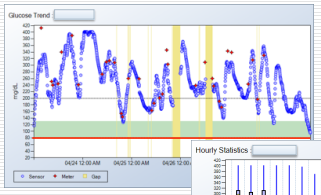
Example: Amy's avg TDD is 40 u/day, average meter BG is 10.3 mmol/L (with few lows), and average BG goal is 7.0 mmol/L:

10.3 mmol/L – 7.0 mmol/L = 3.3 mmol/L

3.3 mmol/L x 3 = 10% rise needed in TDD

40 units x 1.10 = 44 units a day

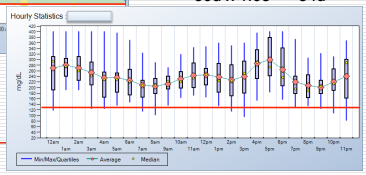
Example – Frequent Highs



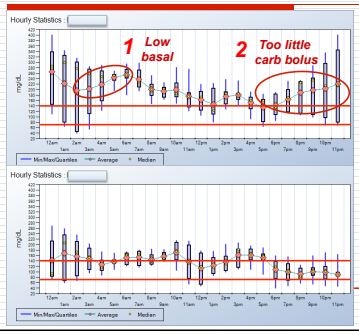
27 yo male, A1c = 8.6%, TDD = 50 u/day

8.6% - 7.0% = 1.6% x 5 = an 8% increase in TDD

50u x 1.08 = 54u



TDD Before & After Adjustment

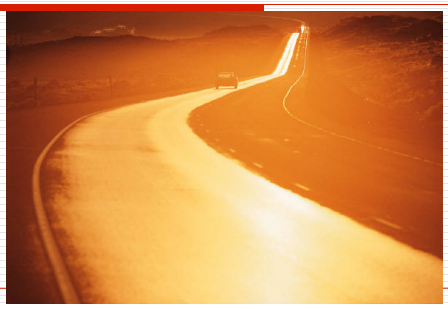


53 yo female
TDD = 36 u

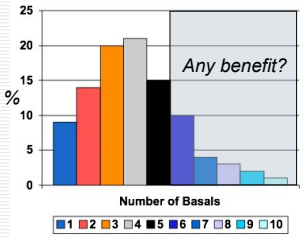
- Raise basal by 0.05 u/hr all day (+1.2 u/day)
- Lower CarbF from 1u/13g to 1u/12g (+1.8 u/day)

TDD = 39 u

Steps To Control – Too many Basals: "Over-Steering"



How Many Basal Rates?



Number of basal rates used per day from self-reports of hundreds of pumpers at insulin-pumpers.org

Once basal rate changes, it takes 3-5 hrs to have its full effect.*

Using more than 5 basals may have little benefit.

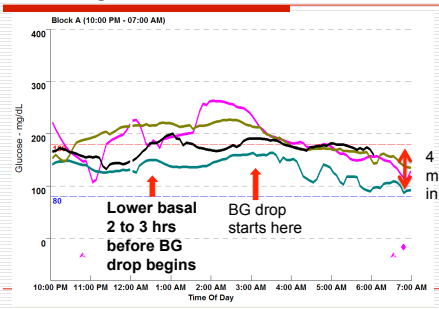
** Heinemann L, Nosek L, Kapitza C, et. al. Changes in basal insulin infusion: time until a change in metabolic effect is induced in patients with type 1 diabetes. Diabetes Care. 2009;32(8):1437–1439.*

Basal Tips – Avoid Over-Steering

- Basal rates are usually similar through day, such as between 0.5 to 0.8, or 1.0 to 1.5 u/hr
- Adjust basal rates in small steps (0.025 to 0.1 u/hr) **2 hours** before BG **starts** to rise or fall
- Over 5 basals a day probably has little benefit.[1]

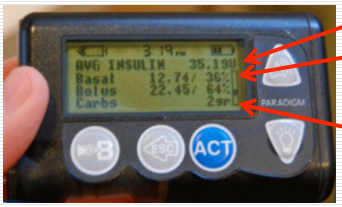
[1] Heinemann L, Nosek L, Kapitza C, et. al. Changes in basal insulin infusion: time until a change in metabolic effect is induced in patients with type 1 diabetes. Diabetes Care. 2009;32(8):1437–1439.

