Emerging Technology Pumps And CGM

Children With Diabetes
Charlotte, NC
Sept. 4, 2010

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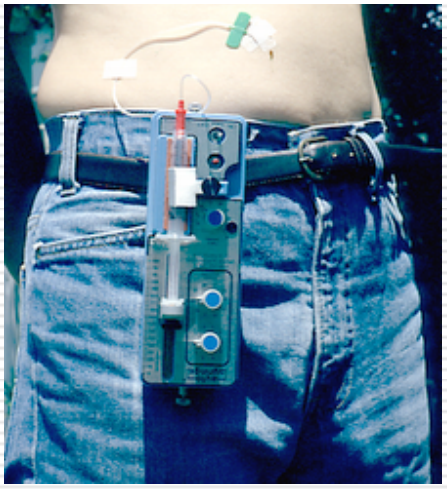
Disclosure

- Book sales – to all pump companies
- Advisory Boards – Tandem Diabetes, Unomedical
- Consultant – Bayer, Roche Accu-Chek, Abbott, Tandem, Medingo
- Speakers Bureau – Tandem Diabetes
- Instructor – J&J Diabetes Institute
- Sub-Investigator – Glaxo Smith Kline, Animus, Sanofi-Aventis, Bayer, Biodel, Dexcom, Novo Nordisk
- Pump Trainer – Accu-Chek, Animas, Medtronic, Omnipod
- Web Advertising –Sanofi-Aventis, Sooil, Medtronic, Animas, Accu-Chek, Abbott, etc.

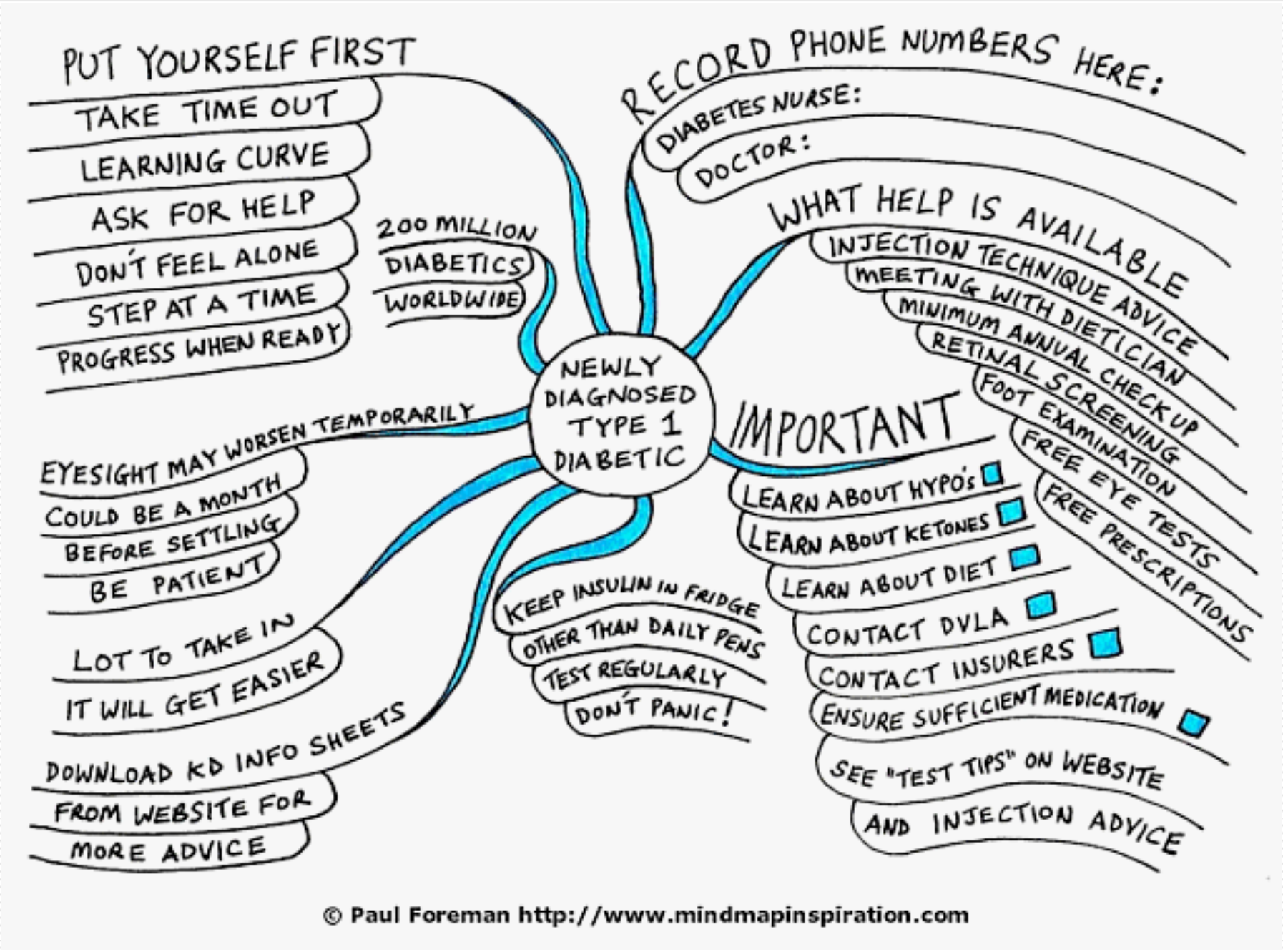
Outline

- Goals
- CGMS
- Special Pump Features
- Pump Settings
- DIA and BOB
- Future Pump Features

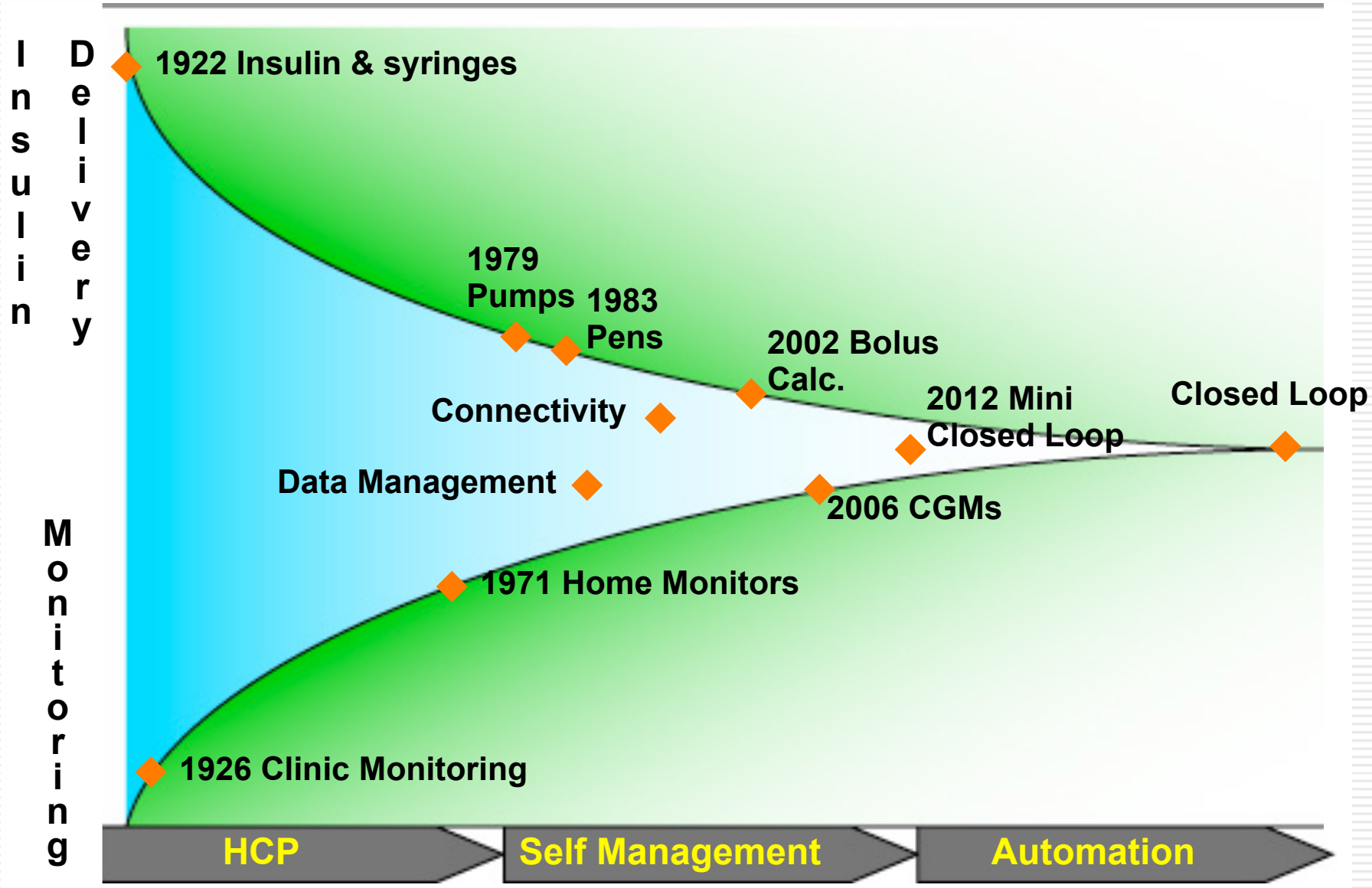


Terms

- **TDD** – total daily dose of insulin (all basals and boluses)
- **Basal** –background insulin released slowly through the day
- **Bolus** – a quick release of insulin
  - Carb bolus – covers carbs
  - Correction bolus – lowers high readings that arise from deficits in basal rates or carb boluses
- **Bolus On Board (BOB)** – bolus insulin still active from recent boluses, active insulin, insulin on board
- **Duration of Insulin Action (DIA)** – time that a bolus will lower the BG – used to measure BOB



