Advanced Pumping Techniques

TCOYD San Diego 2013
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See slides at www.diabetesnet.com/presentations/

Pump Advantages

- Convenience
- Easier to match varying needs
- Less insulin stacking
- Lower A1c, less severe hypoglycemia, less BG variability *
- More freedom of lifestyle
- Better data (clinicians, pumpers, parents)

* Pickup JC, Sutton AJ: Severe hypoglycaemia and glycaemic control in Type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med 2008 Jul;25(7):765-74.

Line Pumps

Asante Snap

Accu-Chek Combo

Animas Ping

Medtronic Revel

Tandem t:slim

Patch Pumps

Accu-Chek Solo

CellNovo

Valeritas V-Go

Calibra Finesse

Insulet
Omnipod

Early Closed Loop – Medtronic 530G

- Low Glucose Suspend (LGS) – CGM can suspend basal up to 2 hrs for a low.
- May reduce length of night lows.
- 6 day Enlite sensor
- CGM alarm excess and wear-ability may be an issue for some

Dexcom – Animas Vibe or Tandem t:slim

- High contrast color screens
- 1 week Dexcom G4 sensor
- Internet access via Diasend or t:connect software
- No low glucose suspend

FDA approvals pending ~2-8 mos?

Accu-Chek and Omnipod CGMs

Accu-Chek Insight Pump

Accu-Check CGM has 4 sensor areas on each sensor

- Mean ARD is ~9.2%,[1] compared to ~10.7% for upcoming Dexcom Gen4 algorithm and 13.9% for Enlite[2]

Omnipod is developing its own CGM system

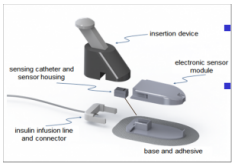
An independent study for the AP found a MARD of 10.8% for current Dexcom G4, 12.3% for Abbott Navigator, and 17.9% for MiniMed Enlite.[3]

1. E. Zschornack et al: DJST Vol 7(4), July 2013
2. B. Keenan et al: DTT Vol 14(3) 2012
3. Dr. Steven Russell of Mass. General Hosp. report at Insulindependance 2013, SD

Navigator II CGM

- Available in UK, Germany, Scandinavia, Holland & Israel
- Sensor is 40% smaller than Navigator
- 1 min updates on BG
- 5 day use with 4 cals on day one and one more on day 3
- Projected low and high

CGM Advances



Pacific Diabetes Technologies

- Factory calibration
- Abbott Flash
  - Intermittent CGM, test strip pricing
- Dual sensors on one set
  - 2 glucose oxidase
  - 1 glucose oxidase and 1 fluorescent
- CGM on infusion set cannula
  - 6-8 sensors on cannula (15% BG drop)

Remote Control

Accu-Check Combo

Animas Ping

Cellnovo

Omnipod

Advantages:

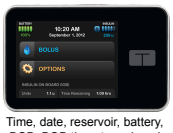
- Allows discreet bolusing (and basaling in some)
- BG and bolus doses sent via radio wave or Bluetooth
- Keeps data in one location

Disadvantage:

- Omnipod remote must be present to give boluses

Ideal Home Screen Data

Time, basal, reservoir, battery



Time, date, reservoir, battery, BOB, BOB time, temp basal

- **CGM BG and trendline**
- **BOB and time left**
- Time and date
- Battery life
- Reservoir units
- Basal rate

Time, date, pump connection

Time, reservoir, battery, CGM trend/BG/arrow/ connection

Connectivity

- Bluetooth can be found in
  - Some pumps
  - Some meters and CGMs
  - Most cell phones
  - Activity monitors – FitBit, FuelBand JawBone, MotoActv, BodyMedia
- Integration of devices from different manufacturers is key
  - Tidepool, etc.

