Insulin Pump Therapy and Continuous Glucose Sensor Use in the Management of Diabetes Mellitus

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Dr. Louis Haenel IV has disclosed that he is a consultant and member of the Speakers Bureaus for sanofi-aventis, Novo Nordisk, AstraZeneca, Medtronic
Discuss the basics of insulin pump therapy
Review the role and mechanisms of continuous glucose monitoring
- Discuss the use of CSII in patients with diabetes mellitus who are taking insulin
A healthy pancreas releases insulin automatically, on average, every 10-to 14-minutes\(^1\), in amounts appropriate for your varying blood glucose levels.

There Are Big Gaps Between Pancreas Insulin Production and Conventional Therapy

**NPH and Short-Acting Insulin**

- Normal Insulin Secretion
- Short-acting Insulin
- NPH

Schematic representation only
Intensive Diabetes Management with Injections Is Better But Leaves Room for Opportunity

- Basal insulin glargine plus rapid-acting insulin before meals
- Requires 4 – 5 injections / day

Schematic representation only.

Normal Insulin Secretion
Rapid-acting Insulin
Insulin glargine

0 hr 12 hrs 24 hrs
A typical profile of basal insulin rates in CSII. Many people are more active in the late afternoon, and more sedentary after dinner, necessitating adjustment to the basal rate. Note higher basal rate in pre-dawn hours.

Insulin Pumps Also Deliver Customized Boluses for Different Types of Meals

Insulin pumps offer smart calculators to help determine how much bolus insulin is needed, and can deliver precise amounts of insulin based on the amount of carbs to be taken.

Insulin Pumps Use Only Rapid Acting Insulin which Has the Least Intrapatient Variability

Pharmacodynamic Variability in Insulin Action*

*Percentages represent the coefficients of variation (CV) for insulin action as measured by the maximum glucose infusion rate in these euglycemic glucose clamp studies.

- Rapid-acting insulin: 16%
- Glargine: 36%
- NPH insulin: 46%

Rapid-acting insulin has the lowest intrapatient variability

### Pump therapy vs MDI: Consistently lower HbA1c in meta-analyses

<table>
<thead>
<tr>
<th>Meta-analyses</th>
<th>HbA1c (CSII vs MDI)</th>
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<tr>
<td><strong>Misso ML, et al. 2010 (Cochrane)</strong></td>
<td>-0.3% (95% CI, -0.4, -0.1) improvement in HbA1c¹</td>
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<tr>
<td><strong>Fatourechi, et al. 2009</strong></td>
<td>-0.2% (95% CI, -0.1 to -0.3) improvement in HbA1c²</td>
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<td><strong>Pickup and Sutton 2008</strong></td>
<td>-0.62% (95% CI, -0.47 to -0.78) improvement in HbA1c³</td>
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<tr>
<td><strong>Jeitler, et al. 2008</strong></td>
<td>-0.6 (95% CI, -0.87 to -0.22) improvement in HbA1c; with reduced insulin requirement⁴</td>
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<tr>
<td><strong>Weissberg-Benchell, et al. 2003</strong></td>
<td>-0.95 (95% CI, -0.8 to -1.1) improvement in HbA1c⁵</td>
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</tbody>
</table>

1. Meta-analysis of 23 randomized controlled trials in more than 976 patients with type 1 diabetes (T1D).
2. Meta-analysis of 15 studies, randomized controlled trials in patients with T1D.
3. Meta-analysis of 22 randomized controlled trials in patients with T1D.
4. Meta-analysis of 22 studies, with 12 studies reporting reductions in glucose in T1D.
5. Meta-analysis of 52 studies with 11 studies reporting reductions in glucose in patients with T1D.

MDI = multiple daily injections
CSII = continuous subcutaneous insulin infusion
Pump therapy vs MDI: Fewer episodes of severe hypoglycemia

- Pumps decrease risk of severe hypoglycemic episodes by 2.9-fold\(^1\)
- Data from 15 trials suggest insulin pumps “may be better than MDI for reducing the incidence of severe hypoglycemic events”*\(^\dagger\)
- Severe hypoglycemic events significantly reduced following CSII introduction: from 37/year to 14/year; \(p<0.05\)^3

*Meta-analysis of 23 randomized controlled trials in more than 976 patients with type 1 diabetes (T1D)
\(^\dagger\)No difference in non-severe hypoglycemia
MDI = multiple daily injections
CSII = continuous subcutaneous insulin infusion

INSULIN PUMP THERAPY
Insulin pump therapy

- Also known as continuous subcutaneous insulin infusion (CSII)
- Infuses rapid acting insulin in precise programmable doses to meet individual patient needs
- Delivers insulin through a soft cannula under the skin
- Replaces multiple injections

The insulin pump closely mimics normal pancreatic insulin delivery
Consensus statement:

“CSII is the most physiological method of insulin delivery currently available”¹

Why do you think more patients are not on insulin pump therapy?

