Chapter 2
Subcutaneous Insulin: A Guide for Dosing Regimens in the Hospital

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Basal-Bolus Insulin

Insulin continues to be the preferred method for the management of hyperglycemia in the inpatient setting. It can be titrated easily, does not have a ceiling dose, and can be administered intravenously and subcutaneously. Details of IV insulin, including the transition from IV to subcutaneous, are discussed in Chapter 3: IV Insulin. In this chapter, we focus on subcutaneous insulin regimens.

Many patients who require subcutaneous insulin in the hospital will already have a diagnosis of diabetes; some will have been on insulin prior to admission. However, some nondiabetic patients may develop hyperglycemia as well. For all inpatients with hyperglycemia, we recommend a proactive insulin regimen that includes two components: (1) basal insulin, to cover basal insulin needs (mainly due to hepatic glucose production) and (2) bolus (or prandial) insulin, to cover any forms of caloric intake—meals, enteral feedings, or total parenteral nutrition (TPN). This strategy is referred to as basal-bolus insulin. For patients with type 1 diabetes, the basal-bolus insulin strategy is optimal, and these patients should always receive basal insulin, even during periods of fasting. Patients with type 1 diabetes require exogenous insulin to prevent the production of ketones and the subsequent development of diabetic ketoacidosis (DKA). For patients with type 2 diabetes also, the basal-bolus insulin strategy is preferred; however, the insulin requirement may decrease over periods of prolonged fasting. Current evidence supports the basal-bolus regimen as more effective, easier to design and adjust, better for blood glucose control, and lower risk for hypoglycemia than alternative strategies.

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An optional insulin regimen component is the correctional insulin scale (so-called sliding scale). The scale is used before meals along with the bolus insulin to correct hyperglycemia. The correctional insulin scale should not be used alone for patients with diabetes; this reactive strategy will not be effective to prevent hyperglycemia or inpatient complications such as hypoglycemia.

Special Care Situations

Subcutaneous insulin may not always be appropriate for patients in the intensive care unit, particularly those with severe sepsis, requiring vasopressors, with acute hepatic failure, or with severe hypoalbuminemia. In these patients IV insulin may be a better choice. An endocrinology consultant can assist with decision making in situations such as these.

Key Points: Basal-Bolus Insulin

- Insulin strategy: Basal + bolus + correctional insulin scale (optimal insulin regimen)
- Correctional insulin scale: avoid using as only insulin regimen. It is only good for patients who are at risk for hyperglycemia, but who do not currently have hyperglycemia.
- Patients with type 1 diabetes always require basal insulin, even if they are not eating.

Transition from Outpatient to Inpatient Care

A patient's outpatient regimen may not be appropriate in the inpatient setting for a variety of reasons.

- Stress can either increase or decrease a patient's insulin requirements.
- Nutrition in the hospital may be different from that at home (i.e., carbohydrate content, total calories, periods of fasting, etc., may be different).
- Medical conditions, such as hypotension, vasopressor use, edema, acute renal failure, surgical procedures, may alter insulin requirements.
- The insulin dose at home may not have provided adequate control.
- For patients who use premixed (2 shots/day) insulin products, such as 70/30 (Humulin 70/30; Novolog® Mix 70/30) and 50/50 (Humulin 50/50; Humalog Mix 50/50) at home: These components are not easily titrated in the inpatient setting. We recommend transition to a basal-bolus insulin regimen while these patients are hospitalized.
- Patients who have no prior diagnosis of diabetes, but who are at risk for developing hyperglycemia in the hospital (such as those receiving glucocorticoids or other medications, or TPN or enteral nutrition [EN]), should have their glucose closely monitored. If a patient develops consistent hyperglycemia, scheduled basal-bolus insulin should be initiated.

Glucose Monitoring

How Often to Monitor?

The frequency of monitoring will depend on the patient's nutrition pattern and insulin regimen.