Background on Pump Doses

Bolus Calculator Settings

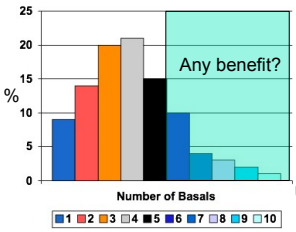
This Setting	Helps
Basal rates	Sound sleep (~50% of TDD)
CarbF or I:C ratio	Cover carbs well
CorrF or ISF	Lower highs safely
Target glucose	Correct to specific goal
DIA	Minimize insulin stacking

APP Study – BGs and Basal Rates

Glucose, Insulin and Carb Data				
Group:	All 396 Pumps	Low Third	Mid Third	High Third
Avg. Meter BG	144 mg/dL 8.0 mmol/L	181 mg/dL 10.0 mmol/L	227mg/dL 12.6 mmol/L	144 mg/dL 8.0 mmol/L
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

How Many Basal Rates Do You Need?



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

When a basal is changed, 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

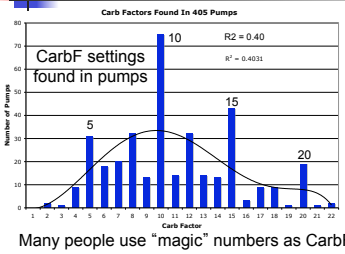
- Basals usually make up 45 to 65% of TDD
- Basal rates should be similar, such as between 0.5 to 0.7, or 1.0 to 1.4 u/hr
- Adjust basal rates in small steps (usually 0.025 to 0.1 u/hr) **<u>3 to 8 hours</u>** before the need arises

APP Study – Carb Boluses and CarbFs

Glucose, Insulin and Carb Data				
Group:	All 396 Pumps	Low Third	Mid Third	High Third
Avg. Meter BG	184 mg/dL 10.2 mmol/L	144 mg/dL 8.0 mmol/L	181 mg/dL 10.0 mmol/L	227 mg/dL 12.6 mmol/L
CarbBolus U/d	20.4 u	20.9 u	20.4 u	19.8 u
CarbBolus/Day	4.14	4.07	4.20	4.14
CarbGram/Day	189.9	185.2	196.3	187.9
CarbF	11.4	10.8	12.2	11.2

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

APP Study – Carb Factors are Often Incorrect[1,2]



CarbFs from 400 pumps were not evenly distributed.

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

Use formulas to derive accurate pump settings –> better than WAG!

Many people use "magic" numbers as CarbFs!

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

Check Bolus Recommendations

With 4.35 u of BOB from an earlier bolus, would you give 2.9 more units for a bedtime snack?

BOB = remaining glucose-lowering activity from recent boluses

Pumps usually cover carbs fully regardless of BOB

When BOB is larger than your correction bolus, consider taking less than the recommended bolus

APP – Occlusions Worsen Control

BG Tertile	Low	Middle	High
Avg BG	146.6	181.6	229.3
Blocks/month	1.36	3.04	3.57

132 pumps in each tertile; avg. BG for 73 days per pump

Unpublished data – Actual Pump Practices Study by J Walsh, R Roberts, and T Bailey

APP Study – Unexpected Outcomes

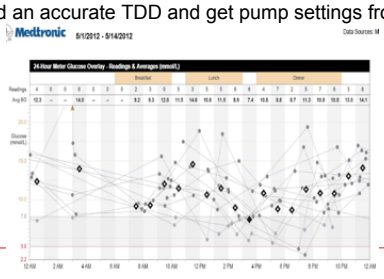
Between low, medium, and high avg. BG groups:

- Basal was 48% of TDD in all groups
- Groups ate same grams of carb and took same number of carb boluses and correction boluses per day
- BG testing had no meaningful impact on glucose – the high BG group tested almost as often as low group
- High BG group used MORE insulin a day
- Occlusions significantly raise avg BG

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

APP Study – Major Conclusion

Find an accurate TDD and get pump settings from it



APP Study – Use your TDD to Check Pump Settings[1]

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

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

Corr. Factor = 1960/TDD (mg/dl) (actually 1500 to 2400)

