10

Prevention of Hospital Hypoglycemia by Algorithm Design: A Programming Pathway for Electronic Order Entry

Susan S. Braithwaite[1], Lisa Clark[1], Lydia Dacenko-Grawe[1], Radha Devi[1], Josefina Diaz[2], Mehran Javadi[1] and Harley Salinas[1]
[1]*University of Illinois-Chicago; Saint Francis Hospital, Resurrection Health Care*
[2]*University of Illinois-Chicago; Saint Joseph Hospital, Resurrection Health Care*
United States of America

1. Introduction

Caregivers treating hospitalized patients are confronted with the necessity both to control hyperglycemia and also to avoid iatrogenic hypoglycemia. Despite controversy about optimal glycemic targets, a large body of evidence associates uncontrolled hyperglycemia with adverse outcomes, both in the intensive care unit and also on general hospital wards (American Diabetes Association, 2011; Moghissi et al., 2009). On general wards, glycemic control during use of scheduled subcutaneous insulin is superior to that seen during use of sliding scale regimens (Baldwin et al., 2005; Umpierrez et al., 2007). When scheduled insulin was compared to sliding scale treatment among general surgical patients, glycemic control was improved (mean blood glucose 145 ± 32 mg/dL vs. 172 ± 47 mg/dL, $p < 0.01$), and a composite outcome of complications was reduced from 24.3 to 8.6%with odds ratio 3.39 (95% CI 1.50-7.65), $p = 0.003$ (Umpierrez et al., 2011). Nevertheless, the problem of hypoglycemia is a barrier to successful control of hospital hyperglycemia. Among 1718 adult patients admitted at academic medical centers and having hyperglycemia or receiving insulin therapy, hypoglycemia occurred on 2.8% of all hospital days (Boord et al., 2009). Predisposing factors and adverse outcomes associated with hypoglycemia have been examined in observational studies and in clinical trials studying the effect of glycemic control upon nonglycemic outcomes (Bagshaw et al., 2009; Fischer et al., 1986; Finfer et al., 2009; Kagansky et al., 2003; Krinsley et al., 2007; Maynard et al., 2008; Smith et al., 2005; Stagnaro-Green et al., 1995; Turchin et al., 2009; Van den Berghe et al., 2006; Varghese et al., 2007; Vriesendorp et al., 2006; Wexler et al., 2007). Mortality of patients having myocardial infarction is higher at the lowest as well as the highest ranges glucose, such that the relationship between mortality and glucose is described by a J-shaped curve (Kosiborod et al., 2008). Outcomes of hospitalized patients that have been linked to hypoglycemia include increased ICU mortality or hospital mortality rates, adverse events such as seizures, and increased length of stay. In the intensive care unit and on general wards, associated factors

identified among patients having hypoglycemia include use of bicarbonate-based substitution fluid during continuous venovenous hemofiltration, need for inotropic support, greater severity of illness, co-administration of octreotide with insulin, comorbidities including chronic kidney disease, sepsis, advanced age, history of diabetes or severe diabetes, and history of prior episodes of hypoglycemia. Of special importance, because of the implication for prevention, is the frequency with which the literature on hospital hypoglycemia describes interruption of normal feedings attributable to hospital routine, or episodes of reduced enteral intake without adjustment of insulin therapy, as a factors predisposing to hypoglycemia.

Mechanisms of potential harm from hypoglycemia are partially understood, but the causal relationships between hypoglycemia or iatrogenic hypoglycemia and outcomes is unclear. Concerning the association of hypoglycemia with adverse outcomes, it remains a tenable explanation at least in part that severity of illness may predispose both to adverse outcomes and to hypoglycemia (Kosiborod et al., 2009; van den Berghe et al., 2006). Proof of permanent injury ascribed to a hypoglycemic episode in the hospital setting sometimes is available, but the case ascertainment rate is low. Although proof of direct harm from identifiable hypoglycemic events within large studies may be not discerned by statistical analysis, yet the harm is uniquely damaging to the individual suffering the hypoglycemic event, so that the reporting of isolated cases remains important (Bhatia et al., 2006; Scalea et al., 2007). Life-changing morbidity or mortality may result from a severe hypoglycemic reaction. It is also suspected that some harms may result from hypoglycemia that are not directly traceable to immediate consequences of a specific hypoglycemic event. Since hospital patients will not be randomized to hypoglycemia or non-hypoglycemia, our understanding of the causes and clinical impact of hypoglycemia will be observational, resulting from analyses of hypoglycemia as a secondary outcome, within trials of therapeutic strategies or interventions aiming at targets other than hypoglycemia, or resulting from analysis of hypoglycemia within cohort studies. For the present, the association of hypoglycemia with adverse outcomes justifies development of strategies for prevention of hypoglycemia in the hospital.

The goal of this chapter is to describe attributes of a programming pathway for computerized order entry that may incorporate the best elements of paper protocols for subcutaneous insulin and that may help prevent hospital hypoglycemia. In designing treatment for the hyperglycemic patient, it is necessary to anticipate events that create risk for hypoglycemia and to meet those events with appropriate revisions of nutritional therapy and scheduled insulin. When insulin orders are in place but patient risk for hypoglycemia is predicted to increase, the components of insulin therapy that might be withheld or reduced may differ, depending upon co-morbidities, anticipated disruption of carbohydrate exposure, alteration of other medical therapies, and classification of diabetes. By juxtaposing elements of care within a checklist of orders, paper protocols present reminders to the prescriber about strategies for hypoglycemia prevention. We believe the main opportunity for improvement within computerized order entry systems is the need to present several different packages of orders at the user interface that match differing patterns of carbohydrate exposure. For each pattern of carbohydrate exposure, the package must include default and acceptable alternative orders that encompass monitoring of blood glucose, scheduled and correction-dose insulin orders, and menus of additional directions associated with the insulin orders.

2. Algorithms for glycemic management in the hospital

Any algorithm must identify a target blood glucose or a target range and define a safe and effective method for attainment and homeostatic maintenance of target range control. Provisions must be in place regardless of algorithm design to make anticipatory adjustments to prevent hypoglycemia in case of sudden change of any of the usual determinants of insulin requirement, such as carbohydrate exposure or concomitant medications. After making brief reference to an algorithmic method for protection against hypoglycemia during intravenous insulin infusion, the literature on electronic order entry of glycemic management plans is briefly referenced, and idealized examples of programmable branching pathways for patients who are eating and not eating will be presented.

2.1 Intravenous insulin infusion

Computerization of intravenous insulin algorithms may be successfully accomplished either through a free standing electronic decision support system or as part of a hospital computer system (Dortch et al, 2008; Hermayer et al. 2007; Junega et al, 2007). The method of computerized order entry that we will use is under construction and will not be presented here, except to say that the algorithms are related to those previously published (Bellam and Braithwaite, 2010; Devi at al, in press 2011). The choice of intravenous insulin protocol depends upon the population treated. The protocols will be designed according to a mathematical rule having population-specific parameters. The protocols are related to column-based tabular protocols in which each column of the table is associated with an assumed maintenance rate of insulin infusion that is thought to be the rate necessary to maintain target range control. Each row of the table represents a range of blood glucose values. The assumed maintenance rate (column assignment) is determined with knowledge of the previous assumed maintenance rate (column assignment) together with the rate of change of blood glucose, at the previous insulin infusion rate. The next insulin infusion rate, at each nursing interaction, depends upon the blood glucose (the row) and the reassigned maintenance rate (column re-assignment, if any). The conservative protocol differs from the standard critical care protocol for intravenous insulin infusion not in the target range blood glucose values, but in the column change rules that result in changing from a lower to a higher maintenance rate (column), or from a higher to a lower assumed maintenance rate (column). That is to say, by analogy with a paper protocol, the column change rules based on rate-of-change of glucose are more conservative under the conservative protocol. We believe that two design features of the intravenous insulin infusion protocols will be shown to be protective against hypoglycemia, namely (1) the column change rules based on rate of change of blood glucose and (2) the near-sigmoidal relationship, at given maintenance rate (within-column), between the insulin infusion rate and the blood glucose.

The protocols for diabetic ketoacidosis and hyperglycemic hyperosmolar state each differ from each other and from the critical care protocols for intravenous insulin infusion by having different column change rules and additionally different target ranges for blood glucose. The target range for blood glucose in treatment of diabetic ketoacidosis or hyperglycemia hyperosmolar coma is higher than for other patients likely to be treated with intravenous insulin infusion. An initially fixed-dose weight-based method for assigning insulin infusion rate during the initial hours of treatment is advocated in the consensus statement of the American Diabetes Association for use during the first several hours of treatment of DKA (Kitabchi et al., 2009). In contrast, a dynamic rule to assign the insulin

infusion rate during treatment of hyperglycemic crisis is employed at our institutions (Devi et al., 2011). The deactivation time for intravenous insulin infusion may be as long as 90 minutes (Mudaliar et al., 2008). A rationale for a dynamic insulin infusion rate in the early hours of treatment for hyperglycemic emergency is that under conventional management late hypoglycemia sometimes complicates the treatment course.

2.2 Algorithms for subcutaneous insulin

Many protocols for hospital care were developed in the era of handwritten order entry. Order sets were developed that served as a checklist to prevent omissions of elements of care. For example, a reminder to have a standing "prn" order for intravenous dextrose under selected conditions or to order an A1C may be part of the order set. Order sets help integrate the components of care with each other. Timing of testing, insulin, and meals may be coordinated by justaposition of related orders on a paper order set. A lynchpin of successful order writing is the coordination of the patterns of glucose monitoring and insulin administration with carbohydrate exposure (Bellam and Braithwaite, 2010; Braithwaite et al., 2007; Campbell et al., 2004; Thompson et al., 2005). If an order set is well designed, by checking boxes and entering numbers the prescriber creates orders that are familiar to and readily interpreted by pharmacy and nursing staff. Lengthy narrative is reduced. Standardization of order entry protects patient safety. A well designed order set facilitates individualization of patient care. Guidelines may be appended to or embedded within order sets, together with references to supportive medical literature (Donaldson et al. 2006; Hermayer et al, 2009; Lee et al. 2008; Maynard et al., 2009; Schnipper et al., 2010; Trujillo et al., 2008; Wexler et al., 2010). Protocols executed through order sets were thought to reduce medical errors, improve safety, and increase adherence to those guidelines that were supported by medical evidence.

