**Novel and Basic Pump Ideas**

**San Diego**

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View slides at www.diabetesnet.com/presentations/

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**Dexcom G6**

- Slick applicator, 10 day wear, 2 yrs and older
- No fingersticks (But calibrate if it's off)
- See BGs on display device, phone, or watch
- Sensible alarms
- Covered by Medicare
- First FDA approval as a fully interoperable CGM or iCGM
- Used for AP systems in Tandem, Omnipod, Solo, OpenAPS

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**Tandem's Unique Remote Upgrade**

Remote software upgrades similar to phones and PCs. Existing hardware rapidly upgraded for artificial pancreas and other features. A new pump in seconds, not years!


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**Tandem t:sport Insulin Pump**

Small wearable insulin pump

200u easy fill reservoir

Precise motor with 0.008 u accuracy

Short or long infusion set

On-pump bolus button

Small t:slim-like control unit and cell phone control

7 day rechargeable battery

Closed loop capabe with just a CGM

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**TDDS AND SETTINGS TO OPTIMIZE PUMPS**
Especially for Control.IQ –
To Optimize Control, Pumpers Need

- An accurate TDD – major control for BG
- Accurate basals (~50% of TDD) for sound sleep
- An accurate CarbF for postmeal control
- An accurate CorrF to lower highs safely
- A correction target that aims well
- An accurate DIA – to minimize insulin stacking
- A higher TDD or stoppage of insulin losses

Brittle diabetes or frequent highs usually = the wrong settings

The Actual Pump Practices Study

- Data downloaded from >1,000 Cozmo insulin pumps during a 2007 routine software upgrade
- 396 pumps with direct BG entered from an attached CozMonitor Freestyle meter into avg. glucose tertiles
- Average of >73 days data and >300 BGs per pump
- 92.7% of wearers used the BC to cover carbs (ie, > 2 meals a day)
- 96.5% used the BC to correct high readings


APP Study – BGs and Basal Rates

<table>
<thead>
<tr>
<th>Glucose, Insulin and Carb Data</th>
<th>Group: All 396 Pumps</th>
<th>Low Third</th>
<th>Mid Third</th>
<th>High Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG Tests/Day</td>
<td>4.38 4.73 4.41 4.01</td>
<td>4.14 4.07 4.20 4.14</td>
<td>189.9 185.2 196.3 187.9</td>
<td></td>
</tr>
<tr>
<td>TDD</td>
<td>49.4 47.9 49.1 51.1</td>
<td>47.3 47.6 47.2 47.8</td>
<td>11.4 10.8 12.2 11.2</td>
<td></td>
</tr>
</tbody>
</table>

The high BG tertile used MORE insulin (larger TDD). They need more insulin OR they need to stop losing it!


APP Study – Carb Boluses and CarbFs

<table>
<thead>
<tr>
<th>Glucose, Insulin and Carb Data</th>
<th>Group: All 396 Pumps</th>
<th>Low Third</th>
<th>Mid Third</th>
<th>High Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. Meter BG</td>
<td>144 mg/10.2 mmol</td>
<td>144 mg/dl (8.0)</td>
<td>181 mg/dl (10.0)</td>
<td>227 mg/dl (12.6)</td>
</tr>
<tr>
<td>CarbBolus U/d</td>
<td>20.4 u 20.9 u 20.4 u 19.8 u</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CarbBolus/Day</td>
<td>4.14 4.07 4.20 4.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CarbGram/Day</td>
<td>189.9 185.2 196.3 187.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CarbF</td>
<td>11.4 10.8 12.2 11.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


OCCLUSIONS & INFUSION SET ISSUES → LOSS OF INSULIN

<table>
<thead>
<tr>
<th>Occlusions Worsen Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG Tertile</td>
</tr>
<tr>
<td>Avg BG</td>
</tr>
<tr>
<td>Blocks/Month</td>
</tr>
</tbody>
</table>

**APP Data – BGs Pre/Post Infusion Set Change**

Average glucose levels for 6-hour intervals before and after infusion set change in 396 pumps (>20 set changes/pump).