The Way To A Closed Loop



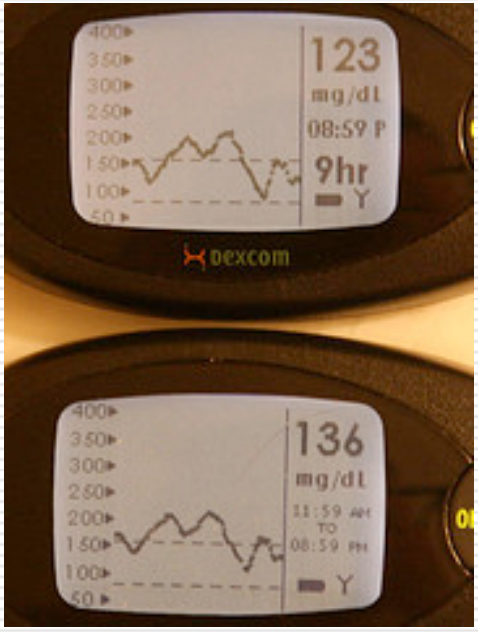
Adapted courtesy Roche/Disetronic

Progress In Monitoring

1300 BC

1971 AD

2010 AD



What If There Were A Pill...

...that:

- Decreased amount of time spent high
- Decreased amount of time spent low
- Warned you of impending highs and lows

Thanks to Dr. Grazia Aleppo

CGM

Components

Sensor

Receiver

Transmitter

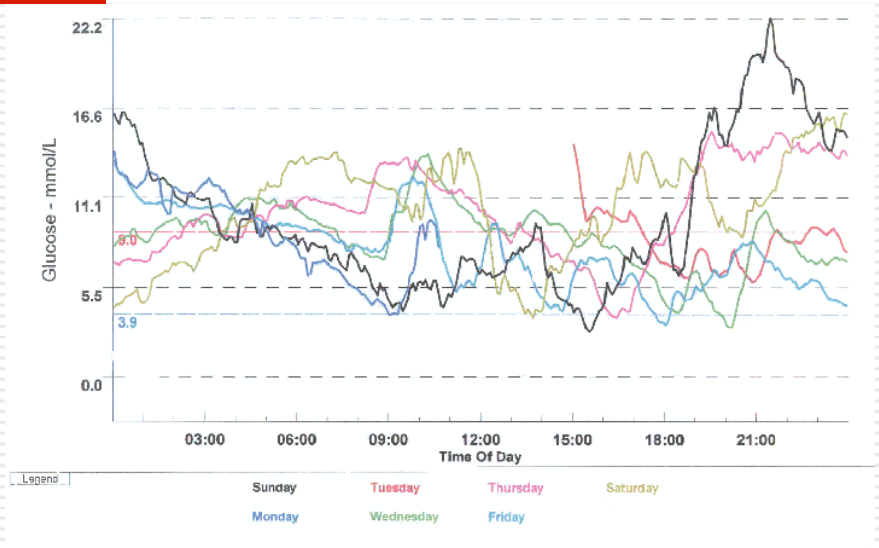
Why CGM Helps

Short Term Benefits

- Minimize extreme BGs – tracking and trending minimizes extremes
- Immediate feedback for what each meal/snack/ exercise does – behavior mod made easy
- Know the direction you're going
- Fingersticks become more useful

Why CGM Helps

Long Term Benefits



- See your patterns
- Test and tune basals, CarbF, CorrF
- Avoid night lows and hypo unawareness
- Peace of mind from fear of lows

Systems

Abbott FreeStyle Navigator®

DexCom™ SEVEN® PLUS

Medtronic MiniMed Revel® REAL-Time*

* Medtronic Guardian® REAL-Time and I-Port also available.

Why Don't My CGM & Meter Agree?

- "Accurate" meter when control solution reads between 106 and 143 mg/dl (BG = ~120 mg/dl)
- Excellent meter accuracy (+/– 10%) = 108 to 132 mg/dl for BG of 120
- CGM is calibrated FROM meter
- CGM accuracy is excellent when deviation is +/– 15% or 102 to 138 mg/dl for BG of 120
- SO....meter may read low (108) and CGM high (138) and BOTH be excellent with real BG of 120!

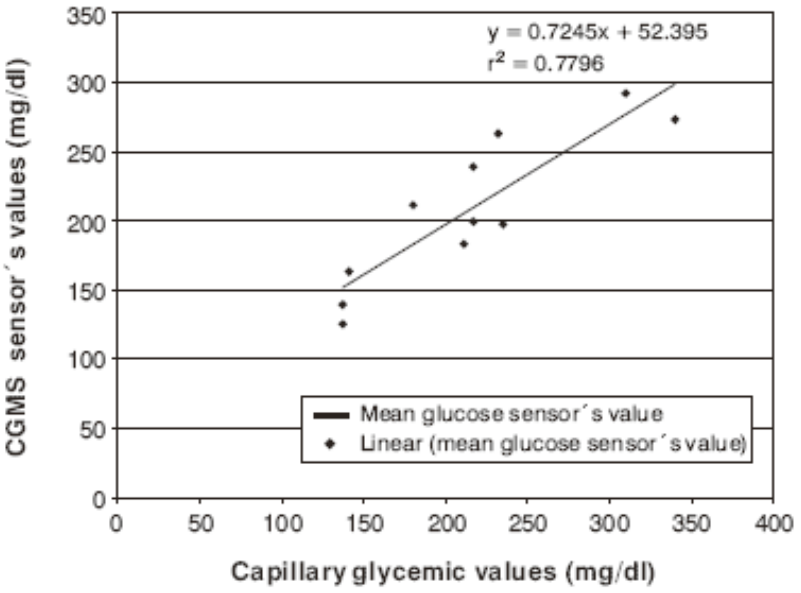


Figure 1 - Correlation of glucose values detected by the continuous glucose monitoring system (CGMS) sensor vs. fingerstick sampling values in pediatric type 1 diabetic patients ($r^2 = 0.77$; $p = 0.001$)

Trends Are Better Than Points

Insight

No clue what to do

Photo courtesy Bernard Farrell

Exercise With Confidence

Experimental CGMs

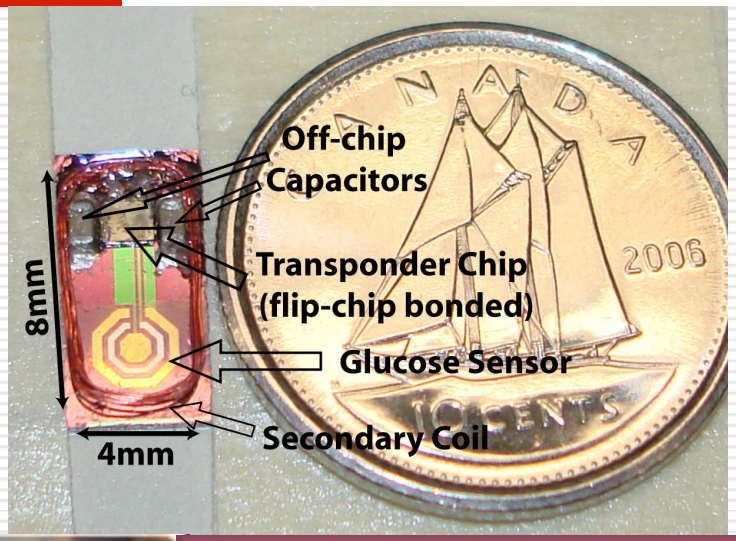
Invasive and Non-Invasive

Implanted CGM Systems

MicroCHIPS Illume

GlySens

Implanted CGM Systems



MicroCHIPS Illume

GlySens

Continuous Osmotic Glucose Sensor

- LifeCare (Bergen, Norway) is working on a CGM to be implanted without surgery
- Currently testing immune system compatibility

Implanted Flourescent Sensors

Flourescent molecule changes color as glucose rises and falls. LED serves as light source.

