The Latest on Pumps and Exercise

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*View slides at www.diabetesnet.com/diabetes-resources/pump-presentation

Highlights
- Introduction to Exercise and Pumps
- Line and Patch Pumps
- Tuning The Bolus Calculator
- Infusion Set Issues
- On the Horizon

The Challenge Of Diabetes
Bringing the A1c down smoothly takes effort

Ways To Get There

Things That Affect Glucose in Exercise
- Current glucose and trend
- BOB at start
- Carbs on board and carb intake
- Length and intensity of exercise
- Training/glycogen level
- Recent lows
- Aerobic versus anaerobic exercise
- Stress hormones/competition

Pump Advantages
- Convenience (fewer missed doses)
- Less insulin, less insulin stacking
- Easier to exercise and match varying insulin needs
- Lower A1C & less severe hypoglycemia, less BG variability *
- More social freedom
- Better data (clinicians, pumpers, parents)

Performance With Optimal BGs

Team Type 1 set a new RAAM course record in 2009:
3,021 miles (4,861 km)
5 days, 9 hrs and 5 min
23.41 mph

Plus 1st place in 2007 and 2nd in 2008

Infusion Line Pumps

- Accu-Chek Combo
- Asante Snap
- Animas Ping
- Medtronic Revel
- Tandem t:slim

Patch Pumps

- Valeritas V-Go
- Accu-Chek Solo
- Calibra Finesse
- Insulet Omnipod

Accu-Chek Solo

- Precise dispensing screw
- Auto-inserter
- 200 units
- Weighs 1 oz
- Bolus button on pump
- Remote with color screen
- Accurate bolus calculations
- FDA approved

CellNovo Wax Motor Pump

- Small wax cube is heated to pump 0.05 u of insulin
- ✋ slow bolus delivery
- Controller sends data via phone lines to internet site/cell phone
- Connects to short infusion set
- 2 rechargeable pumps
- Unclear operation in heat/cold
- CE approved in Europe

Debiotech Jewel

- Micro-Electro-Mechanical Systems tiny silicon motor
- Silicon wafer nanotechnology for mass production of motor
- Very light, 0.02 u delivery
- Separate infusion site
- Current 400 u insulin bladder makes it large
- ✋ Cost
- CE approved
Finesse Type 1 or 2 Bolus Device

- Simple, low cost design
- Manual bolus, no basal
- 0.5, 1, 2, & 5 unit options
- Convenient for those who also use a long-acting insulin
- 200 u reservoir, 27 gauge metal needle, 2" × 1" × 0.25"
- No electronics

Remote Controls – PDA + Meter

- Discreet bolus delivery (and basal in some) from PDA
- Sends BG and bolus dose to pump via radio wave or Bluetooth
- All data in one location
- Some remotes (Cellnovo and Omnipod) must be present to give a bolus

Why The Glucose Falls With Exercise

- Excess basal or bolus insulin
- Excess BOB at start
- Too few carbs
- Longer, more intense exercise
- Lack of training

Why The Glucose Rises With Exercise

- Too little basal or bolus insulin*
- Too many carbs
- Anaerobic exercise
- Competition/stress
- Dehydration
- Muscle trauma (extreme sports)

* Limits exist for the duration and degree for insulin reductions

Benefits Of Training

Basals and boluses are already lowered

- Better access to internal glucose and fat stores

Muscle glycogen stores are already enlarged

- About 25% less glucose is removed from blood after exercise because glycogen stores are already enlarged

Glycogen – nature’s glucose shock absorber

Intensity Affects Fuel Preference

As intensity rises, more glucose is required
Percentage Of Carb and Fat Used As Fuel During Aerobic Exercise

<table>
<thead>
<tr>
<th>% fuel coming from carbs during aerobic exercise</th>
<th>More Carbs</th>
<th>Less Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>% fuel coming from carbs during aerobic exercise</td>
<td>Still More Carbs</td>
<td>More Fat</td>
</tr>
</tbody>
</table>

Your insulin level controls access to both carbs and fat as fuel.

