Glycemic Control

Insulin In The Hospital Setting

- The Evidence For Insulin’s Benefit
- The Mechanism of Insulin’s Benefit
- The Achievement of Insulin’s Benefit
- A Few Cases...

Hyperglycemia In The Setting Of Acute Coronary Syndromes

The Evidence For Tight Glycemic Control In The Critically Sick

- The Early Story
- The Rest Of The Story
Hyperglycemia In The Setting Of Acute Coronary Syndromes
The Evidence For Insulin's Benefit

- Many Observational Studies
- Major Prospective Studies

Hyperglycemia In Critical Illness
From The VA Inpatient Evaluation Center

- From 177 ICUs In 73 VA Hospitals
- 216,000 Patients
- Glycemia Independent Predictor Of Mortality Starting At 1 mg% Above Normal (Normal = 70-110 mg%)  
- True In Medical, Surgical & Cardiac ICUs

DIGAMI Study

620 Randomized to 2 Groups At 19 Swedish Hospitals
- Control: Standard Coronary Care for Their Center
- Intensive: Insulin Glucose Infusion for >24 Hrs for >24 Hrs
  - Target Serum Glucose 126 – 180 mg/dl
  - Multidose (4/day) Insulin for Minimum of 3 Months Following Discharge

Glucose Achieved:
Control  211 mg/dl
Intensive 173 mg/dl

Cardiovascular Risk
Mortality After MI Reduced by Insulin Therapy in the DIGAMI Study

- Standard treatment
- IV Insulin 48 hours, then 4 injections daily

Risk reduction (28%)
P = .011

Low-risk and Not Previously on Insulin (N = 272)
Risk reduction (51%)
P = .0004

Tight Glycemic Control in Diabetic Coronary Artery Bypass Graft Patients Improves Perioperative Outcomes and Decreases Recurrent Ischemic Events

Tight Glycemic Control in Diabetic Coronary Artery Bypass Graft Patients Improves Perioperative Outcomes and Decreases Recurrent Ischemic Events

Glucose Achieved:
- Control: 267 mg/dl
- Intensive: 134 mg/dl

The Effect of GIK Infusion For CABG in Type 2 Diabetes

Other Important Studies
Other Important Studies

- Furnary et al.  
  Prospective Observational Study Of 3554 Diabetic Patients Showing Decreased Mortality After CABG With Better Glycemic Control

- Krinsley  
  Prospective Observational Study Of 800 Patients Before And 800 Patients After Institution Of Tight Glycemic Control, Showing Reduced Mortality And Morbidity In Mixed Med-Surg ICU With Better Glycemic Control


Hyperglycemia In The Setting Of Acute Coronary Syndromes

The Evidence For Tight Glycemic Control In The Critically Sick

- The Early Story
- The Rest Of The Story

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**Glucose-Insulin-Potassium Therapy**

Insulin Therapy for Critically Ill Hospitalized Patients

A Meta-analysis of Randomized Controlled Trials


**Glucose-Insulin-Potassium Therapy**

- Meta-Analysis of 35 Studies
- 8,478 Patients
- Overall, A 15% Reduction In Mortality With GIK

Glucose-Insulin-Potassium Therapy
Control Of Glycemia

- In Trials That Targeted Glucose, 29% Reduction In Mortality With Insulin
- No Benefit When Insulin Was Administered Without Regard To Glucose Levels


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Arch Intern Med 164: 2005-11, 2004

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Effect of Perioperative Insulin Infusion on Surgical Morbidity and Mortality: Systematic Review and Meta-analysis of Randomized Trials
Ann Surg 249: 1574-81, 2009

Benefits and Risks of Tight Glucose Control in Critically Ill Adults
A Meta-analysis
Arch Surg 140: 1022-8, 2005
Characteristics Of Negative Trials

- Lack Of Glycemic Separation

The Issue Of Statistical Power

More Recent Trials

GIST - UK
VISEP
Glucontrol
Characteristics Of Negative Trials

- Lack Of Glycemic Separation
  - Underpowered

Insulin In The Hospital Setting

The days of casual glycemic control for critically ill patients should be over!

So, Reducing Glucose Is Good!!

