Inpatient Management of Hyperglycemia and Diabetes

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Uncontrolled hyperglycemia in hospitalized patients with or without a previous diagnosis of diabetes is associated with adverse outcomes and longer lengths of stay. In addition to the increasing prevalence of diabetes in the United States, many patients without preexisting diabetes experience stress-related hyperglycemia during hospitalization.[1] It is estimated that one-third of hospitalized patients will experience significant hyperglycemia.[2] The cost associated with hospitalization for patients with diabetes accounts for half of all health care expenditures for this disease.[3–5] Controlling glucose levels for inpatients should be a priority for hospitals and practicing physicians. Recent guidelines for optimal glucose goals in hospitalized patients have been developed by the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA).[6]

Controlling glucose and avoiding hypoglycemia is challenging even for experienced clinicians. Acute illness, inconsistent caloric intake, changes from home medications, and limitations regarding the timing of glucose monitoring and insulin administration are all significant obstacles to managing inpatient hyperglycemia.

A good understanding of the principles of physiological insulin delivery is essential to overcoming these obstacles and achieving glucose goals. The purpose of this article is to provide practical advice on managing inpatient hyperglycemia.

General Guidelines

Hyperglycemia is defined as blood glucose > 140 mg/dl, and treatment is recommended when glucose levels are persistently > 140–180 mg/dl.[6] A1C is an important laboratory test that should be ordered in nondiabetic hyperglycemic patients and diabetic patients who have not had a recent test. An A1C value ≥ 6.5% can now be used for diagnosing diabetes and is valuable in distinguishing between preexisting diabetes and acute stress hyperglycemia. In patients with preexisting diabetes, A1C testing will indicate the adequacy of prehospitalization treatment and can help guide discharge planning. Red blood cell transfusion during hospitalization will falsely decrease A1C levels.[7]

Patients with diabetes or hyperglycemia who are eating should be on a consistent-carbohydrate diet, and glucose monitoring should be ordered before each meal and at bedtime. Typically, oral agents should be discontinued during acute illness unless it is a very brief hospitalization. Oral agents can be restarted as patients approach discharge or transfer to a nonacute setting.

Metformin cannot be used when there is any possibility of the need for iodinated contrast studies or renal insufficiency. Sulfonylureas and metaglinides can cause unpredictable hypoglycemia in patients who are not eating reliably. Thiazolidinediones can cause fluid retention, especially in combination with insulin. Parenteral glucagon-like peptide-1 and amylin agonists can cause nausea and should be withheld in acutely ill patients. For these reasons, inpatient hyperglycemia is best managed with insulin only.

Insulin works reliably, and doses can be rapidly adjusted depending on changes in glucose levels and food intake. Use of insulin does not necessarily commit patients to chronic insulin therapy as outpatients, and this should be discussed with patients to allay any potential anxiety. If the A1C value indicates the need for chronic insulin therapy, it is a good idea to begin discussion and training as soon as possible.

IN BRIEF

Control of hyperglycemia in hospitalized patients is important for optimal clinical outcomes, but can be very challenging. This article provides practical recommendations for insulin therapy for common situations that arise during hospitalization.

Subcutaneous Insulin Therapy in Hospitalized Patients

Many types of insulin and insulin regimens can be used effectively to control glucose in the outpatient setting. Insulin therapy during hospitalization requires flexibility to change rapidly with the patients' condition and is best provided by what

has been termed a basal/bolus insulin regimen. It should be emphasized that using a correction scale insulin regimen, also known as "sliding scale insulin," alone is not appropriate to treat sustained hyperglycemia (> 140 mg/dl). Scheduled basal/bolus insulin is designed to prevent hyperglycemia, whereas correction scale insulin only attempts to lower hyperglycemia after it has occurred. A study comparing scheduled basal/bolus insulin to sliding scale insulin only showed a significantly higher percentage of patients achieving goal glucose levels in the basal/bolus group than in the sliding scale only group (66 vs. 38%) without an increase in hypoglycemia.[8]

There are three components to a basal/bolus regimen: basal insulin, meal or nutritional bolus insulin, and correction insulin (Figure 1).[9] The ideal basal insulin provides a constant 24-hour peakless level of insulin to suppress the liver's release of glucose during the fasting state and between meals. NPH insulin has a pronounced and variable peak and should be avoided during hospitalization because it can cause unpredictable hypoglycemia, especially in patients who are not eating reliably.[10,11] Glargine and detemir are newer insulin analogs that provide relatively peakless basal insulin. Glargine is preferred because of its longer duration of action with once-daily administration.[12] Basal insulin, when dosed correctly, should not cause hypoglycemia when patients are restricted from oral nutritional intake (NPO).