As electronic order entry began to gain widespread use, a body of descriptive studies developed concerning the use of structured order sets for electronic order entry for subcutaneous insulin therapy in the hospital. Hermeyer and colleagues described a comprehensive program, including a web-based calculator for the intravenous insulin protocol (Hermeyer et al., 2009). Maynard and colleagues, in a published study of computerized order entry with paper guidelines used on the side, defined time periods 1, 2 and 3 (TP1, TP2, and TP3) during rolling out of the program. Paper statements of guidelines adjunctive to computerized order entry were developed (Lee et al., 2008). The relative risk (RR) of an uncontrolled patient-stay was reduced from baseline to 0.91 (CI 0.85-0.96) in TP2, and to 0.84 (CI 0.77-0.89) in TP3, with more marked effects in the secondary analysis limited to patients with at least 8 point-of-care glucose values (Maynard et al., 2009). The percent of patient-days with hypoglycemia was 3.8%, 2.9%, and 2.6% in the 3 time periods, representing a RR for hypoglycemic day in TP3:TP1 of 0.68 (CI 0.59-0.78). Similar reductions were seen in risk for hypoglycemic patient-stays.

Evidence from cluster randomized studies supports the use of structured order sets to improve glycemic outcomes. Schnipper and colleagues in several stages developed a computerized version of their order entry system for glycemic control (Schnipper et al., 2009; Schnipper et al., 2010; Trujillo et al., 2008). In a cluster randomized design of 179 patients at a single site, two of the four medical services were chosen randomly to receive the intervention using a computerized order set built into the proprietary computer at Brigham and Women's Hospital. The mean percent of glucose readings between 60-180 was

75% in the intervention group and 71% in the usual care group [adjusted RR 1.36 (1.02-1.80)]. With the intervention, there were a lower patient-day weighted mean glucose (148 vs 158, p = 0.04); less use of sliding scale (25% vs 58%, p = 0.01); and no difference in hypoglycemia < 40 mg/dL (0.5% vs 0.3%, p = 0.58). Wexler and colleagues at a single site randomized medical teams to availability of an electronic insulin order template versus usual insulin ordering. Intervention group patients (n=65) had mean glucose of 195 +/- 66 mg/dl. Control group patients (n=63) had mean glucose of 224 +/- 57 mg/dl (P=0.004). In the intervention group, there was no increase in hypoglycemia (Wexler et al., 2010).

With electronic order entry, there is a risk that some of the integration between the components of care might be lost that had been achievable with paper order sets. Under some electronic systems, juxtaposition of related orders is lost. Users might have to navigate between screens to complete a package of orders relating to diabetes encompassing such necessities as a nutrition plan, point-of-care tests, insulin doses, and a treatment plan for hypoglycemia. A plan for continuous enteral tube feedings might be entered on one screen, followed by insulin orders on another screen, and finally orders for point-of-care glucose monitoring and call parameters on a third screen. Orders that are preselected as the likeliest choice, based on absolute rate of utilization, could be programmed as defaults but might be misapplied to subgroups through user failure to deselect and replace the order for the patient at hand. As an example, if the choice "ACHS" appears at the top of a list of possible orders for glucose monitoring as the default (ante cibum and hora somni, before meals and at bedtime), then an order for ACHS timing could be accepted by default, rather than timing more appropriate to the carbohydrate exposure actually planned for a patient who might receive continuous enteral tube feedings.

3. Programming pathway for glycemic management in the hospital

In the United States, in coming years hospitals will strive to comply with "meaningful use" regulations for electronic health records, described in the Health Information Technology for Economic and Clinical Health Act (Blumenthal & Tavenner, 2010). Electronic order entry will gradually replace handwriting of orders. Some systems will sharply restrict the use of free-text entries, creating necessity for a system that will link orders to preprogrammed comments that may be selected by the user. A template similar to that of electronic order entry might be used to facilitate communication among caregivers at the time of patient transfers and discharge. The remainder of this chapter will describe the design of an idealized proposal for a programming pathway for electronic order entry for glycemic management of hospitalized patients.

Within the figures showing the programming pathway, orders that are members of a category or subcategory have the same level of indentation. Pre-assignment of a default choice within-category sometimes is justified either based on frequency of use or medical indications. The user may select or deselect an order by clicking on a button associated with an order at the user interface. In some cases, selection by a provider of one order results in de-selection of another order within the same subcategory or category. In other cases, choices within-category or within sub-category are not mutually exclusive; selection of one order does not result in de-selection of another order (Figure 1). It is envisioned that the user will move through a sequence of those screens within the programming pathway that are determined by having made an early commitment to one branch of the algorithm. When the provider is satisfied that no modifications are required, the provider enters an electronic signature.

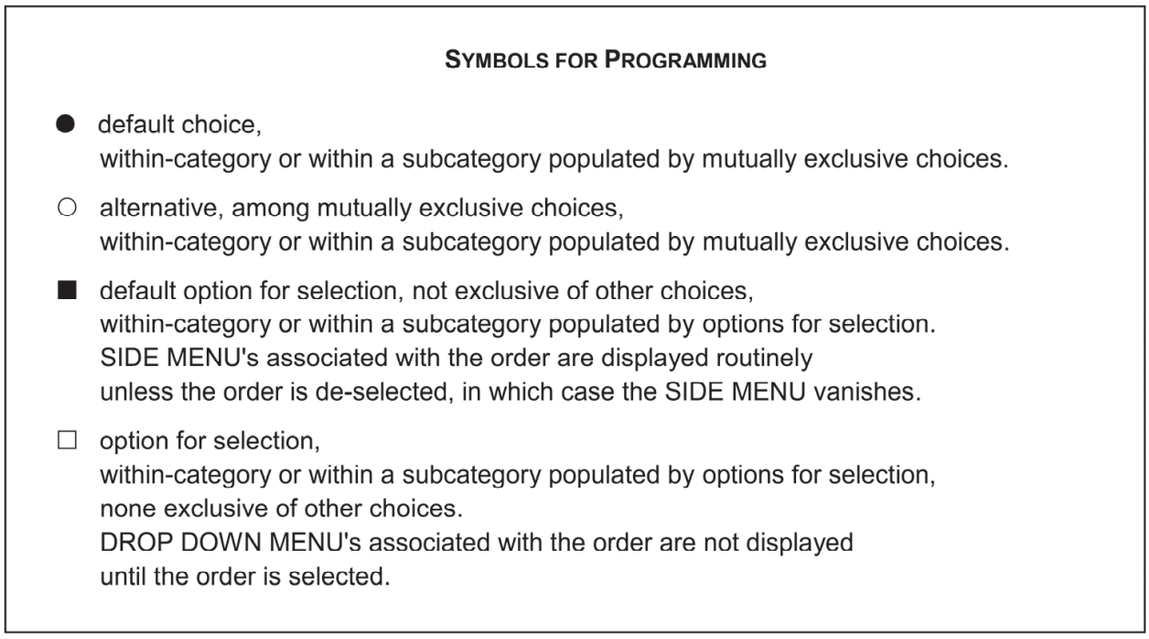


Fig. 1. Instructions to programmer. Symbols signify the function of buttons at the user interface and define the structure of the program.

