GLUCOSE CONTROL WITH TODAY'S INSULIN PUMPS & CGMS

May 10, 2015
3rd Annual Diabetes Type 1 Conference
ANA Intercontinental Tokyo
Sanofi

John Walsh, PA, CDTC
Advanced Metabolic Care and Research
Escondido, CA

Early Days: AutoSyringe As2c & As6c

Courtesy Lilly Museum

Courtesy www.phlex.org

Know The Bolus Calculator Settings

This Setting	Helps
TDD (total daily dose of insulin)	Best guide to initial pump settings – controls A1c, avg glucose, frequency of lows
Basal rates	For sound sleep and skipping meals
CarbF (I:C ratio)	Cover carbs well
CorrF (ISF)	Lower highs safely
Target glucose	BG goal 4-5 hrs after bolus
DIA	Minimize insulin stacking from BOB

Advantages of an Insulin Pump

- Avg. A1c reduction = 0.2%[1,2]
- Convenience = compliance
- Software calculates dose recommendations and tracks BOB

- Reduces insulin stacking, severe hypoglycemia, and BG variability [3,4]
- Plus a freer and more varied lifestyle
- And better data (clinicians, pumpers, and parents)

[1] Hsin-Chieh Y, et al: Ann Intern Med. 2012;157(5):336-347.
[2] Carlsson BM, Attvall S, et al. Diabetes Technol Ther. 2013 Apr;15(4):302-7
[3] Pickup JC, Sutton AJ: Diabet Med 2008 Jul;25(7):765-74.
[4] Hirose M, Kawamura T, Hashimoto T, et al. J Japan Diab Soc. 2009 52(9),

21st Century Line Pumps

Accu-Chek Aviva Combo

Animas Ping or Vibe

Medtronic Revel, 530G, 640G

Tandem t:slim

Asante Snap

21st Century Patch Pumps

Advantages of a CGM

- Average A1c reduction = 0.3%[1]
- Reads glucose every 5 min
- Alarms for lows and highs
- Security for wearer and family
- Trend line and arrows improve bolus doses
- Reduces A1c, severe hypoglycemia, and BG variability
- Better data (clinicians, pumpers, parents)

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

21st Century CGM's

Better BG meters have a mean average relative difference (MARD or error) of 5-6%

Dexcom G4AP (505), MARD 9.0%, 1-2 weeks

Medtronic 530G, MARD 13.9%, 6-10 days

Abbott Libre/Flash, MARD 11.4%, no cal, no alarms, 2 weeks use

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): 277-83

APP Study – What Impacts the Glucose?

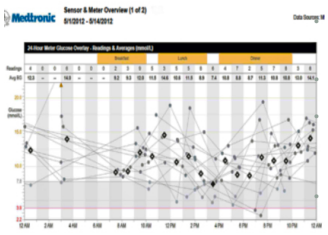
Glucose, Insulin and Carb Data		
Group:	Low BG Tertile	High BG Tertile
Avg. Meter BG	144 mg/dL	227 mg/dL
BG Tests/Day	4.73	4.01
TDD u/d	47.9 u	51.1 u
Basal %	47.6%	47.8%
CarbBolus u/d	20.9 u	19.8 u
CarbBoluses/Day	4.07	4.14
CarbGrams/Day	185.2	187.9

132 people in each tertile with the lowest and highest glucose levels

No significant difference was found in what each group did to reach their average glucose

1. J Walsh, R Roberts, T Bailey. Guidelines for Insulin Dosing in Continuous Subcutaneous Insulin Infusion Using New Formulas from a Retrospective Study of Individuals with Optimal Glucose Levels. J Diab Science & Technology 2010, Vol 4, #5,

Find the Optimal TDD First



- Most people do not get enough insulin
- A few get too much
- An accurate TDD is **the <u>best guide to correct pump settings</u>**
- Pattern management is simpler once TDD and settings are optimized

