DIABETIC CONTROL USING CONTINUOUS INSULIN INFUSION, SUBCUTANEOUS INSULIN, OR ORAL ANTIDIABETIC AGENTS FOR OBSTETRIC INPATIENTS

PHARMACY GUIDELINE

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April 14, 2009
LBMMC + MCH Pharmacy & Therapeutics Committee (April 2009)

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PHARMACY GUIDELINE - OBSTETRIC INPATIENTS

I. BACKGROUND INFORMATION

Diabetes mellitus is the most common medical complication of pregnancy, occurring in 2%-3% of all pregnancies. Approximately 90% of these represent gestational diabetes mellitus (GDM; type 3 diabetes) where the onset or recognition of glucose intolerance occurs during pregnancy. Because suboptimal treatment of this disease is associated with significant maternal, fetal and neonatal morbidity and mortality, tight control of the blood glucose level in pregnant diabetic patients becomes a major goal.

Anticipation of hyperglycemia is a major component of this guideline. Glycosylated hemoglobulin (HbA1c) results when glucose and hemoglobulin A react to form an irreversible compound. The life-span of hemoglobulin A is approximately 120 days, so HbA1c is a measure of the mean blood glucose over that period. Elevated HbA1c is the only known biomarker of diabetes-induced developmental toxicity (growth alteration, structural anomalies, functional and/or neurobehavioral deficits, or death). Normal levels of HbA1c (<6%; mean blood glucose <126 mg/dL) in non-diabetic patients indicate that even euglycemia and/or brief periods of hyperglycemia cause glycosylation of hemoglobulin A and result in accumulation over time. In pregnancy, fetal risks increase directly with increasing HbA1c, but the risk does not exceed the risk in non-diabetic pregnancies until HbA1c concentrations are higher (e.g., >7%; mean blood glucose >154 mg/dL) than the normal range. However, frequent high and low blood glucose concentrations could result in an HbA1c that appears normal. Nevertheless, every effort should be made to prevent accumulation of this biomarker before and during pregnancy because of the extensive morbidity and mortality this disease can cause in the mother and her offspring.

A. Maternal Morbidity

•ketoacidosis and death	•polyhydramnios	•chronic hypertension
•urinary tract infections	•monilial vaginosis	•retinopathy
•spontaneous abortions	•cardiac disease	•infertility

If underlying vascular disease, then increased risk of:

•preeclampsia	•fetal growth restriction	•preterm delivery

B. Embryo-Fetal Toxicity

Congenital anomalies in offspring of mothers with pregestational diabetes mellitus (types 1 and 2) occur with a rate four times that observed in nonpregnant controls. These malformations result from high glucose concentrations occurring before the 7th week of gestation:

•caudal regression syndrome •spina bifida •anal/rectal atresia
•hydrocephalus and other CNS defects such as anencephalus
•cardiac anomalies (transposition of great vessels, ventricular and atrial septal defects)
•renal malformations (agenesis, cystic kidney, ureter duplex)
•situs inversus (transposition of viscera)

•femoral hypoplasia/unusual facies syndrome
•fetal death (spontaneous abortions before 20 weeks; stillbirths in the 3rd trimester)
•intrauterine bone resorption
•macrosomia (due to fetal hyperinsulinemia)

C. Neonatal Toxicity
•birth trauma including asphyxia (due to macrosomia)
•severe neonatal hypoglycemia (due to hyperinsulinemia)
•hyperbilirubinemia
•respiratory distress syndrome (due to inhibition of pulmonary maturation by fetal hyperinsulinemia)
•polycythemia (may involve thrombosis in the neonate)

D. Childhood and Adolescent Toxicity
•attention deficit-hyperactivity disorder
•chronic hypertension
•morbid obesity
•diabetes mellitus

The complications of poorly controlled maternal diabetes listed above can be prevented with early intervention (before conception) diabetic control in types I and 2 and tight control of the disease during gestation in all diabetic types. Although this guideline does not address the issue of preconception diabetes control, it does provide three methods to achieve tight control of the disease during pregnancy - continuous insulin infusion, subcutaneous insulin, and oral antidiabetic agents.

II. Classification of Diabetes

Type 1: autoimmune disease that results in β-cell destruction, usually leading to absolute insulin deficiency; ketoacidosis prone; may have a late onset and slow progression of disease
Type 2: non-autoimmune disease that results in progressive insulin secretory defect on the background of insulin resistance; ketoacidosis resistant
GDM (type 3): diabetes that is diagnosed during pregnancy

III. CALORIE/INSULIN (C/I) RATIO

The Calorie/Insulin (C/I) ratio is defined as the number of calories metabolized by one unit of insulin. The accuracy of the C/I ratio is dependent on many factors, including how well the patient's control has been before admission, how well the patient has followed her prescribed diet, the use of concurrent medications, and other factors. It should only be considered an estimate. The ratio is inversely proportional to the insulin dose and insulin resistance:

i***ncreasing ratio - decreasing insulin dose and decreasing resistance***
decreasing ratio - increasing insulin dose and increasing resistance

IV. INSULIN RESISTANCE IN OBSTETRIC PATIENTS

Some pregnant diabetic women, especially type 2 diabetics (usually White's Class B - see appendix), morbidly obese patients, and/or those newly diagnosed with insulin-dependent diabetes, may be very resistant to normal doses of insulin. These patients require an aggressive approach to dosing and close monitoring of their response to insulin.

PART I. CONTINUOUS INSULIN INFUSION

I. PURPOSE

The purpose of this guideline is to prevent hyperglycemia in diabetic obstetric patients using a continuous intravenous (IV) infusion of insulin.

Exclusion: Treatment of diabetic ketoacidosis (DKA) is the responsibility of the physician and should not be treated with this guideline. These patients require large volumes of dextrose-free IV fluids, electrolyte replenishment, and large amounts of insulin. If requested, however, the pharmacist may regulate the IV insulin dose to control hyperglycemia.

II. BACKGROUND

This guideline for continuous infusion of insulin is for diabetic obstetric inpatients that require tight control of their blood glucose levels to meet stressful situations and for the determination of subcutaneous insulin requirements in obstetric patients with newly diagnosed diabetes mellitus. There are more than 21 different types or subtypes of obstetric diabetic patients that will be treated with this guideline. Brief descriptions of these patient types are described in *Part II. Insulin for Pregnant Diabetics.*

Dosing must be individualized based on the patient's response. For patients who have been receiving insulin before admission, the most common situations that require control with insulin infusions include:

- severe hyperemesis
- surgery
- noncompliance
- infection
- diabetic ketoacidosis
- premature labor
- change of diet
- induction of labor

Because clinical experience in the treatment of obstetric patients with diabetes mellitus with insulin infusions is an integral part of this guideline, the sections below are intended to give general principles only and will not cover every situation that may be confronted in the clinical setting.

III. BLOOD GLUCOSE GOAL RANGE

The blood glucose goal range for IV insulin is 70 - 110 mg/dL.

IV. METHOD FOR DETERMINING BLOOD GLUCOSE

Blood glucose concentrations should be determined using capillary blood obtained by finger stick. On occasion, blood glucose values may be determined by the laboratory and should be indicated on the pharmacy monitoring sheet as such (e.g., 87 mg/dL [L]).