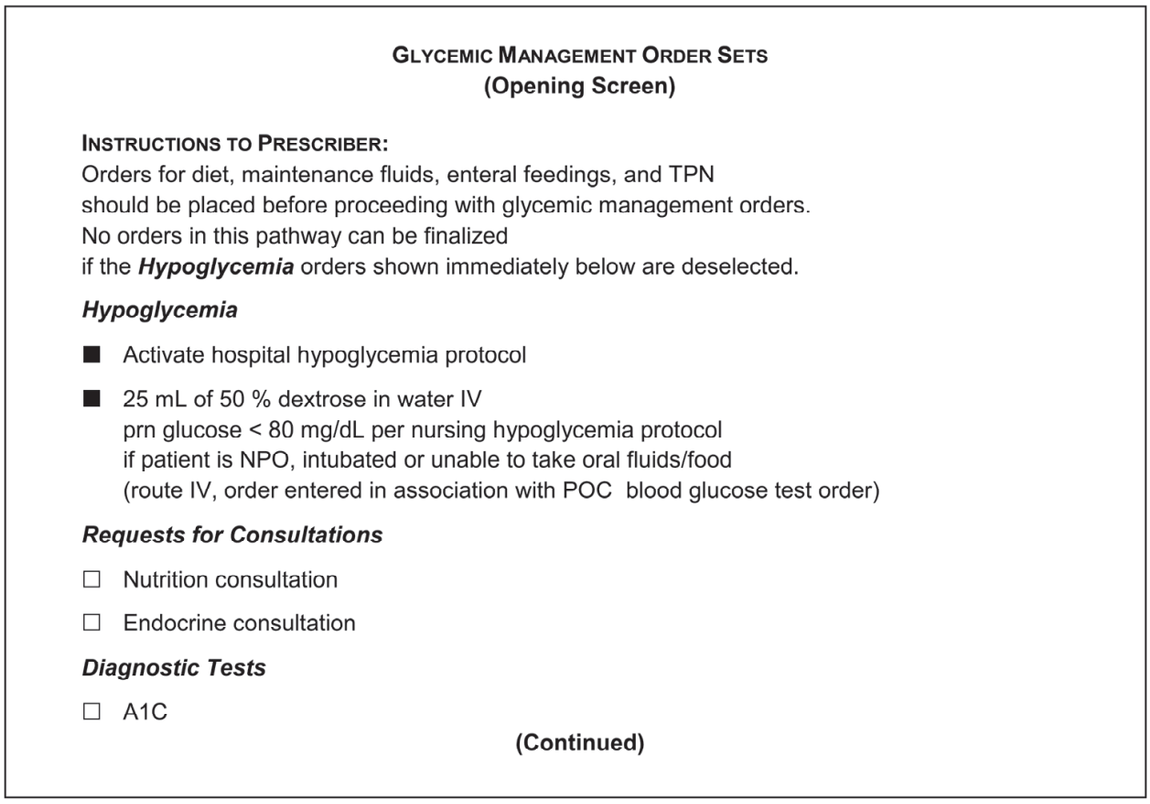
3.1 Programming pathway as checklist

Just as structured paper order sets for subcutaneous insulin therapy may protect the patient from omissions of needed elements of care by presenting a checklist, similarly a checklist of reminders for glycemic management may appear within a branching programming pathway. For example, the main trunk of the branching pathway may call for elements of care that are considered to be potentially universally appropriate, such as a standing "prn" order for concentrated intravenous dextrose for treatment of hypoglycemia, a nutrition consult, or an A1C (Figure 2). The programming pathway that we will present goes on to branch into 8 different treatment plans, each having preventive measures related to hypoglycemia that are specific to the components of the treatment plan, embedded as checklist options for selection, such as “reduce” orders for basal insulin for type 2 diabetes or “hold” parameters for prandial insulin (Figure 3).

3.2 Individualization facilitated under the programming pathway

It is necessary to specify precautions against hypoglycemia, but manual entry can be burdensome. Under the branches of the pathway, measures for hypoglycemia prevention could take different forms depending upon the carbohydrate exposure of the patient, including but not limited to the scheduling the monitoring of blood glucose, assignment of call parameters at alert levels of glucose, pattern of insulin administration, or use of the classification of hyperglycemia or diabetes to determine “hold” parameters for specific components of insulin therapy. We believe the ordering of these protective additional directions is more likely to occur when a complete menu of options is presented to the prescriber than when reliance is placed upon provider initiative and recall. To a large extent, manual entry of such safety provisions can be replaced by checking boxes and entering

numbers. The programming pathway accommodates the spectrum of reasonable provider treatment preferences. By offering a menu of treatment alternatives and additional directions to the insulin orders, the programming pathway facilitates individualization of care for each patient.



GLYCEMIC MANAGEMENT ORDER SETS
(Opening Screen)

INSTRUCTIONS TO PRESCRIBER:
Orders for diet, maintenance fluids, enteral feedings, and TPN
should be placed before proceeding with glycemic management orders.
No orders in this pathway can be finalized
if the ***Hypoglycemia*** orders shown immediately below are deselected.

Hypoglycemia

■ Activate hospital hypoglycemia protocol

■ 25 mL of 50 % dextrose in water IV
prn glucose < 80 mg/dL per nursing hypoglycemia protocol
if patient is NPO, intubated or unable to take oral fluids/food
(route IV, order entered in association with POC blood glucose test order)

Requests for Consultations

☐ Nutrition consultation

☐ Endocrine consultation

Diagnostic Tests

☐ A1C

(Continued)

Fig. 2. Opening screen.

3.3 Intravenous insulin algorithm selection under the pathway

The programming pathway specifies options for four different intravenous insulin infusion protocols. A full discussion of these pathways is beyond the scope of the present discussion. For critical care patients requiring an intravenous insulin infusion, to help the user decide whether to order the conservative critical care intravenous insulin infusion protocol or the standard one, the user may find a link to a drop-down guideline for indications for the conservative IV insulin protocol. This states that the conservative IV insulin protocol will be appropriate for patients with renal failure, malnutrition, hepatic failure, sepsis, severe congestive heart failure, adrenal insufficiency, and other conditions that the caregiver judges to create high-risk for hypoglycemia. The conservative protocol also is the protocol to which the prescriber might default, in case a patient already has demonstrated hypoglycemia while on the standard protocol but still requires intravenous insulin infusion therapy (Figure 3).

An American Diabetes Association consensus statement provides a summary of diagnostic criteria for diabetic ketoacidosis or hyperosmolar hyperglycemic state (Kitabchi et al., 2009). The criteria for each can be summarized in a link to a drop-down guideline for diagnosis,

accessed from the opening menu (Figure 3). Classification as diabetic ketoacidosis (DKA) is suggested by plasma glucose > 250 mg/dL, arterial pH < 7.3, bicarbonate < 15, anion gap > 12 meq/L, and moderate ketonuria or ketonemia. Classification as hyperglycemic hyperosmolar state (HHS) is suggested by plasma glucose > 600 mg/dl, serum osmolality > 320 mosm/L, arterial pH > 7.3, bicarbonate > 15 meq/L, and minimal ketonuria and ketonemia.

3.4 Subcutaneous insulin algorithm selection under the pathway

For patients who will receive subcutaneous insulin, once the pattern of carbohydrate exposure is determined, then the prescriber can select the appropriate branch of the pathway (Figure 3). Selection of a single branch from the list will launch an appropriate submenu, dependent upon carbohydrate exposure, for the schedule of blood glucose monitoring and the selection and timing of components of insulin administration. One branch of the programming pathway presently under construction will provide for a diabetes hospital patient self-management program. Models for patient self-management in the hospital have been described (Braithwaite et al., 2007; Bailon et al., 2009). The focus of this chapter is on orders for subcutaneous insulin therapy for patients who are not candidates for hospital self-management.

GLYCEMIC MANAGEMENT ORDER SETS
(Opening Screen, Continued)

Choose One Branch of the Pathway for Orders Associated with Insulin Therapy

- ○ **GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE EATING**
- ○ **GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE NOT EATING, INCLUDING PATIENTS RECEIVING CONTINUOUS ENTERAL FEEDINGS, CONTINUOUS DEXTROSE-CONTAINING MAINTENANCE FLUIDS, OR NO CARBOHYDRATE EXPOSURE**
- ○ **GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WITH OVERNIGHT ENTERAL FEEDINGS AND DAYTIME MEALS**
- ○ **CRITICAL CARE INTRAVENOUS INSULIN INFUSION, NON-DKA, NONPREGNANT ADULT**
- ○ **CONSERVATIVE CRITICAL CARE INTRAVENOUS INSULIN INFUSION, NON-DKA, NONPREGNANT ADULT**
  (link to drop-down guideline for indications for conservative IV insulin protocol appears here)
- ○ **INTRAVENOUS INSULIN INFUSION PROTOCOL FOR HYPERGLYCEMIC CRISES, NONPREGNANT ADULT, DIABETIC KETOACIDOSIS**
  (link to drop-down guideline for diagnosis appears here)
- ○ **INTRAVENOUS INSULIN INFUSION PROTOCOL FOR HYPERGLYCEMIC CRISES, NONPREGNANT ADULT, HYPEROSMOLAR HYPERGLYCEMIC STATE**
  (link to drop-down guideline for diagnosis appears here)
- ○ **DIABETES HOSPITAL PATIENT SELF MANAGEMENT**

(Go to First Screen within Selected Branch of the Pathway)

Fig. 3. Selection of branch of the pathway.

3.5 Subcutaneous insulin dose titration after pathway initiation

A method for establishing starting doses of insulin is described in sections that will follow. An associated guideline might state that rewriting of the doses of scheduled insulin should be considered daily. Here, a guideline for revision of scheduled insulin is presented that is appropriate to each subcutaneous pathway.

- review comorbidities and medications affecting insulin requirement and carbohydrate exposure or omission.
- review the medication administration record for confirmation of insulin dosing over the preceding 24 hr.
- add the total amount of scheduled and correction dose insulin delivered in the previous 24 hr to determine total daily dose of insulin actually delivered.
- *if all blood glucose readings were > 180 mg/dL, add 10%* to the total daily dose actually delivered in the previous 24 hr to determine the new total daily dose of scheduled insulin.
- *if any blood glucose was < 80 mg/dL, subtract 20%* from the total daily dose actually delivered in the previous 24 hr to determine the new total daily dose of scheduled insulin.

The new dose of scheduled insulin is reapportioned between the components of scheduled therapy. Once the treatment pattern has been entered, changing of dose or correction dose scale can be accomplished outside of the programming pathway. If there are no further specifications, any standing "additional directions" concerning scheduled insulin may be carried forward.

Therapeutic inertia in changing established insulin regimens is a recognized problem in the care of hospitalized patients. In a study of 52 hospitalized patients treated with 50% dextrose for an episode of hypoglycemia, it was found that subsequent to withholding of insulin at the time of the hypoglycemia, 31% of the patients received no other change in treatment (Garg et al., 2004). The guideline above would give caregivers direction on trouble-shooting of the causes of hypoglycemia and making appropriate revisions of treatment.