Potential Advantages:

- Small size
- Low power or locally generated power
- Long life

Non-Invasive Optical CGM

OrSense's NBM-200G uses near infrared light scattering to measure glucose levels.

- Easy to use but likely less accurate than current CGMs
- Tested on over 450 subjects
- Investigational stage

Non-Invasive Eye Patch CGM

Nanoparticles embedded in hydrogel lens reacts with glucose in tears

Chemical reaction changes color of lens.

Exterior device (glasses) read glucose from color change

CGM And Pump Choices

CGM:		Pump:	Available
Dexcom 7+	⟷	Animas	2011
	⟶	Insulet	2011
Paradigm RT	⟷	Medtronic	now
AccuCk Combo	⟷	Combo*	2012?
Navigator	⟷	?	2011?
Dexcom/Navig.	⟷	Tandem	2012?

New Pumps

Tandem 2010

Solo 2012

Calibra 2011/12?

Jewel 2012?

More Patch Pumps

- Roche-Medingo Solo
- Debiotech JewelPump
- Medtronic
- Valeritas V-Go
- Pancreum Beta Wedge
- NiliMEDIX
- Calibra, Medsolve, CellNOVO, Altea

Patch Pump Vs Infusion Set

Patch Pump

- Worn on body
- No external tubing
- Can loosen, leak, be knocked off

Infusion Set

- More site options
- Variety of needle and tubing lengths
- Easy pump removal for showering, sports
- Can loosen, leak, be knocked off

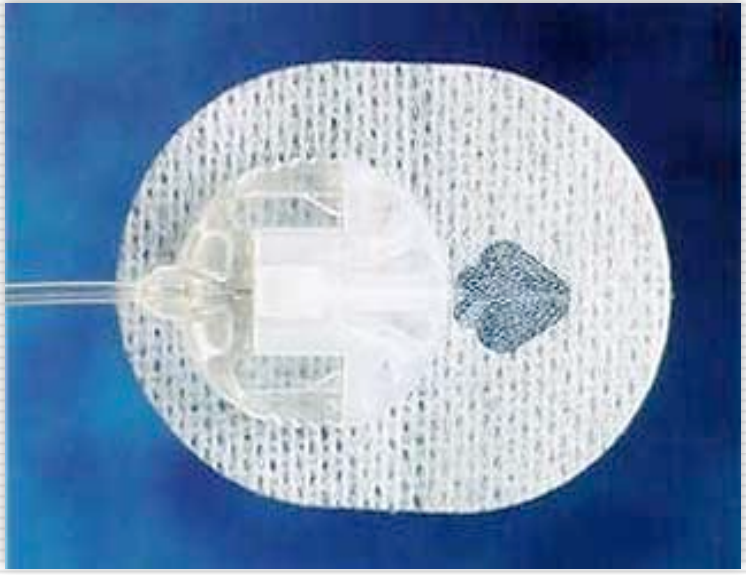
Auto Inserters

Infusion Sets

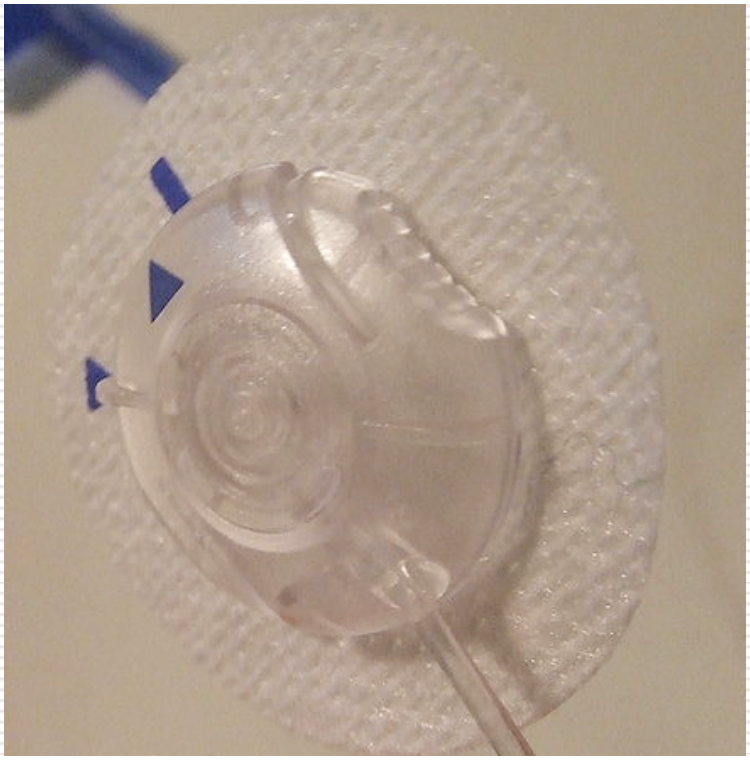
Slanted

Metal

Straight In



Quick Release Sets



Color Screens

Soon: Tandem, Solo, others

CGM Display

Remote Boluses

- Bolusing from meter/PDA lets pump stay hidden
- Meter sends BG to pump
- Carb bolus, correction bolus, basal remotely controlled by meter/PDA
- Accurate, complete history

Bolus and basal adjustments in Accu-Chek Combo (not yet FDA approved)

Combo Boluses – Part Now, Part Later

- DON'T USE for most meals
- Great for Symlin, low GI carbs, hi-protein or hi-fat meals, gastroparesis
- Helps when carb counts or meal timing are uncertain
  - Give part of bolus early to get insulin working
  - Give rest over time – discontinue if meal has fewer carbs than expected. Give 2nd bolus if meal contains more carbs.
- Picky-eater parents love combo boluses

Advanced Carb Counting

The quick way to keep carbs from raising your glucose

Carb lists in Ping, Omnipod, Spirit/Combo, Tandem, others

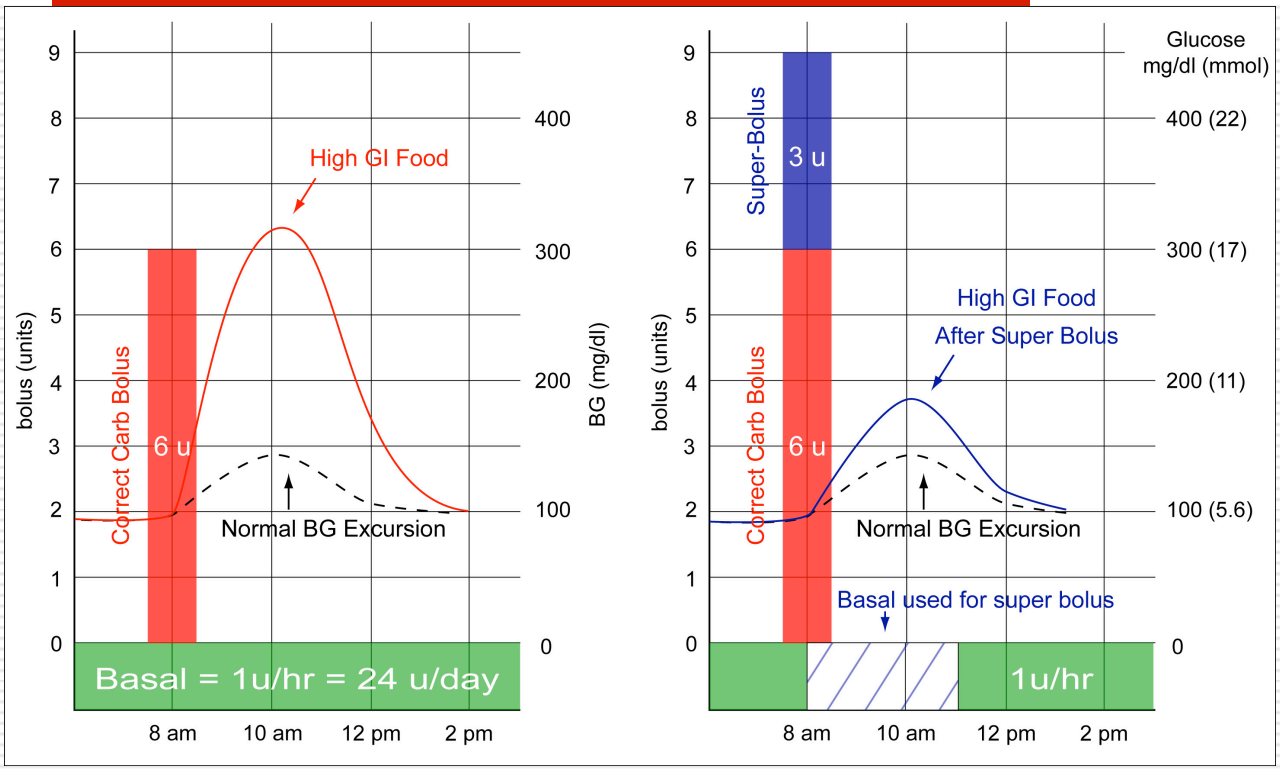
Photo courtesy Emily Boller, emilyboller.com

Temp Basal Rates

Great for:

- Covering exercise ↓
- Handling illness ↑
- Testing new basal rates ↓ ↑
- Offseting excess BOB ↓
- Safely “stopping” a pump and restart on time!