**Clever Pump Trick – Quick Way to Improved TDD (iTDD)**

Most pumper’s BGs are high. If lows are NOT frequent:

**Raise the TDD by 1% for each 6 mg/dl reduction desired in avg BG**

Example: Amy’s avg TDD is 40 units/day, avg BG is 212 mg/dl (rare lows), and her desired avg BG is 140 mg/dl:

- 212 mg/dl = 140 mg/dl = 72 mg/dl
- 72 mg/dl = 6 mg/dl = a 12% increase in TDD
- Amy’s new iTDD = 40 units x 1.12 = 44.8 units

**THE CARB FACTOR**

**Pump Setting Formulas**

- **Basal** = 48% to 58% of TDD
- **CarbF** = \(2.6 \times \frac{Wt(lbs)}{TDD}\)
- **Corr. Factor** = \(1960/TDD\) (mg/dl)

Correction factors are inversely related to TDD and to avg. BG

Based on years of clinical work and research

**Conclusions from APP Study Results**

- Between low, medium, and high glucose groups:
  - Basals identical at 48% of TDD in all 3 tertiles
  - No difference in grams of carb, # of carb boluses, or # of correction boluses per day, or CarbF or CorrF #s
  - Glucose tests per day were “significant” (4.7 vs 4.0) but only minimal impact on glucose outcomes
  - Infusion set failure and occlusions significantly raise average glucose levels


© 2017, Pumping Insulin, 6th ed
Small Change in CarbF = Large Change in BG

\[ \text{CarbF} = \frac{\text{carbs in meal} - \text{carbs in meal}}{1960} \]

<table>
<thead>
<tr>
<th>Meal Size</th>
<th>Fall in BG per meal *</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 grams</td>
<td>0.67u x 49 = – 33 mg/dl</td>
</tr>
<tr>
<td>100 grams</td>
<td>1.1u x 49 = – 54 mg/dl</td>
</tr>
</tbody>
</table>

* Calculated as \( \frac{\text{carbs in meal} - \text{carbs in meal}}{\text{TDD}} \times 1960 \)

When CarbF is lowered from 1/10 to 1/9

\[ \text{TDD} = 40 \text{ u} \]
\[ \text{CorrF} = 49 \text{ mg/dl per u} \]

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 |

\( \text{CarbFs Often Wrong}^{1,2} \)

Only 40% of 405 CarbFs had an expected value

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

Encourage formulas rather than WAG!

\( \text{APP Study – Overrides of Doses Calculated by BC} \)

Who Makes Bolus Adjustments?

- By Bolus Calculator
- Pump User
- Overrides

Less for IOB  | – 1.4 u/day  | – 0.1 u/day
Less for Low BG | + 2.0 u/day | + 0.6 u/day
More for High BG | + 4.2 u/day | + 0.6 u/day
Adjustments Made | – 1.7 u/day | – 0.1 u/day

4.8u added – 1.8u subtracted = 3 additional u/day

* Adjustments in the low glucose tertile.

The BC makes most dose decisions. With good control, about 3 more units a day are needed. Current pumps do not subtract the 1.4 units for excess IOB!

Comparison of Averages Cozmo and Tandem Research Data

- Cozmo (396, 2007)
- Tandem (28,315, 2018)
  - CarbF: 11.5 u/g
  - CorrF: 56.2
  - Basal: 47.6%
  - TDD: 49.4 u/day
  - DIA: 3.1 hr
  - CarbF: 10.7 u/g
  - CorrF: 47.2 u/mg/dl
  - Basal: 50.3%
  - TDD: 49.59 u/day
  - DIA: 3.4 hr

CarbFs Actually Used\(^{1,2}\)

Actual CarbFs for best control tertile (76% had expected value)

Improved mostly by BC subtracting IOB from carb boluses (–1.4u)

Current pumps don’t do this!

Carb boluses reduced also for lows (–0.3u)

Clever Pump Trick – Account for IOB to Get Accurate Bolus

1. When IOB is SMALLER than the CORRECTION bolus, the pump’s recommendation is CORRECT

2. When IOB is LARGER than the CORRECTION bolus, subtract IOB from the combined carb + correction bolus

Example: Carb bolus = 4.0 u

Corr bolus = 1.0 u

IOB = 2.0 u (IOB is larger than Corr bolus)

Accurate bolus = 4 + 1 – 2 = 3 units
USE AN ACCURATE DIA TO ACCOUNT FOR ALL INSULIN ON BOARD

Duration Of Insulin Action (DIA)

Accurate boluses require an accurate DIA

Rapid insulin lowers the glucose for 4 to 5 hrs. This DOES NOT CHANGE in the body when DIA time is changed in pump!

Typical Carb Digestion Times

<table>
<thead>
<tr>
<th>Food</th>
<th>Digestion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>0 m</td>
</tr>
<tr>
<td>fruit/veg juice</td>
<td>5-20 m</td>
</tr>
<tr>
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</tr>
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</tr>
<tr>
<td>broccoli/cauliflower</td>
<td>45 m</td>
</tr>
<tr>
<td>raw carrots/beets</td>
<td>50 m</td>
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<td>60 m</td>
</tr>
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Take Home: most carbs are faster than "rapid" insulin

Short DIAs Hide Insulin Stacking

How much IOB appears to remain 3 hours after a 10 unit bolus using these DIA times:

<table>
<thead>
<tr>
<th>DIA Setting</th>
<th>3 hr</th>
<th>4.5 hr</th>
<th>5.0 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated IOB</td>
<td>0 u</td>
<td>2.5 u</td>
<td>3.4 u</td>
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Short DIAs lead to unexplained lows, erroneous pump setting adjustments, and users ignoring "smart pump" advice.