V. RESPONSIBILITIES OF HEATH CARE TEAM

- **Physician:** ordering insulin (or other antidiabetic therapy) per pharmacy, infusion rates of IV fluids containing drugs other than insulin (e.g., magnesium sulfate, oxytocin), and oversight of team
- **Pharmacist:** insulin and other antidiabetic agent doses, type and rate of supplemental IV fluids,

timing of blood glucose tests, diet (in consultation with Registered Dietician), estimating oral calorie intake (in consultation with Nurse), calculating SC dose, and patient education (e.g., toxicity of diabetes, compliance)
•**Nurse:** routine care and monitoring of the patient, blood glucose tests, and patient education (e.g., injection method)

VI. INTRAVENOUS INFUSION RATE

As noted above, the insulin infusion rate and the infusion rate of the supplemental IV fluids are the responsibility of the pharmacist. IV fluids containing drugs other than insulin is the responsibility of the physician. Typically, the patient will receive approximately 3000 mL/day of supplemental IV fluids containing 5% dextrose. This amount will usually be less in patients consuming oral calories. In addition, the patient also will receive approximately 500 mL/day of normal saline containing insulin. The patient also may receive other IV fluids, such as those from oxytocin and/or magnesium sulfate that must be accounted for in the total caloric intake if they contain glucose.

VII. FLUID RESTRICTION

Changing the concentration of insulin and/or of dextrose may be required if fluid restrictions have been imposed by the physician to prevent pulmonary edema. Women in premature labor receiving $MgSO_4$ infusion, corticosteroids and/or β-sympathomimetics (terbutaline), and those with conditions that predispose to pulmonary edema, such as pyelonephritis, renal disease, gestational hypertension, or preeclampsia may have fluid restriction. Because the necessity to control fluid volumes is not always clear from the medical chart, the pharmacist should clarify the status of each patient with the physician early in the course of therapy.

VIII. INSULIN SOLUTIONS

A. STANDARD SOLUTION

The standard solution consists of 50 units of regular human insulin added to 500 mL of normal saline. This yields a solution containing approximately 0.1 units/mL, but the actual concentration will be less this because of overfilling of the normal saline bottle/bag and the small amount of insulin lost to binding to the container and tubing.

B. DOUBLE CONCENTRATION SOLUTION

Patients with fluid restriction or those requiring very high doses of insulin (e.g., type 2 or 3 diabetics) may require a double concentration insulin solution. The double concentration solution consists of 100 units of regular human insulin added to 500 mL normal saline. This yields a solution containing approximately 0.2 units/mL.

IX. ADMINISTRATION METHOD AND PRIMING

Insulin should be administered by IV infusion. An infusion pump must be used for both the insulin infusion and the supplemental IV fluids. When starting an insulin infusion, and after each tubing change, the nurse should flush the tubing with approximately 50 mL of solution before attaching to the patient.

X. INTRAVENOUS PUSH DOSES

Intravenous push doses of insulin may markedly increase the incidence and severity of hypoglycemic reactions. They are not an option for this guideline and should not be used.

XI. USING THE C/I RATIO

If the patient has been treated with insulin before admission, calculate a C/I ratio by dividing the daily caloric intake prior to admission by the total daily amount of insulin the patient has been receiving (the types of insulin, such as NPH, Lente, or Regular are not a consideration for this calculation). For example, the C/I ratio is 50 if the patient was consuming a 2000 calorie diet and taking 50 units of insulin per day. Typical C/I ratios for each diabetic type, based on patients treated in Womens', are approximately: **>30 (type 1)**; **5-15 (type 2)**; and **10-20 (type 3)**.

XII. INSULIN DOSAGE AND INFUSION RATES

A. BEFORE STARTING INSULIN INFUSION

Determine the patient's current blood glucose level by finger stick. Start a dextrose-containing IV solution (see Exception below). If an IV solution is already infusing, check to determine if it contains 5% dextrose. If not (e.g., Lactated Ringers or Normal Saline), change the solution so that it contains 5% dextrose (e.g., D5LR or D5NS).

Exception: Blood glucose control may be achieved more rapidly if patients with high blood glucose levels (>250 mg/dL) are initially maintained on a non-dextrose IV solution. Change to a dextrose-containing IV solution when the blood glucose concentration is <200 mg/dL.

B. INSULIN RESISTANCE IN OBSTETRIC PATIENTS

Morbidly obese and type 2 diabetics may be very resistant to normal doses of insulin. Frequent glucose checks, as well as frequent increases (or decreases) in the insulin dose, may be required. Double strength insulin solutions should be used. Discussion with another qualified pharmacist also is recommended.

Typical IV insulin doses based on the level of resistance are:

Low resistance (e.g., type 1 diabetes) - fractional doses, such as 2, 2.5, 2.8 units/hr, etc
High resistance (e.g., type 2 or gestational diabetes - whole doses, such as 4, 5, 8 units/hr, etc

C. INITIAL INSULIN INFUSION RATE

1. Patient NPO - No Prior Insulin

The initial insulin infusion rate is dependent on the diabetic type, initial blood glucose (determined immediately before starting the insulin infusion), the infusion rate of supplemental IV fluids (if they contain dextrose), and concurrent administration of other drugs, such as corticosteroids and/or β-sympathomimetics (terbutaline). However, the following general guidelines may be used *(note: clinical experience is a major component of this guideline and the initial doses recommended below may be modified)*:

Blood Glucose mg/dL	Type 1 Initial Dose	Types 2 & 3 Initial Dose
<110	0 units/hr	0 units/hr
110 - 129	2 units/hr	4 units/hr
130 - 149	4 units/hr	8 units/hr
150 - 199	6 units/hr	14 units/hr
>200	10 units/hr	20 units/hr

Check finger stick blood glucose 1 hour after starting the infusion and modify the infusion rate based on that result. For example, if the blood glucose has not changed or has risen, or the decrease is less than 10%, double the insulin rate and check again in 1 hour. In general, when regulating patients on this guideline, an asymptomatic low blood glucose level (within or very close to the Blood Glucose Goal Range) is preferred to a concentration above the Goal Range.

Patients will normally be NPO when an insulin infusion is first ordered. This will allow for easier and faster control of the patient's elevated blood glucose and an estimate of the C/I ratio (*caution: the initial C/I ratio should be considered an estimate only*). Once the blood glucose is within the target range, the diabetic diet may be started. If the diabetic diet is ordered concurrently with the start of the insulin infusion, the pharmacist should discuss with the physician the benefit of a short-term NPO order.

2. Patient NPO - Prior Insulin (types 1 or 2 diabetics)

The initial insulin infusion rate is dependent on the same factors noted above plus the calculated C/I ratio. Use the C/I ratio to determine approximately how much insulin is required to cover the calories received from the supplemental IV fluids (*caution: the C/I ratio provides a rough estimate only; see the comment above on the accuracy of the C/I ratio*). Add the amount of insulin estimated from the C/I ratio to the initial doses recommended above only if the initial blood glucose is <200 mg/dL. If the blood glucose is ≥200 mg/dL, ignore the additional estimated amount of insulin because it will be non-consequential.

Examples

C/I ratio = 50 (type 1)
D5LR at 125 mL/hr
*Calories/hr = 21**
Initial Blood Glucose = 180 mg/dL
Additional insulin required = 21/50 = 0.4 u/hr
Initial starting rate: 6.4 units/hr

C/I ratio = 10 (type 2)
D5LR at 125 mL/hr
Calories/hr = 21
Initial Blood Glucose = 200 mg/dL
Additional insulin required = 0
Initial starting rate: 20 units/hr

*1 gram IV glucose = 3.4 calories

Check finger stick blood glucose 1 hour after starting the infusion and modify the infusion rate based on that result. In general, when regulating patients on this guideline, an asymptomatic low blood glucose level (within or very close to the Blood Glucose Goal Range) is preferred to a concentration above the Goal Range.

