Getting Away from Sliding Scale Insulin
A system-based approach to improve patient outcomes in the inpatient setting
Andrew Ahmann, MD
Harold Schnitzer Diabetes Health Center

Time For A Reality Check
- Diabetes and hyperglycemia are common in the hospital
- Hyperglycemia negatively impacts hospital outcomes
- Glucose goals are somewhat uncertain
- The key is balance between control of hyperglycemia and avoiding hypoglycemia
- Practical approaches have evolved
- Special situations require modifications

Hyperglycemia in the Hospital
- Diabetes:
  - Previously diagnosed
  - Previously undiagnosed
    - HbA1c > 6.5% during admission
- Hyperglycemia without diabetes diagnosis
  - Diabetes diagnosed on follow-up
  - Prediabetes with overt hyperglycemia during acute physiologic stress
  - Hyperglycemia due to physiologic stress without underlying metabolic abnormality
    - normal follow-up testing

Hyperglycemia In The Hospital
- Mortality = 16%
- Mortality = 11%
- Mortality = 63%
- Diabetes
- New Hyperglycemia
- Normal

Hyperglycemia due to physiologic stress without underlying metabolic abnormality

Action And Reaction Over A Decade
- Before 2001 – talk but no action
  - Some evidence for concept

Detrimental Physiologic Impact of Hyperglycemia
Metabolic stress response
- Stress hormones and peptides
- Glucose
- FFA
- Ketones
- Lactate
- Reactive O2 species
- Transcription factors
- Secondary mediators
- Platelet aggregation
- IPA activity
- PAI levels

Thirty-Day Mortality and In-Hospital Complication Rates are Increased in Surgical Patients with Diabetes


Nosocomial Infection Rates Within The First 14 Postoperative Days after Elective Surgery


Hospital Mortality Rates and Glucose Levels in Non-ICU Patients

Absolute risk of adverse outcome (death or prolonged stay) increased 15% per 18-mg/dL increase in glucose levels


Improved Outcomes with Basal-Bolus Insulin in Non-ICU Surgical Patients

Umpierrez et al  Diabetes Care  2011; 34:256-261

Portland Diabetes Protocol: Insulin Infusion Reduces DSWI


Action And Reaction Over A Decade

Before 2001 – Talk but no action
2001 – Van den Berghe SICU study
– Prompted accelerated efforts to improve inpatient glucose control
Intensive Insulin Therapy in the Surgical ICU
Improved Survival

<table>
<thead>
<tr>
<th>Days After Admission</th>
<th>Survival in ICU %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>96</td>
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<tr>
<td>40</td>
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<td>84</td>
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<td>80</td>
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<td>76</td>
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<tr>
<td>140</td>
<td>72</td>
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<tr>
<td>160</td>
<td>68</td>
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<tr>
<td>180</td>
<td>64</td>
</tr>
</tbody>
</table>

Mortality ↓ 42%, P = .04

<table>
<thead>
<tr>
<th>Days After Admission</th>
<th>In-Hospital Survival %</th>
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<tr>
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</tbody>
</table>

Mortality ↓ 34%, P = .01


Glycemic Targets in Hospitalized Patients in 2005

**AACE/ ACE Targets**
- Intensive care unit
  - 110 mg/dL
- Medical/surgical floors
  - 110 mg/dL preprandial
  - 180 mg/dL maximal glucose

**ADA Targets**
- Critically ill
  - As close to 110 mg/dL as possible and usually under 180 mg/dL
- Noncritically ill
  - Premeal glucose 90-130 mg/dl
  - Postprandial glucose < 180 mg/dl

*ADA Standards of Medical Care* Diabetes Care 2006; http://www.aace.com/pub/ICC/inpatientStatement.php

**Action And Reaction Over A Decade**

- **Before 2001** – talk but no action
- **2001** – Van den Berghe SICU study
  - Prompted accelerated efforts to improve inpatient glucose control

Institutional system changes ensued as hospitals attempted to achieve improved glucose control

**System Changes to Improve Glucose Control**

- Multidisciplinary teams/ committees
  - Nursing
  - Hospitalists
  - Anesthesiology
  - Surgeons
  - Pharmacists
  - Quality Assurance
  - Others
- Protocol development
  - ICU insulin infusions
  - Optimal subcutaneous insulin including special situations
  - Transitions
- Forms (orders, flowsheets, kardex)
- Education/ training for all involved individuals
- Monitoring/ glucometrics

**Glucometrics: Guiding Success**

- Data collection:
  - Automatic or manual
  - Must be validated (reviewed)
- Primary parameters
  - Efficacy (according to goals)
  - Safety (frequency of hypoglycemia at various levels)
- Multiple options for meaningful expression
- The process is greatly aided by advancing technology, particularly relating to EMRs