Select a reasonable DIA (4 to 5 hrs) to avoid insulin stacking and unexplained hypoglycemia.

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<tr>
<td>fish</td>
<td>30-60 m</td>
</tr>
<tr>
<td>milk/cot cheese</td>
<td>90 m</td>
</tr>
<tr>
<td>legumes/beans</td>
<td>2 hr</td>
</tr>
<tr>
<td>chicken</td>
<td>1.5-2 hr</td>
</tr>
<tr>
<td>seeds/nuts</td>
<td>2.5-3 hr</td>
</tr>
<tr>
<td>beef/lamb</td>
<td>3-4 hr</td>
</tr>
<tr>
<td>cheese</td>
<td>4-5 hr</td>
</tr>
</tbody>
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Take Home: most carbs are faster than "rapid" insulin

Rapid insulin works here!

IOB Is Present In 65% Of Boluses

APP Results

Insulin stacking is common – 65% of 201,538 boluses are given within 4.5 hours of a prior bolus

Bolus Insulin On Board (IOB)¹
Glucose-lowering activity remaining from recent boluses

An accurate IOB:
- Reduces insulin stacking
- Improves bolus accuracy
- Shows current carb or insulin deficit when BG test is done
- Requires an accurate DIA

Don’t Change DIA to Fix Control Problems
- DIA times are same for children and adults
- If the pump does not “give enough bolus insulin”, do NOT shorten the DIA to get larger boluses. Look for the real reason:
  - a basal rate too low
  - or carb factor too high
- Some things do shorten insulin’s action time:
  - Increased activity and exercise
  - Hot weather
  - Don’t shorten DIA for temporary situations

Clever Pump Trick – Stop Post Meal Spikes
- Count carbs carefully
- Bolus 15 to 45 min before meals when possible
- Eat low GI foods or fewer carbs
- Delay eating till below 140 mg/dl when able
- Add fiber/psyllium/acarbose/Symlyn/GLP-1 agonist
- Use combo bolus (part now/part later) with picky eaters
- Exercise after meals
- Use a Super Bolus

Clever Pump Trick – Bolus Early To Stop Meal Spiking
Figure shows rapid 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 – but too risky to recommend till Basal.IQ !!!
Early boluses – the best-kept secret for better control

Clever Pump Trick – A Super Bolus Turns Basal into Bolus
Super Bolus shifts part of the next 2 to 3.5 hrs of basal insulin into a bolus.
Negligible to no risk for having a low later.¹,²

Faster Insulin Aspart vs Novolog
FIAsp completes phase 1 pump study in people with type 1 diabetes
Eleven people with type 1 diabetes: 18 were treated with an insulin pump using Novolog, and 18 were treated with an insulin pump using FIAsp; postmeal glucose control was measured and compared over a 2-day span. The results showed that the pump groups were more tightly controlled with FIAsp in both the morning and evening. Fasting glucose was lower in the morning, and postmeal glucose was lower in the evening in the FIAsp group. The difference in mean postmeal glucose control was statistically significant (P<.05) for all time points in both the morning and evening. Fasting glucose control was lower in the morning in the FIAsp group; however, the difference was not statistically significant. The study results suggest that FIAsp may be a more effective insulin for people with type 1 diabetes when used in an insulin pump.
Soon – Biochaperone-Lispro

A protein molecule is added to Humalog to speed action. Software update: match default DIA to insulin choice

Hypoglycemia vs Coeff of Variation (CV%)

CV% = standard deviation/average BG

CV or swing in BGs ranged from 11% to 56% in 112 Type 1s

Panel A: CV versus %time per day below 54 mg/dL (1% = ~15 min a day)
Risk of hypo greater when CV% >33%
Panel B: avg BG versus %time per day below 54 mg/dL. Avg glucose has less impact on hypoglycemia
Ideal: a CV% below 34%

How Many Carbs for a Low?

Treat lows with:

Grams of carb = Wt(lbs)/10 + (IOB x CarbF)

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

- At 120 lbs, she needs 12 grams for the low glucose
- Plus 2u IOB x 10 gram/u = 20 grams to cover her IOB

Amy needs 12 g + 20 g = 32 grams for this low

* DIA time MUST be accurate to measure IOB

Closed Loop Algorithms

- Model predictive control (MPC) predicts glucose levels at a specific time point in the near future (some adapt to the user’s routine).
- Proportional integral derivative (PID) responds to measured glucose levels.
- Fuzzy logic (FL) calculates insulin doses based on how an expert would make real-time adjustments based on CGM data.