Mealtime bolus insulin is designed to prevent the predicted postprandial rise in glucose. Bolus insulin is best provided with one of the rapid-acting analogs (lispro, aspart, or glulisine) with each meal. These insulin analogs have a rapid onset of action and usually reach peak levels within 60 minutes. Numerous studies have shown that rapid-acting insulin analogs will control the postprandial rise in glucose and reduce later hypoglycemia better than regular insulin.[13–15] Rapid-acting insulin analogs should be given 0–15 minutes before a meal, whereas regular insulin must be given at least 30 minutes before a meal because of its slower onset of action. The timing requirements for premeal regular insulin administration are not usually realistic in a busy hospital unit. Bolus insulin should be withheld when patients are NPO or when premeal glucose levels are < 70 mg/dl.

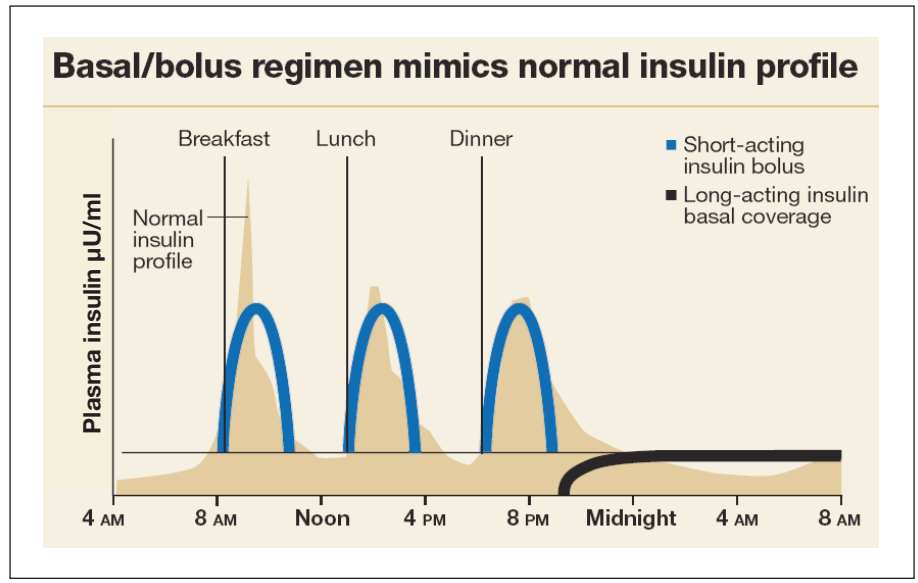
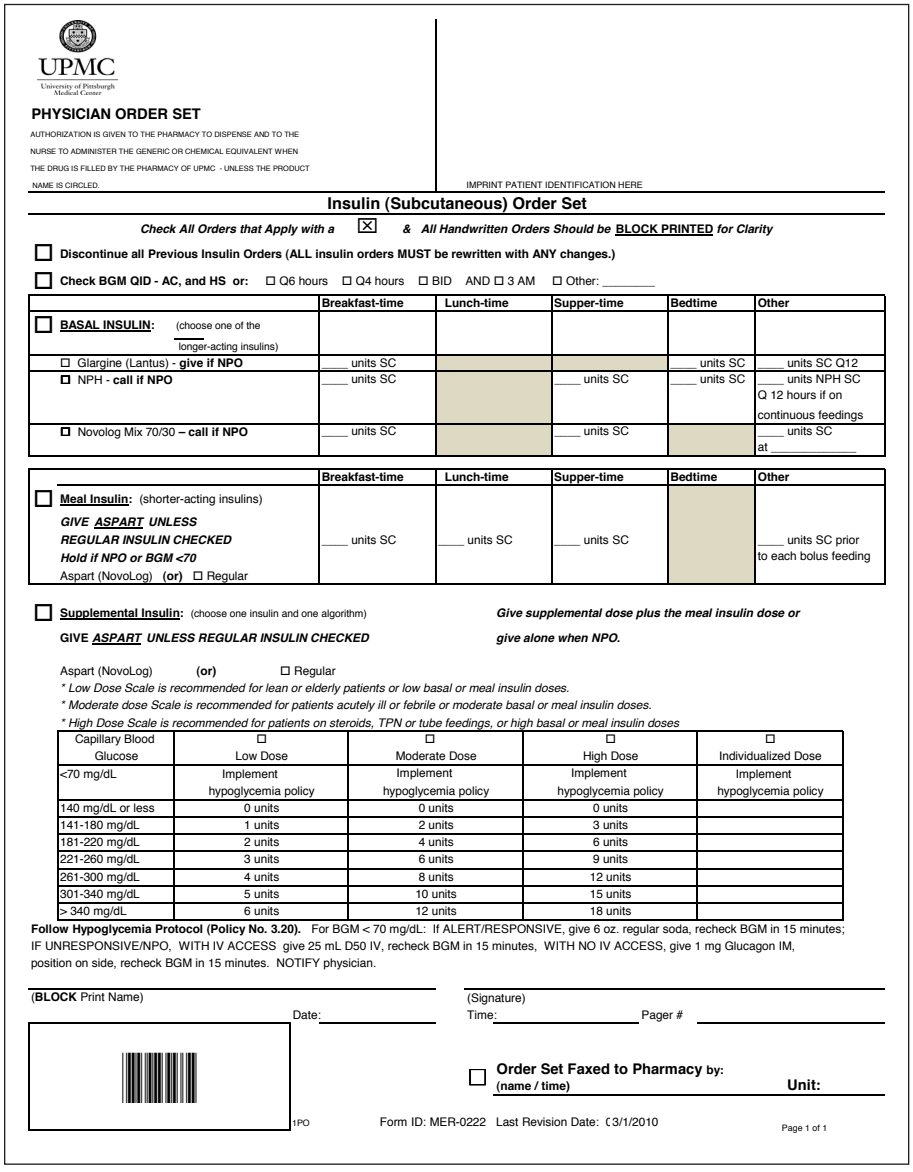


