Improving Glycemic Control in Critical Care Units
Outline

• Objectives
• Review of guidelines and targets
• Treatment principles for DKA
• Building a “perfect” protocol, key ingredients
• Transition from IV to SQ with 2 cases
• Key Points
Learning Objectives

• Implement a IV insulin Infusion protocol within a Critical Care Unit.

• Apply better coordination and communication with bedside nursing related to patient nutrition related to delivery of care and calorie/carbohydrate calculations within a Critical Care Unit.

• Develop or improve protocols around IV infusion, DKA order sets, transitioning from IV to subcutaneous insulin, hypoglycemia protocols, transitions of care, and patient/frontline education within a Critical Care Unit.
Guidelines

**Antihyperglycemic Therapy**
Any patient with a blood glucose >180
Check every patient at least once

- **Insulin**
  - Recommended
  - **Intravenous Insulin**
    - Critically ill patients
    - Goal 140-180
  - **Subcutaneous Insulin**
    - Non-critically ill patients
    - Daily Dose
      - Scheduled
        - Basal
      - Nutritional
      - As needed
      - Correctional

- **Oral Hypoglycemics**
  - Not appropriate
Insulin Infusions: Indications

- DKA/HHS; aggressive and intended to lower blood glucose rapidly
- Critical Illness with hyperglycemia; initiate infusion when BG:
  - ADA/AACE: BG >180 mg/dL
  - SCCM: BG >150 mg/dL

1. Diabetes Care 2016; 39 (Suppl. 1):S99-S104
ADA/SCC Target Glucose Levels in Critical Care/ICU Patients

• American Diabetes Association
  – Starting threshold of >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

• Society of Critical Care Medicine
  – Starting threshold of >150 mg/dL and absolutely at 180 mg/dL
  – Use protocol to achieve low rate of hypoglycemia <70 mg/dL
  – Minimal excursions of <100 mg/dL

Not recommended  
<100-110
Acceptable  
110-150
Recommended  
140-180
Not recommended  
>180

1. Diabetes Care 2016; 39 (Suppl. 1):S99-S104
Controversies Around Point of Care Blood Glucose Meters in the ICU

• January, 2014: Food & Drug Administration (FDA) issued draft guidance stating original premarket studies and approval of hospital blood glucose meters were based on over-the-counter home meters and therefore are off-label use

• January, 2014: New York State Department of Health (NYSDOH) sent letters to all hospital and health care facility lab directors notifying them of CMS’s concerns regarding off-label use and possibility of fines.


Controversies Around BG Meters in the ICU (continued)

Timeline:

• May, 2014 Diabetes Technology Society & FDA held public forum in Arlington, VA to discuss controversies and potential consequences of restricting use.

• September, 2014 Nova StatStrip approved for use in critically ill patients with arterial or venous blood only.

• November, 2014 CMS memo warned that off-label use would be subject to citations and fines during hospital site visits.


Controversies Around BG Meters in the ICU (continued)

- March, 2015 CMS issues new memo calling for temporary withdrawal of previous draft guidance and encouraging manufacturers to conduct studies & apply for clearance for use in ICUs.
- October, 2015 Planning Research in Inpatient Diabetes (PRIDE) group published open letter to CMS urging the restrictions be placed on hold giving hospitals and manufacturers time to complete studies.
NYSDOH Recommendations

• Hospitals can continue to use POC BGMs if they perform validation studies and apply for moderate to high complexity certificate from CLIA

• Hospitals can use FDA approved cartridge based analyzers such as epoc or i-stat with critically ill patients

• Since the Jan 2014 memo from NYSDOH, many hospitals have either performed validation studies or use NovaStat.
DKA: Treatment

- Hydration
- Electrolytes
- Insulin
- Co-morbid conditions and/or precipitating factors

Kitabchi Diabetes Care 2006
Fluids

• Normal saline initially, 1-2L in the first hour
• If (corrected) sodium is normal or elevated, use $\frac{1}{2}$ NS thereafter (± dextrose, ± potassium)
  – Dextrose if BG <200
  – Potassium if K is 3.3-5.2
• Monitor
  – Electrolytes, q2h to start
  – Blood pressure
  – Urine output
  – Osmolality if renal or cardiac disease
Electrolytes

