Achieving Optimal Control
In Type 2 Diabetes

Case Study

- 58 Year Old Journalist
- Type 2 DM Just Diagnosed
- HbA1C 7.1%
Screening For Diabetes….

ADA’s Recommendations:

FBS ≥ 126 mg/dl
Random Glucose ≥ 200 mg/dl
A1C ≥ 6.5%

Incidence of Microvascular Complications in Pre-Diabetes

<table>
<thead>
<tr>
<th>Diabetic Retinopathy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-diabetes HbA₁c = 5.9%</td>
</tr>
<tr>
<td>Pre-diabetes HbA₁c = 6.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neuropathy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-diabetes ........13%*</td>
</tr>
</tbody>
</table>

*Prevalence. 
**Association of Retinopathy and Albuminuria with Glycemia**

A1c Thresholds Similar For Both Retinopathy And Microalbuminuria

Prevalence Of Microalbuminuria Increases With Rising Glucose Levels, Even When Slightly Elevated


---

**Prevention/Delay of Type 2 DM**

- Weight Loss Of 7% Of Body Weight
- Physical Activity At Least 150 Min/Week Of Moderate Activity
- Metformin, Especially If BMI >35, Age > 60 Or Prior Gestational DM
- Screen For Modifiable CVD Risk Factors
Therapy of Diabetes

¬ Diet
¬ Exercise
¬ Medications

What’s The A1C Goal For This Patient??
### Intensive Therapy for Diabetes
Reduction in Incidence of Complications

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Type 1 DCCT</th>
<th>Type 2 Kumamoto</th>
<th>Type 2 UKPDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9 → 7%</td>
<td>9 → 7%</td>
<td>8 → 7%</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>76%</td>
<td>69%</td>
<td>17-21%</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>54%</td>
<td>70%</td>
<td>24-33%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>60%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### What About Glycemic Control And Macrovascular Disease?
Recent Trials Modify The Paradigm
### Diabetic Control and Macrovascular Disease

<table>
<thead>
<tr>
<th></th>
<th>VADT</th>
<th>ACCORD</th>
<th>ADVANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>1,791</td>
<td>10,251</td>
<td>11,140</td>
</tr>
<tr>
<td><strong>Age (Yrs)</strong></td>
<td>60</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td><strong>Gender (% M/F)</strong></td>
<td>97/3</td>
<td>62/38</td>
<td>58/42</td>
</tr>
<tr>
<td><strong>DM Duration (Yrs)</strong></td>
<td>11.5</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td><strong>HbA1c</strong></td>
<td>9.4</td>
<td>8.1</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>CV Events (%)</strong></td>
<td>~40</td>
<td>~35</td>
<td>~32</td>
</tr>
<tr>
<td><strong>Insulin Use (%)</strong></td>
<td>~50</td>
<td>~35</td>
<td>~1.5</td>
</tr>
<tr>
<td><strong>Follow-Up (Yrs)</strong></td>
<td>5.6</td>
<td>3.4</td>
<td>5</td>
</tr>
</tbody>
</table>

**VADT, ACCORD, ADVANCE: Primary Outcome CV Events**

CV Death, MI Stroke

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Standard Control</th>
<th>Intensive Control</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>6</td>
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<td>12</td>
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<td>60</td>
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<td>60</td>
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<tr>
<td>66</td>
<td>66</td>
<td>66</td>
</tr>
</tbody>
</table>

HR 0.94 (0.84-1.06)  
P = 0.32

---

**Hypoglycemia In Recent Major Clinical Trials**

- After the results became available, hypoglycemia was identified as an area of concern in 3 recent major clinical trials in which intensive glucose control was compared with standard glucose control:
  - ACCORD\(^1\)
  - VADT\(^2\)
  - ADVANCE\(^3\)

---

Hypoglycemia and CV Disease

Hemodynamic Responses To Hypoglycemia

- Heart Rate Increases
- Systolic BP Increases
- Diastolic BP Decreases
- Cardiac Output Increases
- Myocardial Contractility Increases
  - EKG Changes
    - T wave flattening or inversion
    - ST depression
    - QT prolongation

Hematologic Responses To Hypoglycemia

- Increased RBCs Leading To Increased Blood Viscosity
- Enhanced Platelet Aggregation
- Increased Platelet Factor 4
- Increased Thromboglobulin
- Increased Coagulation Factor VIII
- Increased Von Willebrand Factor
- Increased Thrombin Generation

Wright R et al Diabetes / Metabolism Research and Reviews, 2008
Is intensive glucose control ever beneficial to the vasculature?