The TDD controls the frequency of lows, A1c, & avg BG

Improve Insulin Doses In Sequence

1. Stop frequent lows first
2. Then correct high A1c/avg BG

Helps you find an ideal TDD from which to select pump settings

3. Set & test basal rates
4. Set & test CarbF for normal pre and post meal readings
5. Set & test CorrF to lower high BGs safely
6. Enjoy good control or return to #1

Brittle diabetes or frequent highs? Usually = wrong pump settings

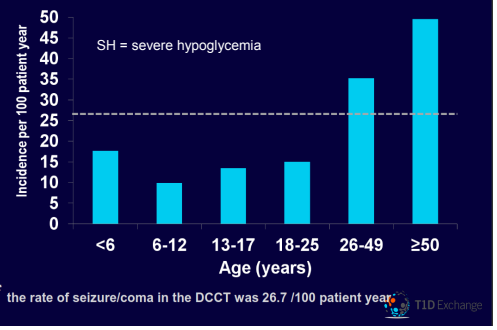
Get an Optimal TDD – Stop Frequent Lows First

You cannot tell how much excess insulin there is!

- Start with a 5% or 10% reduction in TDD
- Or multiply weight(kgs) by 0.55 for "ideal" TDD of someone with an average sensitivity to insulin[1,2]
  - **Example:** Someone who weighs 73 kg (160 lbs) would be expected to have a TDD of 40 units (73 x 0.55 = 40).

1. Davidson PC, Hebblewhite HR, Steed RD, Bode BW. Analysis of guidelines for basal-bolus dosing: basal insulin, correction factor, and carbohydrate-to-insulin ratio. Endocr Pract. 2008;14(9):1095–101.
2. Adamsson U, Lins PE. Clinical views on insulin resistance in type-1 diabetes. Agardh CD, Berne C, Östman J. Diabetes. Stockholm: Almqvist & Wiksell; 1992, 142–50.

Incidence Rate* of SH at various ages



* the rate of seizure/coma in the DCCT was 26.7 /100 patient year

T1D Exchange

Insulin Pumps Reduce Severe Hypoglycemia in Japan

In a 2009 report[1] on 121 patients with Type 1 diabetes followed for 12 months:

- A1c levels were reduced from 8.7% +/- 2.0 to 7.9% +/-1.5
- Severe hypoglycemia decreased from 26.7 to 2.7 per 100 person-years
- Ketoacidosis events were more frequent at the start of therapy (ie, infusion set failures)

[1] Hirose M, Kawamura T, Hashimoto T, et al. J. Japan Diab Soc. 2009 52(9), 767-775

For Low BGs, Optimize the TDD!

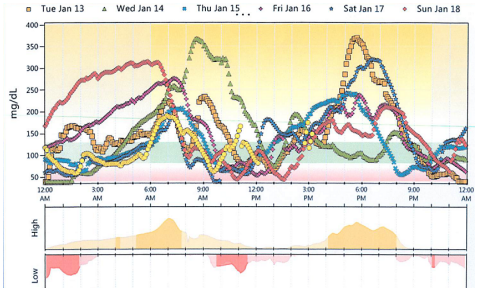
41 yo 69 kg female with A1c = 6.9%

TDD = 50.5 u/d

69 kg x 0.55 = 38.0 u/d

Reset pump settings from a TTD of 41 units

Low BGs with a Pattern



Excess TDD in a 72 yo Type 1 with an A1c of 6.1% who gives boluses after meals and then overcorrects highs

Get an Optimal TDD – Stop Frequent Highs Next

Raise the TDD with the **5 and 6 Rules**:

Raise the TDD by **5%** to lower an A1c by 1%

Or by 1% to lower average BG by **6 mg/dL**

$$\frac{\text{Current BG} - \text{Target BG}}{6} = \%\text{ rise in TDD}$$

Example: Amy's avg TDD is 40 u/day, avg BG 200 mg/dL (few lows, goal = 140 mg/dL):

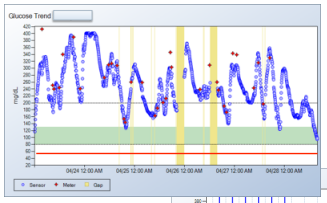
200 mg/dL – 140 mg/dL = 60 mg/dL

60 mg/dL ÷ 6 = 10% rise in TDD

40 units x 1.10 = 44 units a day

© 2013, Pumping Insulin

For High BGs, Optimize the TDD!