- **Potassium**
  - <3.3; replace by IV before insulin
  - 3.3-5.2; add 20-30mEq to IVF
- **Bicarbonate**, only for pH <6.9
  - 3 amps in 1L d5W until pH>7
- **Phosphate**
  - Treat if <1.0mg/dL or if severe cardiac-pulmonary compromise
Insulin Infusion

- Bolus of 0.1 Unit/kg
- Infusion at 0.1 unit/kg/hr
- (Alternatively, infuse at 0.15 units/kg, no bolus)
- Goal is to decrease BG 50-75/hr
- Evaluate hourly and adjust accordingly
- What about the diet?
Diagnostic Work Up

- Urinalysis
- Complete Blood Count
- Electrolytes with calculated anion gap
  - Na – (Cl + CO2)
  - Corrected Sodium
- Osmolality
  - Osmolar gap = Osm – (2xNa + BG/18)
- EKG
- Rule out infection
- Blood Gas (optional)
Insulin Infusions: Highs and Lows

Top Causes of Hyperglycemia in the ICU
- Bad insulin infusion protocol
- Poor utilization of protocol

Top Causes of Hypoglycemia in the ICU
- Bad insulin infusion protocol
- Compliance with the insulin infusion protocol
- Carbohydrate mismatch
- Administration
Ingredients for Insulin Infusion
Order Sets and Protocols

- Identifies the glycemic target range
- Includes clear dosing instructions with acceptable calculation requirements for nurses
- Incorporates glucose monitoring expectations
- Easy physician ordering, check box simplicity
- Criteria for calling the physician
- Includes guidance on steps to follow for interruption of nutrition
- States guidelines on when to initiate the infusion and when to stop
- Defines the insulin concentration clearly and consistently
- Considers changing insulin sensitivity as well as the current glucose value and rate of change in attempting to reach goal and avoid hypoglycemia
- Includes or refers to a standardized hypoglycemia treatment protocol and prevention protocol.
- Incorporates guidelines and cautions for transition to subcutaneous insulin
- Ideally adaptable outside of critical care unit—clear definition of locations where order set is to be used.

J Hosp Med 2008
Ingredients for Insulin Infusion Order Sets and Protocols

Table 2. Components of a Safe and Effective Insulin Infusion Protocol

- Includes appropriate glycemic targets
- Identifies threshold for implementation
- Is nurse-managed and easy to implement
- Provides clear, specific directions for blood glucose monitoring and titration
- Includes titration based on both current blood glucose level and rate of change*
- Is safe: carries a low risk for hypoglycemia and includes an embedded protocol for treatment of hypoglycemia should it occur
- Is effective: gets patients to target quickly and maintains blood glucose within the target range with minimal titration
- Includes a plan for transition to subcutaneous insulin

*Rate of change is calculated based on the slope of the blood glucose trend line and is frequently incorporated into column-based protocols by movement to a more aggressive algorithm if blood glucose is not declining by ~ 40–75 mg/dl or to a less aggressive algorithm if blood glucose is declining too rapidly.
Patient is receiving continuous tube feeds or TPN

Matching Insulin and Intake

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
An interruption in nutrition requires a response!

Mismatched Insulin and Intake

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
You can adjust the insulin

Adjust the Insulin

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
Or start an alternate dextrose source

Matching Insulin and Intake

- Basal Insulin requirements
- Nutritional Insulin Requirements
- Infusion
- Blood Glucose (mg/dL)
Nutrition on Hold Unexpectedly Guideline

This algorithm is a guideline. Contact physician for orders.

Patient on insulin drip

Consider starting D10 at tube feed/TPN infusion rate

(cease patients with cerebral edema or hypotension)

Resume q 1 hour glucose monitoring until glucose is in range for 3 consecutive readings, per MGP 922.1.

If BG < 70 mg/dL or 70-79 mg/dL and asymptomatic,
Follow hospital hypoglycemia protocol

Recheck BG in 15 minutes per protocol.