Super Bolus For A High GI Meal
Shifts Basal To Bolus



A Super Bolus helps when eating more than 30 or 40 grams of carb, esp. high GI meals like cereal.

Max carbs/meal = Wt(lb) X 0.36 [2] to stay in control

Future Feature: Super Bolus shifts part of the next 2 to 3.5 hrs of basal insulin into the bolus with less risk of a low later.[1,2]

[1] J. Walsh: http://www.diabetesnet.com/diabetes_presentations/super-bolus.html September, 2004

[2] J. Bondia, E. Dassau, H. Zisser, R. Calm. J. Vehí, L. Jovanovic, F.J. Doyle III, Coordinated basal-bolus for tighter postprandial glucose control in insulin pump therapy, Journal of Diabetes Science and Technology, 3(1), 89-97, 2008

Tips For Success

1. Stop lows first
2. Find your iTDD – good A1C, stable readings, with basal/carb bolus balance
3. Set & test basals – do overnight readings stay level?
4. Set & test carb boluses – fine-tune premeal BGs
5. Lower post meal BGs – give boluses early, low GI foods, Symlin, etc.
6. Set & test corr. boluses – bring highs down safely

Enjoy good control or return to #1

Brittle diabetes or frequent highs = wrong doses (usually)

Find Your iTDD

If it ain't broke, don't fix it – current doses are great if A1c and avg. meter BG are good with few lows

If not, adjust the current TDD:

1. Lower the TDD by about 5% for:
   - Frequent lows
   - Or highs AND lows IF lows come first
2. Raise the TDD, using the iTDD Table on next slide to adjust for high A1c or high meter average

Keep basal and carb bolus totals balanced

Avg BG on pumps is 183.9 mg/dl (10.2 mmol) – most need larger TDD.

The iTDD Table

10.6 Find Your True TDD

This table helps you find a more accurate TDD when your readings are often above 140 mg/dl (mmol) AND you are not having frequent or severe lows.

Simply find a current 14 day average TDD from your pump on the left and an average glucose from your meter (or a recent A1c) on the bottom. When they intersect provides a better estimate for your TDD.

Current TDD									
100 u	103.0	105.8	108.6	111.4	114.4	117.2	120.0	123.0	125.8
95 u	97.9	100.5	103.2	105.8	108.7	111.3	114.0	116.9	119.5
90 u	92.7	95.2	97.7	100.3	103.0	105.5	108.0	110.7	113.2
85 u	87.6	89.9	92.3	94.7	97.2	99.6	102.0	104.6	106.9
80 u	82.4	84.6	86.9	89.1	91.5	93.8	96.0	98.4	100.6
75 u	77.3	79.4	81.5	83.6	85.8	87.9	90.0	92.3	94.4
70 u	72.1	74.1	76.0	78.0	80.1	82.0	84.0	86.1	88.1
65 u	67.0	68.8	70.6	72.4	74.4	76.2	78.0	80.0	81.8
60 u	61.8	63.5	65.2	66.8	68.6	70.3	72.0	73.8	75.5
55 u	56.7	58.2	59.7	61.3	62.9	64.5	66.0	67.7	69.2
50 u	51.5	52.9	54.3	55.7	57.2	58.6	60.0	61.5	62.9
45 u	46.4	47.6	48.9	50.1	51.5	52.7	54.0	55.4	56.6
35 u	41.2	42.3	43.4	44.6	45.8	46.9	48.0	49.2	50.3
30 u	36.1	37.0	38.0	39.0	40.0	41.0	42.0	43.1	44.0
25 u	30.9	31.7	32.6	33.4	34.3	35.2	36.0	36.9	37.7
20 u	25.8	26.5	27.2	27.9	28.6	29.3	30.0	30.8	31.5
15 u	20.6	21.2	21.7	22.3	22.9	23.4	24.0	24.6	25.2
A1c:	7.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5	11.0
14 day avg BG:	155.0	169.0	183.0	197.0	212.0	226.0	240.0	255.0	269.0

- If frequent lows are main problem, lower current TDD by 5% or more
- If frequent highs are main problem, increase current avg. TDD from recent A1c or a 14 day BG average

J Walsh and R Roberts: Pumping Insulin (5th ed), 2010

Doses That Successful Pumpers Use

2. Optimal Insulin Use

Mean Values For Optimal Doses In Best Control Tertile

Insulin Source	% of TDD	Interquartile Range (%)
Basal	47.8%	39.6% to 54.9%
Carb Boluses	43.1%	35.6% to 51.2%
Corr Boluses	9.0%	6.2% to 11.3%

CorrF Rule Number* = 1960 mg/dl per unit (IQR = 1413 to 2151)

* CorrF Rule Number = Avg CorrF x Avg TDD

Insulin use from best control tertile (132 of 396 pumps with avg BG of 144 mg/dl) in our Cozmo data study

Keep basal rates and carb boluses balanced

- For frequent lows, lower the higher one.
- For frequent highs, raise the lower one

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

Pump Settings

Your Keys To Control

A Smart Pump Arrives Dumb

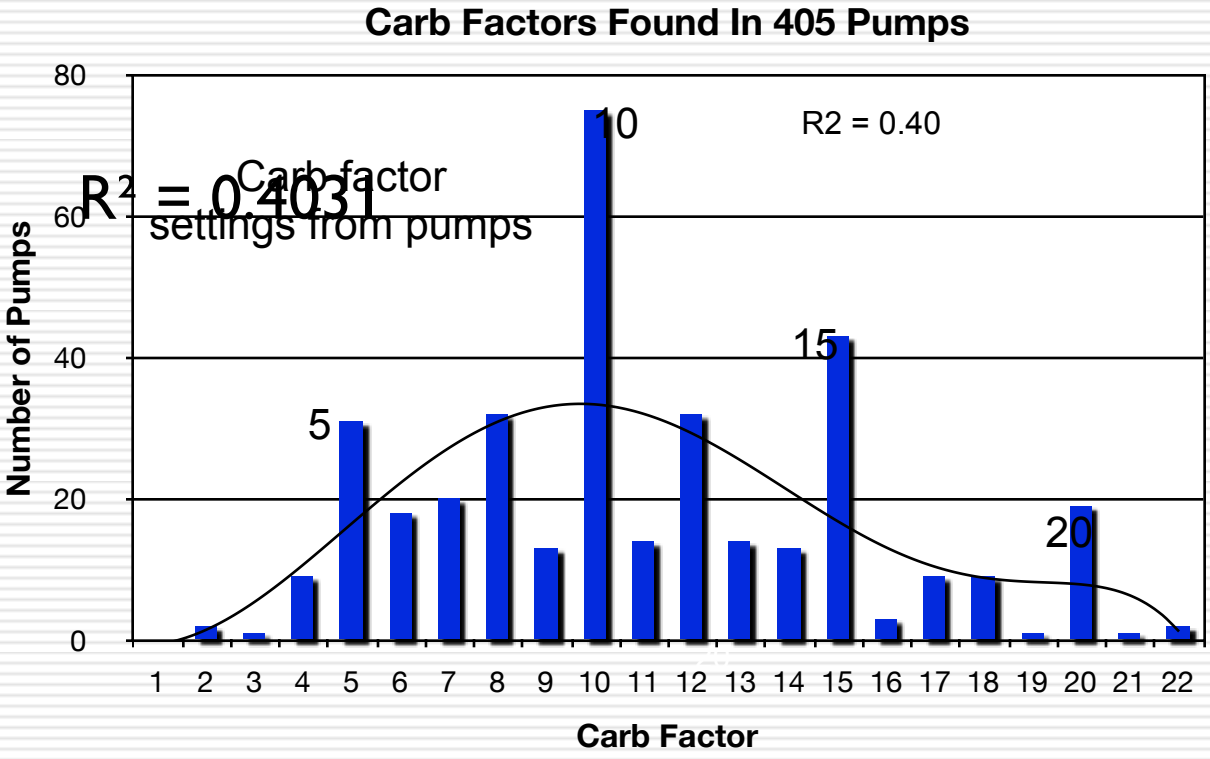
A Smart Pump Arrives Dumb

Set your pump up accurately:

- Accurate TDD
- Accurate basal rates (about 50% of TDD)
- Accurate CarbF
- Accurate CorrF
- Accurate DIA
- Accurate correction target

Don’t rely solely on your bolus calculator!