- Patients eating scheduled meals should be monitored before meals, at bedtime, and, for some, at 3 AM. The 3 AM level can aid in interpretation of an elevated fasting glucose; potential causes include the "dawn phenomenon" and the "Somogyi effect," a rebound rise in blood glucose after hypoglycemia. Once glucoses are stable overnight, the 3 AM check can be discontinued.
- Patients receiving enteral feeding in boluses should be monitored prior to each bolus while the insulin regimen is still being adjusted. Once the insulin dose is stable, monitoring every 6 h is usually sufficient.
- If a patient has symptoms that could be consistent with hyper- or hypoglycemia, the glucose should be checked immediately, even if it is not a prescribed monitoring time.

Blood Glucose Targets

Over the last several years, the optimal glycemic target for the hospitalized patient with hyperglycemia has been the focus of significant discussion and controversy. However, it is reasonable to pursue the following as a straightforward set of goals that can be used in the treatment of most inpatients:

- Pre-meal blood glucose less than 140 mg/dL (7.8 mmol/L)
- Random blood glucose of less than 180 mg/dL (10.0 mmol/L)
- Recent discussions of glycemic control have emphasized the importance of individualizing targets. The selection of a more or less stringent target will depend on the patient's history of previous glucose control and current medical status (e.g., less stringent in patients with terminal illness and those with history of hypoglycemia unawareness).

Choosing an Insulin Regimen

The calculations recommended in this chapter are estimates and are meant to be a starting point. Always use clinical judgment, and make adjustments based on glucose readings obtained over the subsequent 24 h.

Obtain Baseline Information

Subjective: Type of diabetes, new or established, home medications (insulin and non-insulin), total daily dose (TDD) of insulin at home, hypoglycemia frequency, and symptoms.

Objective: Age, weight, height, body mass index (BMI), previous hemoglobin A_{1C} (if available), glomerular filtration rate (GFR), liver function tests, nutritional status in the hospital, use of new medications such as glucocorticoids.

Calculate the Total Daily Insulin Dose

General Considerations

As discussed earlier in this chapter, multiple factors can affect the insulin regimen of a hospitalized patient. Although the degree of glycemic control optimal for the hospitalized patient is still debated, there is no debate regarding the importance of avoiding hypoglycemia. Insulin dosages can be rapidly and easily titrated upward, so it is reasonable to start near the low end of an estimated dose calculation and to ensure that necessary adjustments are made promptly. For patients with GFR less than 60 (stage III or higher chronic kidney disease (CKD), as well as those with acute renal failure), see the section on renal impairment below.

- For patients with type 1 diabetes, the total daily insulin dosage can be estimated at 0.3–0.5 units/kg/day. Patients with type 1 diabetes often are quite sensitive to insulin; thus, it is reasonable to start on the low end.
- For patients with type 2 diabetes, the total daily insulin dosage can start at 0.3–0.7 units/kg/day. Patients with type 2 diabetes have varying degrees of insulin resistance, so a patient who is new to insulin, with uncertain needs, may benefit from a relatively low dose to start. However, some patients may require more than 1 unit/kg/day. If there is uncertainty about the level of insulin resistance, it is simple and safe to start with a TDD of 0.5 units/kg/day.

Scenarios and Examples

Scenario 1: Patient with Hyperglycemia (With or Without Diabetes) Who Is New to Insulin

The patient is new to insulin, so it is reasonable to start with a TDD of 0.3 units/kg/day. However, a higher TDD may be implemented in certain cases. 0.1 units/kg/day can be added to the TDD for the presence of each of the following:

- The patient has type 2 diabetes and is less than 70 years old.
- The patient has evidence of difficult control; that is, he or she takes at least three oral agents at home, or the hemoglobin A_{1C} is greater than 8%, or he or she reports fasting glucoses greater than 200 mg/dL (11.0 mmol/L) prior to admission.
- The patient has a BMI greater than 35 kg/m^2.