If >2 consecutive BG < 80 mg/dL, notify MD. Pharmacy may be contacted for further consultation.

Resume q 1 hour glucose monitoring per MGP 922.1.

Patient on subcutaneous insulin

For patient with glargine insulin order:

Continue glargine insulin. Consider reducing the dose by 20% if tight control or high risk of hypoglycemia.

If dose of scheduled nutritional insulin given in past 1-6 hours, increase frequency of glucose monitoring q 1-2 hours until insulin action complete.

Hold future nutritional insulin until nutrition resumes but continue correction insulin.

For patient with routine scheduled nutritional insulin (regular or lispro):

If BG < 70 mg/dL or 70-79 mg/dL and asymptomatic, Follow hospital hypoglycemia protocol.

Recheck BG in 15-30 minutes per protocol.

Notify MD. Consider starting D10 at tube feed/TPN infusion rate. Pharmacy may be contacted for further consultation.

Resume q 4-6 hour and pm glucose monitoring.

Alternatives:

1. Decrease Rate of Insulin Drip - Contact pharmacy to decrease insulin drip. Insulin Sensitivity Coefficient (ISC):
   - If drip > 6 units/hr decrease ISC by 50% and adjust per insulin protocol
   - If drip < 6 units/hr decrease ISC to 0.01 and adjust per insulin protocol

2. Stop insulin drip and start subcutaneous insulin correction scale insulin with q2-4h monitoring. Suggest administering lispro q4h or regular insulin q6h. (Patients with Type 1 Diabetes Mellitus need basal insulin at all times; do NOT use correction scale alone for Type 1 Diabetes Mellitus.)

3. Call Pharmacy for assistance
Alert for TF on hold + Insulin

• Will appear for pt’s w/ “0” charted for TF rate + “on insulin”
• Wording is as follows:

- Potential Problems
  – RNs don’t consistently chart TF interruptions in I/O
  – Charting, if done, not always timely
Laminated pink caution sign has “Nutrition on Hold Unexpectedly Algorithm” On the back for quick reference
Special Case: Eating on an insulin infusion

- **Nutritional Insulin (SubQ analog)**
- **Basal Insulin (infusion)**
Insulin Concentration

• All insulin infusions should be prepared in the pharmacy

• One standard insulin concentration should be used throughout the hospital whenever possible (or confined to certain locations or patient populations if other concentration is clinically indicated)

• Most common concentration recommended is 1 unit/mL

Jacobi Crit Care Med 2012, ASHP, ISMP
# Our Approaches

<table>
<thead>
<tr>
<th></th>
<th>UCSD</th>
<th>VMMC</th>
<th>NYPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order Set (s)</td>
<td>Computer (EPIC)</td>
<td>Computer (Cerner)</td>
<td>Computer (Sunrise)</td>
</tr>
<tr>
<td>Protocol(s)</td>
<td>Computerized-web-based</td>
<td>Paper (3 sets)</td>
<td>Paper (2 sets)</td>
</tr>
<tr>
<td>BG Target</td>
<td>90-150 (ICU) 90-180 (Step-down) 120-200 (OR)</td>
<td>100-180</td>
<td>100-140 (eg SICU) And/or 140-180 (eg Neuro ICU)</td>
</tr>
<tr>
<td>Formula</td>
<td>BG value and rate of change</td>
<td>BG value and rate of change</td>
<td>BG value and rate of change</td>
</tr>
</tbody>
</table>

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### VMMC (Cerner): DKA/HHS Order Set