Figure 1. Physiological principles of the basal/bolus insulin regimen.[9]

Correction insulin is intended to lower hyperglycemic glucose levels, not to cover nutritional hyperglycemia. But, as with mealtime bolus insulin, rapid-acting analog formulations are the best choice for correctional insulin for patients who are able to eat. Before each meal, the mealtime bolus insulin dose and the correction insulin dose can be added and administered simultaneously. However, it is best to order them separately so they can be adjusted independently. The mealtime bolus insulin should be withheld when patients are not eating, but correction doses should still be given when needed to treat hyperglycemia.

Standardized, preprinted, or computerized insulin order forms improve the ease of ordering insulin and guide physicians to include all three components of subcutaneous therapy. Standardized insulin orders have been shown to improve glucose control and reduce medication errors.[16–18] For these reasons, many hospitals have made the use of such orders mandatory. A sample preprinted insulin order from the authors' institution is provided in Figure 2.

Estimating patients' total daily insulin requirement, or total daily dose (TDD), is the first step in ordering insulin. For patients who were on insulin before admission, the best indicator of insulin requirement is their TDD before admission. Regardless of their previous insulin regimen, it is best to use a basal/bolus regimen during their hospital stay and to explain to patients that this is being done to allow for greater flexibility. Patients with an elevated A1C value may require an increase, and those whose glycemia was



UPMC
University of Pittsburgh Medical Center

PHYSICIAN ORDER SET

AUTHORIZATION IS GIVEN TO THE PHARMACY TO DISPENSE AND TO THE NURSE TO ADMINISTER THE GENERIC OR CHEMICAL EQUIVALENT WHEN THE DRUG IS FILLED BY THE PHARMACY OF UPMC - UNLESS THE PRODUCT NAME IS CIRCLED.