3.6 Integration of the components of care under the pathway during placement of orders for subcutaneous insulin

A decision support system helps the prescriber to recognize the components of care under the pattern of treatment that is ordered and the relationship between these components. During widespread adoption of computerization of order entry, a distinct computer order is required separately for feedings, intravenous dextrose, glucose monitoring, each component of insulin therapy, treatment of hypoglycemia, and call parameters. The relationship of these elements of care to each other and their timing must be coordinated. The integration of the components of care, achieved by many paper protocols and order sets, must be preserved. The prescriber must be able to accomplish the goals of glycemic control and hypoglycemia prevention without navigation through multiple screens of an electronic order entry system. Whether patients are eating or not, interruption of carbohydrate exposure is a well verified risk factor for hospital hypoglycemia. The risk arises from hospital routine that interrupts feedings or patient factors that result in poor oral intake (Fischer et al., 1986). Restrictions on free-text entries will necessitate preprogramming of additional directions. In each branch of the pathway that will be shown, in case of reduction of carbohydrate exposure, the insulin orders may be accompanied by standardized statements concerning hypoglycemia

prevention. Examples include additional directions to “hold” prandial insulin in case of meal omission, “hold” prandial insulin on the mornings of dialysis, or “reduce” insulin in case of poor oral intake.
The order entry system should associate the pattern of blood glucose monitoring, the components of insulin administration together with additional directions, the "call" parameters, and the orders for "prn" oral or intravenous carbohydrate. If an order entry system is well designed, the user will encounter a comprehensive electronic menu for prescribing a glycemic management plan, having internally coordinated components, accessible through a single branch of the pathway of order entry. Under each of the first three branches of the pathway, nursing instructions include an assessment of patient needs, including early attention to patient education and eventual discharge planning.

3.6.1 Subcutaneous Insulin for patients who are eating

Basal-prandial-correction therapy is a prescribing pattern for insulin, described in previous reviews, that is especially well suited to insulin treatment of the hospitalized patient who is eating (Hirsch, 2005; Clement et al., 2004). The orders for monitoring and insulin are written in association with a meal plan, usually a consistent carbohydrate diet. Other specifications to the diet are preserved that may be required for care of comorbidities. The nursing orders for monitoring of blood glucose provide options for testing postprandially but recommend restriction of scheduled postprandial testing to conditions in which retrospective review of the results might be used to revise scheduled therapy for special populations or conditions, such as pregnancy or cystic fibrosis (Figure 4). Most patients require either testing with meals; with meals and at bedtime; or with meals, at bedtime, and midsleep.
Prandial insulin coverage is the treatment given to cover meals, and basal insulin is the treatment necessary to prevent unchecked gluconeogenesis and ketogenesis, required whether or not nutrition is provided. The long-acting insulin analogs glargine and detemir are designed to provide basal coverage. Glargine may be given once daily for most patients, and detemir may be given once or twice daily. The rapid-acting insulin analogs lispro, aspart and glulisine are designed to provide prandial coverage and to provide rapid correction of hyperglycemia. Biphasic or premixed insulin therapy provides both basal and prandial insulin coverage. In the hospital, since there is a risk of interruption of meals, it is desirable to use an insulin treatment plan under which the prandial component of treatment can be interrupted without compromise to the basal insulin coverage. For patients eating discrete meals, biphasic insulin therapy in the hospital generally is replaced by treatment separately with basal coverage and prandial coverage. For correction of hyperglycemia, the rapid-acting insulin analogs are given with meals, sometimes for coverage of snacks, and sometimes at bedtime or midsleep.
Some patients having type 2 diabetes who normally require insulin may experience reduction of insulin resistance during fasting and may produce endogenous insulin sufficient that under conditions of reduced oral intake the requirements for exogenous insulin may decline. Others, who normally are insulin independent, may experience stress-related insulin resistance in the hospital sufficient to produce a requirement for exogenous insulin treatment. Dose initiation guidelines for insulin-requiring patients whose dose requirements are not known might be stated conservatively as follows (with reapportionment as indicated for special conditions, as described below):

- daily basal requirement 0.15 units/kg for type 2 diabetes or for stress hyperglycemia, and 0.25 units/kg for type 1 diabetes

- daily prandial requirement 0.15 units/kg for type 2 diabetes or for stress hyperglycemia, and 0.25 units/kg for type 1 diabetes, apportioned between three meals.

The total daily dose of scheduled insulin is apportioned between the scheduled basal and prandial insulin. A guideline concerning the initial percentage distribution of total daily dose of scheduled insulin between the components of therapy may suggest 50% basal and 50% prandial for most patients, but reapportionment for special conditions:

- 50% basal insulin, 50%prandial insulin for many patients
- > 50% basal insulin, < 50%prandial insulin during immediate recovery following heart surgery
- 33% basal insulin , 67%prandial insulin for renal or hepatic failure, malnutrition, or corticosteroid therapy

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE EATING

Physician Orders for Nursing Staff

■ Point-of-care blood (POC) blood glucose monitoring with frequency

SIDE MENU
(Prescriber guideline: the post cibum (postprandial, PC) options may be appropriate for pregnant patients, patients having cystic fibrosis, and some other patients in special situations, but are not required for general management of diabetes or hyperglycemia.)

Frequency of Monitoring

●	WMEALS, HS (default)	[0800, 1200, 1700 before meals; 2200]
○	WMEALS, HS, 0200	[0800, 1200, 1700 before meals; 2200, 0200]
○	ONCE DAILY	[0800 before breakfast]
○	TWICE DAILY	[0800 before breakfast, 1800]
○	WMEALS	[0800, 1200, 1700 before meals]
○	2HR PC	
○	0800 & 2HR PC	
○	WMEALS & 2HR PC	[0800, 1200, 1700 before meals, and 2HR PC]
○	WMEALS & 2HR PC	[0800, 1200, 1700 before meals, 2HR PC, & HS; 7x/d)
○	WMEALS & 2HR PC, 0200	[0800, 1200, 1700 before meals, 2HR PC, HS, & 0200; 8x/d]

■ Call house officer for point-of-care glucose

SIDE MENU

Call Parameters, High Glucose

● > 350 mg/dL (default)
○ > _____ mg/dL

■ Call house officer for point-of-care glucose

SIDE MENU

Call Parameters, Low Glucose

● < 70 mg/dL (default)
○ < _____ mg/dL

■ Assess patient needs in relation to discharge

□ Teach patient survival skills (capillary glucose monitoring, insulin injection if used, hypoglycemia)

(Go to Next Screen within Pathway)

Fig. 4. Nursing orders for patients who are eating. WMEALS = with meals. WMEALS, HS = with meals and at bedtime. Times of meals may differ according to institutional practices.

Under a treatment plan using basal-prandial-correction dose therapy, typically basal insulin is given once daily as long-acting insulin analog. Before development of insulin analogs, NPH insulin had been used to provide basal coverage, and regular insulin to provide prandial coverage and correction of hyperglycemia. In general, during the treatment of type 2 diabetes, in comparison with NPH-based basal insulin regimens there is less hypoglycemia with use of long-acting insulin analog therapy for basal coverage (Rosenstock et al., 2005; Hermansen et al., 2006). However, some patients prefer to be treated with NPH. Morning dosing with NPH insulin may provide both basal and partial prandial insulin coverage. In the ambulatory setting, some patients use NPH insulin to achieve pattern correction; for example, an evening dose of NPH insulin may cover the dawn phenomenon, correcting a pattern of morning hyperglycemia by meeting predawn insulin resistance with increased insulin levels. Under the branch of the pathway for patients who are eating, prescribers are given the alternatives of using a long-acting insulin analog or NPH for basal insulin coverage (Figure 5).

Not uncommonly, in order to correct fasting hyperglycemia, doses of intermediate or long acting insulin may have been increased during normal dietary intake to a dose higher than true basal requirements. If the basal insulin dose is unchanged during NPO status (nihil per os, nothing by mouth), patients having type 2 diabetes may experience hypoglycemia (Olson et al., 2009). It is important that the programming pathway should present options for basal insulin reduction or interruption in case of planned NPO status. On the other hand, if the basal insulin dose is established correctly in type 1 diabetes, the dose during NPO status usually may be preserved (Mucha et al., 2004). Omission of basal insulin during NPO status in type 1 diabetes may result in ketoacidosis. Therefore, the programming pathway provides options for prescribers to reduce basal insulin in type 2 diabetes but to continue basal insulin in type 1 diabetes, in anticipation of NPO status. A prescriber guideline embedded in the order entry screen warns against interruption of basal insulin for type 1 diabetes (Figure 5).

In the treatment of type 2 diabetes, rapid-acting analogs for prandial coverage may produce less hypoglycemia than regular insulin (Anderson et al., 1997; Raymann et al, 2006; Velussi at al. 2002). The provider may see the need to provide differing doses of prandial insulin at different times of day; the programming pathway permits flexibility in the prescribing of prandial doses, allowing either a fixed dose (best ordered usually with a consistent carbohydrate diet) or a variable dose (Figure 6). This programming pathway is designed for use on the assumption that not all nursing staff are trained on recognition of carbohydrate content of meals; therefore, insulin-to-carbohydrate ratios are not prescribed under the branch of the pathway for subcutaneous insulin for patients who are eating. A modification of the pathway might be used by hospitals that routinely train all nurses on advanced carbohydrate counting so that the provider might order and nurses might use an insulin to carbohydrate ratio to assign prandial insulin doses according to what is on the patient's tray. Patients using the skills of advanced carbohydrate counting and already skilled in self management may best be treated under a different branch of the pathway, for diabetes hospital patient self management.