Deltec Cozmo Study – Carb Factors Found In Pumps[1]

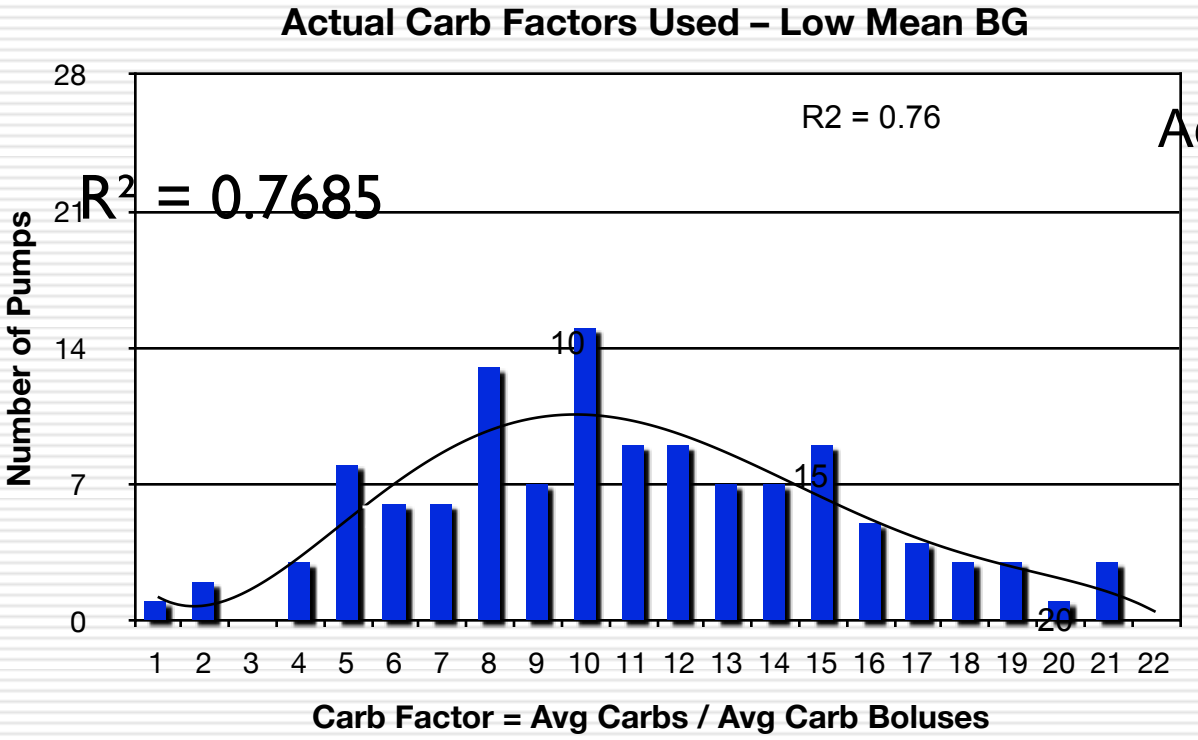


Carb factor settings from pumps are not evenly distributed.

"Magic" numbers – 5, 10, 15, and 20 g/unit – are preferred.

[1] J. Walsh, D. Wroblewski, and TS Bailey: Insulin Pump Settings – A Major Source For Insulin Dose Errors, Diabetes Technology Meeting 2007

Deltec Cozmo Study – Actual Carb Factors Used[1]



Actual Carb Factors change from Pump's CarbF setting when bolus calculator adjusts for BOB, hypoglycemia and hyperglycemia

Carb Factors actually used – avg carbs/avg carb bolus per day

[1] J. Walsh, D. Wroblewski, and TS Bailey: Insulin Pump Settings – A Major Source For Insulin Dose Errors, Diabetes Technology Meeting 2007

Small CarbF Change = Large BG Change

Change in BG/meal when CarbF is lowered from 1/10 to 1/9 TDD = 40 u Corr F = 49 mg/dl per u	
Meal Size	**Fall in BG per meal ***
60 grams	**0.67u x 49 = – 33 mg/dl**
100 grams	**1.1u x 49 = – 54 mg/dl**

*** Calculated as** $\left[\frac{\text{carbs in meal}}{\text{new carb factor}} - \frac{\text{carbs in meal}}{\text{old carb factor}}\right] \times \frac{1960}{\text{TDD}}$

Pump Setting Formulas*

Basal = ~ 48% of TDD

CarbF = 2.6 x $\frac{\text{Wt(lbs)}}{\text{TDD}}$

Carb factor is directly related to insulin sensitivity = average carb factor times individual's insulin sensitivity

Corr. Factor = 1960 / TDD

Correction factor is inversely related to TDD and also inversely related to avg. BG

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

Pump Settings Table

3. Estimates of Basal, CarbF, and CorrF Basal on TDD and Wt												
TDD	**Basal [1] u/day**	**Basal u/hr**	**CorrF[2] (mg/dl) / u**	**Carb Factor[3] in grams/u**								
				100 lbs 45.4 kg	110 lbs 49.9 kg	120 lbs 54.4 kg	130 lbs 60.0 kg	140 lbs 63.5 kg	150 lbs 68.0 kg	160 lbs 72.6 kg	170 lbs 77.1 kg	180 lbs 81.6 kg
16	7.7	0.32	122	16.3	17.9	19.5	21.1	22.8				
20	9.6	0.40	98.0	13.0	14.3	15.6	16.9	18.2	19.5	20.8		
24	11.5	0.48	81.7	10.8	11.9	13.0	14.1	15.2	16.3	17.3	19.5	21.7
28	13.4	0.56	70.0	9.3	10.2	11.1	12.1	13.0	13.9	14.9	16.7	18.6
32	15.4	0.64	61.3	8.1	8.9	9.8	10.6	11.4	12.2	13.0	14.6	16.3
36	17.3	0.72	54.4	7.2	7.9	8.7	9.4	10.1	10.8	11.6	13.0	14.4
40	19.2	0.80	49.0	6.5	7.2	7.8	8.5	9.1	9.8	10.4	11.7	13.0
45	21.6	0.90	43.6	5.8	6.4	6.9	7.5	8.1	8.7	9.2	10.4	11.6
50	24.0	1.00	39.2	5.2	5.7	6.2	6.8	7.3	7.8	8.3	9.4	10.4
55	26.4	1.10	35.6	4.7	5.2	5.7	6.1	6.6	7.1	7.6	8.5	9.5
60	28.8	1.20	32.7	4.3	4.8	5.2	5.6	6.1	6.5	6.9	7.8	8.7
65	31.2	1.30	30.2	4.0	4.4	4.8	5.2	5.6	6.0	6.4	7.2	8.0
70	33.6	1.40	28.0	3.7	4.1	4.5	4.8	5.2	5.6	5.9	6.7	7.4
80	38.4	1.60	24.5	3.3	3.6	3.9	4.2	4.6	4.9	5.2	5.9	6.5
90	43.2	1.80	21.8	2.9	3.2	3.5	3.8	4.0	4.3	4.6	5.2	5.8
100	48.0	2.00	19.6	2.6	2.9	3.1	3.4	3.6	3.9	4.2	4.7	5.2

[1] Basal = TDD x 0.48 [2] Correction Factor = 1960/TDD [3] Carb Factor = 10.8 x relative insulin sensitivity = (2.6 x Wt (lb))/TDD