¹ Consensus statement on use of insulin pumps in pediatrics endorsed by the ADA and European Association for the Study of Diabetes (EASD)
“Consider use of continuous subcutaneous insulin infusion in insulin-treated patients with type 2 diabetes mellitus”

2007 American Association of Clinical Endocrinologists Medical Guidelines For Clinical Practice for the Management of Diabetes Mellitus

“The efficacy and safety of CSII with an insulin pump are comparable to multiple daily injection insulin therapy for patients with type 2 diabetes mellitus”

2007 American Association of Clinical Endocrinologists Medical Guidelines For Clinical Practice for the Management of Diabetes Mellitus
How a Pump Works

The insulin is housed inside the pump in a little cartridge called a “reservoir.”

Insulin travels into your body through a flexible tube that ends with a tiny needle called a “cannula” inserted just under the skin.

The needle is held in place by an “infusion set,” a little adhesive patch stuck to your skin.
Components and their functions:

- A small computerized, battery operated pump
  - Allows the user to control exactly how much insulin is delivered
- A pump reservoir
  - Similar to a regular syringe, holds 2 to 3 days worth of insulin
- A thin plastic tube called an infusion set
  - Has a soft cannula or needle at the end inserted just under the skin, usually on the abdomen

How does it work?

- Insulin passes from the pump reservoir through the tubing into the subcutaneous tissue
An Infusion Set Is the Link Between the Insulin Pump and the Body

Center for Disease Control (CDC) Recommends Changing Infusion Sets Every 2-to-3 days

Insulin Infusion

- Skin
- Subcutaneous Tissue
- Cannula
- Insulin
Normal Pancreatic Insulin Delivery

Normal Pancreas

Diagram showing basal and bolus insulin delivery.
Similarity Between Insulin Pumps and a Normal Pancreas

• Delivery of basal rates
  • Programmed delivery of a constant background rate of insulin (basal rate)
  • Programmable to match the individual’s needs

• Bolus delivery
  • Delivery of a dose of insulin (bolus) to meet the requirements of food intake
  • Calculated based on the amount of carbohydrates contained in the meal or snack
  • Can be used to correct high blood glucose readings
• Delivers continuously/automatically
• Adjusted to match pt’s hepatic glucose production 
  (i.e., fasting & nocturnal, & dawn)
• Similar to a normal functioning pancreas – in maintaining BG stability

Example Basal Rate

1. 12 am @ 0.6 u / hr.
2. 3 am @ 0.7 u / hr.
3. 8 am @ 0.5 u / hr.

Advantages

1. Very precise delivery.
2. Eliminates large insulin depots.
Temporary Basal Rates
- Used to increase or decrease basal insulin during physical activity or during illness

Basal Rate Patterns
- Allows for customized basal rates to be programmed in order to meet the patient’s daily, weekly or monthly needs. This feature is useful in the following circumstances:
  - Changes in sleep times (weekends, shift work)
  - Different schedule during the week vs. weekends
  - High-activity or low-activity days vs. typical day
  - Monthly hormonal shift
Bolus Insulin

- Insulin delivery ‘on demand’
  - Meal Bolus: Given to cover rise in glucose from food
  - Correction Bolus: Given to correct a blood sugar over normal range
- Factors needed to calculate bolus

<table>
<thead>
<tr>
<th>Meal Bolus</th>
<th>Correction Bolus</th>
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<tbody>
<tr>
<td>• Insulin-to-carbohydrate ratio</td>
<td>• Insulin Sensitivity Factor</td>
</tr>
<tr>
<td>• Carbohydrates in the Meal</td>
<td>• Blood Glucose Target</td>
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<tr>
<td>• Activity Level</td>
<td>• Pre-meal Blood Glucose</td>
</tr>
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<td></td>
<td>• Active Insulin</td>
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Bolus Types and How to Set Them

**Bolus type**
1. Normal — all at once
2. Square wave — gradually over time
3. Dual wave — a portion given immediately followed by the remainder over time

**Note:** All bolus types can be given through the Bolus Wizard calculator.

**Ways to set a bolus**
- Bolus Wizard® calculator — automatically calculates bolus dose based on carbohydrate content of food, glucose value, or active insulin. Keeps in memory all the given boluses to prevent stacking of insulin.
- Easy bolus — a pre-set normal bolus that can be increased by fixed amounts. Makes audible beeps to confirm the amount.
- Manual bolus — individual entry of each bolus dose
The OmniPod system: just two simple parts