More Carbs
More Fat

Intensity

Days or Intensity

Duration

When Insulin Levels Need To Change

The LONGER you exercise, The MORE INTENSELY you exercise, and The LESS TRAINED you are, The MORE likely you'll need to lower your basals and boluses.

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More Fat

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More Fat

Glucose Regulation – Aerobic vs Anaerobic

<table>
<thead>
<tr>
<th>Type</th>
<th>Intensity</th>
<th>Duration</th>
<th>Fuel</th>
<th>Glucose</th>
<th>ExCarbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>aerobic</td>
<td>mild to high</td>
<td>hours</td>
<td>30-70% glucose</td>
<td>usually falls</td>
<td>yes</td>
</tr>
<tr>
<td>anaerobic</td>
<td>very high</td>
<td>10 to 15 minutes</td>
<td>up to 100% glucose</td>
<td>usually rises</td>
<td>no</td>
</tr>
</tbody>
</table>

Glucose Regulation

Type:
- aerobic
- anaerobic

Intensity:
- mild to high
- very high

Duration:
- hours
- 10 to 15 minutes

Fuel:
- 30-70% glucose
- up to 100% glucose

Glucose:
- usually falls
- usually rises

ExCarbs:
- yes
- no

Anaerobic Spurts Help Prevent Lows

- Use anaerobic exercise to your advantage for longer aerobic activities
- Short periods of anaerobic effort – 10 to 30 seconds – may be sufficient to raise your glucose and minimize hypoglycemia
- If the insulin level is not excessive

Competition May Raise The Glucose

- Competitive events release stress hormones
  - Hard to predict
  - Bolus as needed
- Short anaerobic events do the same
  - Bolus after event

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Glucose Sources And Timing

Ideally, during exercise most glucose will not come out of the blood

<table>
<thead>
<tr>
<th>During</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local muscle glycogen</td>
<td>– 85%</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>– 15%</td>
</tr>
<tr>
<td>Carb intake</td>
<td>~15%*</td>
</tr>
</tbody>
</table>

* More carbs are needed DURING exercise if insulin level is too high

Reload Glycogen Rapidly

- Glycogen stores in muscle and liver are reduced during exercise
- It is much easier to rebuild glycogen stores in the first 2 hours after exercise
  - Glycogen rebuilding is 2-3 times faster
  - Less risk of night lows
- Use fast carbs: chocolate milk, bagels, potatoes, cereals, dried fruit

Tuning the Bolus Calculator

The BC helps user find bolus recommendations that better match carb intake and the current glucose while minimizing insulin stacking

Bolus Calculator Settings

<table>
<thead>
<tr>
<th>This Setting</th>
<th>Assists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal rates</td>
<td>Safe sleep (~50% of TDD)</td>
</tr>
<tr>
<td>CarbF or I:C ratio</td>
<td>Cover carbs well</td>
</tr>
<tr>
<td>CorrF or ISF</td>
<td>Lower highs safely</td>
</tr>
<tr>
<td>Target glucose</td>
<td>Correct to specific goal</td>
</tr>
<tr>
<td>DIA</td>
<td>Minimize insulin stacking</td>
</tr>
</tbody>
</table>

The average TDD controls the frequency of highs and lows

Training Impacts Your TDD & Settings

As your TDD falls with improved physical fitness, keep your basals and boluses balanced

Example: 160 lb person in good control:

<table>
<thead>
<tr>
<th>Change in BC Settings from Training</th>
<th>TDD</th>
<th>Basal</th>
<th>CarbF</th>
<th>CorrF</th>
<th>Ins Sens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Training</td>
<td>40 u</td>
<td>0.8 u/h</td>
<td>10.4</td>
<td>49</td>
<td>96%</td>
</tr>
<tr>
<td>After Training</td>
<td>30 u</td>
<td>0.6 u/h</td>
<td>13.6</td>
<td>65</td>
<td>125%</td>
</tr>
</tbody>
</table>