For exact calculations, use the Pump Setting Tool at opensourcediabetes.org

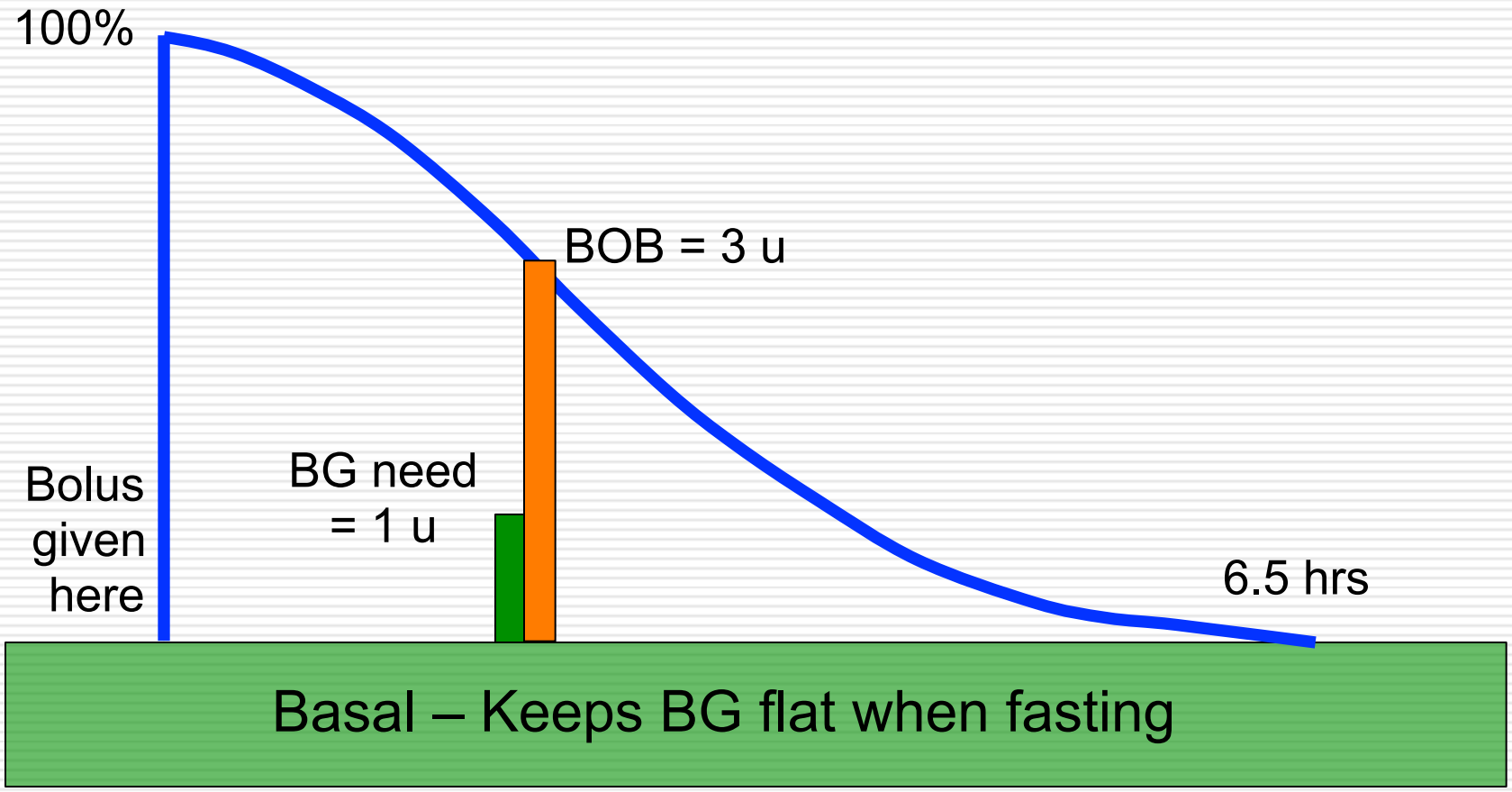
Where Pumps Aim In Target Range

Where In Target Range Does The Pump Aim?	
Accu-Chek Combo	**Middle**
Animas Ping	**Middle**
Insulet Omnipod	**Middle**
Medtronic Revel	**Top and Bottom**

Any BG within target range is NOT corrected.

Avoid target ranges. Choose one correction target.

BOB Explained



Every BG Shows An Insulin Or Carb Deficit

Situation 1

BG = 173 mg/dl (9.6 mmol)

Bolus on board = 0.4 u

Correction bolus: 1.2 u

Insulin deficit = - 0.8 u

Need 0.8 u insulin now

Situation 2

BG = 173 mg/dl (9.6 mmol)

Bolus on board = 4.6 u

Correction bolus: 1.2 u

Insulin excess = 3.4 u

Need 37 grams of carb later to prevent a low

Acts as inexpensive HypoManager™*, helps avoid over-treatment.

* Previously available in Cozmo pump.

How Current Pumps Handle BOB

What's In the BOB & What Is It Applied Against?				
	BOB Includes This Type Of Bolus		BOB Is Subtracted From This Type Of Bolus	
	Carb	Correction	Carb	Correction
Injections	No	No	No	No
Animas Ping	Yes	Yes	No*	Yes
Deltec Cozmo	Yes	Yes	Yes	Yes
Insulet Omnipod	No	Yes	No**	Yes
Medtronic Revel	Yes	Yes	No	Yes

* Except when BG below target BG

** Except when BG is below target and reverse correction is turned on

YES = Safer

Setting Duration Of Insulin Action (DIA)

How long a bolus lowers the glucose

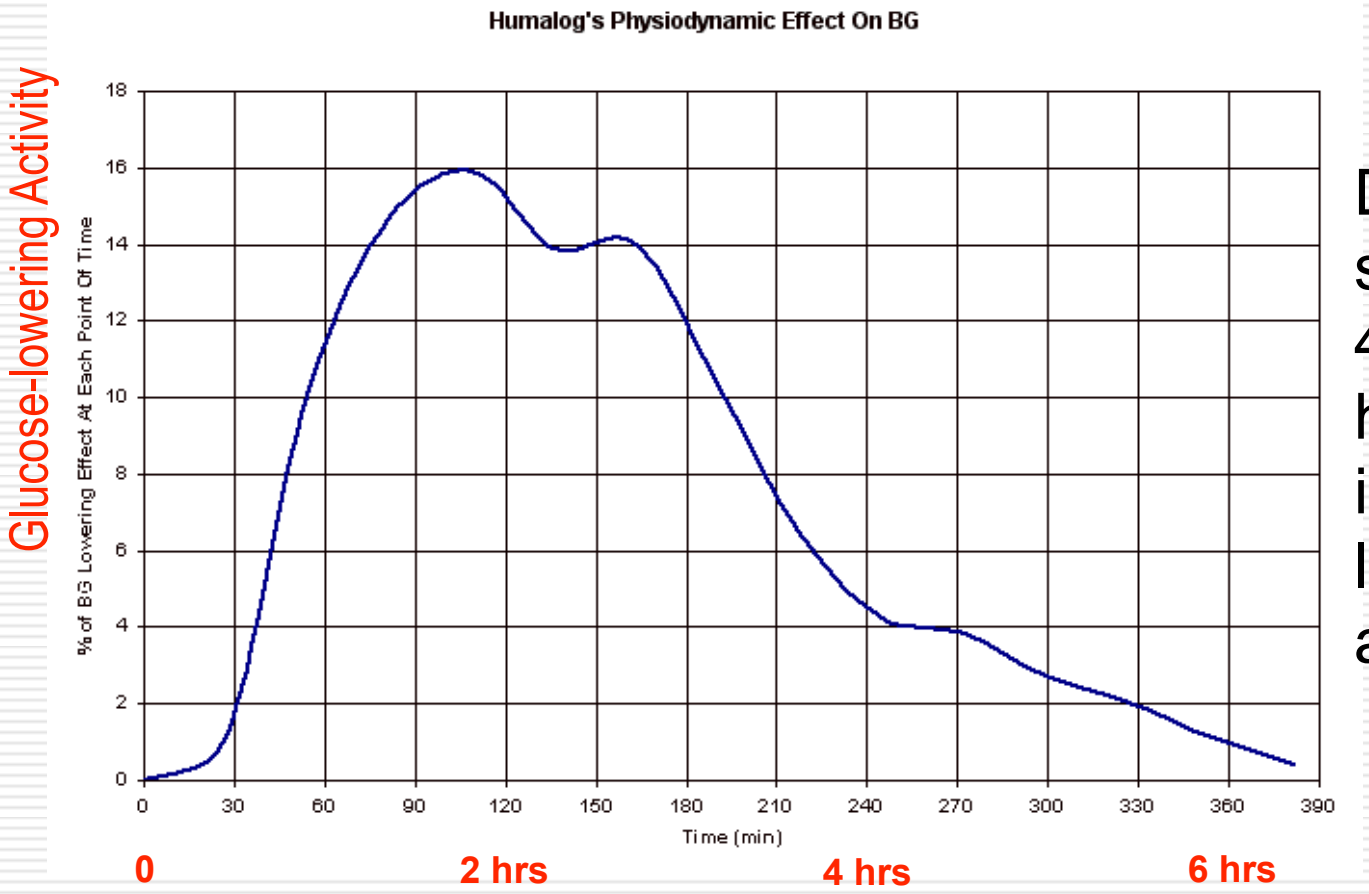
Why The DIA Gets Set Short

Pumpers and clinicians set the DIA too short because:

- Recommended boluses do not bring high BGs down (because basal rates or carb boluses are too small)
- This SEEMS easier than raising basals or lowering a carb factor.
- A low basal rate hides how long a bolus actually lowers the glucose

Duration Of Insulin Action (DIA)