Overnight Basal Check



4 mmol/L (70 mg/dL) drop in 4 hrs

Pump Data – Avg. TDD and Basal/Bolus Balance



***TDD** = 35.19 u*

***Basal** % is low at 36%*

2 grams of carb/day (~20 calories a day) means Bolus Wizard is not being used

The Bolus Calculator

- Better match of bolus with carbs and high glucose
- Shows how much BOB remains – less insulin stacking
- Lower A1c, less glucose variability

Bolus Calculator Settings

This Setting	Helps
Basal rates	Sound sleep
CarbF or I:C ratio	Cover carbs well
CorrF or ISF	Lower highs safely
Target glucose	BG goal 4-5 hrs later
DIA	Minimize insulin stacking

The average TDD determines how often highs and lows occur

Bolus Calculator

Inputs:

Glucose

Photo courtesy www.sixuntilme.com

Grams of carb

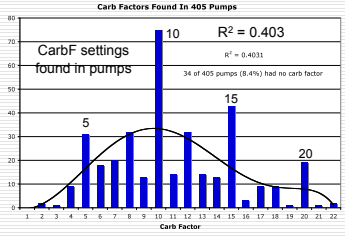
Photo courtesy emilyboller.com

Output: Bolus recommendation with units for carbs and correction, plus how much BOB is still active

Steps To Control – Get Accurate Boluses

- ☐ Use carb counting resources
  - CalorieKing, MyFitnessPal
- ☐ Know portion sizes
  - Measure portions onto plate at home
- ☐ Base CarbF on total daily dose (TDD)
  - CarbF = (2.6 x weight) / TDD

APP Study – Carb Factors Often Wrong[1,2]



CarbFs are not evenly distributed.

People prefer "magic" numbers – 5, 10, 15, and 20 g/unit.

Formulas will provide more accurate settings –> better than WAG!

Don't use "magic" numbers!

1. J Walsh, R Roberts, T Bailey: J Diab Science & Technology 2010, Vol 4, #5, Sept 2010
2. J. Walsh, D. Wroblewski, and TS Bailey: Insulin Pump Settings – A Major Source For Insulin Dose Errors, Diabetes Technology Meeting 2007

Clever Pump Trick – Find Carbs Needed for Lows

1. 1 gram for each 10 lbs of weight (minimum 10 gr)
2. Plus grams = BOB x CarbF

Example: Amy's BG = 52 mg/dL with 2u of BOB (CarbF = 8 gr/u)

- At 140 lbs, she needs 14 grams of carb for the BG
- Plus 2u BOB x 8 gr/u = 16 grams to offset BOB
- She needs 14 g + 16 g = 30 grams for this low

Pump BC May Recommend Excess Bolus Insulin

Recommended Bolus from BC			
Glucose	Units Needed	Animas	Other Pumps
#1: 5.9 mmol/L	0 u	0 u	5 u
#2: 6.1 mmol/L	0 u	5 u	5 u
#3: 12 mmol/L	2 u	5 u	5 u
#4: 18 mmol/L	4 u	5 u	5 u

Pump wearer eats 50 gram dessert 2 hrs after dinner with 5u of BOB on 4 consecutive nights. BG at that time shown for each night, along with the actual bolus needed and the dose current pumps recommend.

CarbF = 10 gr/u; CorrF = 3 mmol/L; Target = 6.0; DIA = 5 hrs

Verify Bolus Recommendations

If 4.35 u of BOB remain from a bolus given 3 hrs earlier, would you give 2.9 more units for a bedtime snack?

Bolus on board (BOB) = glucose-lowering activity that remains from recent boluses

Pumps cover all carbs even when excess BOB is present

BOB of 4.35u is larger than correction bolus need (1.23u), so consider reducing recommended bolus

Ping and Vibe give correct bolus when BG is below target

Clever Pump Trick – Get an Accurate Bolus

1. If BOB is smaller than correction bolus, the recommended pump bolus is CORRECT
2. If BOB is larger than correction bolus, add carb and correction bolus, then subtract BOB

Example: Carb bolus = 3.0 u (Pumps recommend 3.0 u)

Corr bolus = 1.2 u
BOB = 4.0 u
} ***BOB larger than Corr bolus***

Accurate bolus = 3.0 + 1.2 – 4.0 = 0.2 units as needed bolus

Clever Pump Trick – Bolus Early To Stop Meal Spiking

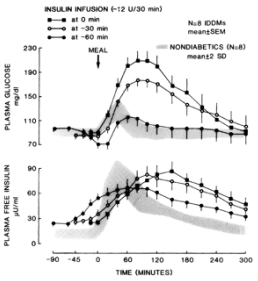


Figure shows Regular insulin injected 0, 30, or 60 min before a meal

Normal glucose and insulin profiles in the shaded areas

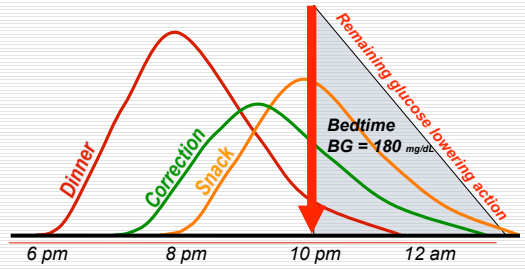
Even though, best glucose occurred with 60 minute bolus – **too risky to recommend!!!**

The best-kept secret for better control

GD Dimitriadis and JE Gerich: Importance of Timing of Preprandial Subcutaneous Insulin Administration in the Management of Diabetes Mellitus.Diabetes Care 6:374-377, 1983.