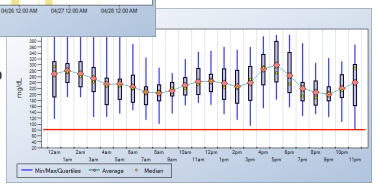
From the A1c

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

Bring downloads to your HCP – They can help you interpret them!



For High BGs, Optimize the TDD

From an avg BG:
53 yo female
TDD = 36 u Avg BG = 190

190 – 140 = 50 / 6 = 8.3%

- 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
an 8.3% increase

Derive Pump Settings from an Optimal TDD[1]

Basal insulin = ~ Half of the TDD (Lower in Japan?)

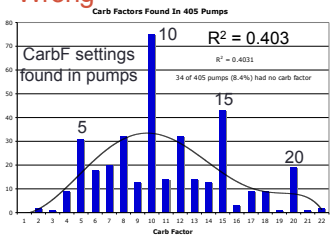
CarbF = 5.7 x Wt(kgs) / TDD *or* 2.6 x Wt(lbs) / TDD

CorrF = 1960 / TDD

CorrF is inversely related to TDD and to avg. BG
A smaller CorrF is required for someone in poor control

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

APP Study – Pump Settings Often Wrong[1,2]



Only 40% of CarbFs have expected value

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

Formulas provide accurate settings – > far 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

Use Decision Support Software to Select Pump Settings

JD is a 20 yo DM1 college student referred to clinic.
Wt 84 kg (180 lb), TDD = 80 u (78-83 u/day), avg BG = 194 mg/dL.

- Basal rate: 1.8 u/hr
- CarbF 10
- CorrF 45
- DIA 4 hrs
- **A1c 8.4%**

Select & Improve Pump Settings with Decision Support Software

Enter Your Information:

Units: English | Metric

Weight: 180 lbs

Avg TDD(?): 80 u/day

Current Avg BG:(?): 194 mg/dl

Target Avg BG(?): 140 mg/dl

Submit

Settings For Target BG (?)

From adjusted TDD to reach target

TDD: 85.5 u/day

Avg Basal: 1.708 u/hr

Carb Factor: 5.5 grams per unit

Correction Factor: 22.9 mg/dl per unit

Relative Insulin Sensitivity: 51%

www.opensourcediabetes.org

Improved Outcome From Decision Support Suggestions

JD's Pump Settings:

	Original	New
• TDD	80 u	85 u
• Basal rate:	1.8 u/hr	1.7 u/hr
• CarbF	10	5.6
• CorrF	45	23
• DIA	4 hrs	5 hrs
• A1c	8.4%	6.9%

www.opensourcediabetes.org

Which Way Do You Adjust Settings?

12.6 Which Way Do You Change Your Pump Settings?			
If you are having:	This is the direction to change your:		
	Basal Rates	Carb Factor	Corr Factor
Frequent lows	↓	↑	↑
Frequent highs	↑	↓	↓

Smaller factors = larger boluses

APP Study – 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 usage in tertile of 132 pumps with the lowest average glucose

J. Walsh, R. Roberts, T. Bailey. Guidelines for Insulin Dosing in Continuous Subcutaneous Insulin Infusion Using New Formulas from a Retrospective Study of Individuals with Optimal Glucose Levels. *J Diabetes Sci Technol*, 4: 1174-1181, 2010.

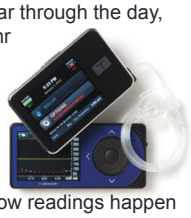
Does Basal Percentage Differ in Japan?

- Average basal percentage of the TDD in most US/European studies is 48 to 52%, although individuals vary.
- In a hospital-based study of 35 Japanese Type 1 patients with an average age of 40, Dr. Kuroda et al found an average basal need of 27.7% +/- 6.9% (16.6% to 43.8%).
- In a younger Japanese population with an average age of 16, Dr. Hashimoto found an average basal need of 35% with a strong association between basal requirements and dietary fat intake
  (p <0.001, R^2 = 0.22).