Accurate boluses require an **accurate DIA**



DIA times shorter than 4.5 to 6 hrs hide BOB and its glucose lowering activity

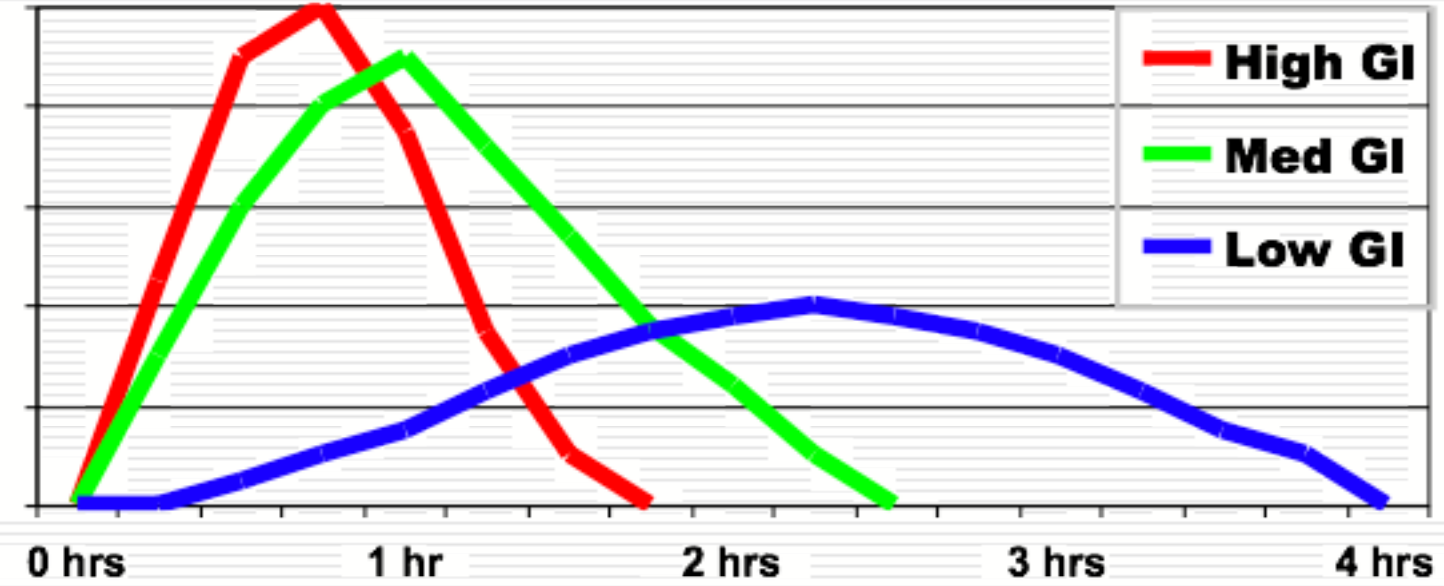
Why A Short DIA Causes Problems

When the DIA time is set too short:

1. Hidden bolus insulin makes the pump recommend boluses that are larger than really needed.
2. People lower daytime basal rates because the basal seems excessive due to the hidden bolus insulin.
3. Then the carb and correction factor numbers get lowered to offset the missing basal.
4. The stronger carb and correction factors cause lows after high carb meals and higher than normal BGs

Example: if BG is 120 at bed with DIA at 3 hrs and a large bolus was taken 3 hrs before – it's to go to sleep without a snack because there is no BOB and the basal gets blamed for the low that follows.

Duration Of Carb Action (Digestion)



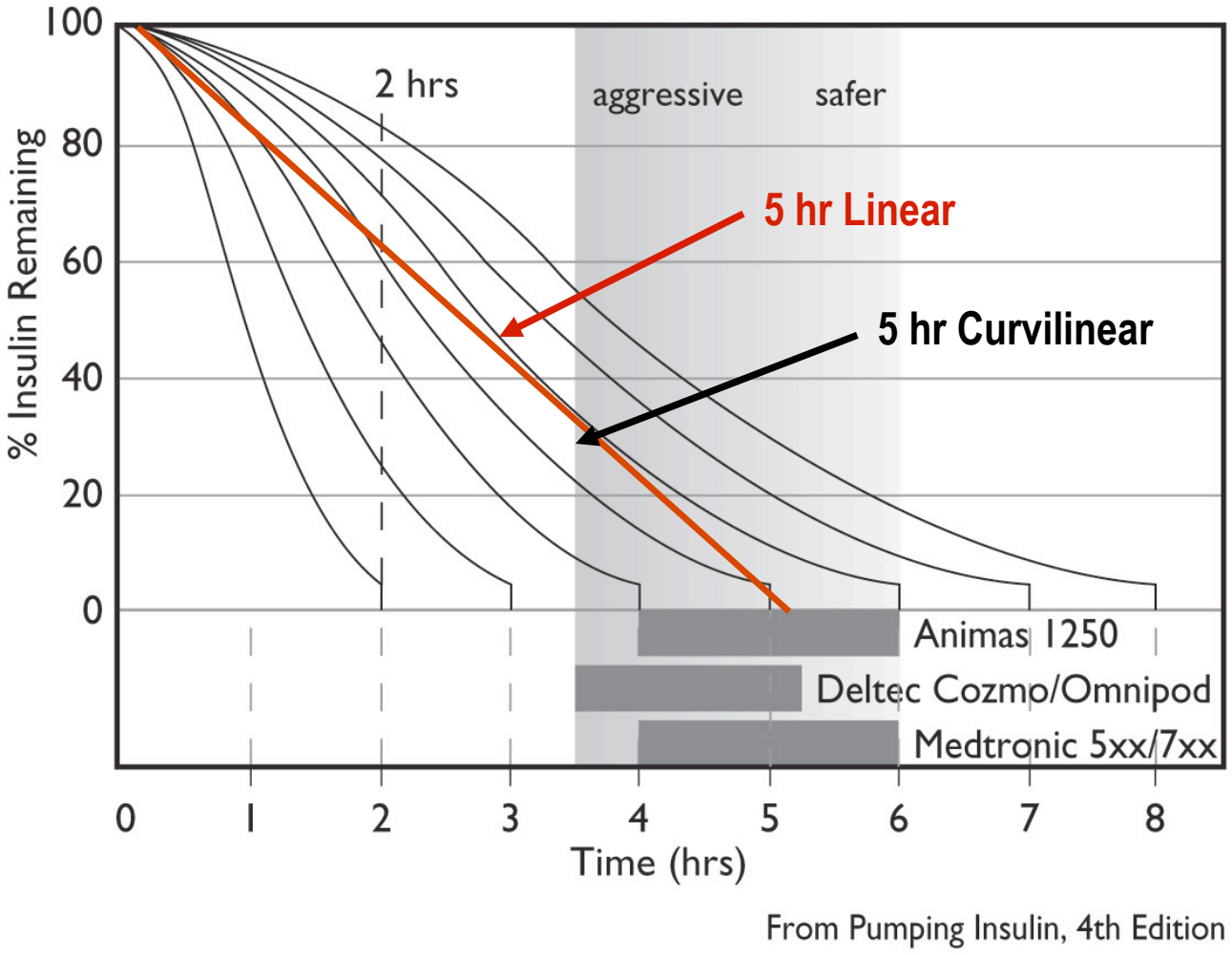
Most carbs affect the BG only 1 to 2.5 hours

Slower digestion with complex carbs, more fiber, more fat, etc

BG impact varies considerably

Thanks to Gary Scheiner, MS, CDE

Recommended DIA Times

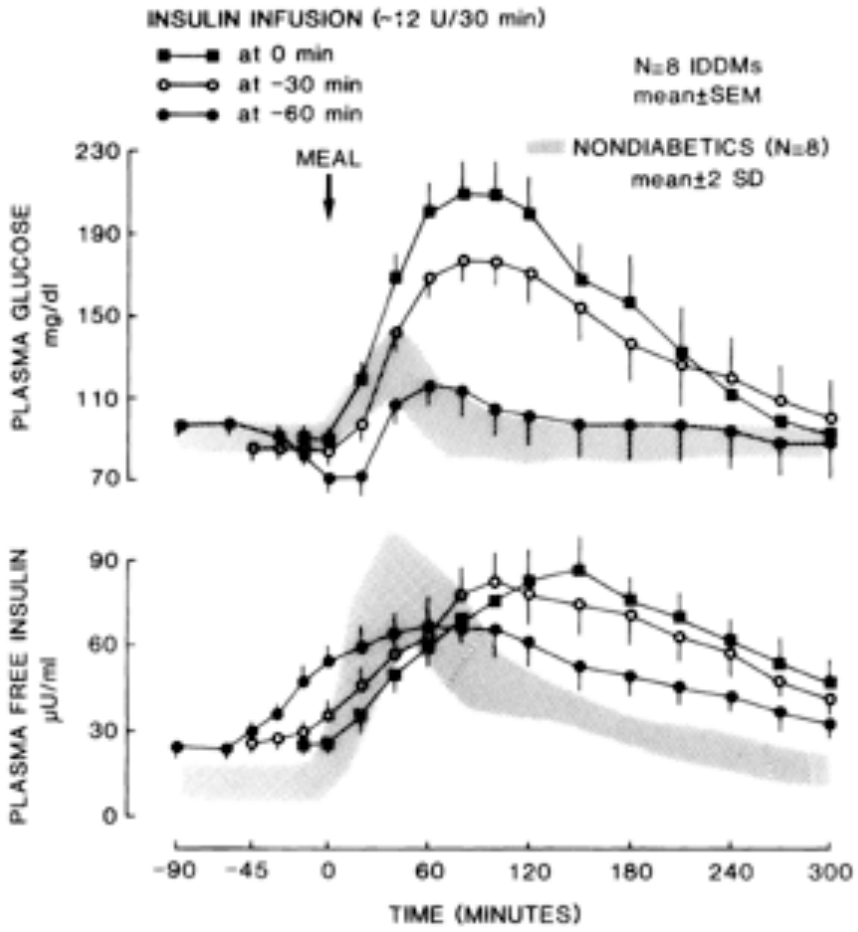


A DIA of 4.5 to 6 hrs makes BOB calculations more accurate.