<table>
<thead>
<tr>
<th>Component</th>
<th>Order Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IV FLUIDS</strong></td>
<td></td>
</tr>
<tr>
<td>Step 1: Resuscitation - Most patient with hyperglycemic crises have moderate to severe dehydration. Begin resuscitation with isotonic normal saline at 1 L/hr up to four hours.</td>
<td></td>
</tr>
<tr>
<td><strong>IV Fluid: Bolus, HOSP</strong></td>
<td></td>
</tr>
<tr>
<td>Step 2: Maintenance while blood glucose is &gt; 200 mg/dL. Supplement potassium in IV fluids if potassium is normal or low, but k+ &gt; 3.1. If k+ &lt; 3.3, then replace potassium by IV prior to starting insulin therapy.</td>
<td></td>
</tr>
<tr>
<td>Sodium Chloride 0.9% 1000 ml + potassium chloride-additive 30 meq</td>
<td>Rate 120 mL/hr, Infuse each bag over 0.7 hr, Volume: 1000 ml, IV, Routine, Start: 08/08/2018 13:18</td>
</tr>
<tr>
<td>Potassium supplementation not required if potassium &gt; 3.3</td>
<td></td>
</tr>
<tr>
<td>Sodium Chloride 0.9%</td>
<td>Rate 120 mL/hr, Volume: 1000 ml, IV, Routine</td>
</tr>
<tr>
<td>Step 3: Maintenance fluid while blood glucose &lt;= 200 mg/dL. Use 0.9% normal saline for patients with a low corrected serum sodium</td>
<td></td>
</tr>
<tr>
<td>Dextrose 5% with 0.9% NaCl</td>
<td>Rate 120 mL/hr, Volume: 1000 ml, IV, Routine. Note: Begin when blood glucose &lt;= 200 for patients with low serum sodium</td>
</tr>
<tr>
<td>Use 0.45% normal saline for patients with a high or normal corrected serum sodium</td>
<td></td>
</tr>
<tr>
<td>Dextrose 5% with 0.45% NaCl</td>
<td>Rate 150 mL/hr, Volume: 1000 ml, IV, Routine. Note: Begin when blood glucose &lt;= 200 for patients with high or normal serum sodium</td>
</tr>
</tbody>
</table>

**Medication(s)**

Pharmacy to Dose medication. Pharmacy will select initial bolus and infusion rate. RN to manage infusion titration per protocol. Contact Pharmacy at d77575 to communicate additional information that may alter standard dosing.

<table>
<thead>
<tr>
<th>Pharmacy to Dose Med</th>
<th>Insulin Infusion - DKA/HHS Protocol, Indications per DKA/HHS insulin protocol, Dose per Pharmacist, IV, Routine, Start: 08/08/2018 13:18, Initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td><strong>Insulin Infusion - DKA/HHS Protocol, Indications per DKA/HHS insulin protocol, Dose per Pharmacist, IV, Routine, Start: 08/08/2018 13:18, Initiation</strong></td>
</tr>
<tr>
<td>&gt;112.4 kg</td>
<td>12.5 units, 12.5 units/hr</td>
</tr>
<tr>
<td>112.5-122.4 kg</td>
<td>12 units, 12 units/hr</td>
</tr>
<tr>
<td>112.5-117.4 kg</td>
<td>11.5 units, 11.5 units/hr</td>
</tr>
</tbody>
</table>

**Details for Pharmacy to Dose Med**

- **Pharmacist to Dose Med:**
  - **Insulin Infusion - DKA/HHS Protocol**
  - **Insulin Infusion - Medical Protocol**
  - **Insulin Infusion - Surgical Protocol**
  - **Insulin Infusion - Bedside IV Protocol**
  - **Insulin Infusion - Other Protocol**
  - **Insulin Infusion - Other Protocol**
  - **Additional Instructions**
  - **Route of Administration:** INS
  - **Priority:** Routine
  - **Duration Unit:** Day
  - **For Insulin Infusion Only:** Initiation
  - **Requested Start Date/Time:** 08/08/2018 13:19
  - **Stop Date/Time:** 
  - **PRN:** Yes
  - **Dose per Pharmacist:** Yes

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HOSPITALISTS. TRANSFORMING HEALTHCARE. REVOLUTIONIZING PATIENT CARE.
# UCSD (Epic): Insulin Infusion Order set

## Order Sets

**IP/ED GEN Intravenous Insusion Therapy**

### Patient Care

- **Patient Care Orders**
  - **Glucose (POC)**
    - Routine, **E**VERY **H**OUR **F**irst occurrence **T**oday at 1400 **U**ntil **S**pecified
    - Check fingerstick glucose hourly per computer protocol. May check glucose every 2 hours if 3 consecutive blood sugars are within the protocol target range.
  - **Nursing Misc Order**
    - Please page pharmacist with insulin computer protocol questions.
    - Routine, **O**NGOING starting **T**oday at 1345 **U**ntil **S**pecified
    - Specify: Please page pharmacist with insulin computer protocol questions.