IMPRINT PATIENT IDENTIFICATION HERE

Insulin (Subcutaneous) Order Set

Check All Orders that Apply with a ☒ *& All Handwritten Orders Should be* **BLOCK PRINTED** *for Clarity*

☐ **Discontinue all Previous Insulin Orders (ALL insulin orders MUST be rewritten with ANY changes.)**

☐ **Check BGM QID - AC, and HS or:** ☐ Q6 hours ☐ Q4 hours ☐ BID AND ☐ 3 AM ☐ Other: _____

	Breakfast-time	Lunch-time	Supper-time	Bedtime	Other
☐ **BASAL INSULIN:** (choose one of the longer-acting insulins)					
☐ Glargine (Lantus) - **give if NPO**	____ units SC			____ units SC	____ units SC Q12
☐ NPH - **call if NPO**	____ units SC		____ units SC	____ units SC	____ units NPH SC Q 12 hours if on continuous feedings
☐ Novolog Mix 70/30 **– call if NPO**	____ units SC		____ units SC		____ units SC at _____

	Breakfast-time	Lunch-time	Supper-time	Bedtime	Other
☐ **Meal Insulin:** (shorter-acting insulins) ***GIVE ASPART UNLESS REGULAR INSULIN CHECKED Hold if NPO or BGM <70*** Aspart (NovoLog) **(or)** ☐ Regular	____ units SC	____ units SC	____ units SC		____ units SC prior to each bolus feeding

☐ **Supplemental Insulin:** (choose one insulin and one algorithm) ***Give supplemental dose plus the meal insulin dose or give alone when NPO.***

GIVE *ASPART* *UNLESS REGULAR INSULIN CHECKED*

Aspart (NovoLog) **(or)** ☐ Regular

** Low Dose Scale is recommended for lean or elderly patients or low basal or meal insulin doses.*
** Moderate dose Scale is recommended for patients acutely ill or febrile or moderate basal or meal insulin doses.*
** High Dose Scale is recommended for patients on steroids, TPN or tube feedings, or high basal or meal insulin doses*

Capillary Blood Glucose	☐ Low Dose	☐ Moderate Dose	☐ High Dose	☐ Individualized Dose
<70 mg/dL	Implement hypoglycemia policy	Implement hypoglycemia policy	Implement hypoglycemia policy	Implement hypoglycemia policy
140 mg/dL or less	0 units	0 units	0 units	
141-180 mg/dL	1 units	2 units	3 units	
181-220 mg/dL	2 units	4 units	6 units	
221-260 mg/dL	3 units	6 units	9 units	
261-300 mg/dL	4 units	8 units	12 units	
301-340 mg/dL	5 units	10 units	15 units	
> 340 mg/dL	6 units	12 units	18 units	

Follow Hypoglycemia Protocol (Policy No. 3.20). For BGM < 70 mg/dL: If ALERT/RESPONSIVE, give 6 oz. regular soda, recheck BGM in 15 minutes; IF UNRESPONSIVE/NPO, WITH IV ACCESS give 25 mL D50 IV, recheck BGM in 15 minutes, WITH NO IV ACCESS, give 1 mg Glucagon IM, position on side, recheck BGM in 15 minutes. NOTIFY physician.

(**BLOCK** Print Name) (Signature)

Date: Time: Pager #

☐ **Order Set Faxed to Pharmacy by: (name / time)** **Unit:**

HPO Form ID: MER-0222 Last Revision Date: 03/1/2010 Page 1 of 1

Figure 2. Standardized subcutaneous insulin orders at the University of Pittsburgh Medical Center, Pennsylvania.[35]

too tightly controlled or who were admitted with hypoglycemia may require a reduction in their prehospitalization TDD. For patients who are insulin naive, insulin can safely be initiated at a TDD of 0.3–0.6 units/kg body weight.[16,17] The lower starting dose is recommended for leaner patients and for those with renal insufficiency, and the higher starting dose is recommended for obese patients and those on glucocorticoids (Table 1).

Studies in both type 1 and type 2 diabetes have consistently shown that optimal glycemic control can be achieved with subcutaneous insulin in patients who are eating normally when approximately 50% of their TDD is provided as basal insulin, and 50% is provided as bolus insulin.[16,17] However, it is important to remember that mealtime bolus doses must be adjusted according to how much patients are actually eating. Mealtime doses may need to be adjusted daily based on patients' anticipated caloric intake and withheld if patients are not eating or if their premeal glucose level is < 70 mg/dl. For patients who are eating unreliably, rapid-acting analog insulin can be ordered to be given immediately after they have eaten, and the mealtime dose can then be adjusted to match their actual intake (e.g., reducing the dose by 50% if only half of the food on the tray was consumed).

Correctional insulin requirements depend on individuals' insulin sensitivity. Many physicians mistakenly order a scale depending on the degree of hyperglycemia, but the appropriate scale is based on each patient's insulin sensitivity, which is best estimated by their TDD.