But how low should we go...
### AACE Position Statement 12/16/03: Hospital Glycemic Goals

**Intensive Care Units:** 110 mg/dL

**Non-Critical Care Units:**
- **Pre-Prandial:** 110 mg/dL
- **Max. Glucose:** 180 mg/dL

### Clinical Benefit Study Year

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### The Leuvan SICU Study

**The New England Journal of Medicine**

Glucose Achieved:
- **Control 153 mg/dL**
- **Intensive 103 mg/dL**

The NICE-SUGAR Study Investigators. *NEJM* 360: 1283-1297, 2009

**NICENG-SUGAR**

*Normoglycemia in Intensive Care Evaluation - Survival Using Glucose Algorithm Regulation*

- 6104 Patients From ICUs of 42 Hospitals in Australia, New Zealand, and North America
- 2 Glycemic Treatment Groups:
  - Insulin Given For Glucose > 180 mg/dl and Stopped For Glucose < 144 mg/dl
  - Glucose Target: 81 – 108 mg/dl
- Median Duration of Treatment 4.2 - 4.3 Days

**Primary Outcome**

Death from Any Cause Within 90 Days After Randomization

90% Power To Detect Absolute Mortality Difference of 3.8% Assuming Baseline Mortality of 30%
The NICE-SUGAR Study Investigators. NEJM 360: 1283-1297, 2009

144±23 mg/dl
115±18 mg/dl

OR 1.14 (CI, 1.02, 1.28)
P = 0.02

CV Death More Common With Intensive Control, 42 vs. 36%, p = 0.02
Number Needed To Harm: 38
Hypoglycemia (<40 mg/dl) More Common With Intensive Control, 6% vs. 0.5%, p < 0.001
NICE-SUGAR
Normoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation

Intensive Glycemic Control Led To No Difference In
- Single or Multiple Organ Failure
- Number Of Ventilator Days
- Renal Replacement Therapy
- Positive Blood Cultures
- RBC Transfusion

The NICE-SUGAR Study Investigators. NEJM 360: 1283-1297, 2009

Insulin In The Hospital Setting

The days of casual glycemic control for critically ill patients should be over!

AACE Position Statement 12/16/03: Hospital Glycemic Goals

Intensive Care Units: 110 mg/dL

Non-Critical Care Units:
  Pre-Prandial 110 mg/dL
  Max. Glucose 180 mg/dL
**ADA/AACE Consensus Statement on Inpatient Glycemic Control 2009**

- **Critically Sick Patients**
  - Threshold to Start Insulin Therapy No Greater Than 180 mg%
  - On Therapy Goal Is 140-180 mg%

- **Non Critically Sick Patients**
  - Pre-Meal < 140 mg%
  - Random < 180 mg%

Moghissi, E et al. Endocrine Practice May/June, 2009

---

**Insulin In The Hospital Setting**

*The Evidence For Insulin’s Benefit*

**Question:**

Does Hyperglycemia, New Or Established, Predict Mortality

---

**Hyperglycemia: An Independent Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes**

- **Question:** Does Hyperglycemia, New or Established, Predict Mortality?
- 2030 Consecutive Records of Adults Admitted to Georgia Baptist Hospital
- Hyperglycemia: FBG ≥ 126 mg/dl or Random Glucose ≥ 200 mg/dl
- **New Hyperglycemia 223 Pts. (12%)**

Umpierrez GR et al. J Clin Endocrinol Metab 2002; 87:978
Hyperglycemia: An Independent Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes

1.7% 3.8% 16.0%
0% 5% 10% 15% 20%

Normoglycemia Known Diabetes New Hyperglycemia

Umpierrez GR et al. J Clin Endocrinol Metab 2002; 87:978

A Marker of In-Hospital Mortality in Patients with Undiagnosed Diabetes

- New Hyperglycemia Patients ~3 x’s As Likely to Be Admitted to ICU
- New Hyperglycemia Patients Had Twice the Length of Stay

Umpierrez GR et al. J Clin Endocrinol Metab 2002; 87:978

Glycemic Control

- The Evidence For Insulin’s Benefit
- The Mechanism of Insulin’s Benefit
- The Achievement of Insulin’s Benefit
- A Few Cases…
Beneficial Effects Of Insulin In The Critical Care Setting

- Hyperglycemia Is Bad
- Since Insulin Reduces Glucose, It Is Good…
- But Beyond Glucose…

Insulin In The Critical Care Setting

- Vasodilates
- Acts As Metabolic Modulator
- Enhances Cell Survival
- Restrains Platelets
- Promotes Fibrinolysis
- Enhances Granulocyte Function
- Is A Potent Anti-Inflammatory Agent

Glycemic Control

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- A Few Cases…
IV Insulin Infusion Protocols

IV Insulin Protocol Based On Insulin Sensitivity

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</table>

Algorithm 6

Algorithm 5

Algorithm 4

Algorithm 3

Algorithm 2

Algorithm 1
Insulin Drip Algorithm

< 70 Off
70-109 0.2
110-119 0.5 Suppose The Patient
120-149 1.0 Starts With BG = 254 mg/dl
150-179 1.5
180-209 2.0
210-239 2.0
240-269 3.0
270-299 3.0
300-329 4.0
Etc.