D. PATIENT CONSUMING SWEET SUCCESS DIABETIC DIET

Typically, a patient will be NPO when started on this guideline and then, when clinically appropriate, changed to a Sweet Success diabetic diet. The total number of calories on the diet should be determined by the dietician in consultation with the pharmacist. Insulin dosing must anticipate (rather than react to) changes in the patient's glucose level.

Sweet Success Diets

	Calories				
Meal	**1800**	**2000**	**2200**	**2400**	**2600**
Breakfast	325	325	325	280	325
Snack (AM)	60	60	215	325	325
Lunch	495	540	540	600	675
Snack (PM)	60	215	215	215	295
Dinner	615	615	615	640	640
Snack (HS)	245	245	245	325	325

The pharmacist and/or the nurse should estimate the number of calories the patient has consumed at each meal or snack. This information must be entered on the pharmacy flow sheet (e.g., ate 80% of breakfast = 260 calories) and will be used when converting to a subcutaneous dose.

Using either a C/I ratio from before admission, or a C/I ratio determined while NPO, divide the estimated caloric intake of the meal or snack by the C/I ratio to obtain the amount of insulin required in the next 2 hours (the approximate duration of the effect from the meal. For snacks, assume the effect of the calories will last for 1 hour. Calories received from the IV fluids during the 1 or 2 hour periods must be included in the total calories. The result of this calculation will provide an estimate of the units of insulin required during the specified interval.

Example: 2000 Diabetic diet started at breakfast (0800)
Glucose at 0745: 88 mg/dL
Current infusion rate: 2.5 units/hr
C/I ratio prior to admission: 20
Current supplemental IV rate: 125 mL/hr
Calories/hr from supplemental IV: 21
Calories from breakfast = 325
Total Calories = 325 + 21 = 346
Estimate of dose required: 346/20 = 17 units/2 hours
Estimate of hourly dose required: 17/2 ≈ 9 units/hr

Therefore, increase the infusion rate to 9 units/hr when the patient begins her breakfast.

E. PATIENT RECEIVING BETAMETHASONE FOR FETAL LUNG MATURITY

Patients receiving insulin infusions, who have premature labor, may receive betamethasone

for fetal lung maturity. This therapy, administered as two 12 mg IM injections 24 hours apart, will result in transient higher blood glucose concentrations due to gluconeogenesis and decreased tissue sensitivity to insulin. Ketoacidosis may occur if inadequate insulin is given. The onset of hyperglycemia is approximately 12-24 hours after the first dose and may persist for 24-48 hours after the last dose. Markedly increased amounts of insulin may be required to maintain control of the patient's glucose levels. The pharmacist must anticipate the rise in glucose and should initiate increased monitoring of finger stick blood glucose concentrations to prevent hyperglycemia.

F. PATIENT RECEIVING β-SYMPATHOMIMETIC TOCOLYTIC THERAPY

Terbutaline is used as a tocolytic and may cause a transient increase in blood glucose levels, usually within 4 hours, by the dual mechanisms of glycogenolysis and gluconeogenesis. Ketoacidosis is a theoretical possibility. Typically, blood glucose levels return to baseline approximately 48 hours after starting therapy, regardless of the duration of therapy. During this time, markedly increased amounts of insulin will be required, as well as more frequent monitoring of blood glucose concentrations.

G. PATIENT RECEIVING BETAMETHASONE AND β-SYMPATHOMIMETICS

A patient receiving both betamethasone and terbutaline for preterm labor represents a challenge for the pharmacist controlling her diabetes. Large increases in glucose levels are typically encountered and require correspondingly large doses of insulin. Frequent glucose concentration monitoring is required with increases, sometimes aggressive, in the insulin infusion rate. Typically, the hyperglycemic response to the therapy will persist for 24-48 hours after the last corticosteroid dose and an appropriate response should be planned for this duration.

H. INSULIN INFUSION RATE FROM 2400 TO 0700

In most patients, but not all, the insulin infusion should be decreased during the period of 2400 to 0700 to correspond to the reduced activity and caloric intake during these hours and to prevent hypoglycemic episodes. However, patients covered under sections E, F, and G above may still require large amounts of insulin during this period.

I. ADDITIONAL PHARMACIST RESPONSIBILITIES DURING INFUSION

The pharmacist must verify each change of insulin dose on the pump. The patient must be checked frequently to assess variables, such as the amount of calories consumed per meal (the patient's nurse should be included in this assessment), occurrence of vomiting, administration of corticosteroids and β-sympathomimetics, and infiltration of IV sites.

XIII. MONITORING PATIENTS WHILE ON INSULIN INFUSION

A. MONITORING PATIENTS WHO ARE NPO

Glucose levels in patients who are NPO and who are receiving insulin infusions should be monitored at approximately 2-hour intervals during the first 24 hours. Once a patient's response to the insulin dose has been determined (usually at or more than 24 hours), the monitoring interval can be lengthened (e.g., to 3- or 4-hour intervals).

B. MONITORING PATIENTS WHO ARE CONSUMING A DIABETIC DIET

Pre- and postprandial glucose levels should be determined when a patient is consuming a diabetic diet. Glucose levels should be determined just before a meal (i.e., preprandial) and 1 hour after a meal (i.e., postprandial). *(Note: When the patient is receiving SC insulin, emphasis will be placed on postprandial glucose levels)* The sample plan below assumes that the patient completes each meal in 15 minutes:

Time	Event	Time	Event
0745	Fasting	0800	Breakfast
0915	1-Hr Postprandial Glucose	1015	Snack
1145	Preprandial Glucose	1200	Lunch
1315	1-Hr Postprandial Glucose	1500	Snack
1645	Preprandial Glucose	1700	Dinner
1815	1-Hr Postprandial Glucose	2045	HS Glucose
2100	Snack	2330	Glucose
0200	Glucose	0500	Glucose

Modification of this schedule is often necessary, and may also include more frequent glucose determinations in patients with poorly controlled diabetes.

XIV. MANAGEMENT OF HYPOGLYCEMIA

A. SIGNS AND SYMPTOMS OF HYPOGLYCEMIA

By definition, hypoglycemia is blood glucose concentration <70 mg/dL, a level at which some patients will exhibit symptoms.

Early Warning Symptoms of Hypoglycemia

•blurred vision	•generalized sweating	•tremor	•hunger
•sweaty palms	•cold feeling	•headache	•palpitation
•piloerection	•tingling of the lips & tongue		

Signs and Symptoms of Decreased Cerebral Function

•lethargy	•confusion	•agitation	•nervousness
•convulsions			

The following may be used to determine the potential severity of a low blood glucose concentration:

Blood glucose concentration: <70 mg/dL: Usually not symptomatic
Blood glucose concentration: <60 mg/dL: May or may not be symptomatic
Blood glucose concentration: <50 mg/dL: Usually symptomatic
Blood glucose concentration: <30 mg/dL: Seizures or coma may occur

B. BLOOD GLUCOSE <70 MG/DL - PATIENT ASYMPTOMATIC

If a blood glucose is <70 mg/dL, and the patient is exhibiting no signs of hypoglycemia (see above), stop the insulin and observe the patient's response. The rate of the dextrose containing

supplemental IV should be increased (see below) until the patient's glucose level is within the Goal Range of 70-110 mg/dL. Recheck the blood glucose level at frequent intervals, but no less than once per hour, and then adjust the insulin infusion rate to reflect the decreased insulin requirement.

C. BLOOD GLUCOSE UNKNOWN - PATIENT SYMPTOMATIC

Stop the insulin infusion if the patient is symptomatic (see symptoms listed above) and obtain a finger stick sample to determine the blood glucose level.

