Diabetes Update
New Insulins
and
Insulin Delivery Systems

Bruce W. Bode, MD, FACE
Atlanta Diabetes Associates
Atlanta, Georgia
Prevalence of Diabetes in the US

Diagnosed
Type 2 Diabetes
10.3 Million

Diagnosed Type 1 Diabetes
0.5 – 1.0 Million

Undiagnosed Diabetes
5.4 Million

Causes of Death in People With Diabetes

<table>
<thead>
<tr>
<th>Condition</th>
<th>% of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>44</td>
</tr>
<tr>
<td>Other Heart Disease</td>
<td>10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
</tr>
<tr>
<td>Cancer</td>
<td>7</td>
</tr>
<tr>
<td>Stroke</td>
<td>5</td>
</tr>
<tr>
<td>Infection</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
</tbody>
</table>

Goals of Intensive Diabetes Management

- Near-normal glycemia
  - HbA1c less than 6.5 to 7.0%
- Avoid short-term crisis
  - Hypoglycemia
  - Hyperglycemia
  - DKA
- Minimize long-term complications
- Improve QOL

Relative Risk of Progression of Diabetic Complications by Mean HbA1C Based on DCCT Data

Skyler, Endo Met Cl N Am 1996
HbA1c and Plasma Glucose

- 26,056 data points (A1c and 7-point glucose profiles) from the DCCT
- Mean plasma glucose = (A1c x 35.6) – 77.3
- Post-lunch, pre-dinner, post-dinner, and bedtime correlated better with A1c than fasting, post-breakfast, or pre-lunch

Rohlfing et al, Diabetes Care 25 (2) Feb 2002
Emerging Concepts

The Importance of Controlling Postprandial Glucose
<table>
<thead>
<tr>
<th>Test</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA(_{1c})</td>
<td>&lt; 6.5 %</td>
</tr>
<tr>
<td>Fasting/preprandial glucose</td>
<td>&lt; 110 mg/dL</td>
</tr>
<tr>
<td>Postprandial glucose</td>
<td>&lt; 140 mg/dL</td>
</tr>
</tbody>
</table>

ACE / AACE Consensus Conference, Washington DC August 2001
Natural History of Type 2 Diabetes

R.M. Bergenstal, International Diabetes Center
Major Metabolic Defects in Type 2 Diabetes

- Peripheral insulin resistance in muscle and fat
- Decreased pancreatic insulin secretion
- Increased hepatic glucose output

Haffner SM, et al. Diabetes Care, 1999
Insulin Resistance: An Underlying Cause of Type 2 Diabetes

- Obesity and inactivity
- Genetic abnormalities
- Aging
- Medications
- Rare disorders
- Type 2 diabetes
- Hypertension
- Dyslipidemia
- Atherosclerosis
- PCOS

Reaven GM. *Physiol Rev.* 1995;75:473-486
Type 2 Diabetes: Two Principal Defects

- Genes → Insulin resistance → ± Environment → IGT → Type 2 diabetes
- Genes → β-cell dysfunction/failure → ± Environment → IGT → Glucose Toxicity

Reaven GM. *Physiol Rev.* 1995;75:473-486
Reaven GM. *Diabetes/Metabol Rev.* 1993;9(Suppl 1):5S-12S;
Role of Free Fatty Acids in Hyperglycemia

Adipose tissue insulin resistance

Muscle

Lipolysis

↑ FFA mobilization

Liver

Liver insulin resistance

↑ FFA oxidation

↓ Glucose utilization

↑ Gluconeogenesis

Hyperglycemia

HbA$_{1c}$ in the UKPDS

Conventional

Intensive

6.2% upper limit of normal range

0 3 6 9 12 15

Years from randomisation

0 1 2 3 4 5

HbA$_{1c}$ (%)

Years from randomisation

0 3 6 9 12 15

HbA$_{1c}$ (%)
UKPDS: β-Cell Function for the Patients Remaining on Diet for 6 Years

Multiple Factors May Drive Progressive Decline of β-Cell Function

Hyperglycemia (glucose toxicity) → Insulin resistance → “Lipotoxicity” (elevated FFA, TG)

Protein glycation → β-cell

## UKPDS: Benefits of Glycemic Control in Type 2 Diabetes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk Reduction</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes-related endpoint</td>
<td>12%</td>
<td>0.029</td>
</tr>
<tr>
<td>Microvascular endpoints</td>
<td>25%</td>
<td>0.0099</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>16%</td>
<td>0.052</td>
</tr>
<tr>
<td>Cataract extraction</td>
<td>24%</td>
<td>0.046</td>
</tr>
<tr>
<td>Retinopathy at 12 years</td>
<td>21%</td>
<td>0.015</td>
</tr>
<tr>
<td>Microalbuminuria at 12 years</td>
<td>33%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Metformin Prevents Heart Attacks and Reduces Deaths in Type 2 Diabetes

**Heart Attacks**

- Conventional Metformin Therapy: 20
- Metformin Therapy: 13

- Reduction: 39%

**Coronary Deaths**

- Conventional Metformin Therapy: 10
- Metformin Therapy: 5

- Reduction: 50%

*P = 0.01*  
*P = 0.02*
Management of Type 2 DM

Step Therapy

- Diet
- Exercise
- Sulfonylurea or Metformin
- Add Alternate Agent
- Add hs NPH vs TZD
- Switch to Mixed Insulin bid
- Switch to Multiple Dose Insulin

Utilitarian, Common Sense, Recommended

Prone to Failure from Misscheduling and Mismanagement
Management of Type 2 DM Stumble Therapy

- WAG Diet
- Golf Cart Exercise
- Sample of the Week Medication
  - Interrupted
  - Not Combined
- Poor Understanding of Goals
- Poor Monitoring

HbA1c >8% (If Seen)
Consider A New Treatment Paradigm

- Treatment designed to correct the dual impairments
- Vigorous effort to meet glycemic targets
- Simultaneous rather than sequential therapy
- Combination therapy from the outset
- Early step-wise titrations to meet glycemic targets
Goals in Management of Type 2 Diabetes

- Fasting BG < 110 mg/dL
- Post-meal < 140 mg/dL
- HbA1c < 6.5%
- Blood Pressure < 130/80
- LDL < 100 mg/dl
- HDL > 45 mg/dl
Thiazolidinediones: Mode of Action

Peroxisome Proliferator-Activated Receptors

- **PPAR\(\gamma\)**
  - Affects glucose, lipid and protein metabolism

- **PPAR\(\alpha\)**
  - Affects lipoprotein metabolism
  (some TZDs)
Thiazolidinediones: Rationale for Type 2 Diabetes Therapy

● Proven characteristics
  – Target insulin resistance, a core defect
  – Improve glycemic control
  – Do not cause hypoglycemia
  – Improve lipid profile (pioglitazone and troglitazone)

● Potential benefits
  – Preservation of pancreatic b-cell function
  – Prevention of progression from impaired glucose tolerance to type 2 diabetes
  – Improvement in cardiovascular outcomes

Change in Lipid Profile at Endpoint: ACTOS Added to Sulfonylurea

Δ from baseline at 16 weeks

<table>
<thead>
<tr>
<th></th>
<th>SU + Placebo (n = 187)</th>
<th>SU + ACTOS 30 mg (n = 189)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>-15.89 % *</td>
<td>10.15 %</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>2.33 %</td>
<td>4.07 %</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>-0.95 %</td>
<td>12.00 %</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>6.57 %</td>
<td>7.02 %</td>
</tr>
</tbody>
</table>

Baseline (mg/dL)

Triglycerides: 258.6, 259.5
Total cholesterol: 211.5, 214.4
HDL cholesterol: 42.9, 41.8
LDL cholesterol: 123.7, 126.5

LOCF

* p ≤ 0.05 vs. placebo

Takeda Pharmaceuticals America, Data on file Study 010
Incidence of Edema

U.S. Placebo-controlled Studies

- Placebo
- ACTOS

2 patients from combination therapy trials and 0 from the monotherapy trials discontinued due to edema

Pioglitazone HCl Package Insert July, 1999
### Approach to Combination Oral Therapy

#### Intensifying of Oral Therapies

- **metformin &/or glitazone**
  - **sulfonylurea/repaglinide**
    - **&/or glucosidase inh**

  **If FPG < 120 mg/dl and HbA1c < 7.0%**
  - Continue

  **If FPG > 120 mg/dl and HbA1c > 7.0%**
  - Add Insulin

- **sulfonylurea/repaglinide**
  - **&/or glucosidase inh**
    - **+**
      - **metformin &/or glitazone**

  **If FPG < 120 mg/dl and HbA1c < 7.0%**
  - Continue

  **If FPG > 120 mg/dl and HbA1c > 7.0%**
  - Add Insulin
Insulin

The most powerful agent we have to control glucose
## Comparison of Human Insulins / Analogues

<table>
<thead>
<tr>
<th>Insulin preparations</th>
<th>Onset of action</th>
<th>Peak</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>30–60 min</td>
<td>2–4 h</td>
<td>6–10 h</td>
</tr>
<tr>
<td>NPH/Lente</td>
<td>1–2 h</td>
<td>4–8 h</td>
<td>10–20 h</td>
</tr>
<tr>
<td>Ultralente</td>
<td>2–4 h</td>
<td>Unpredictable</td>
<td>16–20 h</td>
</tr>
<tr>
<td>Lispro/aspart</td>
<td>5–15 min</td>
<td>1–2 h</td>
<td>4–6 h</td>
</tr>
<tr>
<td>Glargine</td>
<td>1–2 h</td>
<td>Flat</td>
<td>~24 h</td>
</tr>
</tbody>
</table>
Short-Acting Insulin Analogs
Lispro and Aspart Plasma Insulin Profiles

Pharmacokinetic Comparison
NovoLog® vs Humalog®

Hedman, *Diabetes Care* 2001; 24(6):1120-21
Lispro Mix 75/25
Pharmacodynamics

Limitations of NPH, Lente, and Ultralente

- Do not mimic basal insulin profile
  - Variable absorption
  - Pronounced peaks
  - Less than 24-hour duration of action
- Cause unpredictable hypoglycemia
  - Major factor limiting insulin adjustments
  - More weight gain
Insulin Glargine
A New Long-Acting Insulin Analog

- Modifications to human insulin chain
  - Substitution of glycine at position A21
  - Addition of 2 arginines at position B30
- Gradual release from injection site
- Peakless, long-lasting insulin profile
Glargine vs NPH Insulin in Type 1 Diabetes
Action Profiles by Glucose Clamp

Glucose Infusion Rate

n = 20 T1DM
Mean ± SEM

SC insulin

Overall Summary: Glargine

Insulin glargine has the following clinical benefits:

- Once-daily dosing because of its prolonged duration of action and smooth, peakless time-action profile (23.5 hours on repeat injections)
- Comparable or better glycemic control (FBG)
- Lower risk of nocturnal hypoglycemic events
- Safety profile similar to that of human insulin
Type 2 Diabetes ... A Progressive Disease

Over time, most patients will need insulin to control glucose.
Insulin Therapy in Type 2 Diabetes

Indications

- Significant hyperglycemia at presentation
- Hyperglycemia on maximal doses of oral agents
- Decompensation
  - Acute injury, stress, infection, myocardial ischemia
  - Severe hyperglycemia with ketonemia and/or ketonuria
  - Uncontrolled weight loss
  - Use of diabetogenic medications (eg, corticosteroids)
- Surgery
- Pregnancy
- Renal or hepatic disease
Mimicking Nature
The Basal/Bolus Insulin Concept
The Basal/Bolus Insulin Concept

- **Basal insulin**
  - Suppresses glucose production between meals and overnight
  - 40% to 50% of daily needs

- **Bolus insulin (mealtime)**
  - Limits hyperglycemia after meals
  - Immediate rise and sharp peak at 1 hour
  - 10% to 20% of total daily insulin requirement at each meal
Basal vs Mealtime Hyperglycemia in Diabetes

- Basal hyperglycemia
- Mealtime hyperglycemia

Type 2 Diabetes

△ AUC from normal basal >1875 mgm/dL·hr; Est HbA1c >8.7%

When Basal Corrected

Basal vs Mealtime Hyperglycemia in Diabetes

△ AUC from normal basal 900 mgm/dL·hr; Est HbA1c 7.2%
Basal vs Mealtime Hyperglycemia in Diabetes

When Mealtime Hyperglycemia Corrected

△ AUC from normal basal 1425 mgm/dL·hr; Est HbA1c 7.9
When Both Basal & Mealtime Hyperglycemia Corrected

Basal vs Mealtime Hyperglycemia in Diabetes

△ AUC from normal basal 225 mgm/dL·hr; Est HbA1c 6.4%
Over time, most patients will need both basal and mealtime insulin to control glucose.
Starting With Basal Insulin

Advantages

- 1 injection with no mixing
- Insulin pens for increased acceptance
- Slow, safe, and simple titration
- Low dosage
- Effective improvement in glycemic control
- Limited weight gain
Starting With Basal Insulin

Bedtime NPH Added to Diet

Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Type 2 DM on 1 or 2 oral agents (SU, MET, TZD)
- Age 30 to 70
- BMI 26 to 40
- A1C 7.5 to 10% and FPG > 140 mg/dL
- Anti GAD negative
- Willing to enter a 24 week randomized, open labeled study
Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Add 10 units Basal insulin at bedtime (NPH or Glargine)
- Continue current oral agents
- Titrate insulin weekly to fasting BG < 100 mg/dL
  - if 100-120 mg/dL, increase 2 units
  - if 120-140 mg/dL, increase 4 units
  - if 140-160 mg/dL, increase 6 units
  - if 160-180 mg/dL, increase 8 units
Treatment to Target Study; A1C Decrease

Mean HbA1c %

Weeks in Study (N = 691)
Patients in Target (A1c < 7%)
Treatment to Target Study: NPH vs Glargine in DM2 patients on OHA

- Nocturnal Hypoglycemia reduced by ?% in the Glargine group
Advancing Basal/Bolus Insulin

- Indicated when FBG acceptable but
  - HbA1c > 7% or > 6.5%
  - SMBG before dinner > 140 mg/dL
- Insulin options
  - To glargine or NPH, add mealtime aspart / lispro
  - To suppertime 70/30, add morning 70/30
  - Consider insulin pump therapy
- Oral agent options
  - Usually stop sulfonylurea
  - Continue metformin for weight control
  - Continue glitazone for glycemic stability?
Starting With Bolus Insulin

Combination Oral Agents + Mealtime Insulin
Starting With Bolus Insulin
Mealtime Lispro vs NPH or Metformin Added to Sulfonylurea

Case #1: DM 2 on SU with infection

- 49 year old white male
- DM 2 onset age 43, wt 173 lbs, Ht 70 inches
- On glimepiride (Amaryl) 4 mg/day, HbA1c 7.3% (intolerant to metformin)
- Infection in colostomy pouch (ulcerative colitis) glucose up to 300 mg/dL plus
- SBGM 3 times per day
Case #1: DM 2 on SU with infection

- Started on MDI; starting dose 0.2 x wgt. in lbs.
- Wgt. 180 lbs which = 36 units
- Bolus dose (lispro/aspart) = 20% of starting dose at each meal, which = 7 to 8 units ac (tid)
- Basal dose (glargine) = 40% of starting dose at HS, which = 14 units at HS
- Correction bolus = (BG - 100)/ SF, where SF = 1500/total daily dose; SF = 40
Correction Bolus Formula

\[
\text{Current BG} - \text{Ideal BG} \over \text{Glucose Correction factor}
\]

Example:

- Current BG: 220 mg/dl
- Ideal BG: 100 mg/dl
- Glucose Correction Factor: 40 mg/dl

\[
\frac{220 - 100}{40} = 3.0\text{u}
\]
Case #1: DM 2 on SU with infection

- Started on MDI
- Did well, average BG 138 mg/dL at 1 month and 117 mg/dL at 2 months post episode with HbA1c 6.1%
Strategies to Improve Glycemic Control: Type 2 Diabetes

- Monitor glycemic targets – Fasting and postprandial glucose, HbA$_{1c}$
- Self-monitoring of blood glucose is essential
- Nutrition and activity are cornerstones of therapy
- Combinations of pharmacologic agents are often necessary to achieve glycemic targets
Intensive Therapy for Type 1 Diabetes

- Careful balance of food, activity, and insulin
- Daily self-monitoring BG
- Patient trained to vary insulin and food
- Define target BG levels (individualized)
- Frequent contact of patient and diabetes team
- Monitoring HbA$_{1c}$
- Basal / Bolus insulin regimen
Options in Insulin Therapy

- **Current**
  - Multiple injections
  - Insulin pump (CSII)

- **Future**
  - Implant (artificial pancreas)
  - Transplant (pancreas; islet cells)
Multiple Injection Therapy
Intermediate & Short-Acting Insulin Pre-Meal
Multiple Injection Therapy
Intermediate & Short-Acting Insulin Pre-Meal
Multiple Injection Therapy
Intermediate & Short-Acting Insulin Pre-Meal
Multiple Injection Therapy

Glargine & Short-Acting Insulin Pre-Meal
Case #2: DM 1 on MDI

- 46 year old white male power line supervisor
- DM 1 age 40
- On MDI: 10 u lispro pre-meal, 20 u NPH HS
- HbA1c 7.4%
- SMBG avg 124 mg/dL based on 1.9 tests/day (fasting 171 mg/dL, noon 105 mg/dL, pm 125 mg/dL, HS 75 mg/dL)
Case #2: DM 1 on MDI

- Lantus (glargine) 20 u HS added in place of NPH
- No change in behavior (diet, SMBG frequency)
- Seen three months later (8-16-01)
- HbA1c 6.3%
- SMBG average 104 mg/dL (fasting BG 91 mg/dL, noon 126 mg/dL, pm 116 mg/dL, HS 126 mg/dL)
- NO HYPOGLYCEMIA
- HAPPY
Insulin Pens
Introducing InDuo™

- The world’s first combined insulin doser and blood glucose monitoring system
- A major breakthrough in Diabetes Care
InDuo™ - Integration

Feature

- Combined insulin doser and blood glucose monitor
InDuo™ - Compact Size

**Feature**
- Compact, discreet design

**Benefit**
- Allows discreet testing and injecting anywhere, anytime
InDuo™ - Doser Remembers

**Feature**
- Remembers amount of insulin delivered and time since last dose

**Benefit**
- Helps people inject the right amount of insulin at the right time
Variability of Insulin Absorption

CSII <2.8%
Subcutaneous Injectable 10% to 52%

Pump Therapy
Basal & Bolus Short-Acting Insulin
Pump Therapy
Basal & Bolus Short-Acting Insulin
Pump Therapy
Basal & Bolus Short-Acting Insulin

- Combined with SMBG, physiologic insulin requirements can be achieved more closely
- Flexibility in lifestyle
History of Pumps
PARADIGM PUMP

Paradigm.
Simple. Easy.
Paradigm Pump: Advantages

- 29% smaller, water resistant
- Menu driven: 
  - bolus, suspend, basal, prime, utilities
- Reservoir based (easier to fill)
- Silent motor
- AAA batteries
Paradigm Pump: Advantages

- Various bolus options
  - normal, square, dual, and “easy bolus”
- Enhanced memory
- Enhanced safety features
  - (low reservoir alarm, auto off, etc.)
Pump Infusion Sets

Softset QR

Silhouette
Pharmacokinetic Advantages
CSII vs MDI

● Uses only regular or very rapid insulin
  – More predictable absorption than modified insulins (variation 3% vs 19 to 52%)

● Uses 1 injection site
  – Reduces variations in absorption due to site rotation

● Eliminates most of the subcutaneous insulin depot

● Programmable delivery simulates normal pancreatic function

Metabolic Advantages with CSII

- Improved glycemic control
- Better pharmacokinetic delivery of insulin
  - Less hypoglycemia
  - Less insulin required
- Improved quality of life
Glycemic Control

Atlanta Diabetes Associates
CSII
Factors Affecting $\text{HbA}_1\text{c}$

- **Monitoring**
  - $\text{HbA}_1\text{c} = 8.3 - (0.21 \times \text{BG per day})$

- **Recording** 7.4 vs 7.8

- **Diet practiced**
  - CHO: 7.2
  - Fixed: 7.5
  - Other: 8.0

- **Insulin type**
  - Lispro: 7.3
  - R: 7.7
CSII Usage in Type 2 Patients
Atlanta Diabetes Experience

Mean HbA$_{1c}$ (%)

- Baseline: 9.2
- 6 months: 7.57 (P = 0.026)
- 18 months: 7.19 (P = 0.040)

N = 11
Glycemic Control in Type 2 DM: CSII vs MDI in 127 patients

- A1C

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End of Study (24 wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Raskin, *Diabetes* 2001; 50(S2):A106
DM 2 Study: CSII vs MDI

- Overall treatment satisfaction improved in the CSII group: 59% pre to 79% at 24 weeks
- 93% in the CSII group preferred the pump to their prior regiment (insulin +/- OHA)
- CSII group had less hyperglycemic episodes (3 subjects, 6 episodes vs. 11 subjects, 26 episodes in the MDI group)
CSII Reduces Hypoglycemia

Insulin Reduction Following CSII

Baseline (MDI) 15 days 6 mos 18 mos 36 mos

48.1 34.5 * 39.3 * 40.1 * 39.8 *

-28% -18% -16% -17%

n = 389 n = 389 n = 298 n = 246 n = 187

* P < 0.001
Normalization of Lifestyle

- Liberalization of diet — timing & amount
- Increased control with exercise
- Able to work shifts & through lunch
- Less hassle with travel — time zones
- Weight control
- Less anxiety in trying to keep on schedule
Current Continuation Rate
Continuous Subcutaneous Insulin Infusion (CSII)

Continued 97%
Discontinued 3%

N = 165
Average Duration = 3.6 years
Average Discontinuation <1%/yr

U.S. Pump Usage
Total Patients Using Insulin Pumps

- '90: 6,600
- '91: 8,700
- '92: 11,400
- '93: 15,000
- '94: 20,000
- '95: 26,500
- '96: 35,000
- '97: 43,000
- '98: 60,000
- '99: 81,000
- 2000: 120,000
- 2001: 162,000
Pump Therapy Indications

- HbA$_{1c}$ >7.0%
- Frequent hypoglycemia
- Dawn phenomenon
- Exercise
- Pediatrics
- Pregnancy
- Gastroparesis
- Hectic lifestyle
- Shift work
- Type 2

Poor Candidates for CSII

- Unwilling to comply with medical follow-up
- Unwilling to perform self blood glucose monitoring 4 times daily
- Unwilling to quantitate food intake
Current Candidate Selection

Patient Requirements

– Willing to monitor and record BG
– Motivated to take insulin
– Willing to quantify food intake
– Willing to follow-up
– Interested in extending life
Pump Therapy

Basal rate
- Continuous flow of insulin
- Takes the place of NPH or glargine insulin

Meal boluses
- Insulin needed pre-meal
  - Pre-meal BG
  - Carbohydrates in meal
  - Activity level
- Correction bolus for high BG

[Graph showing Basal rate and Meal bolus at different times of the day]
What Type of Bolus Should You Give?

- 9 DM 1 patients on CSII ate pizza and coke on four consecutive Saturdays
- Dual wave bolus (70% at meal, 30% as 2-h square):
  - 9 mg/dl glucose rise
- Single bolus: 33 mg/dl rise
- Double bolus at -10 and 90 min: 66 mg/dl rise
- Square wave bolus over 2 hours: 80 mg/dl rise

Chase et al, Diabetes June 2001 #365
If HbA$_{1c}$ is Not to Goal

Must look at:

- SMBG frequency and recording

- Diet practiced
  - Do they know what they are eating?
  - Do they bolus for all food and snacks?

- Infusion site areas
  - Are they in areas of lipohypertrophy?

- Other factors:
  - Fear of low BG
  - Overtreatment of low BG
Future of Diabetes Management
Improvements in Insulin & Delivery

- Insulin analogs and inhaled insulin
- External pumps
- Internal pumps
- Continuous glucose sensors
- Closed-loop systems
Pulmonary Insulin
Oral Agents + Mealtime Inhaled Insulin Effect on HbA$_{1c}$

*P < .001

GLUCOSE MONITORING SYSTEMS - Telemetry

Consumer Product

- “Real time” glucose readings
- Wireless communication from sensor to monitor
- High and low glucose alarms
- FDA panel pending
Closed-loop control using an external insulin pump and a subcutaneous glucose sensor

subcutaneous glucose sensor + Insulin infusion pump (currently MiniMed 508)
Closed-Loop Setup for Canine Studies
24-h Closed-Loop Control (diabetic canine)
Implantable Pump

- Average HbA$_{1c}$ 7.1%
- Hypoglycemic events reduce to 4 episodes per 100 pt-years
MiniMed 2007 System

Implantable
Insulin Pump
Placement
Implantable Insulin Pumps Indications for Use

- Diabetes out of control (frequent, rapid ρBG)
- Frequent hypoglycemic episodes
- Subcutaneous insulin absorption resistance
- Injection or infusion site reaction
Long-Term Glucose Sensor
Combine Pump and Sensor Technology

LTSS => Long Term Sensor System ("Open Loop Control")
Using an RF Telemetry Link......
Medtronic MiniMed’s Implantable Biomechanical Beta Cell
Today’s Reality
Open-Loop Glucose Control
Summary

- Insulin remains the most powerful agent we have to control diabetes
- When used appropriately in a basal/bolus format, near-normal glycemia can be achieved
- Newer insulins and insulin delivery devices along with glucose sensors will revolutionize our care of diabetes
Conclusion

Intensive therapy is the best way to treat patients with diabetes
QUESTIONS

● For a copy or viewing of these slides, contact

● WWW.adaendo.com

● Email: Minimedtalk@adaendo.com