Suppose The Patient
Starts With BG = 254 mg/dl

But After 1 Hour The BG
Remains About The Same

Insulin Drip Algorithm

< 70 Off
70-109 0.2
110-119 0.5 Suppose The Patient
120-149 1.0 But After 1 Hour The BG
150-179 1.5 Remains About The Same
180-209 2.0
210-239 2.0
240-269 3.0
270-299 3.0
300-329 4.0
Etc.

Etc.

Etc.

The Next Algorithm

< 70 Off < 70 Off
70-109 0.2 70-109 0.5
110-119 0.5 110-119 1.0
120-149 1.0 120-149 1.5
150-179 1.5 150-179 2.0
180-209 2.0 180-209 3.0
210-239 2.0 210-239 4.0
240-269 3.0 240-269 5.0
270-299 3.0 270-299 6.0
300-329 4.0 300-329 7.0
Etc. Etc.
**Recommended IV Fluids**

To Prevent Hypoglycemia, Hypokalemia & Ketosis:

- Glucose: 5-10 gms/hour
- Potassium: 20 meq/L
- The Primary Service Should Choose the Type and the Rate of the Fluid Depending on the Underlying Disease

---

**Life After The Drip....**

Transition From IV to SQ Insulin In The Adult Patient

---

**Basal - Bolus**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Basal Glucose</th>
<th>Prandial Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-8 A.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9-11 A.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12-2 P.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3-5 P.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6-8 P.M.</td>
<td>0</td>
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</tr>
<tr>
<td>9-11 P.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12-2 A.M.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3-5 A.M.</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

---

- Bolus Insulin
- Basal Insulin
- Prandial Glucose
Currently Available Basal Insulins

- Neutral Protamine Hagedorn (1946)
- Insulin Glargine (2001)
- Insulin Detemir (2006)

NPH/Reg Vs. Glargine Insulin After Cardiovascular Surgery

Yeldandi, R et al Diabetes Technology & Therapeutics 8: 609-616, 2006

Transition to SQ: An Approach

To Transition A Patient From An IV Insulin Infusion To SQ Insulin
Multiply Last Drip Dose By 20, And Give This Amount As Glargine
Turn The IV Drip Off 2 Hours Later
Example: Last Drip Dose Is 1.0 Unit/Hour; Give 1.0 × 20 = 20 Units Of Glargine SQ; Discontinue Drip Two Hours Later

This Is Basal Insulin

Basal - Bolus

Transition From IV to SQ Insulin In The Adult Patient

- Basal Insulin
- Bolus Insulin
- Prandial Insulin
- Correction Factor Insulin
Currently Available Bolus Insulins

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

Insulin Profiles

First, The Prandial Dose...
When Patient Is Able To Eat,

- Add Rapid Acting Insulin For Mealtime Coverage
- Rule Of Thumb
  - 50% Basal
  - 50% Prandial, Divided Over 3 Meals

Example: Patient Is On 20 Units Glargine Daily; Give 7 Units With Each Meal Of Lispro (Humalog) Or Aspart (Novolog) Or Glulisine (Apidra)

This Is Prandial Insulin

Basal-Bolus Insulin Therapy: Glargine at HS and Mealtime Insulin Lispro, Aspart, Or Glulisine

Insulin Effect

- Lispro/Aspart/Glulisine
- Glargine

7 units

20 units
Transition From IV to SQ
Insulin In The Adult Patient

- Basal Insulin
- Bolus Insulin

Prandial Insulin
Correction Factor Insulin

Correction Factor Dose, Added To Prandial Dose

<table>
<thead>
<tr>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Insulin Dose &lt;40 units/day</td>
<td>Total Insulin Dose 40-80 units/day</td>
<td>Total Insulin Dose &gt;80 units/day</td>
</tr>
<tr>
<td>Premeal BG</td>
<td>Additional Insulin</td>
<td>Premeal BG</td>
</tr>
<tr>
<td>120-170</td>
<td>1 unit</td>
<td>120-170</td>
</tr>
<tr>
<td>171-220</td>
<td>2 units</td>
<td>171-220</td>
</tr>
<tr>
<td>221-270</td>
<td>3 units</td>
<td>221-270</td>
</tr>
<tr>
<td>271-320</td>
<td>4 units</td>
<td>271-320</td>
</tr>
<tr>
<td>&gt;320</td>
<td>5 units</td>
<td>&gt;320</td>
</tr>
</tbody>
</table>

What About Patients Admitted With Hyperglycemia On The Floor?
A Word on In-Patient Sliding Scale Management...