Blood Glucose within Goal Range or Above

If the concentration is within the blood glucose goal range or above, wait until the patient is asymptomatic then restart the insulin at a reduced rate. Check blood glucose levels at more frequent intervals. Administering extra glucose is rarely needed, especially if the blood glucose level is above the goal range, but is a clinical option. If a high glucose concentration is reduced too rapidly, patients may experience symptoms, even when the blood glucose level is still relatively high.

Blood Glucose less than 70 mg/dL

Administer dextrose by one of the following methods:

a. increase the rate of the 5% Dextrose infusion (e.g., 250 mL/hr x 15 minutes provides 10.6 calories)

b. administer 50% Dextrose by IV push (e.g., 50 mL provides 85 calories). It may only be necessary to administer a partial dose depending on the patient's response; an overly aggressive approach may make control difficult after correction of the hypoglycemic episode

c. if the IV infiltrates, administer either orange juice (40 calories per 120 mL) or grape juice (80 calories per 120 mL)

d. if the IV infiltrates and the patient cannot be aroused:

i. Glucagon is the treatment of choice in the unconscious patient. Glucagon elevates blood glucose by the dual mechanism of hepatic glycogenolysis and gluconeogenesis and should produce a response within 5-20 minutes. Because there must be a physician order before administrating the drug, an order for "Glucagon 1 mg IM/SC/IV x 1 PRN" must be included in the initial order set for insulin management per pharmacy. Glucagon should be available in all of the Pyxis machines in Womens'. IV glucose should also be given as soon as possible.

ii. second-line treatment is to administer 40% glucose gel (three products that are commercially available are Insta-Glucose, Insulin Reaction, or Glutose), Dex4 Glucose tablets, and BD Glucose chewable tablets. Glucose is not absorbed from the buccal cavity and must be swallowed to be effective. A response should occur in 10 minutes, by which time an IV line should have been started. If not, repeat the oral glucose dose.

CAUTION: Swallowing reflexes may be preserved in the unconscious patient, but the absence of a normal gag reflex may lead to aspiration.

Following correction of the hypoglycemia, restart the insulin at a reduced rate to reflect the decreased insulin requirement. Blood glucose concentrations should be checked more frequently.

D. TREATMENT OF HYPOGLYCEMIC REACTIONS WITH UNORDERED CALORIES

Patients exhibiting signs or symptoms of hypoglycemia are occasionally given available snacks, such as crackers and fruit juices. Although this action will usually rapidly reverse the condition, the ingestion of nonscheduled calories often results in markedly elevated blood glucose levels and, because the exact number of calories ingested may be difficult to establish, makes subsequent short-term control of the hyperglycemia and the estimation of the C/I ratio difficult. Therefore, the pharmacist should be immediately notified of any hypoglycemic signs or symptoms and initiate immediate action as described in the above sections. The administration of unordered calories is discouraged, but may be appropriate under the following emergency conditions when the pharmacist or physician do not respond within a reasonable time interval based on the patient's condition (the nurse is to use clinical judgment of what constitutes a "reasonable time interval"):

• Patient has signs/symptoms of severe hypoglycemia (e.g., lethargy, confusion, agitation, nervousness, coma or impending coma, or convulsions); if patient is conscious, administer oral calories such as grape juice (preferred), orange juice, or apple juice; administer IV calories if patient unable to take oral calories (e.g., increase rate of supplemental dextrose IV solution to "wide open" or give 50 mL of 50% dextrose IV push); if patient is unconscious and/or convulsing and no IV site is available, obtain Glucagon from a Pyxis machine and give 1 mg IM/SC/IV.

• Patient has signs/symptoms of less severe hypoglycemia (e.g., blurred vision, generalized sweating, tremor, hunger, sweaty palms, a cold feeling, headache, palpitation, piloerection, or tingling of the lips and tongue); administer IV or oral calories as stated above.

XV. CONVERSION OF INSULIN INFUSION TO SUBCUTANEOUS DOSES

A major purpose of this guideline is the determination of the daily insulin requirement for a pregnant patient. This calculation, if required, is accomplished as follows:

1. Determine the total amount of insulin infused over a 24-hour period (0700 to 0700) by multiplying the units per hour infused by the hours at that rate;
2. Determine the total caloric intake over a 24-hour period (calories consumed from the prescribed diet + IV calories) (IV calories = 3.4 calories/gram dextrose);
3. Divide the total calories by the total insulin to determine the C/I ratio (rounded to nearest whole number);
4. Divide the calories from the prescribed diet (does not include IV calories) by the C/I ratio to determine the daily subcutaneous (SC) insulin requirement (DIR)
5. Divide the DIR into three doses as follows (rounded to even numbers):
    a. multiple the DIR by 0.44 to obtain the morning dose of NPH and by 0.22 for the morning dose of regular insulin; (*total morning dose is 66% of DIR*)
    b. multiple the DIR by 0.17 to obtain the before dinner regular insulin dose;
    c. multiple the DIR by 0.17 to obtain the bedtime dose of NPH.

6. Upon completion of this calculation, the pharmacist is responsible for writing a chart progress note with the following data:
    (a) total insulin infused over 24 hours;

(b) total calories ingested over 24 hours;
(c) calculated C/I ratio;
(d) recommended daily SC insulin dose.

7. After completing the progress note, the pharmacist should order the SC insulin dose to start 30 minutes (15 minutes for lispro or aspart insulins) before breakfast (e.g., 0730 or 0745).
8. Discontinue the insulin infusion and IV fluids 60 minutes (30 minutes for lispro or aspart) after the first SC insulin dose. Order the IV site to be maintained with a saline-lock for 24 hours.

Example: Total insulin infused over 24 hours: 100
Total calories consumed over 24 hours: 2050
C/I Ratio: 21
Post-infusion Diet: 2000 calories
2000 ÷ 21 = 95 units (DIR)
Before breakfast NPH dose: 95 x 0.44 = 42 units
Before breakfast Regular dose: 95 x 0.22 = 20 units (rounded to even number)
Before dinner Regular dose: 95 x 0.17 = 16 units
Before bedtime NPH dose: 95 x 0.17 = 16 units

Chart Note Example (the exact wording is not required):
The patient received approximately 100 units of insulin over 24 hours while consuming approximately 2050 calories (IV + PO). The C/I ratio is 21. If the patient consumes a 2000-calorie diet, her recommended daily insulin requirement is 42 units NPH + 20 units regular insulin in the morning, 16 units regular insulin before dinner, and 16 units NPH at bedtime. /s/_____

9. Caution should be used with patients who were receiving SC insulin before admission. If the calculated SC dose, based on the insulin infusion, is more than 100% of the preadmission dose (e.g., the preadmission dose was 50 units/day and the new calculated dose is >100 units/day), the patient should be given a pre-breakfast dose that is 50% higher than the preadmission pre-breakfast dose. Determine subsequent doses based on the following 1-hour postprandial result:
   a. <100 mg/dL - use preadmission dose;
   b. 100-150 mg/dL - continue with doses that are 50% higher than the preadmission dose;
   c. >150 mg/dL - immediately give the remainder of the calculated morning dose (NPH + regular) and continue with the calculated doses before dinner and at bedtime.

XVI. DISCONTINUING INSULIN INFUSION IMMEDIATELY BEFORE DELIVERY

The insulin infusion should be discontinued immediately before delivery. Generally, a non-dextrose-containing IV solution is substituted at this time. For patients requiring bolus hydration for epidural anesthesia, a non-dextrose-containing IV should be used to avoid transient hyperglycemia that could aggravate neonatal hypoglycemia.