A "1700 rule" has been used to estimate how much 1 unit of insulin will lower glucose.[19] A sensitivity, or correction, factor is calculated by dividing 1700 by the TDD. Most hospitals use low, medium, and high scales that provide doses of insulin when glucose levels exceeds 140–150 mg/dl and increase with additional glucose increments of 40–50 mg/dl (Figure 2). A low scale increases by 1 unit of insulin for each increment of 40–50 mg/dl and corresponds to a sensitivity factor of 40–50 or a TDD of 20–42 units. Therefore, patients requiring insulin doses in this range would be ordered a low-dose correctional scale. A moderate scale would be used for patients requiring a TDD of 43–84 units, and a high-dose scale should be ordered for patients requiring 85–126 units/day. An individualized correctional scale may be necessary for patients with extremely low or high insulin TDDs (< 20 or > 126 units). An example for ordering subcutaneous insulin is provided in Table 2.

Guidelines for insulin initiation dosing are just a starting point.

Table 1. Determining a TDD for Insulin-Naive Patients	
TDD Estimation	**Patient Characteristics**
0.3 units/kg body weight	• Underweight • Older age • Hemodialysis
0.4 units/kg body weight	• Normal weight
0.5 units/kg body weight	• Overweight
≥ 0.6 units/kg body weight	• Obese • Insulin resistant • Glucocorticoids

Insulin doses may need to be adjusted on a daily basis depending on patients' blood glucose testing results and caloric intake. Fasting glucose is the best indicator of adequacy of the basal insulin dose. Glargine can be adjusted every 24–48 hours until fasting glucose is < 120–140 mg/dl. Glucose levels during the rest of the day reflect the appropriateness of mealtime bolus insulin doses. Prelunch glucose measurements reflect the adequacy of the breakfast dose, predinner glucose reflects the lunchtime insulin dose, and bedtime glucose reflects the dinnertime dose of rapid-acting insulin.

Because the correctional scale is based on insulin sensitivity, it is unlikely to be changed unless there is a significant change in a patient's TDD.

Managing Hyperglycemia in Critical Illness

Although there are extensive data indicating that uncontrolled hyperglycemia is associated with adverse outcomes in critically ill patients, the optimal glucose range remains the topic of ongoing research and debate. Recent consensus guidelines have recommended a goal range of 140–180 mg/dl in acute critical illness.[6] However, in specific subgroups of patients, such as open heart surgery patients, there is evidence that a tighter goal of 110–140 mg/dl may be beneficial.[6,20] Severe hypoglycemia (< 40 mg/dl) during critical illness should be avoided because it has been associated with increased mortality.[21,22]

Continuous intravenous (IV) insulin is the safest and most effective way to achieve glucose control within a specified range and respond rapidly to changing clinical conditions. IV insulin should be initiated when glucose is > 180 mg/dl and adjusted to maintain glucose in the 140–180 mg/dl range as much as possible.[6]

Standardized orders promote familiarity with guidelines among physicians and nursing staff and minimize errors.[19] Many IV insulin regimens have been used safely and effectively. An analysis of IV insulin infusion protocols has indicated that orders that adjust insulin based on current glucose values and rate of change of glucose are more effective than protocols that adjust insulin dose based on current glucose levels.[24] Each institution should implement a standard IV insulin protocol that is feasible and best suited to the needs of specific units.[23,28]

IV insulin provides basal insulin for critically ill patients who are not eating. Once patients start eating, mealtime bolus insulin should be provided. If IV insulin is increased to respond to postprandial hyperglycemia, there is a significant risk of hypoglycemia occurring after the postprandial hyperglycemia declines. Therefore, it is best to transition to subcutaneous basal/bolus insulin once patients are eating reliably. IV insulin should be continued for at least 4 hours after the glargine insulin dose is administered or, more conveniently, can be discontinued sooner after the glargine is given by

Table 2. Sample Order for Subcutaneous Insulin in a Hospitalized Patient	
Sample: Basal/bolus insulin dose calculation for a patient weighing 80 kg with a BMI of 28 kg/m^2 and normal renal function	
Step 1	**TDD calculation** TDD = 0.5 units/kg body weight × 80 = 40 units
Step 2	**Basal insulin dose calculation** Basal insulin dose = 50% of TDD = 50% of 40 units = 20 units glargine
Step 3	**Bolus insulin dose calculation** Bolus insulin dose per meal = (50% of TDD)/3= (50% of 40 units)/3 = 20/3 = 6.3 units, or ~ 6 units of rapid-acting insulin before each meal. If the patient or nurse estimates that the patient is only eating 50% of the food on the tray, a reduced dose of 3 units should be ordered instead of the full dose of 6 units
Step 4	**Correctional scale estimation** Assessment of correctional scale insulin is based on TDD. For a patient with a TDD of 40 units, the low correctional scale should be ordered

discontinuing it immediately after a rapid-acting analog is provided as a mealtime bolus dose.[25]