For example, a 40-year-old patient with type 2 diabetes who has never used insulin, whose preadmission A_{1C} is 9%, and whose BMI is 36 kg/m^2, could reasonably be given a TDD of 0.6 units/kg/day.

Scenario 2: Patient with Type 2 Diabetes, on Known Dosages of Insulin at Home

The first step is to determine the patient's true TDD. Consistency of usage is an important component of the history. Does the patient always take the prescribed dosage, or does he or she make modifications? How often does he or she miss an insulin dose?

In order to determine the safety of the patient's reported TDD, it is helpful to calculate a weight-adjusted TDD based on units per kilogram per day. For example, a patient has type 2 diabetes and normally takes 40 units of insulin per day. He weighs 80 kg. His weight-based TDD is 40 units/80 kg/day, or 0.5 units/kg/day. This is reasonable and likely to be safe for a patient with type 2 diabetes. Based on this calculation, it is reasonable to continue with the patient's home TDD in the hospital. If the dose seems too high, a smaller dose can be used initially, with prompt increases as deemed necessary from monitored glucose values.

A list of situations for which the insulin dose can be modified is found in Table 2.1.

Table 2.1 Situations warranting cautious modification of home total daily dose of insulin[a]

Situation	Modification
Type 1 diabetes and uncontrolled glucoses (A_{1C} >8%) or fasting glucoses >200 mg/dL (11 mmol/L)	↑home TDD by 10%
Type 2 diabetes and uncontrolled glucoses (A_{1C} >8%) or fasting glucoses >200 mg/dL (11 mmol/L)	↑ home TDD by 20%
Patient is ABOUT TO BEGIN corticosteroids (newly prescribed for the inpatient stay)	↑ home TDD by 20%
Patient reports hypoglycemia unawareness	↓ home TDD by 20%[b]
Hypoglycemia within the past 24 h: Glucose 50–70 mg/dL (2.8–3.9 mmol/L)	↓ home TDD by 30%[b]
Hypoglycemia within the past 24 h: Glucose <50 mg/dL (2.8 mmol/L)	↓ home TDD by 40%[b]

TDD, total daily dose

[a]These recommendations are based on the algorithm developed by the Duke University Medical Center Glycemic Safety Committee

[b]Always consider making further adjustments if the patient continues to develop hypoglycemia despite changes

Scenario 3: Patient with Type 2 Diabetes Who Is Not Using Insulin and Is Not Hyperglycemic in the Hospital

This situation can occur in patients with type 2 diabetes who are overnourished at home but who are admitted after periods of fasting, as in gastrointestinal illnesses, or who have had moderate weight loss related to illness or other factors. Patients who are not hyperglycemic can be followed with glucose monitoring alone, at least four times daily, usually before meals and at bedtime. However, a scheduled insulin regimen must be added if glucoses rise above the target ranges. It is

not appropriate to follow hyperglycemia with only a correctional insulin scale; this retroactive approach does not effectively prevent future hyperglycemic episodes and will increase the risk for hypoglycemia.

Insulin for Patients with Renal Impairment

For patients with renal impairment, it often is necessary to decrease the TDD depending on the stage of kidney failure due in large part to changes in insulin clearance (Table 2.2). This applies to patients with both chronic and acute renal failure, although patients with improving renal function after acute failure may have increasing insulin requirements. As always, prompt adjustments should be made according to monitored glucoses.