XVII. MANAGEMENT OF DIABETES IN THE POSTPARTUM PERIOD

A. INSULIN REQUIREMENTS POSTPARTUM

Insulin requirements generally decrease markedly in the postpartum period due to the loss

of the hormone secreting placenta. Often, little or no insulin is required for the first 24 hours after delivery. These patients may be extremely sensitive to small amounts (e.g., 4 units) of insulin. (See Part III)

B. POSTPARTUM BLOOD GLUCOSE GOAL RANGE

A glucose concentration of approximately 90-180 mg/dL is adequate for postpartum control. It may be achieved by giving small SC doses of regular insulin (e.g., ≥4 units) for concentrations over 200 mg/dL. Non-dextrose-containing IV solutions are normally used during this period, unless the patient becomes hypoglycemic or ketotic. (See Part II. Section VI.)

C. POSTPARTUM INSULIN INFUSION

Although rarely required, the physician, or the pharmacist in consultation with the physician, may determine that an insulin infusion should be continued postpartum. In this situation, a new rate must be established without regard to the patient's antepartum and intrapartum insulin requirements. Start the infusion at a low rate (e.g., 1 unit/hour) and monitor the glucose concentrations at least every 2 hours until the patient's response to insulin has been established. Maintain a dextrose-containing IV solution. In the event of a hypoglycemic reaction, stop the insulin infusion and increase the dextrose IV rate. Giving orange or grape juice is an option if the patient is not NPO.

D. POSTPARTUM SUBCUTANEOUS INSULIN

1. Patients will typically be type 1 (insulin-dependent) diabetics with a White's classification of C or lower. However, type 2 diabetics (non-insulin dependent) (White's Classification B or lower) may be included if oral hypoglycemic agents are not appropriate for their clinical situation.
2. The physician must order "SC insulin per pharmacy".
3. Blood glucose goals are as follows:
•fasting: 90 - 110 mg/dL
•1-hour postprandial: <180 mg/dL
•2-hour postprandial: <140 mg/dL
4. Postpartum period until diabetic diet started
    a. Order non-glucose IV fluids (e.g., LR) at a rate specified by the physician (if not specified, start at 125 mL/hr)
    b. Order finger stick glucose checks every 6 hours
    c. Order sliding scale insulin as follows:
        •blood glucose ≤200 mg/dL - No insulin
        •blood glucose 201-250 mg/dL - 4 units Regular Insulin
        •blood glucose 251-300 mg/dL - 6 units Regular Insulin
        •blood glucose 301-350 mg/dL - 8 units Regular Insulin
        •blood glucose 351-400 mg/dL - 10 units Regular Insulin
    d. Order: "Do not give insulin more frequently than every 6 hours" **(Important!)**
5. Postpartum period when diabetic diet started
    a. Start scheduled insulin only if patient is tolerating a diabetic diet.
    b. If patient can recall her pre-pregnancy dose, order that dose to start.

c. If the patient cannot recall her pre-pregnancy dose (type 1 diabetics), or she is a type 2 diabetic that will be continued on SC insulin, estimate the insulin dose as follows:

i. determine her total daily insulin dose immediately prior to delivery;
ii. multiple the total daily dose by 0.50 to obtain the starting total postpartum daily SC insulin dose;
iii. distribute the total postpartum daily SC dose in the following manner:
(a) 0.44 as NPH and 0.22 as regular before breakfast (round to even numbers)
(b) 0.22 as NPH and 0.12 as regular before dinner (round to even numbers)
iv. Order finger stick glucose checks for Fasting (goal: 90-110 mg/dL) and 1 hour postprandials (goals: <180 mg/dL)
v. Insulin dose adjustments should be made in 2 unit increments for each type of insulin (i.e., maximum daily change would usually be no more than 8 units).

E. POSTPASTUM ORAL ANTIDIABETICS (Type 2 Diabetics)

1. The physician must order "oral antidiabetic agents per pharmacy".
2. If the patient can recall her pre-pregnancy dose, order that dose to start.
3. If the patient cannot recall her pre-pregnancy regimen, metformin or glyburide should be considered first-line oral agents. The starting dose for metformin is 500 mg BID, whereas the starting dose for glyburide is 2.5-5 mg/day.
4. Serum creatinine must be checked before starting metformin. If the creatinine is >1.4 mg/mL, metformin should not be given because of an increased risk of lactic acidosis.
5. Both metformin and glyburide are considered compatible with breastfeeding.
6. Check finger stick glucose at fasting (goal: 90-110 mg/dL) and 1 hour postprandials (goal: <180 mg/dL).

XVIII. REQUIRED DATA ON PHARMACIST'S FLOW SHEET

The following data are required on the pharmacist's flow sheet: patient's name, identification number, age, room number, height, weight, allergies, ordering physician, White's diabetic Class (see appendix A), diet, gestational age in weeks/days, insulin dosing prior to admission, time of the last dose, and the concentration of the insulin solution. In addition, the following data should be entered as it is obtained (see sample flow sheet attached):

1. Date and Time
2. Blood glucose level (indicate if laboratory determined)
3. Rate of insulin infusion
4. Urinary acetone four times daily if the patient is NPO, or if infection is present, or if blood glucose concentration is greater than 200 mg/dL
5. Any hypoglycemic reactions (symptoms/treatment, if any)
6. Type and rate of supplemental IV fluids
7. Type and rate of any other IV fluids (e.g., Magnesium sulfate)
8. Oral caloric intake (each meal and snack); estimation of amount consumed (in % and number of calories) together with the time consumed.

Original: 04.05.96jb; Revised: 1997, 2002, 2003, 2004; April 2009jb-ku

PART II. INTRAVENOUS INSULIN FOR PREGNANT DIABETICS

I. Newly Diagnosed Diabetic

A. Type 1 (Insulin Dependent)

White's Class C or lower (but could be Class B if less than 10 years)
Blood Glucose Goal (No retinopathy): 70-110 mg/dL
Blood Glucose Goal (retinopathy): 90-130 mg/dL
Insulin Solution: 50 units/500 mL saline (0.1 unit/mL)

A newly diagnosed type 1 diabetic in pregnancy should be extremely rare. If it does occur, use the same method outlined in Section II. A. below.

Conversion to SC insulin
The best approach is to use the 4-dose method with Humulin NPH and Humalog (lispro) insulin. If the fasting values are elevated and have not been controlled by adjusting the bedtime NPH and/or the diet, consider adding a dose at about 0300 using Regular insulin.

B. Type 2 (Non-Insulin Dependent)

White's Class B (but could be Class C or lower if 10 years or more)
Blood Glucose Goal: 70-110 mg/dL
Blood Glucose Goal (retinopathy): 90-130 mg/dL (uncommon)
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Nearly all women diagnosed with diabetes before 20 weeks' gestation will be type 2. This type of diabetes is marked by insulin resistance, either secondary to obesity, pregnancy, or both. The usual C:I ratio range is 5-15, thus aggressive dosing is required. For women in the first trimester (<14 weeks' gestation), rapid control is desired to prevent further embryo toxicity (structural anomalies, spontaneous abortions, and setting the basis for macrosomia in the second and third trimesters).

Rapid lowering of high glucose levels should be avoided in patients with impaired vision, whether or not retinopathy has been diagnosed. If the patient does have retinopathy, rapid lowering of glucose might worsen the condition. Although a specific reference has not been located, lowering the glucose to the goal range over 24-48 hours seems reasonable.

Conversion to SC insulin
Use the 3-dose method with Humulin NPH and Regular insulin.