When TDD changes, so should your pump settings

Bolus Calculator

User Inputs: Glucose

Grams of carb

Photo courtesy: www.sixuntilme.com

Photo courtesy: emilyboller.com

BC Output: Recommended bolus with list of units for carbs, correction (if any), and BOB (if any)
APP Study –
Carb Factors are Often Incorrect\(^1,2\)

<table>
<thead>
<tr>
<th>Carb Factor</th>
<th>Number of Pumps</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>5</td>
</tr>
</tbody>
</table>

Pump carb factors from 400 pumps are not evenly distributed.
People like “magic” numbers – 5, 10, 15, and 20 g/unit.
Always use formulas to get more accurate pump settings — better than WAG!

\(^2\) J. Walsh, D. Wroblewski, and TS Bailey: Insulin Pump Settings – A Major Source For Insulin Dose Errors, Diabetes Technology Meeting 2007

APP Study –
Use the TDD to Find Pump Settings\(^1\)

\[ \text{Basal} = \sim 48\% \text{ of TDD or } 0.02 \times \text{TDD} \]
\[ \text{CarbF} = 5.7 \times \frac{\text{Wt (kg)}}{\text{TDD}} \quad \text{or} \quad 2.6 \times \frac{\text{Wt (lbs)}}{\text{TDD}} \]
\[ \text{Corr. Factor} = \frac{110}{\text{TDD} \ (mmol/L)} \quad \text{or} \quad \frac{1960}{\text{TDD} \ (mg/dl)} \]

CorrF is inversely related to TDD and to avg. BG

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


Verify Bolus Recommendations

BOB = glucose-lowering activity that remains from recent boluses
Almost all pumps cover carbs fully regardless of BOB.
If BOB exceeds correction bolus, consider reducing recommended bolus, especially before events and before going to sleep.

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

Avoid Short DIA

A short DIA hides your true BOB and leads to:
- Hidden insulin stacking and “unexplained” lows
- Errors in adjustments of basal rates, carb factors, and correction factors
- Ignoring your “smart” pump’s advice

Set DIA for real action time: 4.5 to 6 hrs.
Don’t modify DIA time to fix control problems

How To Reduce Boluses

- Bolus reductions are ideal for exercise that takes place shortly after a meal and lasts less than 60 to 90 minutes
- For exercise before meals, eat extra free carbs and reduce bolus for the meal that follows
- For long and more strenuous exercise, meal boluses can be greatly reduced and sometimes eliminated

Clever Pump Trick –
Super Bolus – Shift Basal To Bolus

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.\(^1,2\)

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

Max carbs/meal = \( \text{Wt (lbs)} \times 0.36 \) to stay in control
How Many Basals?

Percentage of pumpers who use 1 to 10 basals per day from self reports of several hundred pumpers at insulin-pumpers.org.

Basal changes take at least 3-5 hours to have their full effect* when basal rates are doubled, so >5 basals has dubious benefit.

Temp Basal Reduction

- Short, large basal reductions can be used right before exercise to offset excess BOB
  - ~80% reduction for up to 90 min
- Smaller reductions for exercise that lasts over 90 min
  - Max reduction usually 50%
  - Reduce basal an hour or so before activity starts
- After a long exercise, glucose may fall for 12 to 36 hrs
  - Temp basal reductions are often needed
  - Plus additional carbs to rebuild glycogen stores

Don’t suspend your pump!