Several additional directions may be selected in conjunction with orders for prandial use of rapid-acting insulin analog that provide protection against hypoglycemia. Most obviously, the direction "HOLD IF NPO" is intended to reduce the risk of administration of prandial insulin at times when meals might be omitted. The order to hold prandial insulin for

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE EATING
(Continued)

Scheduled Basal Insulin

☐ Long-acting insulin analog (Long-AA) for basal insulin coverage

DROP DOWN MENU

Long-Acting Analog of Insulin (Long-AA)

● Glargine insulin (route SC, priority routine), dose _____ units
○ Detemir insulin (route SC, priority routine), dose _____ units

Frequency and Time of Medication

● Once daily at 2200 (default for Long-AA)
○ Once daily at 0800
○ Twice daily at 0800 and 2200

Additional Directions

(Prescriber guideline:
true basal insulin requirements should not be withheld for type 1 diabetes)

○ DO NOT WITHHOLD
○ CUT 20% IF NPO
○ CUT 50% IF NPO
○ HOLD IF NPO

☐ NPH for basal insulin coverage, morning dose

DROP DOWN MENU

Morning Dose of NPH

● NPH insulin (route SC, priority routine), _____ units, once daily at 0800

Additional Directions

(Prescriber guideline:
true basal insulin requirements should not be withheld for type 1 diabetes.)

○ DO NOT WITHHOLD
○ CUT 20% IF NPO
○ CUT 50% IF NPO
○ HOLD IF NPO

☐ NPH for basal insulin coverage, evening dose

DROP DOWN MENU

Evening Dose of NPH

○ NPH insulin (route SC, priority routine), _____ units, once daily at 1700
○ NPH insulin (route SC, priority routine), _____ units, once daily at 2200

Additional Directions

(Prescriber guideline:
true basal insulin requirements should not be withheld for type 1 diabetes.)

○ DO NOT WITHHOLD
○ CUT 20% IF NPO
○ CUT 50% IF NPO
○ HOLD IF NPO

(Go to Next Screen within Pathway)

Fig. 5. Basal insulin orders for patients who are eating. The start time and duration for each recurring medication order are to be programmed, but will not shown. SC = subcutaneously; NPO = nihil per os (nothing by mouth). Abbreviations may differ according to institutional policy.

glucose below a given threshold replicates a conservative practice pattern that many users of multiple daily insulin injections employ at home. Acceptable control may be achieved by postprandial administration of rapid-acting insulin analog (Jungmann, 2005). For patients whose oral intake is uncertain, the programming pathway provides the option that the use of prandial insulin might be withheld until 50% of the tray has been taken. For patients with stage V chronic kidney disease having hemodialysis, there may be greater risk for hypoglycemia on hemodialysis days (Kazempour-Ardebili et al., 2009). To permit insulin dose reduction by dose omission of rapid-acting analog at breakfast and lunch on dialysis days, a checkbox is provided specifying that the nurse should withhold the scheduled rapid-acting analog before breakfast and lunch on hemodialysis days (Figure 6).

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE EATING
(Continued)

Scheduled Rapid-Acting Analog of Insulin (Rapid-AA)

● Rapid-AA insulin (route SC, priority routine), dose _____ units, every day (default)

SIDE MENU

Frequency and Time of Medication

● WMEALS (default) [0800, 1200, 1700]

Additional Directions

☐ HOLD IF NPO
☐ HOLD IF BG < XXX
☐ HOLD UNTIL 50% OF TRAY IS TAKEN
☐ HOLD SCHEDULED RAPID-AA BEFORE BREAKFAST AND LUNCH ON HEMODIALYSIS DAYS

○ Rapid-AA insulin (route SC, priority routine) every day, dose specified for each meal separately

DROP DOWN MENU

Dose with Frequency and Time of Medication

☐ dose _____ units, every day with breakfast. [0800]
☐ dose _____ units, every day with lunch. [1200]
☐ dose _____ units, every day with supper. [1700]
☐ dose _____ units, every day with HS snack. [2200]

Additional Directions

☐ HOLD IF NPO
☐ HOLD IF BG < XXX
☐ HOLD UNTIL 50% OF TRAY IS TAKEN
☐ HOLD SCHEDULED RAPID-AA BEFORE BREAKFAST AND LUNCH ON HEMODIALYSIS DAYS

(Go to Next Screen within Pathway)

Fig. 6. Prandial insulin (nutritional insulin) for patients who are eating. BG = point-of-care blood glucose.

Frequent dosing with rapid-acting analogs for correction of hyperglycemia creates the risk of "stacking" of effect. When a patient has had hyperglycemia prior to a meal, consideration of another correction dose may arise in the postprandial state. The effect of a previously administered correction dose may not have been fully exerted when the blood glucose is retested. Use of a fixed glucose-dependent correction dose rule, designed to meet specific

pre-meal targets, may result in hypoglycemia when applied postprandially, prior to full dissipation of the effects of any earlier correction dose. Therefore, orders for correction doses under the programming pathway are restricted to the following three time plans for administration: with meals; HS (bedtime); 0200. The orders may provide a different scale for each of those three time plans (Figure 6).

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE EATING
(Continued)

Bridging Doses of Insulin for Transition from Intravenous Insulin Infusion to Scheduled Subcutaneous Therapy

☐ NPH insulin for transitioning from insulin drip (route SC), dose _____ units

DROP DOWN MENU
(Prescriber guideline: if intravenous insulin infusion will terminate at a time of day when the first daily basal insulin dose is not yet due, a bridging dose of subcutaneous NPH insulin may be used once, to be given at least 2 hr prior to interruption of intravenous insulin infusion.)

Priority

○ Priority stat
○ Priority routine, once at _____

☐ Regular insulin for transitioning from insulin drip (route SC), dose _____ units

DROP DOWN MENU
(Prescriber guideline: if intravenous insulin infusion will terminate at a time of day when the first daily basal insulin dose is not yet due, a bridging dose of subcutaneous regular insulin may be used once, to be given at least 2 hr prior to interruption of intravenous insulin infusion.)

Priority

○ Priority stat
○ Priority routine, once at _____

(Go to Next Screen within Pathway for Correction Dose Insulin, Having Separate Selections "With Meals," "HS," and "0200", Not Shown)

Fig. 7. Bridging doses of insulin for patients who are eating, at the time of transition from intravenous insulin infusion to subcutaneous insulin.

Transitioning guidelines from intravenous insulin infusion to subcutaneous insulin recommend that the provider should order subcutaneous insulin before interruption of insulin infusion (Osburne et al., 2006). Infrequently small amounts of basal and prandial insulin (but not subcutaneous correction doses) may be started more than 2 - 4 hr prior to interruption of intravenous insulin infusion. In order to transition from intravenous insulin to subcutaneous insulin, the 24-hr requirement for scheduled subcutaneous basal insulin that is to be started or added may be about 80% of the 24-hr amount of basal insulin, extrapolated from observation of insulin requirement during the last 6-8 hr of intravenous insulin infusion. To avoid overestimation of basal dose requirement, observation must be made during a timeframe of medical stability during which there have been no meals, such as midnight to 0800; there must be no change of carbohydrate-containing maintenance fluids, enteral feedings, or total parenteral nutritional at the time of transition to

subcutaneous insulin therapy; there must have been independence from pressors and continuous veno-venous hemodialysis; and there must be no change of corticosteroid dose. If the time of transition occurs at a time of day that differs from the usual time of administration of long-acting insulin analog, then a bridging dose of regular or intermediate-acting insulin may be given (Figure 7).

3.6.2 Subcutaneous insulin for patients who are not eating

The patient receiving continuous exposure to carbohydrate as intravenous dextrose or enteral feedings, or the patient receiving no carbohydrate, generally should have glucose monitoring at time intervals that are equally spaced (Figure 8). The order "ACHS" for a patient who has been made "NPO" is meaningless. Therefore, the branch of the programming pathway for patients who are not eating starts with the default order for monitoring of point-of-care blood glucose every 6 hr.

During NPO status, the dose of insulin required to cover dextrose-containing maintenance fluids, total parenteral nutrition (TPN), or enteral tube feedings is described as nutritional insulin. Outside of the programming pathway, the provider may include insulin among the TPN additives. long-acting insulin analog sometimes is used for coverage of continuous enteral feedings. Under such a regimen, safety precautions must be in place for dextrose infusion in case of interruption of enteral feedings. A barrier to creating a universal rule is that patient tolerance for intravenous fluids differs according to condition. Safety data about use of basal insulin during enteral feedings, conducted with careful definition of insulin dose, has been generated in the context of a clinical trial, such that close supervision of the patients can be assumed to have occurred (Koryotkoski et al., 2009).

Personal observation of isolated cases of severe hypoglycemia outside of the research context has led to concern that safety of covering enteral feedings with long-acting analog, demonstrated under controlled research conditions, is not generalizable. In actual practice, use of long-acting analog to cover enteral feedings can be complicated by protracted hypoglycemia, a special risk in case of unforeseen interruption of enteral feedings. When NPH and regular insulin are used every 6 hours, each insulin dose is smaller than under a once-daily glargine program, and the frequency of insulin administration provides deliberate stacking of effect. The use of more frequent and smaller doses of intermediate acting insulin achieves control superior to that of sliding scale insulin; such therapy is intended to reduce the risk of prolonged exposure to high doses of long-acting insulin in case of sudden interruption of enteral feedings, and to reduce the importance of reliance upon the antidote of intravenous dextrose, in case of feeding interruptions.

A "sliding scale" regimen of NPH insulin every 4 hr or every 6 hr has been examined, compared to sliding scale aspart insulin alone for treatment of patients receiving enteral feedings (Cook, A. et al., 2009). Amber Cook and colleagues use a standardized rule for altering the NPH dose based on response of blood glucose. In our programming pathway, and on the antecedent paper order sets, in contrast to the closely related regimen of Amber Cook at al., we specify an option for use of mixtures of NPH and regular insulin every 6 hours. The prescribing style is intended to achieve flat-line coverage of insulin effect. The method described in our guideline is to administer equal doses of insulin every 6 hours, apportioned as 2/3 NPH and 1/3 regular insulin, with instructions to withhold the regular insulin in case of glucose below a given threshold.