C. Type 3 (Gestational)

White's Class A2
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

The majority of newly diagnosed diabetes in pregnancy will be gestational diabetics. Furthermore, most will be started on treatment as outpatients, either with insulin or oral agents (e.g., glyburide). However, if admitted, it is important to recognize that insulin resistance, usually secondary to pregnancy, is a hallmark of this type. This type of patient typically presents after 20 weeks' gestation, but could present earlier if morbidly obese. The usual C:I ratio range is 10-20. Dosing should be moderately aggressive.

Conversion to SC insulin or Glyburide

If the patient is less than 30 weeks' gestation, convert to SC insulin using the 3-dose method. Consider converting to glyburide 2.5-5 mg before breakfast if the patient is 30 weeks' gestation or more, the fasting values before admission were <110 mg/dL, and the physician agrees. However, insulin is the gold standard and the first choice regardless of gestational age.

II. OUT-OF-CONTROL DIABETES

A. Type 1 (Insulin Dependent)

White's Class C or lower (but could be Class B if less than 10 years)
Blood Glucose Goal (no retinopathy): 70-110 mg/dL
Blood Glucose Goal (retinopathy): 90-130 mg/dL
Insulin Solution: 50 units/500 mL saline (0.1 unit/mL)

Calculate a C:I ratio when the insulin dose and prescribed diet are known. However, the ratio may not reflect the patient's true requirement because of noncompliance with the diet, insulin dose, or both, and change in the insulin requirements. Relatively small IV doses (in comparison to types 2 and 3) of insulin are usually required. Hypoglycemic reactions are a risk with aggressive dosing. For women in the first trimester (<14 weeks' gestation), rapid control is desired to prevent further embryo toxicity (structural anomalies, spontaneous abortions, and setting the basis for macrosomia in the second and third trimesters). The C:I ratio is typically greater than 30.

Rapid lowering of high glucose levels should be avoided in patients with impaired vision, whether or not retinopathy has been diagnosed. If the patient does have retinopathy, rapid lowering of glucose might worsen her retinopathy. Although a specific reference has not been located, lowering the glucose to the goal range over 24-48 hours seems reasonable.

Conversion to SC insulin

The best approach is to use the 4-dose method with Humulin NPH and Humalog (lispro) insulin. If the fasting values are elevated and have not been controlled by adjusting the bedtime NPH and/or the diet, consider adding a dose at about 0300 using Regular insulin.

B. Type 2 (Non-insulin Dependent)

White's Class B (but could be Class C or lower if 10 years or more)
Blood Glucose Goal: 70-110 mg/dL

Blood Glucose Goal (retinopathy): 90-130 mg/dL (extremely rare)
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Calculate a C:I ratio if the patient has been on insulin and the prescribed diet is known. However, many of these patients will have been on oral agents prior to admission so a C:I ratio cannot be calculated. Moreover, even in those who were receiving insulin prior to admission, the ratio may not reflect the patient's true requirement because of noncompliance with the diet, insulin dose, or both, and changes in insulin requirements. For women in the first trimester (<14 weeks' gestation), rapid control is desired to prevent further embryo toxicity (structural anomalies, spontaneous abortions, and setting the basis for macrosomia in the second and third trimesters). Aggressive dosing is required because of high insulin resistance. The usual C:I ratio range is 5-15.

In those rare cases where there is visual impairment, whether or not retinopathy has been diagnosed, dose insulin as for a type 1 patient with retinopathy (see Section II. A. above).

Conversion to SC insulin
Use the 3-dose method with Humulin NPH and Regular insulin. If the calculated SC dose is 300 units/day or more consider adding metformin 500 mg twice daily (before breakfast and dinner), if the physician agrees. If metformin is started, the calculated insulin dose should be decreased 60% (i.e., the insulin dose will be 40% of the original calculated dose).

C. Type 3 (Gestational)
White's Class A2
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

An out-of-control gestational diabetic admitted to the Hospital is uncommon. However, if it does occur, use the same method as described for newly diagnosed gestational diabetics.

Conversion to SC insulin or Glyburide
If the patient is less than 30 weeks' gestation, convert to SC insulin (Humulin NPH and Regular) using the 3-dose method. Consider converting to glyburide 5 mg before breakfast if the patient is 30 weeks' gestation or more, the fasting values before admission were <110 mg/dL, and the physician agrees. However, insulin is the gold standard and the first choice regardless of gestational age.

III. DIABETIC ADMITTED IN PRETERM LABOR
A. Type 1 (Insulin Dependent)
White's Class C or lower (but could be Class B if less than 10 years)
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 unit/mL)

Betamethasone
Patients admitted for preterm labor may receive betamethasone (12 mg IM every 24 hours x 2 doses) to accelerate fetal lung maturity if they are <34 weeks' gestation. These patients will require IV insulin to manage the corticosteroid-induced hyperglycemia and to prevent possible diabetic ketoacidosis and subsequent fetal toxicity. The onset of hyperglycemia is approximately 12-24 hours after the first dose and the duration is approximately 24-48 hours after the last dose. Anticipation of the high glucose levels that will occur is required (see Guideline for further details).

Terbutaline
Hyperglycemia may occur within 4 hours if the tocolytic agent, terbutaline, is given. Typically, blood glucose levels return to baseline approximately 48 hours after the first dose, regardless of the duration of therapy. Anticipation of the high glucose levels that will occur is required (see Guideline for further details).

Betamethasone and Terbutaline
This combination requires very aggressive insulin therapy. Anticipation of the high glucose levels that will occur is required (see Guideline for further details).

B. Type 2 (Non-Insulin Dependent)
White's Class B (but could be Class C if 10 years or more)
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Same as Section III. A. above.

C. Type 3 (Gestational)
White's Class A2
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Same as Section III. A. above.

IV. DIABETIC ADMITTED IN LABOR

A. Type 1 (Insulin Dependent)
White's Class C or lower (but could be Class B if less than 10 years)
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 50 units/500 mL saline (0.1 unit/mL)

The goal of therapy is to maintain the blood glucose at less than 110 mg/dL. If the blood glucose is greater than 110 mg/dL with a non-dextrose IV solution (e.g., LR), start IV insulin and change to a dextrose IV solution (e.g., D5LR). The insulin dose should be based on the pre-admission

C:I ratio The maximum total IV rate (IV insulin + mainline IV) should be determined in consultation with the physician. Check blood glucose levels at least every 2 hours. The nurse will discontinue the insulin when delivery is imminent.

If insulin has not been started and a non-dextrose IV solution (e.g., LR) is infusing, check urine ketones (by dipstick) at every void or every 2 hours if the patient is catheterized. Start IV insulin and change the IV to a dextrose solution (e.g., D5LR) when the urine is positive for ketones. The insulin dose should be based on the pre-admission C:I ratio. When the patient is receiving insulin, check the blood glucose at least every 2 hours.

If the patient has received NPH within the past 12 hours, a dextrose IV solution (e.g., D5LR) will most likely be needed to prevent hypoglycemia. When it has been more than 12 hours since the NPH dose, change the IV to a non-dextrose IV solution (e.g., LR) if the blood glucose is greater than 90 mg/dL. Start IV insulin if the change results in a glucose >110 mg/dL.

Usually, patients will be NPO during labor. However, if the labor is prolonged, a diabetic diet may be ordered. In such a case, cover the meal with IV insulin. The insulin dose should be based on the pre-admission C:I ratio. A dextrose IV solution should be infused when insulin is infusing.

B. Type 2 (Non-insulin Dependent)
White's Class B (but could be Class C if 10 years or more)
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Same as Section IV. A. above.

C. Type 3 (Gestational)
White's Class A2
Blood Glucose Goal: 70-110 mg/dL
Insulin Solution: 100 units/500 mL saline (0.2 units/mL)

Same as Section IV. A. above.