### Medications

- **Insulin Infusion**
  - **Insulin Infusion**
    - insulin regular (HUMULIN, NOVOLIN) 100 Units in sodium chloride 0.9 % 100 mL infusion
      - IntraVENOUS, CONTINUOUS starting today at 1400 until Discontinued
      - Infuse per insulin computer protocol
  - **And**
    - insulin regular (HUMULIN, NOVOLIN) IV bolus from bag 1-15 Units
      - 1-15 Units, IntraVENOUS, ONCE PRN, 1 dose starting Today at 1331 until Discontinued. Per insulin computer protocol
      - Bolus dose per insulin computer protocol. Do NOT administer a bolus dose upon initiation of the insulin infusion if a separately ordered bolus dose of insulin was administered within the last two hours.
  - **Fingerstick Glucose Orders for Hypoglycemia Protocol**
    - **Glucose (POC)**
      - Routine, PRN starting Today at 1331 until Specified
      - Test blood glucose within 15 to 30 minutes of the initial glucose test showing blood glucose < 70 mg/dL with or without symptoms OR glucose < 80 mg/dL with symptoms (e.g., shakiness, diaphoresis, confusion, irritability). If blood glucose is still below 80 mg/dL after treatment, RETREAT and check blood glucose again in 15 to 30 minutes. Continue to check blood glucose every 15 to 30 minutes until the glucose is greater than or equal to 80 mg/dL for TWO consecutive values.
UCSD: Insulin Infusion Calculator (web-based, lives outside of EPIC)

- RNs utilize the **Insulin Computer Calculator** per UCSD protocol
  - **Log-in** to the secure web-based insulin computer protocol site
  - **Select** the patient’s unit and patient
  - **Enter** the blood glucose levels as directed
  - **Add comments** (as needed) where indicated
UCSD: Insulin Infusion Calculator (web-based, lives outside of EPIC)

• Computer program provides recommendation for bolus and rate on initiation and then recommendations for hourly adjustment of infusion rate per hourly BG checks thereafter.
NYPH Critical Care Drips

[Image of a form for requesting critical care drips, with options for date, time, type, and reason, along with a list of insulin drip medications with their respective costs.]
# Criteria for Transition to SubQ Insulin

<table>
<thead>
<tr>
<th>DKA</th>
<th>HHS</th>
<th>Hyperglycemia in CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG &lt;200</td>
<td>BG &lt;300</td>
<td>Resolution critical illness</td>
</tr>
<tr>
<td>Two of the following:</td>
<td>Normal osmolality</td>
<td>Off vasopressors</td>
</tr>
<tr>
<td>Gap &lt;12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicarbonate &gt;15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH &gt;7.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal mentation</td>
<td></td>
<td>Stable infusion rate for ~6hrs</td>
</tr>
</tbody>
</table>

Kitabchi *Diabetes Care* 2006
Transition to SubQ

• Overlap IV and SubQ by two hours
• Know the home regimen and whether or not this was adequate.
• Formulae
  – Average rate method
  – Weight based dosing
• Insert brain between protocols, formulae and your patient!!
Transition to SubQ Insulin

• Step 1
  • Is patient ready for transition from IV to SubQ insulin?
    – Critical illness resolved? Off pressors?
    – DKA/HHS resolved?
    – Rate stable for ~ 6hrs?
Transition to SubQ Insulin

• Step 2
  – Does patient have history of DM? A1C?
    • No DM and A1C <6.0% --> correction scale only
    • Yes DM or A1C >6.0% --> basal bolus regimen

• Step 3
  – Use 80% of the lowest of the following to determine TDD:
    • the dose administered over the last 12 hours multiplied by 2
    • the dose administered over the last 24 hours
    • Use average hourly rate over the last 6hrs (if stable) and multiply by 20 (80%)
    • Weight
Transition to SubQ Insulin

• Step 4
  – Determine if TDD = basal or basal+nutritional
    • If basal dose only, then dose can be doubled and divided accordingly when nutrition added
    • If basal+nutritional, then give 50% as basal and 50% as bolus

• Give basal insulin dose and turn off insulin drip 2 hrs later
Transition from IV to SQ Insulin Protocol

Step 1: Is the patient ready for transition?
- Patient meets following criteria:
  - Pt is not critically ill or requiring vasopressors
  - Blood glucose in target range all of last 6 hours

Yes → Continue insulin drip

No → Transition to correction scale only

Step 2: Does patient need scheduled subcutaneous insulin?
- NO:
  - Patients with no history of diabetes AND HbA1C < 6.0%
- YES:
  - All patients with DM 1
  - Patients with DM 2 and insulin drip rate > 1.0 unit/hour
  - Patients with HbA1C > 6.0%

Yes → Calculate total daily dose insulin requirement

Step 3: Calculate total daily dose insulin requirement (call pharmacy to use insulin calculator to transition and/or use equation below)
- Average the rate of insulin infusion over the previous 6 hours and multiply this number by 20. (24 is not used for safety reasons.)

\[(\text{avg drip rate}) \times 20 = \text{(calculated insulin)}\]

Step 4: Evaluate patient nutrition while on drip to determine insulin distribution
- Full nutrition: Pt is currently eating >50% of their meals, on goal tube feeds, goal TPN or receiving Dextrose IVF > 50mL/hr
- Minimal nutrition: Pt is currently NPO, taking <50% of their meals, on a zero carbohydrate clear liquid diet, or 6 hours used in Step 3 calculation is period of fasting (i.e. overnight)

Full Nutrition: calculated insulin = TDD
1. Give 50% of the TDD as basal insulin ordered as Lantus (glargine) once daily to be administered 2 hours before stopping the insulin infusion.
2. Give 50% of the TDD as nutritional insulin divided TID if tolerating meals (Lispro) or 6 hours if on continuous tube feeds (Regular) using CPOE orderset.
3. Order appropriate correction scale once drip is discontinued using CPOE orderset.

Minimal Nutrition: calculated insulin = basal insulin
1. Give 100% of calculated insulin as basal insulin ordered as Lantus (glargine) once daily to be administered 2 hours before stopping the insulin infusion.
2. Add nutritional insulin when clinically indicated.
3. Order appropriate correction scale once drip is discontinued using CPOE orderset.

Address all questions to ICU Pharmacist or Endocrine/Diabetes pager HC 290-4320, LJ 290-5272.
Case 1

- 49 y/o male w/ DM2 s/p CABG
- Home regimen is metformin 1000mg bid and Humalog 75/25 mixed insulin, 50 units in am and 30 units in pm
- A1C 9.0%
- Weight 120 kg
- BG well controlled on insulin drip, pt remains NPO on NS IVF’s
- Insulin infusion rates (units/hr): 2.3, 3.2, 3.0, 2.3, 2.2, 2.5 (avg 2.6 units/hr)
- Pt extubated, off pressors, ready to start diet
Yes

Yes

Avg 2.6 units/hr X 20 = 52 units

NPO on NS IVFs, so 52 units = basal

Basal insulin 52 units daily

When patient starts carb controlled diet start:

Analog insulin 16 units qac

High/aggressive correction scale
Example of hardwired transition algorithm at VMMC
Common Pitfalls

• No overlap between infusion and subcutaneous insulin

• Premature transition, so that it is difficult to determine a stable rate

• Mismatch between insulin infusion and nutritional status on infusion and at transition
  – Interruptions of tube feeds/TPN
  – Unclear about whether or not the infusion is being used to meet nutritional needs
Key Points

• Per guidelines, insulin infusions are indicated for:
  – DKA/HHS
  – Critically ill patients with a BG >180

• Treatment of DKA centers around the four pillars of hydration, electrolytes, insulin, and appropriate diagnostic evaluation for etiology

• Safe and effective insulin infusion protocols are clear, concise, account for the trajectory of BG values and address hypoglycemia

• The transition from insulin infusion to a subcutaneous regimen is complex and involves a delicate balance of art and science
Thank you