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE NOT EATING, INCLUDING PATIENTS RECEIVING CONTINUOUS ENTERAL FEEDINGS, CONTINUOUS DEXTROSE-CONTAINING MAINTENANCE FLUIDS, OR NO CARBOHYDRATE EXPOSURE

Physician Orders for Nursing Staff
(Orders to "call," assess," and "teach" to be programmed, but not shown here)

■ POC (point-of-care) blood glucose monitoring Q6HRS [0600, 1200, 1800, 2400]

Scheduled Intermediate-Acting Insulin

● NPH insulin (route SC, priority routine), dose _____ units
(Prescriber guideline: Prescribe equal total doses of scheduled insulin every 6 hr, apportioned as 2/3 NPH, 1/3 regular insulin.)

SIDE MENU
(Start time for order and duration of order to be programmed, but not shown here)
Frequency and Time of Medication
● Q6HRS (default for NPH insulin)
○ Q12HRS
Additional Directions
☐ HOLD IF TUBE FEEDS STOP
☐ HOLD X6 HR BEFORE TUBE FEEDS WILL STOP
☐ HOLD IF INFUSION RATE OF DEXTROSE-CONTAINING MAINTENANCE FLUIDS IS REDUCED
☐ CALL M.D. IF UNPLANNED INTERRUPTION OF TUBE FEEDS OCCURS TO CONSIDER DEXTROSE-CONTAINING FLUID ORDER

Scheduled Regular Insulin

● Regular insulin (route SC, priority routine), dose _____ units
(Prescriber guideline: Prescribe equal total doses of scheduled insulin every 6 hr, apportioned as 2/3 NPH, 1/3 regular insulin.)

SIDE MENU
(Start time for order and duration of order to be programmed, but not shown here)
Frequency and Time of Medication
● Q6HRS (default for regular insulin)
○ Q12HRS
Additional Directions
☐ HOLD IF TUBE FEEDS STOP
☐ HOLD X6 HR BEFORE TUBE FEEDS WILL STOP
☐ HOLD IF INFUSION RATE OF DEXTROSE-CONTAINING MAINTENANCE FLUIDS IS REDUCED
☐ HOLD IF BG < XXX
☐ CALL M.D. IF UNPLANNED INTERRUPTION OF TUBE FEEDS OCCURS TO CONSIDER DEXTROSE-CONTAINING FLUID ORDER

(Go to Next Screen within Pathway)

Fig. 8. Nursing orders and scheduled insulin orders for patients who are not eating, including patients receiving continuous dextrose-containing maintenance fluids, continuous enteral feedings, or no carbohydrate exposure.

The algorithm we use does not provide a protocolized rule for changing the NPH dose based on glycemic response, but rather alters insulin delivery below a given glucose

threshold by protocolized omission of scheduled regular insulin. The prescriber within the programming pathway is invited to provide the additional direction for scheduled regular insulin "HOLD FOR BG < XXX" (where BG = point-of-care blood glucose).

Transitioning guidelines from intravenous insulin infusion to subcutaneous insulin for the prescriber include the following, with recognition that the guidelines may not be appropriate for every case, and that individualization is required:

- Order subcutaneous insulin before interruption of insulin infusion. Infrequently small amounts of scheduled NPH and regular insulin (but not sliding scale) may be started more than 2 - 4 hr prior to interruption of intravenous insulin infusion.
- Prescribe equal total doses of scheduled insulin every 6 hr, apportioned as 2/3 NPH, 1/3 regular insulin.
- In order to transition from intravenous insulin to subcutaneous insulin, the 24-hr requirement for scheduled NPH and regular insulin that is to be started or added may be about 80% of the 24-hr amount of intravenous insulin, extrapolated from observation of insulin requirement during the last 6-8 hr of intravenous insulin infusion. To avoid overestimation of dose requirement, observation must be made during a timeframe of medical stability; there must be no change of carbohydrate-containing maintenance fluids, enteral feedings, or total parenteral nutrition at the time of transition to subcutaneous insulin therapy; there must have been independence from pressors and CVVHD; and there must be no change of corticosteroid dose.

A set of dose initiation guidelines is given for insulin-requiring patients whose dose requirements are not known. The total daily dose of insulin for coverage of enteral feedings or continuous intravenous dextrose exposure may be calculated conservatively as follows:

- 24 hr basal requirement is 0.15 units/kg for type 2 diabetes or for stress hyperglycemia, and 0.25 units/kg for type 1 diabetes.
- nutritional requirement is 1 unit per 10 gm of carbohydrate per 24 hr, as determined by review of maintenance fluid or enteral tube feeding composition and delivery rate.
- for type 2 diabetes or stress hyperglycemia, during continuous carbohydrate exposure, the total daily dose of insulin is the sum of the 24 hr basal and nutritional components of therapy.
- the total daily dose of insulin is apportioned between NPH and regular insulin as above.

On a periodic basis, the caregiver then may alter the scheduled NPH and insulin by revising the scheduled insulin orders, using a guideline as shown above for re-establishing total daily dose (see section 3.5), and reapportioning the dose between NPH and regular insulin.

To prevent inadvertent interruption of basal insulin for type 1 diabetes patients who are not eating, a special provision is available, in the branch of the programming pathway for patients who are not eating, to maintain basal dose requirements of long-acting insulin analog treatment when interruption of carbohydrate exposure necessitates interruption of nutritional insulin (Figure 9).

3.6.3 Subcutaneous insulin for patients with overnight enteral feedings and daytime meals

For patients whose oral intake is temporarily poor but likely to improve, overnight enteral tube feedings may be used during transition from negligible oral intake to a full meal plan. Premixed 70% human insulin isophane suspension/30% human insulin (70/30 NPH / regular insulin) may be used as premedication to cover overnight enteral feedings (Figure

10). The need for correction dose insulin is likely to occur during and at the end of each feeding. As the patient's intake of oral feedings improves, correction dose insulin during the day may be required. For patients having type 1 diabetes, additionally daily use of long acting insulin analog should be ordered, in an amount restricted to the basal dose, together with the regimen of premixed insulin that is being used for nutritional coverage and regular insulin for correction dose coverage. Once dietary intake is adequate, overnight enteral feedings and the accompanying premedication with 70/30 isophane NPH/regular insulin no longer are required. Once the patient is eating, a new basal-prandial-correction insulin regimen may be required.

3.6.4 Diabetes hospital patient self management

In the ambulatory setting, skilled use of a flexible insulin program may reduce the frequency of hypoglyemia (Samann et al., 2006). Patients competent at diabetes self-management, for example patients using multiple daily injections or insulin pump therapy, under defined conditions can be treated in the hospital with continuation of their usual program of self-management (Braithwaite et al., 2007; Bailon et al., 2009). A full description of such a program is beyond the scope of this chapter. A hallmark feature is the utilization of the skills of advanced carbohydrate counting to permit matching of mealtime insulin bolus doses to carbohydrate intake, and the use of a rule for establishment of correction doses for treatment of hyperglycemia.

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WHO ARE NOT EATING INCLUDING PATIENTS RECEIVING CONTINUOUS ENTERAL FEEDINGS, CONTINUOUS DEXTROSE-CONTAINING MAINTENANCE FLUIDS, OR NO CARBOHYDRATE EXPOSURE
(Continued)

Scheduled Long-Acting Analog of Insulin (Long-AA)
(Prescriber guideline: this order for type 1 diabetes is restricted to basal dose requirements;
the order may be used for the basal dose requirement, together with
an NPH and regular insulin regimen for nutritional coverage and/or correction dose insulin coverage.)

○ Glargine insulin (route SC, priority routine), dose _____ units
○ Detemir insulin (route SC, priority routine), dose _____ units

DROP DOWN MENU
(Start time for order and duration of order to be programmed, but not shown here)
Frequency and Time of Medication
● Once daily at 2200 (default for glargine)
○ Once daily at 0800
○ Twice daily at 1000 and 2200
Additional Directions
(Prescriber guideline:
true basal insulin requirements should not be withheld for type 1 diabetes.)
● DO NOT WITHHOLD

(Go to Next Screen within Pathway, Correction Dose Insulin As Needed Every 6 hr, Not Shown)

Fig. 9. Basal insulin orders for type 1 diabetes patients who are not eating.

GLYCEMIC MANAGEMENT AND SUBCUTANEOUS INSULIN FOR PATIENTS WITH OVERNIGHT ENTERAL FEEDINGS AND DAYTIME MEALS

Physician Orders for Nursing Staff
(Orders to "call," assess," and "teach" to be programmed, but not shown here)

■ POC (point-of-care) blood glucose monitoring with frequency

SIDE MENU
Frequency of Monitoring
● WMEALS, HS, 0200 [0800, 1200, 1700 before meals; 2200, 0200]
○ WMEALS, HS [0800, 1200, 1700 before meals; 2200]

Scheduled Premixed 70% Human Insulin Isophane Suspension and 30% Human Insulin
(Prescriber guideline: this order provides coverage for overnight enteral feedings;
cancel this order when overnight enteral feedings are discontinued.)

■ Premixed 70% human insulin isophane suspension and 30% human insulin
(route "SC", priority "premedication"), dose _____ units.

SIDE MENU
(Start time for order and duration of order to be programmed, but not shown here)
Frequency and Time of Medication
● Once q PM as premedication to enteral feeding (default)
○ Once daily at 1800 as premedication to enteral feeding
○ Once daily at 2000 as premedication to enteral feeding
○ Once daily at 2200 as premedication to enteral feeding
Additional Directions
■ HOLD IF NO TUBE FEEDS (tube feedings, enteral feedings)
□ CALL M.D. IF UNPLANNED INTERRUPTION OF TUBE FEEDS OCCURS
TO CONSIDER DEXTROSE-CONTAINING FLUID ORDER

Scheduled Long-Acting Analog of Insulin (Long-AA, Abbreviated Display of Order)
(Prescriber guideline: this order for type 1 diabetes is restricted to basal dose requirements;
the order may be used for the basal dose requirement together with
an NPH and regular insulin regimen for nutritional coverage and/or correction dose coverage)

○ Glargine insulin (route SC, priority routine), dose _____ units
○ Detemir insulin (route SC, priority routine), dose _____ units

DROP DOWN MENU
(Frequency and time of medication, start time for order,duration of order,
and additional directions to be programmed, but not shown here)

(Go to Next Screen within Pathway, Correction Dose Insulin ACHS and 0200, Not Shown)

Fig. 10. Insulin orders for patients having overnight enteral tube feedings and daytime meals.