CorrF is inversely related to TDD and to avg. BG

Or use Pump Settings Tool to compare current to "ideal" settings at www.diabetesnet.com/diabetes_tools/pumpsettings/

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

Dosing Tips

Help Your Health Care Provider

- Check glucose 6 x a day or wear a CGM
- Download and bring your records
- Use the bolus calculator for all boluses, count or measure carbs, and override when needed
- Don't over-treat lows with carbs nor highs with insulin
- Know when to change your pump settings

Size Up the Problem

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

Steps To Control

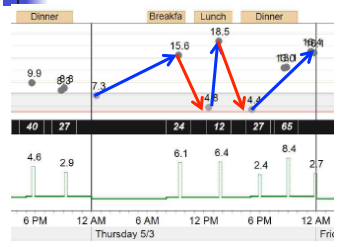
- Stop lows first
- Bolus 15 to 30 min before meals when able
- Periodically check basal/carb bolus balance
- Look for and correct unwanted patterns

Stop Frequent Lows First

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

156lb/4 = 38.0 u/d

Then Stop Frequent Highs

When your average BG is high **with few lows**:

Raise TDD by 1% for each 6 mg/dl in BG (or for each 0.2% in A1c) you want to lower your glucose

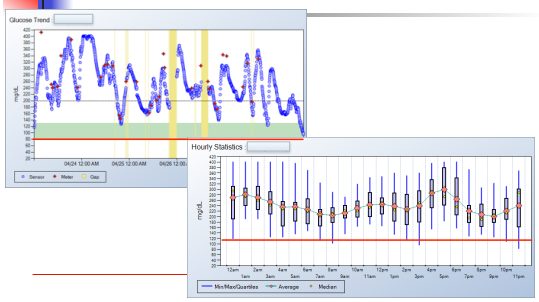
Example: Amy's avg TDD is 40 u/day. Her average meter BG is 205 mg/dl with few lows. Her BG goal (average) is 145 mg/dl:

205 mg/dl – 145 mg/dl = 60 mg/dl

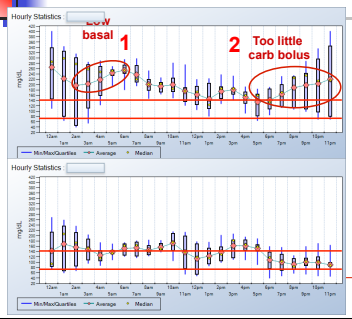
60 mg/dl ÷ 6 mg/dl = 10% rise needed in TDD

40 units x 1.10 = 44 units

Example – Frequent Highs



TDD Before & After Adjustment



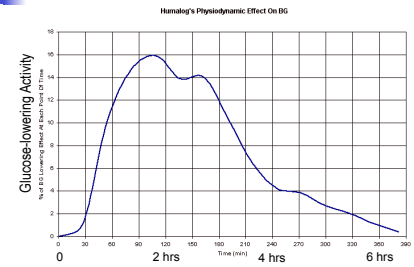
Start TDD = 36 u

- Raised basal by 0.05 u/hr all day (+1.2 u/day)
- Lowered carb factor from 1u/13g to 1u/12g (+1.8 u/day)

End TDD = 39 u

Duration Of Insulin Action

Accurate boluses require an accurate DIA



Why Short DIAs Cause Problems

3 hours after a 10 unit bolus, table shows how much BOB a pump thinks is left with each DIA time:

	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

Always set the DIA from an insulin's real action time

Do not change DIA to fix control problems

Don't Set Your DIA Short

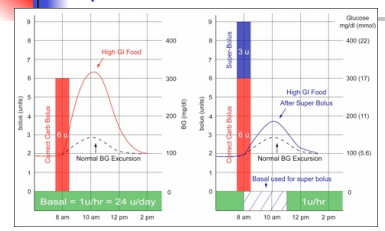
A short DIA hides BOB and leads to:

- Hidden insulin stacking
- "Unexplained" lows
- Errors in adjustments of basal rates, carb factors, and correction factors
- Or just ignoring your "smart" pump's advice

Set DIA for real action time: 4.5 to 6 hrs.