Multiple Temp Basal Reductions

- 3 hrs activity at 5 of 5 intensity
- % of usual basal

Adjacent basals before the need arises

Disconnect Bolus

- Disconnect up to 2 hrs for sports, mini-vacation, etc.
- User estimates time off and pump gives up to 50% of missed basal as bolus
- Alarm reminds user to re-connect
- After reconnecting, pump shows how much basal was lost and offers to supply the missing amount

Infusion Sets – The Achilles Heel Of Pumps

Survey of 1142 pump wearers seen in 40 German diabetes clinics

- 54% reported an increase in glycemia for unknown reasons until their infusion set was changed
- 26% of patients report that their auto-insertion device did not always work (in 10% ± 12% of all cases)
- 19% reported kinking, 12% had leakage, 12% air bubbles, and 33% had other issues
- 58% use Teflon and 39% use steel needle, with 82% straight and 12% bend sets

Pump Plumbing

Glucose Levels Around Infusion Set Changes

Reasons that Infusion Sets Fail

- Complete pullout
- Insulin leak along Teflon to skin
- Hematoma (pool of blood)
- Occlusion
- Cannula kink
- Loose hub
- Punctured line

ALL should rarely or never happen

Anchor Your Infusion Line!

Place a strip of 1" tape across infusion line to:

- Stop tugging on Teflon catheter under the skin to reduce skin irritation or "pump bumps"
- Stop "unexplained highs" caused by insulin leaking back to skin surface
- Prevent most pull outs

Use tape so you don’t lose insulin!

Tapes

Some 1" tapes that work well

- Transpore
- Micropore
- Durapore
- Hypafix
- Blenderm

Infusion Set Auto-Inserters

- Inset 30
- Accu-Chek Link Assist
- Inset/Mio
- Quick-Serter
- Cleo
- Spring
- Omnipod

Tackies

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

Remove with Goo B Gone or Detechol
Line Disconnect Mechanisms

Pinch & pull; Easiest
Pinch, twist, & lift; Hardest
Twist & pull; Easiest
Pinch & lift; Harder

Tubing lengths: 24”, 32”, and 43” for most sets

On The Horizon

Easy Adjustment for Exercise

Enter planned exercise into pump:
1. Intensity (1-7 scale)
2. Duration (15-480 min)
3. Training level for activity (1-5 scale)

With your current BOB and CGM BG/trend, pump calculates likely carb intake and insulin reduction needed during and after the exercise

Easy Adjustment for Exercise

Add activity monitor to pump
Combined with your current BOB and CGM BG/trend, this lets your pump calculate likely basal and bolus reductions after exercise

Future Pump Feature

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

Early Closed Loop – Animas Vibe

- Insulin pump with high contrast color screen
- 1 week Dexcom G4 sensor with smallest needle
- Internet access via Diasend software

Future Pump Feature

CE approved in Europe
Early Closed Loop – Medtronic Veo

- Low Glucose Suspend (LGS)
- Uses CGM to suspend basal for up to 2 hrs when low
- User can reactivate basal
- Reduce prolonged nighttime lows
- Ability to detect low BGs remains an issue

CE approved in 2009, submitted for FDA approval

Challenges to an Artificial Pancreas
JDRF Closed Loop – 2012

1. Develop alternate glucose sensing for reliability
   a) Multiple sensors on one platform
   b) Alternate technologies: florescence, etc.
2. Develop dual delivery pump (insulin + other drug)
3. Evaluate alternate non-insulin drugs to prevent hypoglycemia (glucagon, Symlin, GLP-1 agonist, leptin, or ?)
4. Modular testing of software control algorithms

Faster Insulins

Problem: Carb digestion is often < 2 hrs
Insulin action lasts > 5 hrs

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

Microneedle Intradermal Delivery

- Becton Dickinson 1.5 mm intradermal needle speeds up insulin action
- Painless
- Reliable attachment of infusion set is critical to success

Hyaluronidase

- Recombinant human hyaluronidase temporarily degrades local hyaluran, a structural protein in the interstitial space
- Faster insulin uptake
- DIA ~4 to 4.5 hrs – Phase 3 clinical testing with 435 pump wearers now underway
- Release in early 2014?

Long-Lasting Implanted CGMs

- Few disposables
- Minor surgery
- Funded as rental?

Sensors For Medicine

MicroCHIPS Iliume

OlySens
Implanted Fluorescent CGM

Molecules fluoresce & change color as glucose rises or falls
- Small size, low power, low cost, long life, great accuracy, minimal lag time

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

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