DON'T reset your DIA without discussing this with your physician!

From Pumping Insulin, 4th ed., adapted fom Mudaliar et al: Diabetes Care, 22: 1501, 1999

Bolus Early To Stop Meal Spikes



- Figure shows rapid insulin injected 0, 30, or 60 min before a meal
- Normal glucose and insulin profiles shown in the shaded areas
- Best glucose profile when bolus is given 60 min ahead, but too risky to recommend!!!

DIA Tips

- DIA times don't differ between children and adults
- Use of short DIA hides true BOB:
  - Causes "unexplained" lows
  - Leads to incorrect adjustments in basal rates, carb factors, and correction factors to compensate for excess boluses
  - Makes user ignore their "smart" pump's bolus recommendations
- If the pump does not "give enough bolus insulin", look for real reason:
  - A low TDD, low basal rates, or a carb factor number that's too high

Don't change DIA to fix control problems!

Where Are Pumps & CGMs Going?

Cool Colors

Pump Styling

- Styling now competitive for pumps
- Don’t give up function/ safety/ease-of-use for style

Communication – Pump + Phone

- Several companies are developing meters for phones using Bluetooth
- Rapid alerts for care-givers of young, elderly, hypo-unaware
- Adds food databases, carb counters, apps, analysis
- Eventually management via cell phone

Diabetes Phone Apps

- Wavesense Diabetes Manager, Gluco Buddy, Diabetes Log, Bant, Glucose Mate, Diabetic Meal Planner Lite
- Many apps available for I–Phones, Pre, Blackberry
- Help for dosing, logging, carb counting

Future Pump Features

- Show How Setting Changes Will Impact TDD & BG
- Temp Basal + Bolus Doses
- Super Bolus
- Meal Size Boluses
- Excess BOB Alert
- Exercise Compensator
- Infusion Set Monitor
- Automated Bolus and Basal Testing

Better Guidance From Smart Pumps

"Why can't my smart pump learn?"

John Rodosevich, President of SD Pump Club

Wanted: a pump that

- Recognizes glucose patterns
- Alerts user and provider about helpful basal or bolus setting adjustments
- Simplifies and speeds up data collection and its analysis
- Thinks and learns

Future Pump Modifications

- Smart phones integration that controls pump, shows sensor data, acts as BG meter, and analyzes data in a single device
- Smaller, flatter patch pumps with bolus buttons
- Dual chamber pumps – glucagon, amylin, or GLP-1 agonists along with insulin
- Better, more reliable infusion sets
- CGM integration into closed loop

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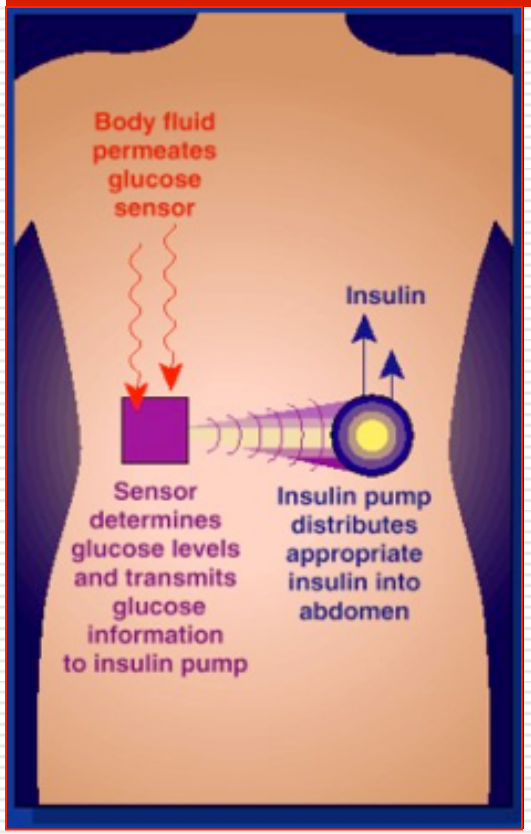
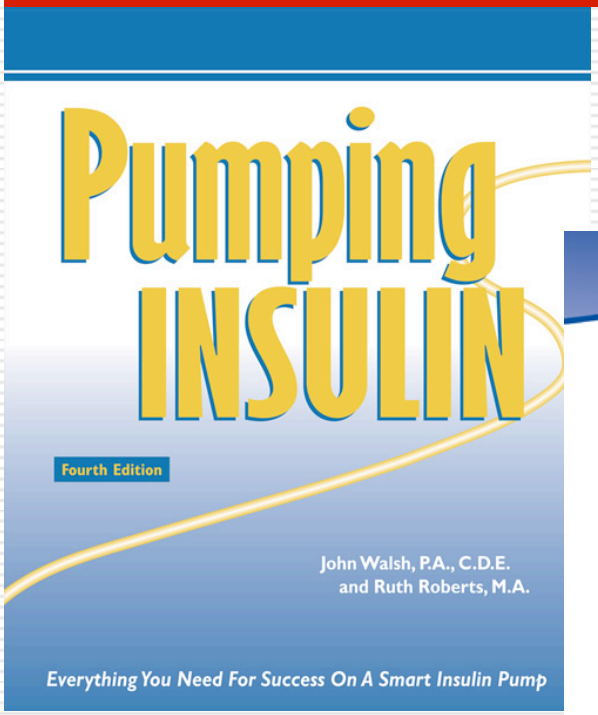
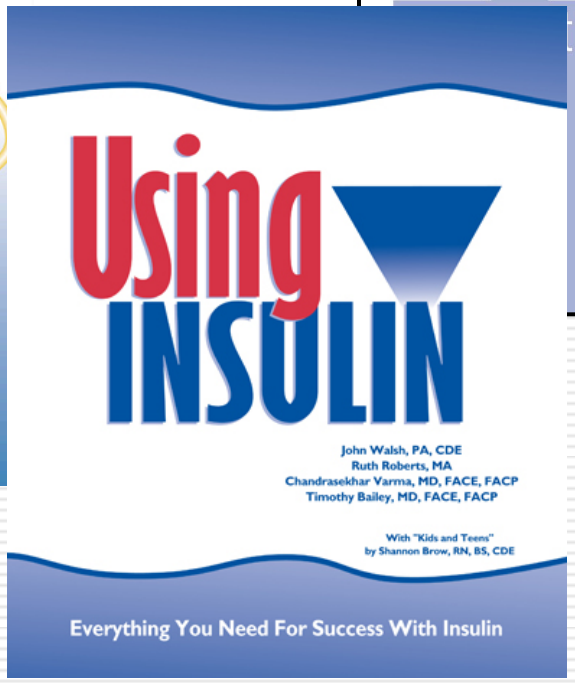
How Long To A Closed Loop?

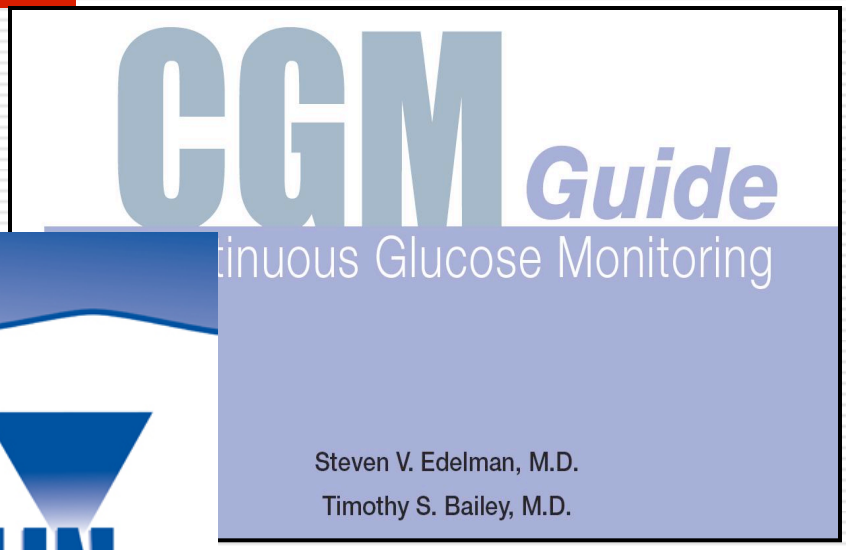


- Still needed:
  - Faster insulins
  - Better CGM accuracy
  - Less sensor lag time
- Dual pumps with glucagon
- Glucose control algorithms that don't fail

Reading – Still The Best Way To Learn







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