Don't change your DIA to fix control problems

Clever Pump Trick – Super Bolus – Shift Basal To Bolus



Good for:

Meals with over 30 to 40 grams of carb

High BGs

Future: 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

Clever Pump Trick – How Many Carbs do You Need for a Low?

1. 10 grams for each 80 lbs of weight
2. **plus** grams = the current BOB* x CarbF

Example:

- Amy weighs 160 lbs = 20 grams of carb
- And she has 2 units of BOB with a CarbF of 8 grams/unit
  2 u x 8 g/u = 16 grams
- For this low she needs:
  20 g + 16 g = 36 grams

Add extra carbs as needed for recent or planned exercise.

Infusion Set Issues

- Little research has been done
- Clinician and wearer reports and blogs suggest infusion set issues are widespread
- Set leaks and failures create random hyperglycemia, making their source difficult to identify.
- A major source for calls to pump companies and for pump discontinuation
- Less than 10% of inspected pumps have any defect

Pump Failure Modes

- Most of the 16,849 adverse pump events reported to the FDA between 2006-2009[1] involved infusion sets: failure, disconnection, or bent cannula[1]
- A 2006 review of pumps in France also found most serious adverse events involved infusion sets: obstruction, leakage, infection, or inflammation[2]

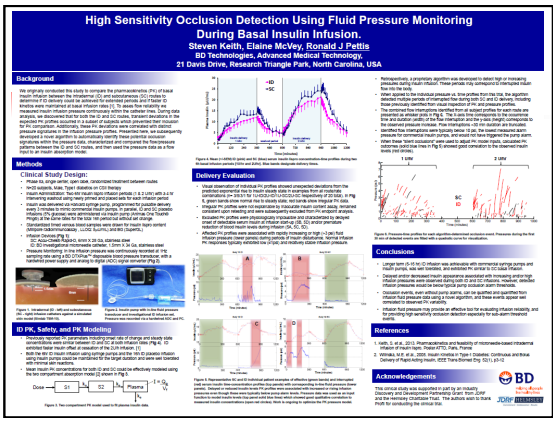
1 www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralHospitalandPersonalUseDevicesPanel/UCM202779.pdf
[2] Maugendre D. Technical risks with subcutaneous insulin infusion. Diabetes Metab. 2006;32:279-284.

Infusion Sets – The Achilles Heel Of Pumps

Survey of 1142 pumpers in 40 German diabetes clinics

- 54% reported an increase in glycemia for unknown reasons until their infusion set is changed
- 19% reported kinking, 12% had leakage, 12% air bubbles, and 33% had other issues
- 36% used auto-insertion devices – 72% of them reported that the device failed to work ~10% of the time

Gabriele and Lutz Heinemann: Reality of insulin pump treatment in Germany: Results from a survey with 1142 patients treated in 40 specialized practices. Abstract # 2013 ADA Meeting. winDiab, Scientific Institute of the Specialized Diabetes Practices, Düsseldorf, Germany


High Sensitivity Occlusion Detection Using Fluid Pressure Monitoring During Basal Insulin Infusion.

Steven Keith, Elaine McVey, Ronald J Pettis
BD Technologies, Advanced Medical Technology,
21 Davis Drive, Research Triangle Park, North Carolina, USA

Background

Methods

Clinical Study Design:

ID PK, Safety, and PK Modeling

Delivery Evaluation

Conclusions

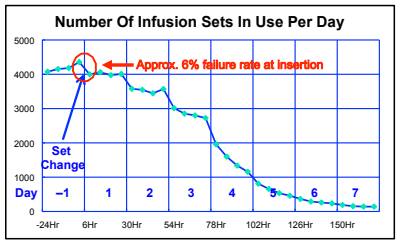
References

Acknowledgements

BD

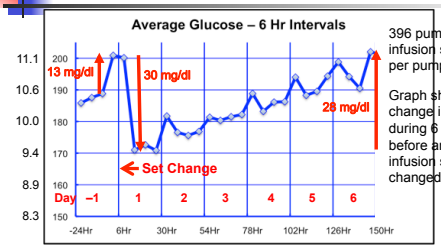
7

How Long Do People Use Infusion Sets?