**Glucometrics**

- more easily determined by IT systems with EMR -

Oregon Health & Science University
Strategies To Improve Glucose Control

- Staff education to facilitate change in practices
- Hospital protocols to include all staff providers
  - Paper vs computerized
- Glycemic consult team
  - Diabetes educator driven
  - NP or Pharm D model
  - Endocrinologist model
  - Hospitalists
    - Alone
    - In concert with an endocrinologist and nurse.
  - Hybrids

Hospitalist Based Glycemic Treatment Team Improves Mean Full Hospitalization CBG in Surgical Patients

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Month</th>
<th>Mean Full Hospitalization CBG (mg/dL)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-6 to 0</td>
<td>196</td>
<td>36</td>
</tr>
</tbody>
</table>

**Glycemic Treatment Team**

|          | 0 to 3 | 165* | 29 |
|          | 12-15  | 162**| 22 |

*p<0.005, **p<0.001 vs. baseline

Action And Reaction Over A Decade

- **Before 2001** – talk but no action
- **2001** – Van den Berghe SICU study
- **2003** – AACE guidelines with ICU goal <110
  - ADA involved but slightly modified the guidelines
- **2004** – ADA Technical Review published
- **2004-2008** – Incomplete studies and many questions
  - Meta-analyses failed to confirm generalized value of intensive therapy in the ICU

Characteristics of These Studies

- Many used modifications of the Leuven protocol extended to a multicenter trial
- High frequency of hypoglycemia
  - 10-20% of patients having a glucose <40 mg/dl
- In most cases the targets were not met
- Control group targets were lower
- Most of the studies stopped early (underpowered) but didn’t show statistical differences
- Raise questions of the consequences of hypoglycemia

Glucose Control in the ICU/CCU: The Questions

<table>
<thead>
<tr>
<th>Trial</th>
<th>Setting</th>
<th>G1 Target</th>
<th>G2 Achieved*</th>
<th>G2 Achieved**</th>
<th>End Points</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIGAMI2 2006</td>
<td>ICU (2004-2005)</td>
<td>110-140 mg/dL (6-8 mmol/L)</td>
<td>70 mmol/L</td>
<td>14.5%</td>
<td>30.9%</td>
<td>3.04 (1.6-5.8)</td>
</tr>
<tr>
<td>Van der Berghe 2006</td>
<td>ICU (2001-2002)</td>
<td>80-110 mg/dL (4.4-6.1 mmol/L)</td>
<td>78 mmol/L</td>
<td>18.5%</td>
<td>24.7%</td>
<td>2.42 (0.98-6.0)</td>
</tr>
<tr>
<td>ISS 2006</td>
<td>ICU (2004-2005)</td>
<td>80 mmol/L</td>
<td>60-70 mmol/L</td>
<td>34.6%</td>
<td>37.9%</td>
<td>1.19 (0.8-1.8)</td>
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<td>Goellner 2007</td>
<td>ICU (2005-2007)</td>
<td>80 mmol/L</td>
<td>60-70 mmol/L</td>
<td>41.9%</td>
<td>45.9%</td>
<td>1.21 (0.36-4.4)</td>
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<td>23.4%</td>
<td>26.0%</td>
<td>1.3% (0.8-2.1)</td>
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The Story of Inpatient Glucose Control Over the Last Decade (cont)

2009 – Nice Sugar study completed
- Accentuated concerns about intensive therapy in ICU

2009 – New Guidelines from AACE / ADA
- Target glucose 140-180 mg/dL

AACE/ADA Target Glucose Levels in Non–ICU Patients
- Premeal glucose targets <140 mg/dL
- Random BG <180 mg/dL
- To avoid hypoglycemia, reassess insulin regimen if BG levels fall below 100 mg/dL
- Occasional patients may be maintained with a glucose range below and/or above these cut-points

Hypoglycemia = BG <70 mg/dL
Severe hypoglycemia = BG <40 mg/dL

AACE/ADA Target Glucose Level in ICU Patients
- Starting threshold of no higher than 180 mg/dL
- Once IV insulin is started, the glucose level should be maintained between 140 and 180 mg/dL
- Lower glucose targets (110-140 mg/dL) may be appropriate in selected patients
- Targets <110 mg/dL or >180 mg/dL are not recommended

NICE-SUGAR Study: Results
- 3054 received ITT goal: 81-108 mg/dL
- 3050 received CIT goal: <180 mg/dL

- 90-day mortality: ITT, 829 patients (27.5%); CIT, 751 (24.9%)
- Absolute mortality difference: 2.6% (95% CI, 0.4-4.8)
- Odds ratio for death with ITT: 1.14 (95% CI, 1.02-1.28; P =.02)


The Story of Inpatient Glucose Control Over the Last Decade (cont)

2009 – Nice Sugar study completed
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AACE/ADA Target Glucose Consensus Statement