Table 2.2 Renal impairment warranting cautious modification of total daily dose[a]

Situation	Modification
Patient on insulin at home, no history of hypoglycemia, and stable CKD stage I and II (GFR >40 mL/min per BSA 1.73 m^2)	None: May use home TDD
CKD stage III (GFR 30–39 mL/min per BSA 1.73 m^2)	↓ home TDD by 30%
CKD stage IV (GFR 15–29 mL/min per BSA 1.73 m^2)	↓home TDD by 50%
CKD stage V (GFR 15 mL/min per BSA 1.73 m^2) or ESRD or acute renal injury	↓home TDD by 60%

BSA, body surface area; CKD, chronic kidney disease; ESRD, end-stage renal disease; GFR, glomerular filtration rate; TDD, total daily dose

[a]These recommendations are based on the algorithm developed by the Duke University Medical Center Glycemic Safety Committee

Insulin for Patients Taking Glucocorticoids

For patients taking glucocorticoids, it is recommended by some diabetologists that regular (Novolin R®, Humulin R®) insulin be used in order to adjust for the delayed increase in prandial glucose that may be seen in this scenario. In patients taking glucocorticoids, the fasting glucose may be minimally increased, with a substantially more exaggerated increase in postprandial glucose. Occasionally, patients without a previous diagnosis of diabetes might require only prandial insulin. As with other patients with hyperglycemia, the insulin dose should be based on the patient's weight, calorie consumption, meal time, and other associated factors that might be affecting glycemic levels (e.g., the patient's status following major surgical intervention).

Distribution of the Total Daily Dose

Most experts agree that a basal-bolus insulin regimen is the best approach for patients requiring intensive insulin treatment. The variable timing of nutrition,

medications, and procedures in the hospital makes premixed and split-mix insulin regimens unreliable and dangerous. Basal-bolus insulin regimens will be different for patients who are eating regular, discrete meals than for those who have continuous nutrition (through EN or TPN routes) and those who are fasting.

The Patient Who Is Eating Discrete Meals

A basal-bolus regimen for this patient can be accomplished in two ways: (1) a long-acting peakless insulin (i.e., glargine [Lantus®] or detemir [Levemir®]), for the basal component with a rapid-acting insulin (i.e., aspart [Novolog®], lispro [Humalog®], or glulisine [apidra®]) at mealtime, or (2) an intermediate-acting insulin (i.e., NPH [Neutral Protamine Hagedorn]) at bedtime with a short-acting insulin (i.e., regular [Novolin R® or Humulin R]) at mealtime.

Long-Acting Insulin (Glargine[Lantus] or Detemir[Levemir]), with Rapid-Acting Insulin (Aspart[Novolog], Lispro[Humalog], or Glulisine[Apidra])

Long-acting insulin serves as the entire basal component; 50% of the TDD usually is administered as one or two long-acting insulin injections over 24 h. (If this component is greater than 50 units, it is advisable to give it as two injections to maximize absorption). This can be done at the same time or divided into morning and evening doses, according to the physician and patient preferences. The remaining 50% of the dose is divided into three mealtime injections of rapid-acting insulin such that approximately 17% is administered at each meal. It should be noted that this equal distribution of mealtime doses must be adjusted subsequently based on glucose levels; it is rare for a patient to consume equal amounts of carbohydrates for each meal of the day. If the patient skips a meal, rapid-acting insulin should not be given.

Although a basal insulin such as glargine or detemir can be given at any time of the day, it is commonly given at bedtime, in part to prevent the mistake of mixing it with a short- or rapid-acting insulin.

Intermediate-Acting Insulin (NPH[Neutral Protamine Hagedorn]), and Short-Acting Insulin (Regular [Novolin R or Humulin R])

In this strategy, the basal and bolus components are not distinctly divided into separate insulins. Thus, the role of each insulin is not as intuitive as with the long- and rapid-acting insulins. Nonetheless, the strategy is simple. Here, 25% of the TDD is administered as short-acting (regular) insulin before each of the three meals. The remaining 25% is administered as intermediate-acting (NPH) insulin at bedtime.

An important feature of this type of plan is that, unlike the long- and rapid-acting insulin plan, mealtime insulin must be given even when a meal is omitted or reduced. This is because the mealtime insulin covers part of the basal-insulin requirement. When a patient is fasting, the “mealtime” insulin dose should be reduced by half,

and the full bedtime dose should be continued unchanged (see below). Additionally, it is important to consider proper timing of the short-acting insulin in relation to meals. The most challenging aspect of this regimen in the inpatient setting is to ensure the delivery of short-acting insulin 30–45 min before a meal, for optimal efficacy.