The basal insulin dose can be estimated by calculating the IV insulin requirement while the patient was not eating. The stress of surgery or critical illness will increase insulin requirements, and, as stress decreases, basal insulin requirements will also decrease. During transition from IV to subcutaneous insulin, a reduction in the basal dose by 20–33% to account for decreasing requirements has been found to be safe and effective.[25,26] For patients with stress-induced hyperglycemia only, insulin may continue to be decreased and discontinued as their condition improves.

Mealtime bolus doses depend on patients' caloric intake. Patients recovering from critical illness will not be eating full meals, so a convenient starting dose would be 10% of the basal dose, given at each meal. Mealtime boluses will likely need to be increased daily as the diet advances. Table 3 provides an example of converting from an insulin drip to a basal/bolus regimen.

Table 3. Sample Conversion From IV to Basal/Bolus Insulin

Sample: Basal/bolus insulin dose calculation for a patient started on diet who required 2 units/hour of insulin overnight while NPO	
Step 1	**Basal dose calculation** Patient's hourly insulin infusion rate while NPO = 2 units/hour 24-hour basal insulin dose during stress = 24 × hourly infusion rate = 24 × 2 = 48 units Adjusted basal dose accounting for stress reduction = 2/3 × 24-hour basal rate = 2/3 × 48 = 32 units of glargine
Step 2	**TDD calculation** TDD = dose is 2 × adjusted basal dose = 2 × 32 = 64 units
Step 3	**Mealtime bolus dose calculation** Patient just started to eat, so 10% of basal dose can be started with each meal = 0.1 × 32 = 3 units with each meal
Step 4	**Correctional scale estimation** A moderate-level correctional scale is most appropriate for an estimated TDD of 64 units

Management of Hyperglycemia With Enteral Feedings

Hyperglycemia is a common complication of enteral feedings and can contribute to adverse clinical outcomes.[28] Enteral formulas with reduced carbohydrate and modified fat content have been shown to result in lower glucose levels and should be used if possible in hyperglycemic patients.[29] Persistent hyperglycemia should be treated with scheduled insulin doses. Once-daily glargine insulin, premixed human 70/30 insulin given every 8 hours, or a combination of NPH given every 12 hours and regular insulin given every 6 hours have all been recommended, with limited data.[30–32] Regular insulin for correction doses may be a better choice with enteral feedings when a less pronounced peak of insulin is desirable and glucose is monitored every 6 hours.

Regardless of the insulin regimen used, the insulin TDD can be calculated at 0.3–0.6 units/kg body weight. This is a starting dose, which should be adjusted daily based on patients' glucose response and the amount of correctional insulin that was required the previous day. It has been recommended that 80% of the correctional insulin be added to the long- or intermediate-acting insulin the next day. The goal is to eventually arrive at a regimen that will maintain glucose in the goal range while patients are on continuous feedings.

If tube feedings are provided only nocturnally, NPH is preferable and should be given to coincide with the onset of the feedings. If patients on nocturnal tube feedings are eating meals, they may require mealtime bolus insulin to prevent postprandial hyperglycemia. Bolus tube feedings should be covered the same as ingested meals with a dose of rapid-acting analog insulin at the time of each bolus feeding.

The biggest challenge in treating hyperglycemia caused by enteral feedings is that unexpected interruption of feedings can lead to hypoglycemia. Insulin should be adjusted appropriately if there is a planned withholding of feedings. If the enteral feeding is unexpectedly interrupted for more than 2 hours, all insulin should be withheld and 10% dextrose should be administered intravenously at the same rate as that of the enteral feedings to prevent hypoglycemia. It is best to have a standardized policy for this common occurrence. Monitoring electrolytes and providing adequate free water is very important. Dehydration is a common complication of enteral feedings and a frequently overlooked cause of hyperglycemia.[28] A sample calculation of insulin requirements for a patient on enteral feeds is shown in Table 4.