- Starting threshold of no higher than 180 mg/dL
- Lower glucose targets (110-140 mg/dL) may be appropriate in selected patients

Hypoglycemia =  BG <70 mg/dL
Severe hypoglycemia =  BG <40 mg/dL

New Guidelines from ACP
- Target glucose 140-200 mg/dL
- Partly the result of Kansagara et al systematic review

Question of wrong message
- Intensive therapy in ICU patients defined by a goal < 110 mg/dL with present insulin infusions is not advisable.
Possible Reasons The Studies Failed to Show Benefit of Tight Glucose Control
- The general hypothesis is wrong.
- Normal glucose levels are bad for some groups.
- The adverse effects of hypoglycemia offsets the benefits of improved mean glucose.
- Glucose variability reduces the benefits of lower mean glucose.

Hyperglycemia-related Mortality in the ICU is Related to Disease State
Study of 259,040 admissions to VA ICUs

Significant Association:
- Unstable angina
- Acute MI
- CVA
- Arrhythmia
- Respiratory failure
- GI bleed
- Pneumonia
- Sepsis
- Acute renal failure
- CVA
- PE
- Colectomy
- Vae surgery
- Gout surgery

Not statistically associated
- COPD
- Hepatic failure
- GI bleed
- GI perforation
- Peripheral arterial bypass
- Muscle skeletal problems
- CABG
- Amputation
- Hip fracture


What Are Some Possible Contributory Factors if Hypoglycemia is the Problem?
- Some disease states are prone to adverse effects of hypoglycemia.
- POC monitoring accuracy is inadequate to support tight glucose goals.
- Our insulin infusion algorithms are inadequate to reach goals without excess hypoglycemia and variability.

POC Meter Interferences

<table>
<thead>
<tr>
<th>Glucose Oxidase</th>
<th>Glucose Dehydrogenase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood</td>
<td>-</td>
</tr>
<tr>
<td>Arterial blood</td>
<td>-</td>
</tr>
<tr>
<td>Capillary blood</td>
<td>-</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>-</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>-</td>
</tr>
<tr>
<td>Hypotension</td>
<td>-</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>-</td>
</tr>
<tr>
<td>Dopamine</td>
<td>-</td>
</tr>
<tr>
<td>Mannitol</td>
<td>-</td>
</tr>
</tbody>
</table>


Dungan K et al. Diabetes Care 2007  30:403
Assessment on POC Glucose in Hospital

- POC testing with meters is common in the acute care setting to direct IV insulin infusions.
- Present accuracy in this setting could contribute to hypoglycemia with intensive targets.
- Advances in glucose meters are likely to help this problem.
- For now, other methods are preferred for tight targets of < 110 mg/dl.

Controlling Glucose In The Hospital
Practical Aspects

Recommendations for Managing Inpatient Hyperglycemia

Antihyperglycemic Therapy

Insulin
- Recommended
- Critically ill patients in the ICU

OADs
- Not Generally Recommended
- Non-critically ill patients

IV Insulin
- NPH 2-4 times daily
  - Give 50% for meals if eating
  - Apportion according to relative meal size
  - Can give after the meal if intake uncertain

SC Insulin
- Detemir (12-24 hours)
  - Can give after the meal if intake uncertain

Insulin Requirements in Health and Illness

Insulin Time-action profiles Duration

Aspart, Lispro, Glulisine (4-6 hours)

starting insulin in the hospital

Patient Previously on Oral Agents

- Consider a 24 hour insulin dose of 0.5-0.6 units/kg/day
  - Lower dose in elderly and thin
- Give 50% of this as basal
  - Glargine or detemir once daily
  - NPH 2-4 times daily
- Give 50% for meals if eating
  - Apportion according to relative meal size
  - Can give after the meal if intake uncertain
- Use supplemental scale and adjust

**Sliding Scales: An Addiction We Can’t Overcome?**

Sliding “Scare” insulin doesn’t work well.

---

**Randomized Basal Bolus versus Sliding Scale Regular Insulin in patients with type 2 Diabetes Mellitus (RABBIT-2 Trial)**

- D/C oral antidiabetic drugs on admission
- Starting total daily dose (TDD):
  - 0.4 U/kg/d x BG between 140-200 mg/dL
  - 0.5 U/kg/d x BG between 201-400 mg/dL
- Half of TDD as insulin glargine and half as rapid-acting insulin (lispro, aspart, glulisine)
  - Insulin glargine - once daily, at the same time/day.
  - Rapid-acting insulin - three equally divided doses (AC)


---

**Rabbit 2 Trial: Changes in Glucose Levels With Basal-Bolus vs Sliding Scale Insulin**

Mean overall BG difference between the groups during hospital stay was 27 mg/dL ($P<.01$)

---

**Rabbit 2 Trial: Treatment Success With Basal-Bolus vs Sliding Scale Insulin**

BG target of <140 mg/dL was achieved in 66% using B/B of patients vs 38% using SSI

14% of patients using SSI remained with BG >240 mg/dL and were switched to B/B


---

**Inpatient Diabetes Management: Supplemental Insulin**

- Supplemental insulin is OK -- *sliding scale is not!*
- May use a protocol with various levels of expected insulin sensitivity or use outpatient rules of sensitivity with allowance for stress
- If supplemental doses do not reduce the next glucose to < 150 mg/dL, increase the scale appropriately
- Supplemental requirements should be reviewed each 24 hours and often added to the next day’s baseline dose at the appropriate times

---

**Transition From IV to SC Insulin: Risk For Loss Of Glucose Control**

P<.001

---

IP, intensive insulin protocol.

**Transition of IV to Subcutaneous Insulin Some Dos & Don’ts**

- Place patients needing significant IV insulin doses on physiologic insulin regimens (meal plus basal).
- Don’t use basal insulin alone in patients with very poor control on two or more oral agents.
- Use correction doses for temporary hyperglycemia.
- Overlap SC and IV to minimize “hyperlglycemia escape” related to short ½ life of IV insulin.
  - Or give 10% bolus of rapid-acting analog at transition
- Use post meal rapid analogs for uncertain ability to consume food.

**Basics of SC Insulin After IV**

**Converting From IV Insulin Infusion to SC In The Hospital Without Rapid Medical Improvement**

- Calculate the IV basal insulin requirement
  - Insulin delivered overnight for 4 hours (stability)
  - Multiply by 6 = 24 hour basal requirement
  - Multiply by 80% to get a safe SC dose /24 hours
    - Example:
      - Overnight the patient averaged 1.2 u/hr = 4.8 u/ 4 hours
      - 4.8 x 6 = 30 units
      - 30 x .8 = 24 units
      - 24 units glargine or detemir before breakfast or bedtime or 24 u N in 2-4 doses
    - Adjust according to overnight glucose control

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**Typical Blood Glucose Pattern With Morning Steroid Therapy**

- Morning glucose is often down to baseline
Inpatient Therapy of Ill Patients Who Have Been on Intravenous Insulin and AM Steroids

- Use intravenous insulin with intravenous glucose until the patient can eat
- Use IV insulin dose of the last 24 hours to estimate the 24 hour SC insulin requirement

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>L</th>
<th>Dinner</th>
<th>HS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular/Analog</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine/Detemir</td>
<td></td>
<td>40%</td>
<td></td>
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</tr>
</tbody>
</table>

Adjust as indicated by CBGs

Treating Steroid Induced Hyperglycemia

U Colorado NPH Approach

- Evaluated 20 patients with CF related DM
  - Given prednisolone in the hospital
  - On glargine + RAA insulin
  - Added NPH to the admission regimen
    - 1 unit per mg of PRED up to 20 mg
    - Add 0.5 u/mg from 21-40 mg
    - Add 0.25 u/mg over 40 mg
  - Compared to increased basal-bolus insulin
  - Both groups had a 40% increase in TDI (90 u/d)
- The group with NPH did better (p < 0.001)


Special Nutrition Considerations

<table>
<thead>
<tr>
<th>Nutrition Method</th>
<th>Insulin Component</th>
<th>Possible Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus tube feedings</td>
<td>Basal insulin 40% of TDD + Nutritional insulin 60% of TDD as RAA</td>
<td>RAA insulin scheduled with each bolus feeding + RAA insulin correction (later increase scheduled) + Basal insulin (glargine or levemir q 12)</td>
</tr>
<tr>
<td>Continuous tube feedings</td>
<td>Basal insulin 40% of TDD + Nutritional insulin as 60% of TDD as divided doses</td>
<td>RAA q 4 hours regular q 6 hours or NPH q 8 hours + Basal insulin</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>Give insulin IV with nutrition</td>
<td>Dose find with IV insulin infusion followed by 80% placed in TPN Plus correction insulin.</td>
</tr>
</tbody>
</table>

RAA = Rapid Acting Analog insulin (aspart, glulisine, lispro)

Features Increasing the Risk of Hypoglycemia in an Inpatient Setting

- Advanced age
- Renal failure
- Liver disease
- Concurrent illness (cerebral vascular accident, congestive heart failure, shock, sepsis)
- Ventilator use
- Concurrent medications (β-blockers, quinolones, steroids, epinephrine)


Events Triggering In-hospital Hypoglycemia

- Transportation off ward, causing meal delay
- Failure to measure blood glucose before insulin doses
- New NPO status
- Interruption of
  - IV dextrose therapy
  - Total parenteral nutrition
  - Enteral feedings
  - Continuous venovenous hemodialysis