Sliding Scale
Episodic Bolus Insulin
WITHOUT Basal Insulin

Basal Bolus Versus SSI
Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes The RABBIT 2 Trial

- 130 Type 2 Diabetic Patients Admitted to General Medicine Services
- Managed By Internal Medicine Residents Who Received A Copy Of Assigned Treatment Protocol
- Basal-Bolus Regime With Glargine And Glulisine Compared To SSI

Umpierrez, G. et al Diabetes Care 30: 2181-2186, 2007
Basal Bolus Versus SSI
Randomized Study Of Basal-Bolus Insulin Therapy In The Inpatient Management Of Patients With Type 2 Diabetes
The RABBIT 2 Trial

- Glucose Difference Between Groups 27 mg% (p < 0.01)
- Percentage Of Patients At Target (< 140 mg%)
  Basal Bolus       SSIBasal Bolus       SSI
  66%              38%
- No Difference In Hypoglcemia (<0.5%)

Umpierrez, G. et al Diabetes Care 30: 2181-2186, 2007
**Starting Basal-Bolus From Scratch**

*Calculate Starting Total Daily Dose (TDD)*

- Previous Total Daily Insulin Units Used or
- 0.4 units/kg (Type 1 DM)
- 0.6 units/kg (New Onset Or Lean Type 2)
- 0.8 units/kg (Type 2 DM)

*This Is Very Conservative and Actual Needs May Turn Out to Be Substantially More*

---

**Starting Basal-Bolus From Scratch**

*Basal Insulin = ½ TDD*

Give All of Calculated Glargine Dose Q 24h

Goal: FBS And Pre-Meal Glucose = 80-110 mg/dl

*Bolus Doses = ½ TDD*

Prandial Dose + Correction Factor

**AFTER THE MEAL**

Goal: 2h Post-Prandial <180 mg/dl

---

**Median inpatient glucose levels**

*Definition: Median inpatient glucose levels in patients with diabetes. Glucose readings below 40mg/dL and above 400mg/dL were excluded. Data Source: Clarity database, FORCE database.*

*Analysis: The median inpatient glucose value, which was previously stable with a median of 157mg/dL, has decreased, and continues to decrease, with the implementation of inpatient insulin protocols.*
A Word About Oral Agents...

Therapy of Type 2 Diabetes Mellitus: Hospital Use of Oral Agents

<table>
<thead>
<tr>
<th>Category</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretagogues</td>
<td>Not for Acute Illness With Variable Intake</td>
</tr>
<tr>
<td>α Glucosidase Inhibitors</td>
<td>Not for Acute Illness With Variable Intake</td>
</tr>
<tr>
<td>Metformin</td>
<td>Hold for Acute Illness of Renal, Cardiac, or Liver Function Unstable, or Surgery, or Radiocontrast</td>
</tr>
<tr>
<td>Glitazones</td>
<td>Can Give or Not</td>
</tr>
</tbody>
</table>

Have A Discharge Plan
**Can A Patient Go Back To Oral Agents At Discharge?**

- If Pre-Admission Control Acceptable, YES!!!
- Admission HbA1C Helpful
- If Not At Goal on Maximum Oral Agents, Needs Adjustment

**Glycemic Control**

- The Evidence For Insulin’s Benefit
- The Mechanism of Insulin’s Benefit
- The Achievement of Insulin’s Benefit

**A Few Cases…**

**Floor Patient**

- 65 y/o male with DM2, hyperlipidemia, HTN, and DJD
- Admitted to General Medicine with chest pain
- Metformin 1000mg BID and glipizide 5mg BID; HbA1c 6.4% 2 weeks ago
- Glucose on floor arrival 275 mg/dl
- Admit orders
  - Serial troponins
  - Possible adenosine myoview
Floor Patient

- 65 y/o male
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl
- Admit orders
  - Serial troponins
  - Possible adenosine myoview

What should be started to control glucose?
- a) Metformin only
- b) Glipizide only
- c) Metformin and glipizide
- d) Glargine and log
- e) Insulin and metformin
- f) Insulin and glipizide

Floor Patient

- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl
- Admit orders
  - Serial troponins
  - Possible adenosine myoview
- Start glargine and log