Cell Novo Closed Loop

Cell Novo pump and Dexcom G5 sensor in 68 people, age 47.2 ±13.4 years, HbA1c 7.6 ±0.9%, diabetes 27.9 ±13.2 years. Randomized 12 weeks on and off of closed loop.

Time in 70-180 mg/dl range: 69.5% [62.4;75.6] in CL vs. 58.7% [45.2;64.9] in OL.
Time in hypoglycemia <70 mg/dl: 2.1% [1.2;2.6] in CL vs. 4.1% [1.9;6.1] in OL.
Insulin + Symlin in Closed Loop

Comparison of 1) rapid insulin-alone + AP (AP), 2) rapid insulin & Symlin (pramlintide) & AP (DAP), and iii) 3) Regular insulin (Humulin R) & amylin & AP (R-DAP) in 12 Type 1 adults.

<table>
<thead>
<tr>
<th>Insulin &amp; Pramlintide</th>
<th>Artificial Pancreas in Type 1 Diabetes—Randomized Controlled Trial. 210-OR ADA 2018 Orlando; Canada study.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Twenty T1D patients aged 11.9 ± 6.9 years used openAPS, Dexcom G4® CGM, and Sool Dana® insulin pump for an average openAPS duration of 180 days:</td>
</tr>
<tr>
<td></td>
<td>• Time in 70-180 mg/dl range increased from 70.1% (± 16.4) to 83.3% (± 10.1), p&lt;0.001.</td>
</tr>
<tr>
<td></td>
<td>• A1C fell from 6.8% to 6.3%, p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>• Time above 180 mg/dl fell from 24.7 ± 16.5% to 13.3 ± 9.4%, p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>• Time below 70 mg/dl fell from 5.1 ± 3.3% to 3.4 ± 2.3%, p= 0.004.</td>
</tr>
</tbody>
</table>

OpenAPS Closed Loop

Open Artificial Pancreas System Reduced Hypoglycemia and Improved Glycemic Control in Patients with Type 1 Diabetes. 964-P ADA 2018 Orlando; South Korea study.

NOVEL PUMP IDEAS

Sensionics Eversense XL

SQ-implanted CGM worn for 90 days
Transmitter to phone is adhered to skin

Improve Set Reliability

Steel versus Teflon Infusion Sets

<table>
<thead>
<tr>
<th>Steel:</th>
<th>Teflon:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No kinking</td>
<td>More versions</td>
</tr>
<tr>
<td>Few silent occlusions¹</td>
<td>Straight or slanted</td>
</tr>
<tr>
<td>Simple insertion</td>
<td>Manual or automatic insertion</td>
</tr>
<tr>
<td>Very few failures</td>
<td>Less needle phobia</td>
</tr>
<tr>
<td>Better biocompatibility, less back pressure²</td>
<td>25 gauge (27-gauge introducer needle)</td>
</tr>
<tr>
<td>Easier to train</td>
<td>FlowSmart: 28 gauge (30-gauge introducer)</td>
</tr>
<tr>
<td>28-30 gauge, 4-6 mm</td>
<td></td>
</tr>
</tbody>
</table>


Innovative OpenAPS Features

- Rapid situational adjustment
- Carbs on board – fast, medium, slow COB
- User selects own glucose target
- Always in AutoMode when CGM is active
- OpenAPS $200; Loop $135 plus $99 a year as Apple developer
- Options: Eating Soon, Autosensitivity (settings optimizer), OpenAPS Simulator (virtual testing of food/insulin options)

**Missing: Real Pump Features**

- Show How a New Setting Impacts TDD & BG
- Eliminate temp basal rates → Temp Insulin Adjustments (basal AND bolus doses)
- Add Super Bolus Option
- Add Meal Size Bolus Option (1 → 7 carb sizes derived from TDD)
- Safety Option (subtract excess IOB from carbs)
- Excess IOB when Carb Bolus is Given Alert (warns when excess IOB is present but no BG reading is entered)

**Missing: Real Pump Features**

- Automated Basal and Bolus Testing
- Low BG Predictor (IOB x CorrF exceeds current BG minus target BG) HypoManager
- Carbs Needed For A Low
- Exercise Compensator (time + intensity → basal and bolus adjustment guidance)
- Infusion Set Leak Detector (analyze end-of-set-use hyperglycemia and/or short and variable usage times)

**Lots More to Learn**

[Image of a book titled "PUMPING INSULIN"]

*Created by Freepik*