Management of Hyperglycemia With Parenteral Feedings

Hyperglycemia occurs commonly with total parenteral nutrition (TPN) and is associated with significant adverse outcomes.[33] Mild hypergly-

Table 4. Sample Insulin Requirement Calculation for a Patient on Enteral Feedings

Sample: Insulin dose calculation for 80 kg patient with a BMI of 24 kg/m^2 on continuous enteral feeding	
Step 1	**TDD calculation.** TDD: 0.4 units/kg × 80 = 32 units
Step 2	**Insulin dosing based on type of insulin.** Glargine insulin dose: 32 units subcutaneously daily or NPH insulin dose: 16 units subcutaneously twice daily
Step 3	**Correctional scale estimation.** Low correctional scale insulin is most appropriate for patient requiring an estimated TDD of 32 units. Order correctional scale every 4 hours with rapid-acting analogs and every 6 hours with regular insulin

cemia can be managed by addition of regular insulin to the TPN using a starting dose of 0.1 units for every gram of carbohydrate in the TPN. If glucose remains elevated, the insulin dose in TPN can be adjusted daily by adding 80% of the previous day's correctional insulin. If glucose levels are extremely elevated, IV insulin can be employed to control hyperglycemia more rapidly.

Once a stable IV rate has been determined, it can be extrapolated to a 24-hour TDD, with 75% of this dose is added to TPN. Patients with preexisting diabetes may benefit from receiving 40% of their TDD as basal insulin subcutaneously and the remainder provided as regular insulin in TPN. When TPN is discontinued, glucose control will be maintained with the basal long-acting insulin, and mealtime bolus insulin can be added as the patient begins to eat.

Glucocorticoids

Glucocorticoids are known to significantly increase glucose levels, primarily by inhibiting glucose uptake into muscle. Postprandial glucose levels are generally most affected, and patients who are treated with a basal/bolus regimen will probably require a higher percentage of their TDD as bolus insulin while they are on glucocorticoids. It is important to reduce insulin doses as glucocorticoids are tapered to avoid hypoglycemia.

Discharge Planning

The A1C test result is valuable in determining the most appropriate treatment strategy at discharge. For patients with diabetes, the current recommendation is a goal A1C of < 7%; however, for patients of advanced age or with life-shortening illnesses, a higher A1C is acceptable.

Although insulin is recommended during hospitalization, many patients will not need insulin at discharge. A newly diagnosed patient should be treated according to the current guidelines for initiating pharmacological therapy based on the severity of their disease.[34] Patients with a history of diabetes with acceptable control and whose A1C is in the goal range can probably be discharged on their prehospitalization medication or insulin regimen. Patients with suboptimal control should have intensification of therapy, either by addition or increase in oral agents, addition of basal insulin, or a complex insulin regimen as warranted by their A1C level.

For patients new to insulin therapy, it is important to begin education as soon as possible. Although the use of a basal/bolus regimen is advocated in the hospital for flexibility, this regimen may not be feasible or necessary in the outpatient setting. For many patients with type 2 diabetes, once-daily basal insulin in combination with oral agents or twice-daily premixed insulin may be adequate. It is necessary to assess the patient's daily schedule, meal plan, insulin self-administration ability, and financial resources. Patients who do not have prescription coverage will probably need to use generic oral agents and human insulin (NPH and regular) individually or premixed whenever possible. With decreasing lengths of stay, it is only possible to provide "survival skills" education in the hospital. This includes the safe administration of insulin and medications, basic understanding of meal planning, and recognition and treatment of hypoglycemia. Patients with newly diagnosed diabetes, those who are new to insulin therapy, and those with educational deficits should be referred to an outpatient diabetes educator for more comprehensive education.

Summary

Managing diabetes and hyperglycemia during hospitalization is vital for optimal clinical outcomes. Insulin is the best treatment for inpatient management but can be very challenging given the stress of illness, frequently changing caloric intake throughout the hospital stay, and limitations to care provided by hospital personnel. An understanding of physiological insulin administration and the use of the three components of subcutaneous insulin therapy (basal, mealtime bolus, and correctional insulin) helps to achieve glucose goals and provide needed flexibility. Standardized

orders for subcutaneous and IV insulin can guide physicians and minimize errors. Early and thoughtful discharge planning will help to ensure continued glucose control in the outpatient setting.

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