Most pump wearers use their infusion sets for 2-3 days.

Average BGs Before & After Set Change



396 pumps with ~20 infusion set changes per pump.

Graph shows change in avg. BG during 6 hr intervals before and after infusion set is changed.

Unpublished data from Actual Pump Practices Study by J Walsh, R Roberts, and T Bailey

Do You Have a Set Problem?

- Do sites often "go bad"?
- Do you have "scarring" or "poor absorption"?
- Often have 2 or more unexplained highs in a row?
- Do correction boluses sometimes not work?
- Have high BGs (often 8-32 hrs) until set is changed?

Solutions for Infusion Set Problems

- Anchor the infusion line with tape
- Review site prep and insertion technique with clinician or trainer
- Insert set by hand
- Switch to a different brand of infusion set

Tapes: Transpore, Micropore, Durapore, Hypafix

Counter-Measures to Sweat

- Skin-Tac
- Mastisol/Detachol
- Tincture of Benzoin
- Toupee glue

New Developments

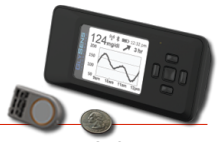
Implanted CGMs

MicroCHIPS Illume

Sensionics

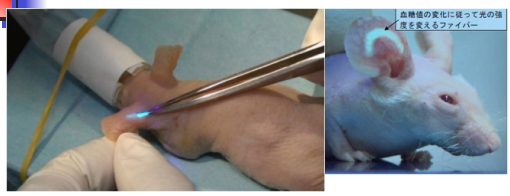
- Months to years of use
- No disposables
- Minor surgery
- Funded as rental?

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

Faster Insulin

For better matching of carbs (< 2 hrs) with insulin (5 hrs)

- Ultra-fast insulin analogs
  - Novo Nordisk FIAsp
  - Biodel
  - MannKind Afrezza (inhaled)
- Diaport intraperitoneal delivery
- Micro-needle intradermal delivery
- Hyaluronidase
- Warming of infusion site

Goal: fewer highs and lows

Accu-Chek Diaport

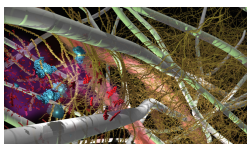
Delivery into the abdominal cavity speeds up insulin action when more insulin goes directly to the liver

BD Intradermal Microneedle

- 1.5 mm intradermal needle speeds up insulin action
- Painless
- Reliable attachment of set will be critical

Hyaluronidase

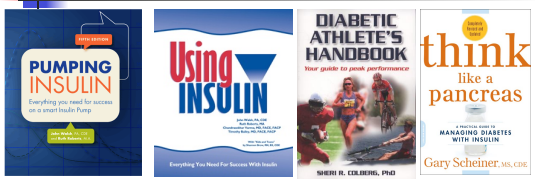
- Recombinant human hyaluronidase temporarily degrades local hyaluran, a structural protein in the interstitial space
- Speeds up insulin uptake
- DIA ~4 to 4.5 hrs?
- Phase 3 clinical trials underway with release in early 2014?



Future Pump Features

- How setting change impacts TDD (& BG)
- Temp basal plus bolus doses
- Super Bolus
- Meal-size boluses
- Excess BOB alert (bolus without BG but BOB is ++)
- Low BG predictor (HypoManager)
- Exercise compensator
- Infusion set monitor/leak detector
- Automated basal and bolus testing

Life Is Easier When You Know More!



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