V. POSTPARTUM MONITORING
A. Type 1 (Insulin Dependent)
White's Class C or lower (but could be Class B if less than 10 years)
Blood Glucose Goal: 100 - 180 mg/dL

Insulin is usually not required in the immediate postpartum period and before the patient consumes food. Use sliding scale SC insulin (e.g., 4 units for 200-250 mg/fL, 6 units for 251-300 mg/dL, 8 units for 301-350 mg/dL, and 10 units for 351-400 mg/dL) to control hyperglycemia. Although rare, the physician may determine that IV insulin is required. If so, start IV insulin at 1 unit/hour when the blood glucose is greater than 180 mg/dL. Check the glucose in 1 hour and

then every 2 hours until a pattern has been established. A dextrose IV solution is required. Patients will be very sensitive to insulin and great care must be taken to avoid severe hypoglycemia.

For patients not receiving IV insulin, cover the first meal with sliding scale insulin. When the patient has demonstrated that she can consume a meal, restart her on SC insulin. The dose should be approximately 50% of the last dose before delivery. Order finger stick blood glucoses at fasting, 1 hour postprandial, and bedtime.

B. Type 2 (Non-insulin Dependent)
White's Class B (but could be Class C if 10 years or more)
Blood Glucose Goal: 100 - 180 mg/dL

Insulin is usually not required in the immediate postpartum period and before the patient consumes food. Use sliding scale SC insulin (e.g., 4 units for 200-250 mg/dL, 6 units for 251-300 mg/dL, 8 units for 301-350 mg/dL, and 10 units for 351-400 mg/dL) to control hyperglycemia.

Cover the first meal with sliding scale insulin. When the patient has demonstrated that she can consume a meal, restart her pre-gestational diabetic regimen. If the regimen was insulin, start her at approximately 50% of the last insulin dose before delivery. If the regimen was an oral agent or agents, restart these at the same dose as pre-gestation. For patients diagnosed during pregnancy, consult with the physician to arrive at the best regimen. Order finger stick blood glucoses at fasting, 1 hour postprandial, and bedtime.

C. Type 3 (Gestational)
White's Class A2
Blood Glucose Goal: NONE

There is no need to check the blood glucoses of postpartum women who had gestational diabetics.

November 2006jb
Revised July 2008; April 2009jb

PART III. SUBCUTANEOUS INSULIN DOSING OBSTETRIC INPATIENTS

I. PURPOSE

To control blood glucose in diabetic obstetric inpatients using subcutaneous (SC) insulin doses.

II. PHYSICIAN ORDER REQUIRED

A physician's order for SC insulin per pharmacy must be in the patient's chart.

III. BACKGROUND

This guideline describes a technique to dose SC insulin to control blood glucose in pregnant diabetic inpatients. For patients who have received insulin by a continuous infusion, conversion to SC dosing usually occurs about 24 hours before discharge. However, some patients, because of other pregnancy complications, may be hospitalized for days to weeks and require SC insulin therapy. As pregnancy progresses, insulin dose requirements increase in a relatively predictable manner, based on the patient's body weight and gestational age. Even though the increase in insulin dose may be partially predictable, the dose must be titrated in each patient to assure optimum blood glucose control and to prevent hypoglycemic/hyperglycemic episodes. Proper dose titration will also reduce the maternal, fetal, and newborn complications outlined in the Background Information to this guideline. Therefore, close monitoring of these patients is required to achieve the goal of well-controlled diabetes during pregnancy.

IV. BLOOD GLUCOSE GOAL RANGE

Unless otherwise specified by the physician, the mean glucose goal range is 60 - 110 mg%. Specific target glucose ranges are:[10]

Fasting (Before Breakfast):	60 - 90 mg/dL
Before Lunch/Dinner/Bedtime Snack:	60 - 105 mg/dL ***(not routinely checked)***
Postprandial (1 Hr):	<130 mg/dL
Postprandial (2 Hr):	<120 mg/dL ***(not routinely checked)***
Bedtime:	<110 mg/dL
Early Morning (0300):	60 - 90 mg/dL ***(not routinely checked)***

V. SUBCUTANEOUS DOSING METHODS

A. INITIAL CALCULATION FOR THREE-DOSE METHOD

		Fraction of Total Dose	
	Time	NPH	Regular
Before Breakfast	0800	0.44	0.22
Before Dinner	1700		0.17
At Bedtime	2200	0.17	

B. INITIAL CALCULATION FOR FOUR-DOSE METHOD

		Fraction of Total Dose	
	Time	NPH	Regular
Before Breakfast	0800	0.28	0.22
Before Lunch	1200		0.17
Before Dinner	1700		0.17
At Bedtime	2200	0.17	

C. COMPARISON OF THREE- AND FOUR-DOSE METHODS

For this guideline, the preferred SC dosing technique, because of better compliance, is the three-dose method. The four-dose method may be required in some individuals if control cannot be achieved, such as in type 1 diabetics, but the majority of women will be adequately controlled using three insulin doses per day.

VI. MONITORING BLOOD GLUCOSE

Glucose concentrations should be determined at bedside using capillary blood. If glucose concentrations are determined by the laboratory, this information should be noted on the patient's record as such (e.g., 120 mg/dL [L]). A study has shown that postprandial in comparison to preprandial blood glucose control results in better maternal and newborn outcome by decreasing the risk of neonatal hypoglycemia, macrosomia, and cesarean delivery. The scheduling of glucose determinations, therefore, emphasizes 1-hour postprandial checks (i.e., ***1 hour after the last bite of the meal***). The only pre-meal determination routinely performed is the morning fasting. A typical plan for blood glucose checking is as follows:

•fasting - before breakfast
•postprandial - 1 hour after the last bite of breakfast, lunch, and dinner
•bedtime
•early morning - approximately 0300 ***optional, not routine***

VII. GLYCOSYLATED HEMOGLOBIN (HbA1c)

Measurement of HbA1c provides a method to measure mean blood glucose control over the preceding 2-3 months. HbA_{1c} was chosen because it makes up most of the glycosylated hemoglobin and because it is the least affected by recent changes in blood glucose. Measurement of HbA1c indicates the amount of hemoglobin that has been irreversibly glycosylated at the N terminal amino group in the beta chain. Its concentration is determined by the plasma glucose level and the life span of a red blood cell (about 120 days). Although normal values vary from laboratory to laboratory, the goal in Women's Hospital is an HbA1c of <6%. The physician will order this laboratory test, especially for any newly diagnosed patient at <20 weeks' gestation. The pharmacist should request these results if they are not on the chart.

Factors Affecting HbA1c	Effect
Hemoglobinopathies	Decreased
Anemias	
Hemolytic	Decreased
Iron deficiency	Decreased (if receiving iron therapy)
	No change (if not treated)
Blood loss	Decreased
Uremia	Increased (if assay based on HPLC or electroendosmosis)
	No change (if assay based on affinity chromatography)
Hemodialysis	No change
Vitamin C (≥1 gm/day)	Decreased
Vitamin E (≥1200 IU/day)	Decreased

VIII. INSULIN DOSE REQUIREMENTS BY GESTATIONAL AGE

The total daily insulin requirement will increase with gestational age and this should be anticipated. In general, but only for diabetic types 1 and 3, this increase may be shown as follows, where the weight is actual body weight:

0.7 u/kg weeks 6 - 18
0.8 u/kg weeks 18 - 26
0.9 u/kg weeks 26 - 36
1.0 u/kg weeks 36 - 41
0.6 u/kg Postpartum

A number of factors may affect the above doses, such as insulin resistance in gestational diabetics, obesity, and the level of exercise. The above doses cannot be used to routinely determine insulin requirements because the insulin regimen for each patient must be individualized, but the expected changes do provide a basis to anticipate rising requirements as pregnancy progresses.