4. Conclusion

A programming pathway for computerized order entry is described that will present templates to the prescriber for well-established strategies for control of hyperglycemia and prevention of hospital hypoglycemia. There is not yet an embodiment of the plan within an existing electronic health record, nor is the content specifically yet endorsed by the healthcare system of the authors, but rather the plan is proposed in general terms as a

springboard for development and for modification to meet local needs. A user of the electronic order entry system may opt out of the programming pathway. The pathway is intended to both standardize order entry and also to facilitate individualization of care by the provider and for the patient. An opening screen offers default orders that will be universally desirable for glycemic management and then asks the user to choose a branch of the programming pathway based on route of insulin (intravenous or subcutaneous) and, for subcutaneous insulin regimens, based upon carbohydrate exposure. Within each branch of the pathway for subcutaneous insulin, it is possible to complete related orders without navigation between screens and without use of free-text, by entering numbers and selecting additional directions from side menus and drop down menus. User guidelines are displayed or available by computer link. By grouping and prioritizing related orders (especially the plans for nutrition, glucose monitoring, and insulin) and by offering appropriate additional directions within a branch of the pathway, the integration of the components of care, achievable on paper order sets by juxtaposition, is preserved under the electronic order entry system by user choice of a branch of the programming pathway.

5. Acknowledgement

The authors would like to acknowledge the work of the Diabetes Council of the Resurrection Health Care System and the input of members of the nursing, nutrition services, pharmacy, resident physician, attending physician, and administrative staff.

6. References

American Diabetes Association. 2011. Standards of medical care in diabetes - 2011. Diabetes Care 34 (Suppl 1):S11-S61.

Anderson, J. H., Jr., R. L. Brunelle, P. Keohane, V. A. Koivistos, M. E. Trautmann, L. Vignati, and R. DiMarchi. 1997. Mealtime treatment with insulin analog improves postprandial hyperglycemia and hypoglycemia in patients with non-insulin-dependent diabetes mellitus. Multicenter Insulin Lispro Study Group. *Arch Intern Med* 157 (11):1249-55.

Bagshaw, S. M., M. Egi, C. George, and R. Bellomo. 2009. Early blood glucose control and mortality in critically ill patients in Australia. *Crit Care Med* 37 (2):463-70.

Bhatia, A., B. Cadman, and I. Mackenzie. 2006. Hypoglycemia and Cardiac Arrest in a Critically Ill Patient on Strict Glycemic Control. *Anesth Analg* 102 (2):549-551.

Baldwin, D., G. Villanueva, R. McNutt, and S. Bhatnagar. 2005. Eliminating Inpatient Sliding-Scale Insulin: A reeducation project with medical house staff. *Diabetes Care* 28 (5):1008-1011.

Bellam, H., and S. S. Braithwaite. 2010. Hospital hypoglycemia: from observation to action. *Insulin Journal* 5 (1):16-36.

Blumenthal, D., and M. Tavenner. 2010. The "Meaningful Use" Regulation for Electronic Health Records. *New England Journal of Medicine* 363 (6):501-504.

Boord, J.A. , R.A. Greevy, SS Braithwaite, et al. 2009. Evaluation of hospital glycemic control at US academic medical centers. Hospital Medicine 4:35–44.

Braithwaite, S. S., B. Robertson, H. P. Mehrotra, L. M. McElveen, and C. L. Thompson. 2007. Managing hyperglycemia in hospitalized patients. *Clin Cornerstone* 8 (2):44-54; discussion 55-7.

Campbell, K B, and S S Braithwaite. 2004. Hospital Management of Hyperglycemia. Clin Diabetes 22 (2):81-88.

Clement S., S.S. Braithwaite, M.F. Magee, et al. 2004. Management of Diabetes and Hyperglycemia in Hospitals. Diabetes Care 27(2):553-591.

Cook, A., D. Burkitt, L. McDonald, and L. Sublett. 2009. Evaluation of Glycemic Control Using NPH Insulin Sliding Scale Versus Insulin Aspart Sliding Scale in Continuously Tube-Fed Patients. *Nutrition in Clinical Practice* 24 (6):718-722.

Bailon, RM, B.J. Partlow, V. Miller-Cage, M.E. Boyle, J.C. Castro, P.B. Bourgeois, C.B. Cook. 2009. Continuous subcutaneous insulin infusion (insulin pump) therapy can be safely used in the hospital in select patients. Endocr Pract. Jan-Feb;15(1):24-9.

Devi, R., G. Selvakumar, L. Clark, C. Downer, and S.S. Braithwaite. 2011. A dose-defining algorithm for attainment and maintenance of glycemic targets during intravenous insulin infusion and fluid therapy of hyperglycemic crisis. *Diabetes Management* 1 (4):397–412

Donaldson, S., G. Villanuueva, L. Rondinelli, and D. Baldwin. 2006. Rush University guidelines and protocols for the management of hyperglycemia in hospitalized patients: elimination of the sliding scale and improvement of glycemic control throughout the hospital. *Diabetes Educ* 32 (6):954-62.

Dortch, M. J., N. T. Mowery, A. Ozdas, L. Dossett, H. Cao, B. Collier, G. Holder, R. A. Miller, and A. K. May. 2008. A Computerized Insulin Infusion Titration Protocol Improves Glucose Control With Less Hypoglycemia Compared to a Manual Titration Protocol in a Trauma Intensive Care Unit. *JPEN J Parenter Enteral Nutr* 32 (1):18-27.

Finfer S., D.R. Chittock, S.Y. Su, et al. 2009. Intensive versus conventional glucose control in critically ill patients. N Engl J Med 360(13):1283-97.

Fischer, K F, J A Lees, and J H Newman. 1986. Hypoglycemia in hospitalized patients. *N Engl J Med* 315:1245-50.

Garg, R., H. Bhutani, A. Jarry, and M. Pendergrass. 2007. Provider response to insulin-induced hypoglycemia in hospitalized patients. *J Hosp Med* 2 (4):258-60.

Hermansen, K., M. Davies, T. Derezinski, G. Martinez Ravn, P. Clauson, and P. Home. 2006. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naive people with type 2 diabetes. *Diabetes Care* 29 (6):1269-74.

Hermayer, K.L., D.E. Neal, T.V. Hushion, M.G. Irving, P.C. Arnold, L.Kozlowski, M.R. Stroud, F.B. Kerr, and J.M. Kratz. 2007. Outcomes of a Cardiothoracic Intensive Care Web-Based Online Intravenous Insulin Infusion Calculator Study at a Medical University Hospital. *Diabetes Technology & Therapeutics* 9:523-534.

Hermayer, K.L., P. Cawley, P. Arnold, A. Sutton, J. Crudup, L. Kozlowski, and T.V. Hushion. 2009. Impact of improvement efforts on glycemic control and hypoglycemia at a university medical center. *J. Hosp. Med.* 4 (6):331-339.

Hirsch, I.B. 2005. Insulin analogues. N Engl J Med. 352(2):174-83.

Juneja, R., C. Roudebush, N. Kumar, A. Macy, A. Golas, D. Wall, C. Wolverton, D. Nelson, J. Carroll, and S. Flanders. 2007. Utilization of a computerized intravenous insulin infusion program to control blood glucose in the intensive care unit. *Diabetes Technol Ther* 9:232-240.

Jungmann E. 2005. Intensified insulin therapy of type 2 diabetes mellitus: pre- or postprandial injection of aspart insulin? Dtsch Med Wochenschr 130(20):1254-1257.

Kagansky, N, S Levy, E Rimon, L Cojocaru, A Fridman, Z Ozer, and H Knobler. 2003. Hypoglycemia as a predictor of mortality in hospitalized elderly patients. *Arch Intern Med* 163:1825-1829.

Kitabchi, A. E., G. E. Umpierrez, J. M. Miles, and J. N. Fisher. 2009. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 32 (7):1335-43.

Kazempour-Ardebili, S., V. L. Lecamwasam, T. Dassanyake, A. H. Frankel, F. W. K. Tam, A. Dornhorst, G. Frost, and J. J. O. Turner. 2009. Assessing Glycemic Control in Maintenance Hemodialysis Patients With Type 2 Diabetes. *Diabetes Care* 32 (7):1137.

Korytkowski, M. T., R. J. Salata, G. L. Koerbel, F. Selzer, E. Karslioglu, A. M. Idriss, K. K.W. Lee, A. J. Moser, and F. G.S. Toledo. 2009. Insulin Therapy and Glycemic Control in Hospitalized Patients With Diabetes During Enteral Nutrition Therapy: A randomized controlled clinical trial. *Diabetes Care* 32 (4):594-596.

Kosiborod, M, S.E. Inzucchi, H.M. Krumholz, L. Xiao, P.G. Jones, S. Fiske, F.A. Masoudi, S.P. Marso, J.S. Spertus. 2008. Glucometrics in patients hospitalized with acute myocardial infarction: defining the optimal outcomes-based measure of risk. Circulation 117(8):1018-27.