**UKPDS**
**United Kingdom Prospective Diabetes Study**

<table>
<thead>
<tr>
<th></th>
<th>VADT</th>
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<th>UKPDS</th>
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<td>5</td>
<td>~10</td>
</tr>
</tbody>
</table>

**UKPDS**
United Kingdom Prospective Diabetes Study Follow-Up

Myocardial Infarction

**Metabolic Memory**

Or

**Legacy Effect**

Summary: Trials and Metabolic Memory

- Get In There Early With Tight Glycemic Control BUT Relax Glycemic Control Later!

- If CV Risk Factors Are Controlled, There Is No Benefit And Potential Harm To Intensive Glycemic Control In High Risk Patients With A Long Duration Of DM
Multiple Factors Drive Progressive Decline Of β-Cell Function

- Hyperglycemia (Glucose Toxicity)
- Insulin Resistance
- "Lipotoxicity" Elevated FFA,TG
- Amyloid Deposition
- Protein Glycation
- Interleukin 1 α and β

Multi-factorial Pathogenesis of Type 2 Diabetes

- Decreased Insulin secretion
- Inefficient glucose uptake (skeletal muscle)
- Increased hepatic glucose production
- Decreased incretin effect
- Increased glucagon secretion
- Increased free fatty acids
- Neurotransmitter dysfunction
- Increased glucose reabsorption
Fat Topography in Insulin Resistance

Adiponectin: Increases Insulin Sensitivity

Fat Topography In Insulin Resistance

HI TG
HI FFA

Intramuscular
Intrahepatic
Subcutaneous
Intra-Abdominal

FFA
TNF α
Resistin
Leptin
IL-6
CRP
Tissue Factor
PAI-1
Angiotensinogen
### Medications To Break Insulin Resistance: Metformin

**The Good**
- Efficacious (↓A1C 1.2%)
- Long Track Record
- ↓ Hepatic Glucose Production (90%)
- Helps Muscle Glucose Uptake (10%)
- Colon Cancer Protection

**Not So Good**
- GI Upset
- Hold For Procedures and CT Dye Load
- Watch Creatinine Stop If > 1.5mg

### Medications To Break Insulin Resistance: Thiazolidinediones

**The Good:**
- Efficacious (↓A1C 1.2%)
- Reasonably Long Experience
- No Hypoglycemia
- β Cell Preservation
**TZD’s**

**The Good:**
- Efficacious
- Reasonably Long Experience
- No Hypoglycemia
- β Cell Preservation

**Not So Good:**
- Increased CV Risk?
- Edema
- Weight Gain
- Fractures
- Bladder Cancer

---

**Multi-factorial Pathogenesis of Type 2 Diabetes**

[Diagram showing various factors contributing to Type 2 Diabetes]

- Decreased Insulin secretion
- Inefficient glucose uptake (skeletal muscle)
- Increased hepatic glucose production
- Decreased incretin effect
- Increased glucagon secretion
- Increased free fatty acids
- Neurotransmitter dysfunction
- Increased glucose reabsorption
GLP-1 Modes of Action in Humans

GLP-1 is secreted from the L-cells in the intestine.

- Stimulates insulin secretion
- Suppresses glucagon
- Slows gastric emptying
- Reduces food intake

Upon ingestion of food...

Drucker DJ. Curr Pharm Des 2001; 7:1399-1412
Drucker DJ. Mol Endocrinol 2003; 17:161-171

One More Point
Going Back to Those β Cells.....
Natural History of Type 2 Diabetes

- **Glucose (mg/dL)**
  - **Fasting glucose**
  - **Post-meal glucose**

- **Relative Function (%)**
  - **Insulin resistance**
  - **Insulin level**

*IFG* = impaired fasting glucose.