[1] Kuroda A, Kaneto H, Yasuda T, et al. Basal insulin requirement Is ~30% of the total daily insulin dose in type 1 diabetic patients, who use the insulin pump. Diab Care 34, May 2011, 1089-1090.
[2] Hashimoto T, Kawamura T, Kashihara Y, et al. Factors associated with basal insulin dose in Japanese children and young adult type 1 diabetics. J Diab Invest 3(3), 2012, 276-282

Basal Tips – Avoid Over-Steering

- Basal rates usually remain similar through the day, such as between 0.75 to 1.0 u/hr
- Adjust basal rates early
  - by 0.025 to 0.1 u/hr **2 hours** before the glucose **starts** to rise or fall,
  - or **5-8 hours** before high or low readings happen



Clever Pump Trick – Bolus Early To Stop Meal Spikes

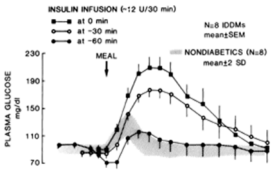


Figure shows Regular insulin injected 0, 30, or 60 min before a meal

Normal glucose profile shown in shaded area

Best glucose occurred with 60 minute bolus – **but too risky!!!**

Bolus 15-30 min before meals – 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.

Clever Pump Trick – Get the Right Number of Carbs for a Low

1. **No BOB:** 1 gram for each 4.5 kg (~10 lbs) of weight
2. **With BOB:** Add grams = BOB* x CarbF

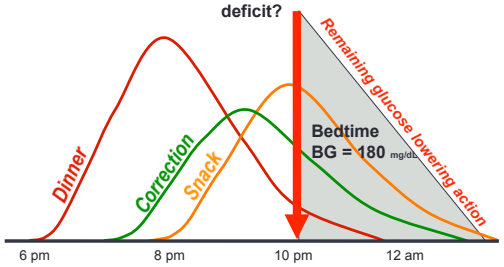
Example: Amy's BG = 52 mg/dL with 2u of BOB (CarbF = 10 g/u)

- At 45 kgs (100 lbs), she needs 10 grams for the low glucose
- ***Plus*** 2u BOB x 8 gram/u = 16 grams to offset BOB
- Amy needs 10 g + 16 g = 26 grams for this low

*** DIA time must be accurate**

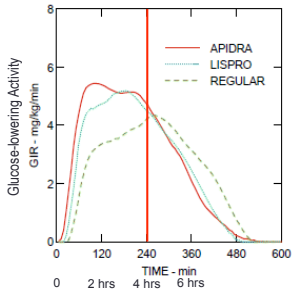
Bolus on Board / Insulin Stacking

Bedtime BG = 180 mg/dL – is there an insulin or a carb deficit?



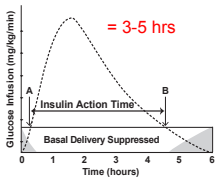
Duration Of Insulin Action in the Body

Accurate boluses require an accurate DIA



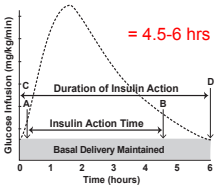
Insulin Action Time ≠ Duration of Ins. Action

Fig. 1 Insulin Action Time



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

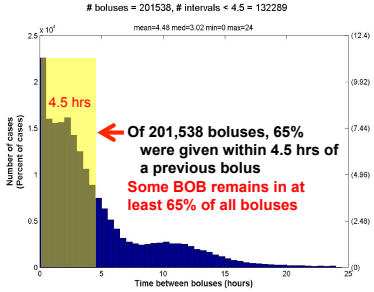
Fig. 2 Duration of Insulin Action



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

J Walsh, R Roberts, L Heinemann. Confusion Regarding Duration of Insulin Action A Potential Source for Major Insulin Dose Errors by Bolus Calculators. *J Diabetes Sci Technol January 2014 vol. 8 no. 1 170-178.*