NPH insulin has a significant peak, albeit fairly broad, which means it has a bolus component as well. Therefore, in some people, it may be helpful when given in the morning, to help cover lunch, and given at bedtime to help with the dawn hepatic glucose output surge. However, for patients who are fasting and who do not exhibit this dawn phenomenon, the dose of evening NPH must be reduced to prevent hypoglycemia. Furthermore, NPH insulin is not recommended for daytime use for patients who are fasting, as the midday peak may result in hypoglycemia.

The Patient Who Is Not Eating

The general principal in this situation is to continue the basal component while removing the bolus component. For the long- and rapid-acting insulin strategy described above, the long-acting insulin can be continued at the usual dose and time. The rapid-acting insulin is not given. When used at an appropriate dose, basal insulin should not cause fasting hypo- or hyperglycemia. However, for patients who will have prolonged periods of fasting or whose basal dose is unknown, administration of a long-acting basal insulin may increase the risk for prolonged hypoglycemia, and use is not recommended. These patients can be transitioned to a regimen of regular insulin every 6 h, as below. For the intermediate- and short-acting insulin regimen, the regimen can be changed in two ways. If the period of fasting is short-term, the existing regimen can be continued, with administration of half doses of the regular insulin at mealtimes. Alternatively, for patients who are not eating for an extended period of time, short-acting (regular) insulin may be given every 6 h without any intermediate-acting (NPH) insulin. In this second strategy, there will still be a small peak in the insulin activity, but it prevents hyperglycemia similar to longer-acting basal insulin, without the danger of prolonged hypoglycemia.

Patients with type 1 diabetes should always receive basal insulin, even if they are not eating, to prevent development of DKA. If necessary, IV dextrose (D5) may be given to support blood glucose during this time.

Correctional Insulin Scale

The correctional insulin scale is a tool designed to correct unpredictable hyperglycemia so that a patient's scheduled insulin regimen can be effective. It should not be used alone. Importantly, correctional insulin is given as a rapid- or short-acting insulin along with bolus insulin (depending on the patient's scheduled insulin type); it should never be given at bedtime.

Although many institutions have a "standard" correctional insulin scale, it is better to calculate an individualized scale to avoid under- or overtreatment. A quick and easy estimation for the scale increment is to use 5% of the TDD of insulin. For

Table 2.3 Example of correctional insulin scale

Glucose	Correctional insulin dose[a]
150 mg/dL (8.0 mmol/L)	None
150–200 mg/dL (8.0–11.0 mmol/L)	3 units
201–250 mg/dL (11.1–13.8 mmol/L)	6 units
251–300 mg/dL (13.9–16.6 mmol/L)	9 units
>300 mg/dL (>16.6 mmol/L)	12 units

[a]In some patients it might be too aggressive to start a correctional insulin scale at 150 mg/dL (8.0 mmol/L); e.g. a patient with hypoglycemia unawareness

example, if a patient has a TDD of 60, then 5% of 60 units is 3 units. Thus, the scale is designed with 3-unit increments as shown in Table 2.3.

Key Points: Choosing an Insulin Regimen

- All of the calculations shown here are estimates. Each patient will have a unique response to insulin, which will vary with inpatient circumstances. Thus, it is critical to reassess the regimen daily and adjust promptly. If this becomes challenging, an endocrine consultant can assist.
- Calculate a weight-based TDD of insulin for a starting point, or use the home TDD, if it appears reasonable.
- Make modifications based on age, type of diabetes, concern for hypoglycemia, use of non-insulin antidiabetic agents, renal function, and concomitant glucocorticoid use.
- Divide into basal and bolus components and, if desired, add a correctional insulin scale.

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