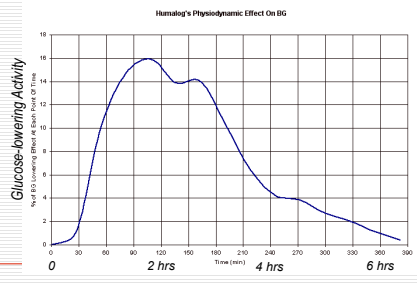
Bolus on Board / Insulin Stacking

Bedtime BG = 10 mmol/L – is there an insulin or a carb deficit?



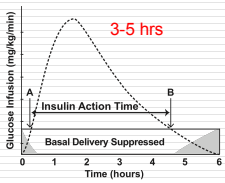
Duration Of Insulin Action

Accurate boluses require an accurate DIA



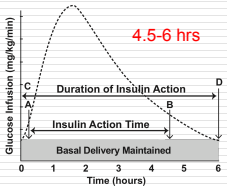
Insulin Action Time ≠ Duration of Action

Fig. 1 Insulin Action Time



IAT is measured between points A and B, and involves suppression of basal delivery.

Fig. 2 Duration of Insulin Action



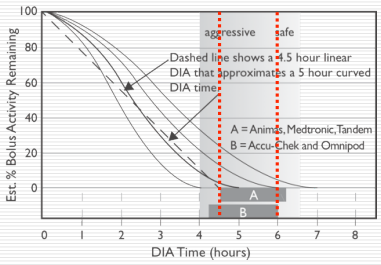
DIA is measured between points C and D. Once basal delivery is maintained, the PD of a bolus insulin can be directly measured.

Why Short DIA Times Cause Lows

How much BOB a pump thinks is left 3 hours after a 10 unit bolus for these DIA times:

	Pump's estimate of Insulin On Board			
If DIA is set to:	3 hr	4.5 hr	5.0 hr	5.5 hr
Estimated BOB is:	0 u	2.5 u	3.4 u	4.0 u

Recommended DIA Times



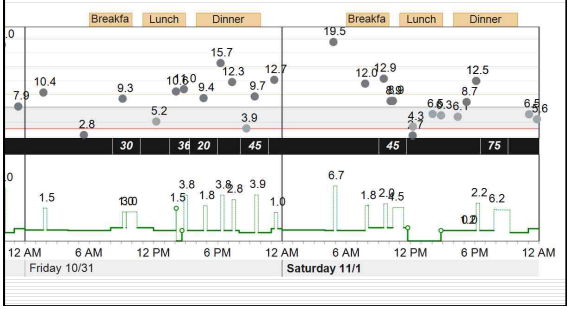
Set DIA to 4.5 to 6 hrs for accurate calculation of BOB and bolus doses

Graphic adapted from Mudaliar et al: Diabetes Care, 22: 1501, 1999

Infusion Set Failure Is Common

- Most of the 16,849 adverse pump events reported to the FDA between 2006-2009[1] involved infusion sets[1]
- A 2006 review of pumps in France likewise found that most serious adverse events involved infusion sets[2]
- Auto-insertion devices have a high failure rate of 8.9%[3]
- In a survey of 1142 pumpers in 40 German diabetes clinics, 36% used auto-insertion devices and 72% reported that the device failed to work ~10% of the time. 54% reported high BGs for unknown reasons until their infusion set was changed

1 www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralHospitalandPersonalUseDevicesPanel/UCM202779.pdf
[2] Maugendre D. Technical risks with subcutaneous insulin infusion. Diabetes Metab. 2006;32:279-284.
[3] Renard E, et al: Lower rate of initial failures and reduced occurrence of adverse events with a new catheter model for continuous SQ insulin infusion. Diabetes Technol Ther 12:769-773, 2010.
[4] Reichert D, et al. Realität der Insulinpumpentherapie in Diabetesschwerpunktpraxen: Daten von 1142 Patienten aus 40 diabetologischen Schwerpunktpraxen. Diabetes, Stoffw. und Herz 22: 367-375, 2013.



Auto-Inserters

Inset 30

Accu-Chek Link Assist

Inset/Mio

Quick-Serter

Cleo

Omnipod

Is The Infusion Set The Problem?