Insulin Stacking Is Common



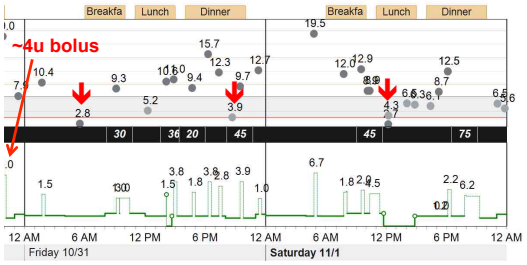
J Walsh, D Wroblewski, T Bailey. Disparate Bolus on Board Recommendations in Insulin Pump Therapy. Poster 2007 AACE Meeting

A Short DIA Hides BOB & Causes Unexplained Hypoglycemia

This is how much BOB a pump thinks is left 3 hrs after a 10-unit bolus using these DIA times:

When DIA is set to:	Pump's estimate of Insulin On Board			
	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

Short DIA Times Cause Lows



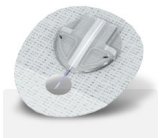
39 yo woman has 2 lows on Friday and another on Saturday from hidden insulin stacking caused by her short DIA time of 3 hours .

Avoid Excess Bolus Recommendations

4.35 u of BOB remain from a bolus given 3 hrs earlier – is 2.9 more units really needed for a bedtime snack?

Infusion Set/Cannula Options

Slanted Teflon | Straight-In Teflon | Straight-In Metal



Comfort/Silhouette/Tender | Accu-Chek Ultraflex | Contact Detach/Sure-T

Type	Teflon	Steel
Recommended use	3 days	2 days
Time of use in US	3.4 days*	3.7 days*

* J. Walsh, R Roberts, D Weber, G Faber-Heinemann, and L. Heinemann. Insulin Pump and CGM Usage in the US and Germany: Results of a Real-world Survey with 985 Subjects. *J Diabetes Sci Technol*. 2015, Vol. 9(5) >500 self-reports of length of use in the US.

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]

1 www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/Medical DevicesAdvisoryCommittee/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.

Auto-Inserters

Inset 30 | Accu-Chek Link Assist | Inset/Mio

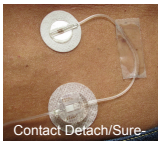
Quick-Serter

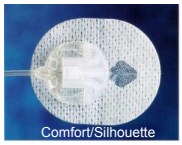
Cleo

Omnipod

Low Failure Infusion Setups


Contact Detach/Sure-T

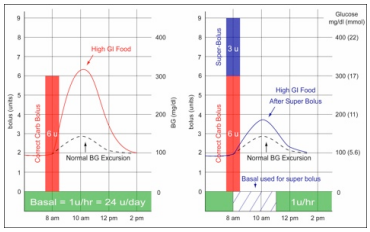

Contact Detach/Sure-


Comfort/Silhouette

Ideal for small child, pregnancy, decreased dexterity, and normal people:

- Place clear adhesive (IV3000, Tegaderm) on top of Sure-T/ Contact Detach infusion sets
- Place 1" tape (Transpore, Durapore, etc) on infusion line of a Teflon set to reduce site irritation and line tugs that cause leaks

Clever Pump Trick – Super Bolus to Stop Meal Spikes

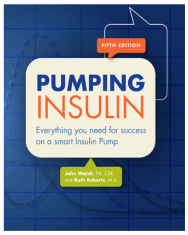


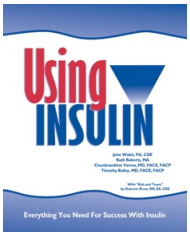
Super Bolus – use temp basal reduction to shift part of the next 2 to 3.5 hrs of basal insulin into a bolus

Less spiking + less risk of a low later.[1,2] Done by user, not the pump

[1] J. Walsh: http://www.diabetesnet.com/diabetes_presentations/#uper-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. JDST, 3(1), 89-97,

Diabetes Is Better When You Know More!





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