1. Built-in BG meter that automatically incorporates BG levels into suggested bolus calculations and history records

2. Waterproof pod

All-in-one
- Infusion set, insulin reservoir, automated inserter and batteries

Automated processes
- Cannula Insertion
- Priming

Intuitive user interface
- Full text navigation
- Set-up wizard
- Easy to teach, easy to learn
Fully integrated design with no assembly required

- Integrated insulin reservoir, infusion set, automated inserter, pumping mechanism, and power supply

Automated processes including cannula insertion and priming:

- Automated and consistent insertion alleviates potential for human error, and this unique design helps ensure that the cannula is inserted at the correct angle and depth
- Automated priming and tubing-free design ensures consistent priming with no concern with bubbles in tubing
CONTINUOUS GLUCOSE MONITORING

Professional vs Personal
Professional CGM Device

Proven Clinical Value

- 3 day evaluation
- Blinded to patient
- Glucose levels every 5 min
- 4 fingersticks per day
- Solutions Software
- No new reports
- No new algorithms

...plus Enhanced Features

- Wireless
- Discreet/Comfortable to wear
- Waterproof (IPX 8)
- Minimal patient training
- Minimal patient interaction
- Enhanced revenue streams
Modal Day Summary Report: Case Study

Dawn Phenomenon

Nocturnal Hypoglycemia

Friday
Saturday
Sunday
Friday
Saturday
Sunday
**First: Look for Hypo**

- For glucose levels BELOW low limit
  - Problem: basal rate is probably too high
  - Solution: decrease basal rate?

**Second: Look for Hyper**

- For glucose levels ABOVE high limit
  - Problem: basal rate is probably too low
  - Solution: increase basal rate?
Step 2: Look at Pre-prandial Periods

First: Look for Hypo
Consider:
- Influence of bolus, previous meal, active insulin
- Exercise and activity
- Food: Timing, Quantity, Composition

Second: Look for Hyper
Consider:
- Same considerations as hypo
- Plus breakfast related dawn phenomenon
Step 3: Look at Post-prandial Periods

First: Look for Hypo
- If hypoglycemia is observed in the PP period (2–3 hours after meal):
  - Suggests issue with the bolus for that meal
  - Consider timing, type, accuracy of bolus
  - Consider influence of exercise

Second: Look for Hyper
- If Hyperglycemia peaks above 180 mg/dl (<10.0mmol/l) post meal:
  - Consider timing, type, accuracy of bolus
  - Consider food intake, food quantity and meal composition
The Cloud

Wireless Internet Connection
Wi-Fi or Cellular; pricing will vary

2. Special Android app reads the G4 data and sends it "to the Cloud"

3. Cloud service stores CGM data, formats it, and publishes the data for viewing as a website.

4. Any device can connect to the web browser to view the data.

*An option to setup the CGM Cloud service is offered by the admins of the "CGM in The Cloud" Facebook Group - please join the group and visit the files section for more details. The system is based on the work of programming parents and friends in the "CGM in the Cloud" community. No guarantees or warranties are given, and there's no official support. Sharing the resource is voluntary.
Introducing MiniMed® Connect
What Is MiniMed Connect?

A better connection to diabetes care

For people with **diabetes**: discreet display of pump and CGM information

For healthcare providers: automatic CareLink®
Personal uploads

For care partners: online access to diabetes information

pump + sensor  uploader  mobile device  any Internet-enabled device
For People with Diabetes

Pump and CGM information now on the smartphone

- App shows sensor glucose values in the context of pump information
  - Active insulin, calibration, reservoir volume, sensor life, battery levels

- Easy-to-use interactive display
  - Display of past and current sensor glucose values
  - 3-hour, 6-hour, 12-hour and 24-hour views
  - Clear color coding and intuitive menu
  - Portrait and landscape modes of home screen

- Up-to-date data sent from pump to phone every 5 minutes
Information available anytime, anywhere through CareLink

- New tab in CareLink Personal called CareLink Connect
- Available on computers and mobile devices
- Displays key diabetes information
  - Sensor glucose values, active insulin, calibration, reservoir volume, sensor life, battery levels
- Text message notifications for uncleared alarms and alerts

Low SG for John Smith
Received by CareLink at 12:33pm
Convenient access to patient diabetes data

- Automatic uploads of pump and sensor glucose data to CareLink Personal every 24 hours
- Minimizes manual data uploads during office visits
- Easier follow-up and tracking of patients who may need more help
- Information can be displayed in CareLink Professional after syncing with CareLink Personal
Integrated Technology

- Artificial Pancreas Platform
- Threshold Suspend Feature
- Predictive Alerts
- Audible alarms/Vibration alarms
Tiny wireless chip and miniaturized glucose sensor embedded between two layers of soft contact lens material.

Accurate glucose monitoring for diabetics using bodily fluids, i.e. tears.

Prototypes can generate one reading per second.

Experimenting with LEDs to serve as early warning for the wearer.

Source: Google X