- Sites often "go bad"?
- Have "scarring" or "poor absorption"?
- Often have 2 or more unexplained highs in a row?
- Do correction boluses sometimes not work?
- Have high BGs until set is changed?

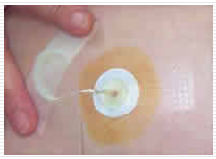
Why Infusion Sets Fail

- Complete pullout
- Insulin leak along Teflon to skin
- Hematoma under the skin
- Autoinserter
- Occlusion
- Loose hub
- Punctured line

ALL should rarely or never happen

Infusion Set Solutions

- Insert set manually
- Anchor the infusion line with tape*
- Review site prep and insertion technique with clinician or trainer
- Switch to a more reliable infusion set



** Transpore, Micropore, Durapore, Hypafix*

Future Developments

Artificial Pancreas Pathway

TODAY

OPEN-LOOP (Patient confirmation)	SEMI-CLOSED LOOP (Semi-automated system)	CLOSED-LOOP (Fully-automated system)

• Insulin pump + glucose sensor + bolus wizard	• Iterative:
	– Threshold suspend
	– Predictive suspend
	– Overnight closed-loop
		• Free-living trials have started
		• Dual hormones?
		• Meal-handling
		  • Announce?
		  • Assist?

Going Beyond Simple Pumps

- Show how a setting change changes the TDD (& BG)
- Temp basal PLUS bolus doses
- Super Bolus
- Meal-size boluses
- Alert for excess BOB (bolus without BG but BOB is ++)
- Low BG predictor (HypoManager)
- Exercise compensator (duration + intensity = gr of carb)
- Infusion set monitor/leak detector
- Automated basal and bolus testing

Connectivity

The next big wave in diabetes devices and care!

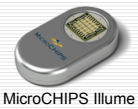
Gadgets
+ Interfaces
+ Intelligence

Eventually, easier for everyone

Connectivity – the Next Big Wave

- Bluetooth LE allows connecting:
  - Pumps or smart insulin pens
  - Meters and CGMs
  - Cell phones
  - Activity monitors – FitBit, FuelBand JawBone, MotoActv, BodyMedia
- Integrate data from different device manufacturers
  - Tidepool, DiaSend, MySugr, etc.

Implanted CGMs



MicroCHIPS Illume

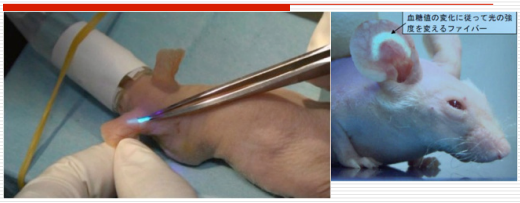
Sensionics

- Months to years of use
- No disposables
- Minor surgery
- Funded as rental?

Biorasis Glucowizzard

GlySens

Implanted Fluorescent CGM

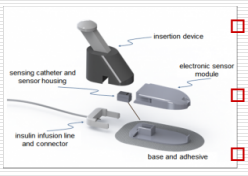


Molecules fluoresce & change color as glucose rises or falls

- Small size, low power, low cost, long life, good accuracy, minimal lag time

From Y. J. Heo et al: Institute of Industrial Science at the University of Tokyo

New CGM Designs



Pacific Diabetes Technologies

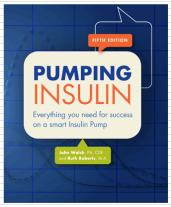
- Factory calibrated
- Abbott Flash -14 day, no cal
  - Intermittent CGM with lower cost
- Glucose oxidase + fluorescent sensors
- 2 to 6 sensors on one CGM wire
- 2 to 6 sensors on infusion cannula

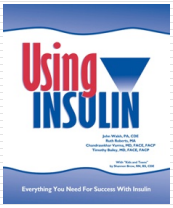
Faster Insulins

- Diaport intraperitoneal delivery
- Ultra-fast insulin analogs
  - Novo Nordisk / Lilly
  - Biodel
  - MannKind Afrezza (inhaled)
- Micro-needles (1.5 mm)
- Hyaluronidase
- Warming of infusion site

Goal: fewer highs and fewer lows

Life Is Better When You Know More!





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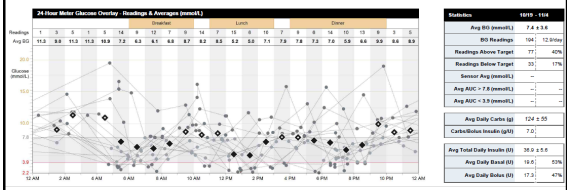
Slides at www.diabetesnet.com/diabetes-resources/diabetes-presentations
Books at www.diabetesnet.com/dmall/ or 800-988-4772

Case Study – Excess TDD



Case Study – Hypos Caused by Pump