Kosiborod, M., S.E. Inzucchi, A. Goyal, H.M. Krumholz, F.A. Masoudi, L. Xiao, and J.A. Spertus. 2009. Relationship between spontaneous and iatrogenic hypoglycemia and mortality in patients hospitalized with acute myocardial infarction. *JAMA* 301 (15):1556-64.

Krinsley, J. S., and A. Grover. 2007. Severe hypoglycemia in critically ill patients: risk factors and outcomes. *Crit Care Med* 35 (10):2262-7.

Lee, J., B. Clay, Z. Zelazny, and G. Maynard. 2008. Indication-based ordering: a new paradigm for glycemic control in hospitalized inpatients. *J Diabetes Sci Technol* 2 (3):349-56.

Maynard, G. A., M. P. Huynh, and M. Renvall. 2008. Iatrogenic Inpatient Hypoglycemia: Risk Factors, Treatment, and Prevention: Analysis of Current Practice at an Academic Medical Center With Implications for Improvement Efforts. *Diabetes Spectr* 21 (4):241-247.

Maynard, G., J. Lee, G. Phillips, E. Fink, and M. Renvall. 2009. Improved inpatient use of basal insulin, reduced hypoglycemia, and improved glycemic control: effect of structured subcutaneous insulin orders and an insulin management algorithm. *J Hosp Med* 4 (1):3-15.

Moghissi E.S., M.T. Korytkowski, M. DiNardo, et al. 2009. American Association of Clinical Endocrinologists and American Diabetes Association Consensus Statement on Inpatient Glycemic Control. Endocrine Practice 15(4):1-17.

Mucha, G. T., S. Merkel, W. Thomas, and J. P. Bantle. 2004. Fasting and Insulin Glargine in Individuals With Type 1 Diabetes. *Diabetes Care* 27 (5):1209-1210.

Mudaliar, S., P. Mohideen, R. Deutsch, T. P. Ciaraldi, D. Armstrong, B. Kim, X. Sha, and R. R. Henry. 2002. Intravenous Glargine and Regular Insulin Have Similar Effects on Endogenous Glucose Output and Peripheral Activation/Deactivation Kinetic Profiles. *Diabetes Care* 25 (9):1597-1602.

Olson, R. P., M. A. Bethel, and L. Lien. 2009. Preoperative hypoglycemia in a patient receiving insulin detemir. *Anesth Analg* 108 (6):1836-8.

Osburne, R. C., C. B. Cook, L. Stockton, M. Baird, V. Harmon, A. Keddo, T. Pounds, L. Lowey, J. Reid, K. A. McGowan, and P. C. Davidson. 2006. Improving Hyperglycemia Management in the Intensive Care Unit: Preliminary Report of a Nurse-Driven Quality Improvement Project Using a Redesigned Insulin Infusion Algorithm. *The Diabetes Educator* 32 (3):394-403.

Rayman, G., V. Profozic, M. Middle. 2006. Insulin glulisine imparts effective glycaemic control in patients with Type 2 diabetes. Diabetes Res Clin Pract. 76(2):304-312.

Rosenstock, J., G. Dailey, M. Massi-Benedetti, A. Fritsche, Z. Lin, and A. Salzman. 2005. Reduced hypoglycemia risk with insulin glargine: a meta-analysis comparing insulin glargine with human NPH insulin in type 2 diabetes. *Diabetes Care* 28 (4):950-5.

Scalea, T. M., G. V. Bochicchio, K. M. Bochicchio, S. B. Johnson, M. Joshi, and A. Pyle. 2007. Tight glycemic control in critically injured trauma patients. *Ann Surg* 246 (4):605-10; discussion 610-2.

Schnipper, J. L., C. D. Ndumele, C. L. Liang, and M. L. Pendergrass. 2009. Effects of a subcutaneous insulin protocol, clinical education, and computerized order set on the quality of inpatient management of hyperglycemia: results of a clinical trial. *J Hosp Med* 4 (1):16-27.

Schnipper, J. L., C. L. Liang, C. D. Ndumele, and M. L. Pendergrass. 2010. Effects of a computerized order set on the inpatient management of hyperglycemia: a cluster-randomized controlled trial. *Endocr Pract* 16 (2):209-18.

Smith, W. D., A. G. Winterstein, T. Johns, E.Rosenberg, and B. C. Sauer. 2005. Causes of hyperglycemia and hypoglycemia in adult inpatients. *Am J Health Syst Pharm* 62 (7):714-719.

Stagnaro-Green, A, M K Barton, P L Linekin, E Corkery, K deBeer, and S H Roman. 1995. Mortalilty in hospitalized patients with hypoglycemia and severe hyperglycemia. *Mount Sinai Journal of Medicine* 62 (6):422-426.

Thompson, C. L., K. C. Dunn, M. C. Menon, L. E. Kearns, and S. S. Braithwaite. 2005. Hyperglycemia in the Hospital. *Diabetes Spectr* 18 (1):20-27.

Turchin, A., M. E. Matheny, M. Shubina, J. V. Scanlon, B. Greenwood, and M. L. Pendergrass. 2009. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. *Diabetes Care* 32 (7):1153-7.

Trujillo, J. M., E. E. Barsky, B. C. Greenwood, S. A. Wahlstrom, S. Shaykevich, M. L. Pendergrass, and J. L. Schnipper. 2008. Improving glycemic control in medical inpatients: a pilot study. *J Hosp Med* 3 (1):55-63.

Umpierrez, G. E., J. P. Kelly, J. E. Navarrete, M. M. C. Casals, and A. E. Kitabchi. 1997. Hyperglycemic Crises in Urban Blacks. *Archives of Internal Medicine* 157 (6):669-675.

Umpierrez, G. E., D. Smiley, A. Zisman, L. M. Prieto, A. Palacio, M. Ceron, A. Puig, and R. Mejia. 2007. Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes (RABBIT 2 Trial). *Diabetes Care* 30 (9):2181-2186.

Umpierrez, G. E., D. Smiley, S. Jacobs, L. Peng, A. Temponi, P. Mulligan, D. Umpierrez, C. Newton, D. Olson, and M. Rizzo. 2011. Randomized Study of Basal Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes Undergoing General Surgery (RABBIT 2 Surgery). *Diabetes Care* 34 (2):256-261.

Van den Berghe, G., A. Wilmer, I. Milants, P. J. Wouters, B. Bouckaert, F. Bruyninckx, R.Bouillon, and M. Schetz. 2006. Intensive Insulin Therapy in Mixed Medical/Surgical Intensive Care Units: Benefit Versus Harm. *Diabetes* 55 (11):3151-3159.

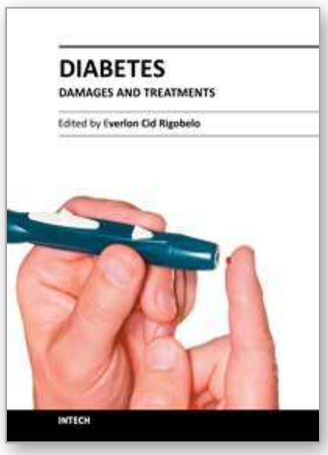
Varghese, P., V. Gleason, R. Sorokin, C. Senholzi, S. Jabbour, and J. E. Gottlieb. 2007. Hypoglycemia in hospitalized patients treated with antihyperglycemic agents. *J Hosp Med* 2 (4):234-40.

Velussi, M. 2002. Lispro insulin treatment in comparison with regular human insulin in type 2 diabetic patients living in nursing homes. *Diabetes Nutr Metab* 15 (2):96-100.

Vriesendorp, T., S. van Santen, H. De Vries, E. de Jonge, F. Rosendaal, M. Schultz, and J. Hoekstra. 2006. Predisposing factors for hypoglycemia in the intensive care unit. *Crit Care Med* 34 (1):96-101.

Wexler, D. J., J. B. Meigs, E. Cagliero, D. M. Nathan, and R. W. Grant. 2007. Prevalence of Hyper- and Hypoglycemia Among Inpatients With Diabetes: A national survey of 44 U.S. hospitals. *Diabetes Care* 30 (2):367-369.

Wexler, Deborah J., Peter Shrader, Sean M. Burns, and Enrico Cagliero. 2010. Effectiveness of a Computerized Insulin Order Template in General Medical Inpatients With Type 2 Diabetes. *Diabetes Care* 33 (10):2181-2183.



Diabetes - Damages and Treatments

Edited by Prof. Everlon Rigobelo

ISBN 978-953-307-652-2
Hard cover, 348 pages
Publisher InTech
Published online 09, November, 2011
Published in print edition November, 2011

Over the last few decades the prevalence of diabetes has dramatically grown in most regions of the world. In 2010, 285 million people were diagnosed with diabetes and it is estimated that the number will increase to 438 million in 2030. Hypoglycemia is a disorder where the glucose serum concentration is usually low. The organism usually keeps the serum glucose concentration in a range of 70 to 110 mL/dL of blood. In hypoglycemia the glucose concentration normally remains lower than 50 mL/dL of blood. Hopefully, this book will be of help to many scientists, doctors, pharmacists, chemicals, and other experts in a variety of disciplines, both academic and industrial. In addition to supporting researcher and development, this book should be suitable for teaching.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Susan S. Braithwaite, Lisa Clark, Lydia Dacenko-Grawe, Radha Devi, Josefina Diaz, Mehran Javadi and Harley Salinas (2011). Prevention of Hospital Hypoglycemia by Algorithm Design: A Programming Pathway for Electronic Order Entry, Diabetes - Damages and Treatments, Prof. Everlon Rigobelo (Ed.), ISBN: 978-953-307-652-2, InTech, Available from: http://www.intechopen.com/books/diabetes-damages-and-treatments/prevention-of-hospital-hypoglycemia-by-algorithm-design-a-programming-pathway-for-electronic-order-e

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen