

The American Association of Clinical Endocrinologists  
*presents*

## Management of Inpatient Hyperglycemia 2012

Today's Session

*Safe and Effective Use of Insulin*



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## Commercial Support

AACE and The Epsilon Group would like to acknowledge the following companies that have provided support for this educational activity:

Lilly USA, LLC

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## Faculty

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University of Pittsburgh School of Pharmacy  
Director, University Diabetes Care Associates

## Disclosure

Dr. Drab reports that he does not have any relevant financial relationships with any commercial interests. He also reports that his presentation will not include discussion of any investigational or unlabeled use(s) of a product. Dr. Drab has no identified conflicts of interest.



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## Management of Inpatient Hyperglycemia 2012

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### Hyperglycemia is Common in Hospitalized Patients

- Hyperglycemia occurred in 38% of patients admitted to the hospital
  - 26% had known history of diabetes
  - 12% had *no prior* history of diabetes
- Noncritically ill medical/surgical: 38%
- Intensive care units (ICU): 29% - 100%
  - Episode of glucose > 110 mg/mL: 100%
  - Episode of glucose > 200 mg/mL: 31%
  - Mean glucose > 145 mg/dL: 39%



Umpteirez G et al. J Clin Endocrinol Metab. 2002; 87:978-92.; Lovietan CS et al. Diabetes Care. 1998; 21:246.; Kinsley JS. Mayo Clin Proc. 2003; 78:1471-8.; Falgouta M et al. Abstract Presented at: American Diabetes Association 66th Annual Scientific Sessions; Washington, DC; 2006 Jun 11. Abstract 19-1B.

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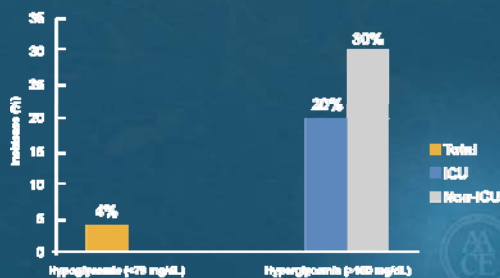
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### Testing Results Show Hyperglycemia Is Common in ICU and Non-ICU Settings



Cook CB, et al. Diabetes Technol Ther. 2007;9(6):493-500.

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## Patients with Diabetes in the Hospital Are Undertreated

- 38% of patients had hyperglycemia while in the hospital
- Of these, two thirds had a previous history of diabetes
  - For these patients,
    - 53% had orders for a special diet
    - 33% were prescribed oral agents
    - 32% received scheduled insulin doses



Umptierrez GE, et al. *J Clin Endocrinol Metab.* 2002;87(3):978-982.

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## Diabetes Care in Hospitalized Non-critically Ill Patients

- More than 20% of hospitalized non-critically ill patients had evidence of sustained hyperglycemia
- 42% of the patients who showed poor glycemic control (glucose >200 mg/dL) during the first 24 hours were discharged in poor control
- Frequency of hyperglycemia was high (25.5 of 100 measurements per person)
- 72% received insulin during hospitalization, but...
  - There was high use of short-acting insulin and less than optimal intensification of therapy
  - Many patients had insulin therapy decreased despite persistent hyperglycemia



Cook CB, et al. *J Hosp Med.* 2007;2(4):203-211.

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## AACE/ADA Recommended Target Glucose Levels in ICU Patients

- **ICU setting:**
  - 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

Not recommended <110*	Acceptable 110 – 180	Recommended 140 - 180	Not recommended > 180
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\* mg/dL

American Association of Clinical Endocrinologists. Available at: <http://www.aace.com/clinicalguidelines>. Accessed March 1, 2011.

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## AACE/ADA Recommended Target Glucose Levels in Non-ICU Patients

- **Non-ICU setting:**
  - 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

Umpletz G et al, J Clin Endocrinol Metabol 97: January 2012

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## Preferred Methods for Managing Hospitalized Persons with Diabetes

- Continuous variable-rate IV insulin drip
  - Regular insulin
- Basal/bolus therapy (MDI)
  - Long-acting and rapid-acting insulin

MDI = multiple daily injections.



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## Increased Hospital Safety Concerns

JCAHO considers insulin to be one of the 5 highest risk medicines in the inpatient setting primarily because the consequences of errors with insulin therapy can be catastrophic

**CMS: Changes to Medicare & Medicaid Services**  
**CMS Moving to Reduce Disastrous but Preventable 'Never Events' in Hospitals**  
August 4, 2008

**Proliferation of insulin combination products increases opportunity for errors**  
November 27, 2002

**Action needed to prevent dangerous HEPARIN-INSULIN confusion**  
May 3, 2007



1. The Joint Commission, <http://www.jointcommission.org>, Accessed January 29, 2009.  
2. The Institute for Safe Medication Practices (ISMP), <http://www.ismp.org>, Accessed January 29, 2009.  
3. New York Media, *Senior Journalist*, Accessed January 29, 2009.

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## Types of Medication Errors with Insulin

1. Prescription/Transcription Errors
2. Dispensing Errors
3. Administration Errors



Adapted from Jackson MA, Reines WG. *US Pharmacist*. 2003;28(6):69-79.

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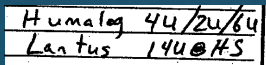
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## Types of Medication Errors

1. Prescription/Transcription Errors
  - Illegible orders
  - Missing or misplaced zeros and decimal points
  - Use of unsafe abbreviations
  - Unintended drug ordered based on variety of drug formulations



Adapted from Jackson MA, Reines WG. *US Pharmacist*. 2003;28(6):69-79.

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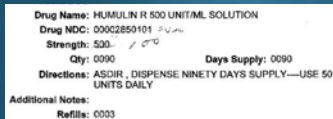
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## Types of Medication Errors

2. Dispensing Errors
  - Look alike/sound alike medications
  - Incorrect preparation
  - Accessibility as floor stock
  - Nonstandard compounded IV solutions and infusion rates



Adapted from Jackson MA, Reines WG. *US Pharmacist*. 2003;28(6):69-79.

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## Types of Medication Errors

### 3. Administration Errors

- Incorrect drug, dose/infusion rate, or timing
- Medication given to the wrong patient
- Incorrect administration technique, route
- Omission errors or extra doses given
- Lack of drug monitoring
- Lack of double checking



Adapted from Jackson MA, Reinos WC. *J Clin Pharm Ther*. 2003;28(6):60-70.

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## Insulin Errors Directly Affect Inpatient Care

- Insulin is a major contributor of injury-induced medication errors within the hospital setting<sup>1</sup>
- Per Institute for Safe Medication Practices (ISMP), 11% of serious medication errors were associated with incorrect insulin administration<sup>2</sup>
- Insulin may be twice as likely to cause patient harm vs. other reported medications based on MEDMARX data compiled by United States Pharmacopeia<sup>3</sup>
- The same errors seen today were documented as far back as 1975<sup>4</sup>
- 80% of inpatient errors are caused by glucose lowering agents and account for 10% of all harmful drug errors<sup>4</sup>

1. Hellman R. *Endocr Pract*. 2004;10(suppl 2):100-108.  
2. Grissinger M. *Pharm Ther*. 2003;28(10):628.  
3. US Pharmacopeia Center for the Advancement of Patient Safety. USP patient safety CAPSLink. July 2003. <http://www.usp.org/pdf/EN/patientSafety/capsLink2003-07-01.pdf>. Accessed January 29, 2009.  
4. Grissinger M. ISMP Teleconference. Prevention Errors with Insulin: A Multidisciplinary Approach.

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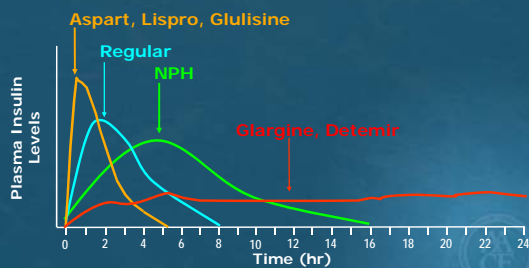
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## Insulin Onset and Duration of Action Affects Inpatient Care



Rosenstock J. *Clin Cornerstone*. 2001;4:50-61.

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## Common Risk Factors for Insulin Errors

- Lack of dose verification
- Mix-up between insulin and heparin vials
- Dangerous abbreviations and dose designations
- Use of the abbreviation "U" in place of "units"
- Handwritten and no carbon required orders
- Sliding-scale orders
- Verbal orders
- Ambiguous orders
- Hold orders
- Wrong infusion rates programmed into infusion pump
- Transcription mismatches

The Joint Commission. *High-alert medications and patient safety*. November 19, 1999. Available at: <http://www.jointcommission.org>. Accessed March 1, 2010.

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## The Potential for Insulin Dosing Errors Using Infusion Protocols

- Multiple protocols have multiple optional starting points
- Instructions are lengthy
- May require complex mathematical calculations
- Frequent adjustments in insulin dosing multiply the potential for error through:
  - Misinterpretation of how to use the protocol
  - Order/administered for incorrect patient
  - Failure to recognize a new order
  - Miscalculations
  - Transcription errors
  - Desensitized to frequent alert alarms may lead to delay in testing

Leasa et al. *Intensive and Crit Care Nurs.* 2010; 26(3): 161-168.

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## The Frequency and Effect of Blood Glucose Transcription Mismatches

- Measured the number of transcription errors when entering BG into a computerized insulin dosing calculator
  - 5.3% mismatched pairs (value entered did not match value of BG meter)
  - Mismatched values initiated 93 false alerts and failed to initiate 170 alerts for nurses to notify MDs
  - Low hypoglycemia rate, (1.1%) however, 6% of those BG values were mismatches resulting in 23% higher insulin doses ( $p < .001$ )
  - Low hyperglycemia rate (0.9%), however 13% of those BG values were mismatches resulting in 42% lower insulin doses ( $p < .001$ ).

Campion et al. *Intensive Care Med.* 2010; 36(9): 1566-1570.

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## Clinical Impact of Insulin Misuse in the Hospital Setting

### Hyperglycemia

Underdosing or missed doses can lead to poor outcomes, such as ketoacidosis<sup>1</sup>

Increases risk of morbidity and mortality<sup>2</sup>

Extends length of hospital stay; can lead to ICU admission<sup>2</sup>

### Hypoglycemia

Less common source of morbidity and mortality, vs hyperglycemia in hospitals<sup>1</sup>

Increases risk of starvation ketosis<sup>2</sup>

Associated with unfavorable patient outcomes, ranging from falls and nausea to myocardial ischemia and death<sup>1</sup>

1. Hellman R. *Endocr Pract.* 2004;10(suppl 2):100-108.  
2. Moghissi E. *Cleve Clin J Med.* 2004;71(10):801-808.

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## Factors Increasing the Risk of Hypoglycemia

- Advanced age
- Decreased oral intake
- Chronic renal failure
- Post renal transplant
- Liver disease
- Beta-blockers
- Lack of coordination between dietary and timing of insulin meal dose
- Inadequate monitoring
- Lack of coordination between transportation and nursing
- Hold/indcipherable orders



ACE/ADA Task Force on Inpatient Diabetes. *Diabetes Care* 2009;31(suppl. 1):S1-S110.

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## Suggested Strategies for Improving Safety With Insulin Therapy in the Hospital Setting

- Standardize pharmacy operations<sup>1</sup>
- Educate nursing and support staff<sup>2</sup>
- Implement hospital-wide initiatives<sup>2</sup>
- Encourage communication and collaboration<sup>2</sup>
- Adopt Joint Commission Diabetes Certification program standards<sup>3</sup>

1. US Pharmacopelia Center for the Advancement of Patient Safety. USP patient safety CAPSLink. July 2003. <http://www.usp.org/pdf/EN/patientSafety/capsLink2003-07-01.pdf>. Accessed January 29, 2009.  
2. Hellman R. *Endocr Pract.* 2004;10(suppl 2):100-108.  
3. The Joint Commission. Inpatient diabetes. <http://www.jointcommission.org/CertificationPrograms/Inpatient+Diabetes>. Accessed January 29, 2009.

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## Standardize Insulin Therapy to Reduce Errors

- Single Insulin Infusion Concentration
- Single Insulin Infusion Protocol
- Guidelines for Transitions: IV to Sub Q
- Guidelines for Special Situations
  - Steroid therapy
  - Enteral Nutrition
  - Parenteral Nutrition
  - Patient Transportation & Other Handoffs
  - Pre-procedure (NPO)
  - Hypoglycemia: BG < 70 mg/dL



ACE/ADA Task Force on Inpatient Diabetes. *Diabetes Care* 2009;31(suppl. 1):S1-S110.

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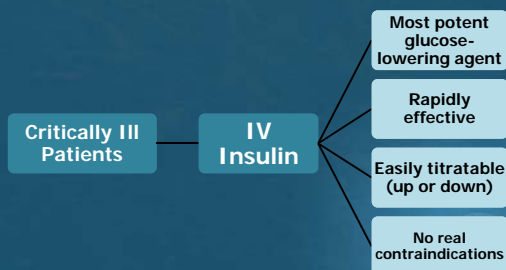
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## Insulin is the Most Appropriate Agent for the Majority of Hospitalized Patients



Moghissi E, et al. *Endocr Pract*. 2009;15:353-369.  
ADA. *Diabetes Care* 2009;32(suppl 1):S1-S110

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## Some Indications for Intravenous Insulin Therapy in the Hospital

- Critical illness (surgical, medical)
- Perioperative period
- Post organ transplant
- Prolonged NPO status in patients who are insulin deficient (T1DM)
- Total parenteral nutrition therapy
- Markedly elevated glucose exacerbated by high-dose glucocorticoid therapy
- Other illnesses requiring prompt glucose control (eg, nonketotic hyperosmolar state, diabetic ketoacidosis)

NPO = nothing by mouth.

Adapted from: Garber AJ, et al. *Endocr Pract*. 2004;10(1):77-82.

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## Characteristics of Safe and Effective IV Insulin Protocols

- **Reaches and maintains** BG successfully within pre-specified target range.
- Includes a **clear algorithm** for making temporary corrective changes in the IV insulin rate, as patient requirements change.
- Incorporates the **'rate of change'** in BG, not just absolute values.
- Incorporates the current **IV insulin rate**.
- Minimizes **hypoglycemia**; provides specific directions for treatment when it occurs.
- Provides specific guidelines for timing / selection of doses for the **transition to SQ insulin**.

ACE/ADA Task Force on Inpatient Diabetes. *Diabetes Care* 2009;31(suppl. 1):S1-S110.

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## Essential Part of Insulin Therapy: Hypoglycemia Protocol

- Clear Definition of Hypoglycemia (BG < 70 mg/dL)
- Nursing Order to Treat **Without Delay**
  1. Stop insulin infusion (if patient is on one)
  2. Oral glucose (if patient is able to take oral) Oral:
  3. IV dextrose or glucagon (if patient is unable to take oral)
  4. Repeat blood glucose monitoring 15 min after treatment for hypoglycemia and repeat treatment if BG < 80 mg/dL
  5. Directions for when and how to restart insulin
- Look for the cause of hypoglycemia and determine if other treatment changes are needed

ACE/ADA Task Force on Inpatient Diabetes. *Endocr Pract* 2006;12:458-468.  
ADA. *Diabetes Care* 2009;31(suppl 1):S1-S110.

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## Essential Part of Insulin Therapy: When to Notify the Physician

- For any hypoglycemia that results in loss of consciousness
- For hypoglycemia that has not resolved after administering 50mL of D50W IV and discontinuing the insulin infusion
- Unexpected changes in blood glucose
- For persistent blood glucose > 300 mg/dL
- Consider endocrinology consult for the most challenging patients.



ACE/ADA Task Force on Inpatient Diabetes. *Endocr Pract* 2006;12:458-468.  
ADA. *Diabetes Care* 2009;31(suppl 1):S1-S110.

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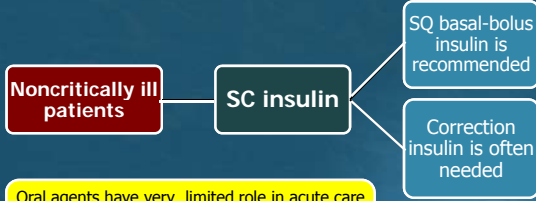
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## Insulin Is the Most Appropriate Agent for the Majority of Hospitalized Patients



Oral agents have very limited role in acute care setting; consider discontinuing in favor of insulin during acute illness

SC = subcutaneous

ACE/ADA Task Force on Inpatient Diabetes. *Endocr Pract*. 2006;12:458-468. ADA. *Diabetes Care*. 2009;31(suppl 1):S1-S110.

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## Considerations with Non-insulin Therapies in the Hospital

- Sulfonylureas/Glinides
- Metformin
- Thiazolidinediones (TZDs)
- DPP-4 inhibitors
- $\alpha$ -glucosidase inhibitors
- GLP1 receptor agonists
- Amylin receptor agonists

*In general, non-insulin agents are suboptimal glucose-lowering agents due to several factors:*

- Contraindications
- Slower onset of action
- Altered nutritional status
- 'Ceiling of effectiveness'

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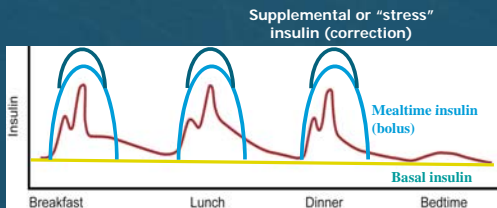
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## Maintaining Physiologic Insulin Delivery in the Hospital



- Basal Insulin for maintenance
- Meal time insulin bolus to cover CHO intake
- Correction bolus if mealtime does not control post-prandial glucose excursion

Clement S et al. *Diabetes Care* 2004;27:553-591

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## Subcutaneous Insulin Therapy

- Principles are borrowed from outpatient therapy
- Provide standing insulin orders
  - Basal / Prandial / Supplemental (correction)
- Assess insulin needs in the context of intercurrent stress / medications affecting glucose
- Do not omit doses for good control or mild hypoglycemia
- Review glucose results and adjust insulin daily
- Review chart for unusual circumstances
  - missed meals, hypoglycemia treatment, late insulin

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## Subcutaneous Insulin Dosing without Prior Intravenous Insulin

- Starting daily insulin doses based on degree of hyperglycemia:
  - 0.4 U/kg/day for BG 140-200 mg/dL
  - 0.5 U/kg/day for BG 201-400 mg/dL
- Divided total daily dose of insulin into 50% basal as long-acting analog and 50% prandial as rapid-acting analog
  - Divide prandial insulin into 3 equal doses

Umplierrez G, et al. *J Clin Endocrinol Metab.* 2009;94(2):564-569.  
Umplierrez G, et al. *Diabetes Care.* 2007;30(9):2181-2186.  
Umplierrez G. *Diabetes Care.* 2009;32(4):751-753.

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## Options for Basal and Prandial Insulin

### Basal Insulin Options

#### Analogs

1. Detemir
2. Glargine

#### Human

1. NPH

### Nutritional Insulin Options

#### Analogs

1. Altered Absorption Characteristics
2. More Physiologic Approach
3. Alleviates the inconvenience and timing issues of NPH & Regular human insulin

#### Analogs

1. Aspart
2. Glulisine
3. Lispro

#### Human

1. Regular

Umplierrez et al. *Diabetes Care.* 30:2181 2007

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## Subcutaneous Insulin Therapy in the Hospital: Practical Guidelines

Programmed/Scheduled		Correction Dose (supplemental)
Basal	Bolus (nutritional)	When BG > target
<ul style="list-style-type: none"> <li>• Long-acting (HS or AM)                             <ul style="list-style-type: none"> <li>• Detemir</li> <li>• Glargine</li> </ul> </li> <li>• Intermediate-acting (HS or BID)                             <ul style="list-style-type: none"> <li>• NPH</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Rapid-acting (AC TID)                             <ul style="list-style-type: none"> <li>• Aspart</li> <li>• Lispro</li> <li>• Glulisine</li> </ul> </li> <li>• Short-acting (AC TID)                             <ul style="list-style-type: none"> <li>• Regular                                     <ul style="list-style-type: none"> <li>• ac (TID)</li> <li>• 30-45 minutes ac</li> </ul> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Rapid-acting                             <ul style="list-style-type: none"> <li>• PRN w/ AC dose</li> </ul> </li> <li>• Short-acting                             <ul style="list-style-type: none"> <li>• PRN w/ AC dose</li> </ul> </li> </ul>
<b>Recommended blood glucose monitoring</b> <ul style="list-style-type: none"> <li>• If patient is eating: AS and HS</li> <li>• If patient is NPO: every 4-6 hours</li> </ul>		

BID = twice daily; AC = before meals; TID = 3 times daily; HS = at bedtime.  
Clement S, et al. Diabetes Care. 2004;27(2):553-591.

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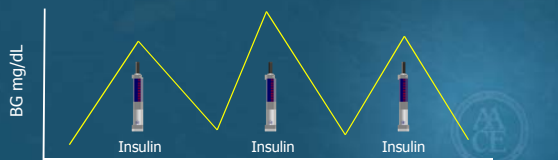
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## Sliding Scale Insulin Regimen

- Sliding-scale insulin (SSI) remains widely used<sup>1</sup>
- Subcutaneous regular human insulin, given as sole modality of insulin Rx, when hyperglycemia occurs<sup>2</sup>
  - Insulin dose based on BG measurements taken 4 times per day before meals and at bedtime<sup>2</sup>
  - Insulin generally is not given until BG is >200 mg/mL<sup>1</sup>



<sup>1</sup>Browning LA et al. *Am J Health-Syst Pharm.* 2004; 61:1611-4.  
<sup>2</sup>Hirsch IB et al. *Resid Staff Physician.* 2007; 53(2).

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## Pitfalls of SSI

- Is reactive, rather than proactive
- Often mismatched with changes in patient's insulin sensitivity
- Does not meet physiologic needs
- Can lead to 'insulin stacking'
  - When several boluses are given in a short period of time; insulin action overlaps, which may cause hypoglycemia



Lavernia F. *Medscape J Med.* 2008;10(9):216.

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## Adopt Diabetes Certification Standards

- The most successful inpatient diabetes programs have the following essential characteristics:
  - Specific staff education requirements
  - Blood glucose monitoring protocols
  - Treatment plans for hyperglycemia and hypoglycemia
  - Data reporting of incidences of hypoglycemia
  - Patient education on diabetes management
  - An identified program champion or team



The Joint Commission. Inpatient diabetes.  
<http://www.jointcommission.org/CertificationPrograms/Inpatient+Diabetes>.  
Approved January 29, 2009.

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## Adopt Joint Commission Diabetes Certification Standards

- Certificate of merit awarded to hospitals that exemplify superior inpatient diabetes management
- Includes adoption of specific American Diabetes Association (ADA) protocols and initiatives to continually improve patient care and outcomes



The Joint Commission. Inpatient diabetes.  
<http://www.jointcommission.org/CertificationPrograms/Inpatient+Diabetes>.  
Approved January 29, 2009.

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## Points to Consider

- What practices do you currently utilize in your hospital to promote a safe patient environment?
- Since insulin is a high-alert medication, what actions can your hospital take to address safety concerns surrounding its use?



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## Summary

- Insulin is the most appropriate agent for majority of hospitalized
- Insulin is a “high alert medication”
- For effective and safe use of insulin, institutions need to consider
  - standardized pharmacy operations
  - Education of nursing and support staff
  - Implementation hospital-wide initiatives
  - Effective communication and collaboration among care givers



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## Questions



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## Resources for More Information

Resource	Contact Information
AACE Inpatient Glycemic Control Resource Center	<a href="http://resources.aace.com/">http://resources.aace.com/</a>
Georgia Hospital Association Diabetes Special Interest Group	<a href="http://www.gha.org/pha/health/diabetes/index.asp">http://www.gha.org/pha/health/diabetes/index.asp</a>
Glucometrics Web site (free service to calculate inpatient glucose control data)	<a href="http://metrics.med.yale.edu/main/">http://metrics.med.yale.edu/main/</a>

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## AACE Inpatient Glycemic Control Resource Center



<http://resources.aace.com/>

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### Part 4 – Management of Inpatient Hyperglycemia: Hyperglycemia Crisis Conditions

Susan S. Braithwaite, MD

February 9, 2012  
1130 AM Eastern  
or  
1 PM Central (10 AM Pacific)

Visit <http://aes.aace.com> for more information and to register.

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