What would be the insulin doses?
1) 75 kg patient
2) 75 x 0.8 = 60 units insulin total
3) 60 / 2 = 30 units
4) 30 units basal (glargine)
5) 30 units prandial (log) -- 10 units after each meal
6) Medium dose correction factor

Floor Patient

- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl
- Admit orders
  - Serial troponins
  - Possible adenosine myoview
- Start glargine and log

Patient NPO after midnight for adenosine myoview

How should insulin orders be changed once he is NPO?
- a) Stop all of the insulin
- b) Hold the prandial log only, continue glargine and correction scale
- c) Hold the glargine only, continue log and correction scale
Floor Patient
- 65 y/o male (75kg)
- DM2, hyperlipidemia, HTN, and DJD
- Metformin 1000mg BID and glipizide 5mg BID
- HbA1c 6.4%
- Glucose 275 mg/dl

Patient NPO after midnight for adenosine myoview
Reversible defect on myoview led to stent

With which diabetes medication(s) should the patient be sent home?
- Glargine and log
- Metformin 1000mg BID and glipizide 5mg BID
- Insulin pump

ICU Patient
- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Metformin 1000mg BID, glipizide 10mg BID, rosiglitazone 8mg qday
- HbA1c 8% 3 months ago
- Glucose on MICU arrival 230 mg/dl
- What therapy should be started for glucose control?
  a. Continue metformin and glipizide
  b. Start glargine and log
  c. Start an insulin drip

ICU Patient
- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started

What diabetes lab should be ordered?
- Urine microalbumin
- Hemoglobin A1c
- Nothing
ICU Patient
- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started

How should new diet be covered?
- a) Adjust the insulin drip
- b) Continue the drip, start SC log with carbohydrate counting
- c) Continue the drip, restart glipizide

ICU Patient
- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What about insulin orders?
- a) Continue the insulin drip
- b) Stop the drip, start sliding scale log
- c) Stop drip, start glargine/log

ICU Patient
- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What are the insulin doses, assuming last drip dose was 1.5 units/hour?
- Glargine (1.5 units x 20 = 30 units)
- Log (30 units / 3 = 10 units)
- 10 units after each meal
- Medium dose correction factor
**ICU Patient**

- 65 y/o female with DM2, HTN, & hyperlipidemia
- Admitted to the MICU with sepsis
- Glucose on MICU arrival 230 mg/dl
- Insulin drip started
- Clear liquids started
- Transferring to Gen Med

What happens to the insulin drip?

Discontinue the insulin drip 2 hours after glargine injected

**Former ICU, Now Floor, Patient**

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor
- Second morning on the floor
  - Fasting glucose 138 mg/dl

**ADA/AACE Consensus Statement on Inpatient Glycemic Control 2009**

- **Critically Sick Patients**
  - Threshold to Start Insulin Therapy No Greater Than 180 mg%
  - On Therapy Goal Is 140-180 mg%
- **Non Critically Sick Patients**
  - Pre-Meal < 140 mg%
  - Random < 180 mg%

Meghissi, E et al Endocrine Practice May/June, 2009
**Former ICU, Now Floor, Patient**

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor
- Second morning on the floor
  - Fasting glucose 138 mg/dl
  - Increase next glargine dose to 34U

---

**Adjust Basal Insulin By FBS:**

- Decrease 4 U if FBS are below 60 mg/dL
- Decrease 2 U if FBS is 60-80 mg/dL
- Increase 6 U if FBS is 141 to 160 mg/dL
- Increase 8 U if FBS is 161 to 180 mg/dL
- Increase 10 U if FBS is > 180 mg/dL

*Or Adjust Based On Previous Days Correction Factor Doses*

---

**Former ICU, Now Floor, Patient**

- 65 y/o female with DM2 and sepsis
- Glargine 30 units daily and log 10 units TID
- Medium dose correction factor
- Second morning on the floor
  - Fasting glucose 138 mg/dl
  - Increase next glargine dose to 34U

- Third morning on the floor
  - Fasting glucose 110mg/dl
  - Continue glargine 34 units
Former ICU, Now Floor, Patient

- Patient going home!!
- Glargine 34 units daily and log T1 units TID
- Medium dose correction factor
- HbA1c 9%

**How should her diabetes medication(s) be adjusted?**

- a) Discontinue insulin and restart oral medications
- b) Reintroduce metformin and rosiglitazone to insulin
- c) Continue insulin only

Glycemic Control

- The Evidence For Insulin’s Benefit
- The Mechanism of Insulin’s Benefit
- The Achievement of Insulin’s Benefit
- A Few Cases…