**β-cell Neogenesis, Proliferation and Apoptosis**

- **Ductal progenitor cells**
- **Neogenesis**
- **Proliferation**
- **Apoptosis**
- **GLP-1**
  - **Stimulates**
  - **Inhibits**
**GLP-1: Effects On The Gastrointestinal, Cardiac And Central Nervous Systems**

- **Learning And Memory Function** (Animal Studies)
- **Neuroprotection** (Animal Studies)
- **Satiety**
- **Food Intake**
- **Gastric Emptying And Acid Secretion**
- **Protection And Improved Function**

---

**GLP-1 Modes of Action in Humans**

- Upon Ingestion of Food...
  - GLP-1 Is Secreted From the L-cells in the Intestine

- This in Turn...
  - Stimulates Insulin Secretion
  - Suppresses Glucagon
  - Slows Gastric Emptying
  - Reduces Food Intake

Long Term Effects Demonstrated in Animals...
- Increases β Cell Mass & Efficiency

---

**References**

Glucose Dependent Effects of GLP-1

Type 2 Diabetics (n=10)

Mean (se) <p.05  Nautack MA Diabetologia 1983

GLP-1 Effect : Blocked By DPP-4

GLP-1(7-36) Active
DPP-IV
Rapid Inactivation

GLP-1(9-36)Inactive
Renal Clearance

Mixed Meal
Intestinal GLP-1 Secretion

Deacon et al. Diabetes 1995; 44:1126
GLP-1: Rapidly Degraded by DPP-4

\[ t_{1/2} = 1-2 \text{ minutes} \]

*Amino acids shown in gold are homologous with the structure of glucagon.

Mentlein, R Regulatory Peptides 85:9-24, 1999

Secreted GLP-1 Rapidly Degraded

- GLP-1 (green) released into intestinal capillaries is immediately exposed to DPP-4 (red)\(^1\)
- >50% of secreted GLP-1 is already degraded before it reaches the general circulation\(^2\)
- >40% of circulating GLP-1 is already degraded before it reaches \(\beta\) cells\(^2\)

\(^1\)Hansen L. et al. Endocrinology. 1999;140:5356-5363;

Mentlein, R Regulatory Peptides 85:9-24, 1999
Enhance GLP-1 Effect By...

GLP-1 RECEPTOR AGONISTS

- Exenatide (Byetta/Bydureon) sc
- Liraglutide (Victoza) sc
- Lixisenatide sc

The Good:
- Efficacious (\(\Delta A1C 1.2-1.5\%\))
- Decrease Post-Prandial Glucose
- No Hypoglycemia
- Potential For Weight Loss
- Perhaps \(\beta\) Cell Preservation

The Not So Good:
- Daily/Twice Daily/Weekly Injection
- GI Upset
- Rare Reports Of Pancreatitis
- Cost
GLP-1 Effect: Blocked By DPP-4

Mixed Meal
- Intestinal GLP-1 Secretion
- GLP-1(7-36) Active
- Rapid Inactivation
- DPP-4
- GLP-1(9-36) Inactive
- Renal Clearance

GLP-1 Agonists
- Deacon et al. Diabetes 1995; 44:1126

Enhance GLP-1 Effect By...

**GLP-1 RECEPTOR AGONISTS**
- Exenatide sc (Byetta/Bydureon)
- Liraglutide sc (Victoza)
- Lixisenatide sc

**DPP-4 INHIBITORS**
- Sitagliptin po (Januvia)
- Saxagliptin po (Onglyza)
- Linagliptin po (Tradjenta)
- Alogliptin po (Nesina)
**DPP-4 Inhibitors**

**The Good:**
- Efficacious (↓A1C 0.7%)
- Decrease Post-Prandial Glucose
- No Hypoglycemia
- Weight Neutral
- Safe In Renal Disease
- No GI Upset
- Perhaps β Cell Preservation

**The Not So Good:**
- Cost
- Rare Reports Of Pancreatitis

**Multi-factorial Pathogenesis of Type 2 Diabetes**

- Decreased insulin secretion
- Inefficient glucose uptake (skeletal muscle)
- Increased hepatic glucose production
- Carbohydrate absorption
- Increased glucagon secretion
- Increased free fatty acids
- Neurotransmitter dysfunction
- Increased glucose reabsorption
**α Glucosidase Inhibitors**

**Good**
- Efficacious (↓A1C 0.6%)
- Long Experience
- No Hypoglycemia
- No Weight Gain

**Not So Good**
- Dosing With Meals
- GI Intolerance

---

**Multi-factorial Pathogenesis of Type 2 Diabetes**

- Decreased insulin secretion
- Inefficient glucose uptake (skeletal muscle)
- Increased hepatic glucose production
- Decreased incretin effect
- Increased glucagon secretion
- Increased free fatty acids
- Neurotransmitter dysfunction
- Increased glucose reabsorption
**Dopamine Receptor Agonists**

Type 2 Diabetics Have Low Levels Of Brain Dopamine

Quick Release Bromocriptine Increases Brain Dopamine Levels

---

**Altered Hypothalamic Function in Response to Glucose Ingestion in Obese and DM Humans**

**Bromocriptine Mesylate: Proposed Mechanism Of Action**

Morning administration (within 2 hours of waking) of Cycloset

Corrects Low dopaminergic tone in hypothalamus in early morning in diabetes

- Sympathetic tone
- HPA axis tone
- Hepatic gluconeogenesis
- FFA and TG
- Insulin resistance
- Inflammation/hypercoagulation

Restoration of morning peak in dopaminergic activity (via D2 receptor-mediated activity)

- Sympathetic tone
- HPA axis tone
- Hepatic gluconeogenesis
- FFA and TG
- Insulin resistance
- Inflammation/hypercoagulation

Impaired glucose metabolism, hyperglycemia and insulin resistance

Decreased postprandial glucose levels

- Sympathetic tone
- HPA axis tone
- Hepatic gluconeogenesis
- FFA and TG
- Insulin resistance
- Inflammation/hypercoagulation

Adverse cardiovascular pathology

Day-long reduction in plasma glucose, TGs and FFAs

- Sympathetic tone
- HPA axis tone
- Hepatic gluconeogenesis
- FFA and TG
- Insulin resistance
- Inflammation/hypercoagulation

Fonseca. Use of Dopamine agonists in Type-2 Diabetes. Oxford American Pocket Cards. OUP, 2010


**Quick Release Bromocriptine**

**The Good**
- Efficacious (ΔA1C 0.6%)
- Resets Hypothalamic Circadian Clock
- Surprisingly Good CV Profile

**Not So Good**
- Hypotension
- Short Track Record
- Cost
Multi-factorial Pathogenesis of Type 2 Diabetes

Sodium-Glucose Transport Inhibitors (SGLT's)

Inhibit Sodium-Glucose Co-Transporter-2 Located In Segment S1 Of Proximal Tubule Of The Nephron

This Transporter Reabsorbs Most Glucose Filtered By The Glomerulus
Renal Handling of Glucose

(180 L/day) (900 mg/L) = 162 g/day

Glucose
SGLT2
S1
90%
S3
10%
No Glucose

Canaglifozin

Selective Inhibitor of SGLT2

Inhibits Renal Glucose Reabsorption, Promotes Glucose Excretion

Decreases Hyperglycemia In Insulin Independent Manner
**Canaglifozin**

**The Good**
- Efficacious (↓A1C 1.0%)
- Inhibits Glucose Reabsorption At Renal Level
- Weight Reduction
- No Drug Interactions

**Not So Good**
- Increased UTI’s/Vaginitis
- Short Track Record
- Cost

**Combination Pills for Type 2 Diabetes**
- Glyburide/Metformin (Glucovance)
- Glipizide/Metformin (Metaglip)
- Sitagliptin/Metformin (Janumet)
- Saxaglitin/Metformin (Kombiglyze)
- Tradjenta/Metformin (Jentadueto)
Anti-Hyperglycemic Monotherapy: Maximum Therapeutic Effect on A1C

- Insulin
- Glimepiride
- Glipizide GITS
- Pioglitazone
- Sita/Saxa/linagliptin
- QR Bromocriptine
- Exenatide/Liraglutide
- Pioglitazone
- Acarbose

Reduction in A1C Level (%)

0 -0.5 -1.0 -1.5 -2.0


A Basic Principle:

Fix The Fasting First
Physiologic Insulin Secretion: Basal/Bolus Concept

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Basal Insulin (µU/mL)</th>
<th>Prandial Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.M.</td>
<td>50</td>
<td>150</td>
</tr>
<tr>
<td>P.M.</td>
<td>25</td>
<td>100</td>
</tr>
</tbody>
</table>

Basal Insulins

- Neutral Protamine Hagedorn (1946)
- Glargine (2001)
- Detemir (2006)
- Degludec (2013)
Starting Basal Insulin

Continue Oral Agent(s) at Same Dosage
(Eventually Reduce)
Add Single Insulin Dose (~ 15 units)
- Glargine (Anytime)
- Increase Insulin Dose 1 unit Daily Until FBS<100 mg &/or HbA1C < 7%

Suggested Titration Options For Glargine

Start with 10-15 units basal insulin and adjust weekly²

<table>
<thead>
<tr>
<th>Mean of self-monitored FPG values from preceding 2 days</th>
<th>Increase in insulin dose (IU/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥180 mg/dL</td>
<td>+8</td>
</tr>
<tr>
<td>140-179 mg/dL</td>
<td>+6</td>
</tr>
<tr>
<td>120-139 mg/dL</td>
<td>+4</td>
</tr>
<tr>
<td>100-119 mg/dL</td>
<td>+2</td>
</tr>
</tbody>
</table>

Or

Increase by 1 unit daily until FBS ≤ 100 mg/dL

**Insulin Pens**

- More Convenient Than Vial And Syringe
- Repeatedly More Accurate Dosages
- Easier To Use For Those With Visual Or Fine Motor Skills Impairments
- Less Injection Pain
  
  Coated Needles Not Dulled By Insertion Into A Vial Before Insertion Into The Skin

**Natural History of Type 2 Diabetes**

*IFG=impaired fasting glucose.*
Glucose Patterns in Type 2 Diabetes Mellitus

Continue SU/Tide/DPP-4 Inhibitor, Metformin, TZD

Currently Available Bolus Insulins

- Regular (1921)
- Insulin Lispro (1996)
- Insulin Aspart (2000)
- Insulin Glulisine (2006)
**Dosing Prandial Insulin**

- **Considerations For Initial Dosing**
  - 5-10 u/meal
  - OR 0.1 - 0.15 u/kg/meal
  - Use Glargine Dose As A Guide → 30% At Breakfast, 30% Lunch, 40% Dinner

- **Considerations For Dosing Adjustments**
  - Variable Meal Dosing To Adjust For Carbohydrate Intake
  - Supplemental Dosing To Correct For BG Before Meals

---

**Fine Tuning The Bolus**

**The Bolus Has 2 Components:**

- **Prandial**
  - Fine Tune By Carbohydrate Counting
  - **Correction Factor**
  - Adjustment For Pre-Meal Hyperglycemia

---

Glucose Patterns in Type 2 Diabetes Mellitus

Case Study

- 58 Year Old Journalist
- Type 2 DM Just Diagnosed
- HbA1C 7.1%
- Metformin Started

Discontinue SU/Tide/DPP-4 Inhibitor; Continue Metformin, TZD
**Case Study**

3 Months Later

- 58 Year Old Journalist
- Type 2 DM Just Diagnosed
- On Metformin
- Hb A1C 6.2%

---

**Case Study**

4 Years Later

- 61 Year Old Journalist
- Type 2 DM x 4 Years
- On Metformin
- Hb A1C 8.2%
Decisions, Decisions…

Failure On 1 Oral Agents
Add 2nd Oral Agent
Add GLP-1 Agent
Add Insulin

Case Study

- 61 Year Old Journalist
- Type 2 DM X 4 Years
- On Metformin
- Hb A1C 8.2%
- Second Oral Agent Added
Case Study

3 Months Later

- 61 Year Old Journalist
- Type 2 DM x 4 Years
- On Metformin + Second Oral Agent
- Hb A1C 6.9%

Case Study

2 Year Later

- 62 Year Old Journalist
- Type 2 DM x 6 Years
- On Metformin + Second Oral Agent
- HbA1C 8.9%
What To Do If/When Two Oral Agents Are Not Enough?

Decisions, Decisions…

- Failure On 2 Oral Agents
- Add 3rd Oral Agent
- Add GLP-1 Agent
- Add Insulin
### Change in Body Weight

<table>
<thead>
<tr>
<th>Weeks</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>18</th>
<th>26</th>
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<tr>
<td>6</td>
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</tbody>
</table>

**Exenatide** vs **Insulin Glargine**:
- **Exenatide**:
  - Mean ± SE shown
- **Insulin Glargine**:
  - Mean ± SE shown

* * p<0.0001, exenatide vs insulin glargine at same time point

---

### Overall Incidence of Adverse Events Occurring in at Least 2% of Treated Patients

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Exenatide Group</th>
<th>Insulin Glargine Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>161 (57.1)</td>
<td>23 (8.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>49 (17.4)</td>
<td>10 (3.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Headache</td>
<td>25 (8.9)</td>
<td>23 (8.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>22 (7.8)</td>
<td>24 (9.0)</td>
<td>0.65</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>24 (8.5)</td>
<td>8 (3.0)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Heine, R. J. et. al. Ann Intern Med 2005;143:559-569
Case Study

- 62 Year Old Journalist
- Type 2 DM x 6 Years
- On Metformin + Second Oral Agent
- Hb A1C 8.9%
- Basal Insulin Added

4 Months Later

- 62 Year Old Journalist
- Type 2 DM x 6 Years
- On Metformin + Second Oral Agent + Basal Insulin
- HbA1C 6.9%
Case Study
2 Years Later

- 64 Year Old Journalist
- Type 2 DM x 9 Years
- On Metformin + Second Oral Agent + Basal Insulin
- HbA1C 7.8% With Fasting Sugars Between 100 and 110 mg%

What’s Going On?

Postprandial Glucose Must Be Elevated
Natural History of Type 2 Diabetes

*IFG=impaired fasting glucose.

Bolus Insulin

- Add Rapid Acting Insulin For Mealtime Coverage

- Rule Of Thumb For Glargine:
  - 50% Basal
  - 50% Prandial, Divided Over 3 Meals
Glucose Patterns in Type 2 Diabetes Mellitus

Continue SU/GLP-1 Agonist/DPP-4 Inhibitor, Metformin, TZD

Case Study

3 Months Later

- 64 Year Old Journalist
- Type 2 DM x 9 Years
- On Metformin + Second Oral Agent + Basal Insulin + 1 Shot Bolus Insulin
- HbA1C 6.7%
Case Study
2 Years Later

- 66 Year Old Journalist
- Type 2 DM X 11 Years
- On Metformin + Second Oral Agent + Basal Insulin + 1 Shot Bolus Insulin
- Hb A1C 8.8%

Glucose Patterns in Type 2 Diabetes Mellitus

Discontinue SU/GLP-1 Agent/DPP-4 Inhibitor; Continue Metformin, TZD
Case Study

- 66 Year Old Journalist
- Type 2 DM x 11 Years
- On Metformin + Basal Insulin + Bolus Insulin Before Each Meal
- HbA1C 6.9%

Finally, For Your Larger Patients....
Extreme Insulin Resistance
> 200 units/day → Consider Using U500

- 5 Times As Concentrated --- 500 units/ml
- Dosed BID or TID
- Cost Savings

Don’t Forget The ABCs

- **A** = Aspirin (if over age 50)
- **B** = Blood Pressure
- **C** = Cholesterol
**BP Goals:**

- SBP <140
- SBP <130 if can achieve without undue treatment burden, such as younger pts.
- DBP <80

- Of note, suggest that at least one anti-hypertensive be administered at bedtime

**Lipid Goals:**

- Goal LDL<100 if no overt CVD
- Goal LDL<70 if CVD or >40 with one or more CVD risk factor (fam hx, HTN, smoking, albuminuria)
- HDL > 40 and TG <150 desirable
  
  *However LDL Targeted Statin Therapy Is Preferred Strategy*
Lipids: Statins Trump Other Meds

- Combination Therapy Provides No Additional CVD Benefit Over Statin And Is Not Recommended
- If Goal LDL Not Reached On Max Tolerated Statin, Treat To Goal Of 30-40% Reduction In LDL From Baseline

Coronary Disease

- Screening Asymptomatic Patients Not Recommended
- β-Blocker For At Least 2 Years After MI
- Metformin May Be Used In Patients With Stable Compensated CHF If Renal Function Normal; Avoid If Unstable CHF Or Hospitalized