In contrast to pregnant patients, the postpartum dose of 0.6 u/kg/day may be used to restart patients on a SC regimen 48-72 hours after delivery. In this case, the body weight should be determined after postpartum diuresis has occurred.

IX. DOSE ADJUSTMENTS (THREE-DOSE METHOD)

Time of Day	Blood Glucose (mg/dL)	Insulin Dose to be Adjusted	Adjustments Required*
Fasting	>90	Bedtime NPH and/or PM Regular	**Check HS glucose (2100):** •if >110, increase PM Regular by 2-4 units and/or decrease HS snack **If HS glucose is normal, check 0300 glucose:** •if >90, increase HS NPH by 2-4 units •if <60, decrease HS NPH by 2-4 units and/or increase HS snack
Fasting	<60	Bedtime NPH	Decrease by 2-4 units
1-Hour Post-Breakfast	>130	AM Regular	Increase by 2-4 units
	<100	AM Regular	Decrease by 2-4 units
1-Hour Post-Lunch	>130	AM NPH	Increase by 2-4 units
	<100	AM NPH	Decrease by 2-4 units
1-Hour Post-Dinner	>130	PM Regular	Increase by 2-4 units
	<100	PM Regular	Decrease by 2-4 units

*dose adjustments are made the next day

Note: Dose adjustments for patients with brittle diabetes should be limited to 10%-15% (i.e., 1-2 units). For diabetic types 2 and 3, dose adjustments should be in the 2-4 units range.

X. DOSE ADJUSTMENTS (FOUR-DOSE METHOD)

Time of day	Blood Glucose (mg/dL)	Insulin Dose to be Adjusted	Adjustments Required*
Fasting	>90	Bedtime NPH	**Check HS glucose (2100):** •if >110, increase PM Regular by 2 units and/or decrease HS snack **If HS glucose is normal, check 0300 glucose:** •if >90, increase HS NPH by 2 units •if <60, decrease HS NPH by 2 units and/or increase HS snack
Fasting	<60	Bedtime NPH	Decrease by 2 units
1-Hour Post Breakfast	>130	AM Regular	Increase by 2 units
	<100	AM Regular	Decrease by 2 units
1-Hour Post Lunch	>130	Lunch Regular or AM NPH	Increase either or both by 2 units
	<100	Lunch Regular or AM NPH	Decrease either or both by 2 units
1-Hour Post Dinner	>130	PM Regular	Increase by 2 units
	<100	PM Regular	Decrease by 2 units

*dose adjustments are made the next day

Note: Dose adjustments for patients with brittle diabetes should be limited to 10%-15% (i.e., 1-2 units). The four-dose method is frequently used for type 1 diabetics who are using rapid acting insulin, such as lispro (Humalog) or aspart (Novolog), before meals. The above table is appropriate for either Regular or rapid acting insulins.

XI. TIMING OF MEALS AND SNACKS

The scheduling of meals and snacks for a diabetic patient is critical for the achievement of good diabetic control. Therefore, it is vital that the pharmacist routinely check that meals are served at scheduled times. However, the nursing staff in Womens' are keenly aware of the importance of delivering the food at the scheduled times. The meal and snack schedule in Womens' is:

Breakfast 0800 (note: nursing will not administer the AM NPH/Reg insulin until the patient's breakfast tray is in the Unit)
Snack 1030
Lunch 1230-1245

Snack	1430
Dinner	1800-1830
Snack	2100

Nursing will ask the patient to notify them when they have completed their meal so that the 1-hour postprandial blood glucose concentration checks can be scheduled. Based on the actual meal and meal completion times, the nurse will modify the ordered schedule of blood glucose determinations.

XII. CALORIE REQUIREMENTS DURING PREGNANCY

Patients treated under this guideline will given the Sweet Success diet (see Part I, Section XII.D).

XIII. EXERCISE AND OTHER FACTORS AFFECTING BLOOD GLUCOSE

Cardiovascular conditioning exercise can affect blood glucose by increasing insulin binding to and affinity for its receptor (i.e., lessening insulin resistance), and by improving hepatic glucose output and glucose clearance. However, even moderate exercise, such as walking for 15-30 minutes after a meal, may affect glucose control and must be anticipated when an inpatient is discharged home. ***This may require a reduction in the insulin dose immediately before discharge.***

XIV. INJECTION SITE

The abdominal wall is the preferred SC insulin injection site during pregnancy. If the patient is using other sites (e.g., arm or thigh), explain to her that the most consistent absorption of her insulin dose comes from using the stomach region and she should use that site. Rotating injections in a wide circle around the navel will allow her to obtain the most stable glucose levels.

07.97jb; 08.03; 02.04
April 2009jb-ku

PART IV. ORAL ANTIDIABETIC AGENTS
OBSTETRIC INPATIENTS

For obstetric inpatients, the oral antidiabetic agents, glyburide or metformin, may be indicated in two situations. In each situation, a physician's order for the specific drug must be obtained and documented in the patient's chart.

A. GESTATIONAL DIABETES

Diabetes first detected during pregnancy is defined as *gestational diabetes*. Depending on the gestational age when detected, however, many of these patients will be newly diagnosed type 2 diabetics and will require antidiabetic therapy after pregnancy. In contrast, when detected late in the second trimester, antidiabetic therapy will not be required after delivery and these patients represent true gestational diabetes. In this latter group, glyburide therapy will usually control the hyperglycemia and may be appropriate under the following conditions:[11]

a. gestational age of ≥30 weeks, and
b. fasting glucose levels <110 mg/dL

The failure rate with glyburide is increased when these conditions are not met. Therefore, glyburide should not be used and insulin therapy should be started. The starting dose of glyburide (non-micronized) should be 2.5-5 mg/day, taken either as a single dose with breakfast or dinner, or divided into two doses with breakfast and dinner. Individual doses can be increased at weekly intervals, in increments no larger than 2.5 mg, to a maximum of 20 mg/day. If control has not been achieved with the maximum dose, the patient should be changed to insulin.[11] Discussion with the physician is required, as is an order to change to "SC insulin per pharmacy".

B. MASSIVE INSULIN RESISTANCE

In some diabetic patients with types 2 or 3 diabetes, massive insulin resistance can result in daily insulin doses ≥300 units per day. Based on the experience in Womens', the addition of metformin 500 mg BID will lower the insulin requirement by approximately 60%. Discussion with the physician is required, as is an order for "Metformin per pharmacy".

Example: calculated insulin dose is 300 units/day
Start metformin 500 mg BID
Start total insulin dose of 120 units/day (divided into 3 doses)

April 2009jg-ku

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APPENDIX A
WHITE'S CLASSIFICATION OF DIABETES DURING PREGNANCY

Class	Age at Onset Years		Duration Years	Maternal Complications
A1	Any		Any	None; diet controlled
A2	Any		Any	None; insulin required
B	≥20	or	<10	No vascular disease
C	10-19	or	10-19	No vascular disease
D	<10	or	≥20	Background retinopathy[1] only or hypertension
F				Nephropathy (>500 mg/day proteinuria)
H				Arteriosclerotic heart disease
R				Proliferative retinopathy[2] or vitreous hemorrhage
T				After renal transplantation

Legend:
1. Background retinopathy = retinal microaneurysms, dot or blot hemorrhages, hard exudates
2. Preproliferative retinopathy = ischemic lesions: "cotton-wool spots", venous beading, and duplications;
3. Proliferative retinopathy = neovascularization may extend into vitreous, lead to hemorrhage, clot retraction, vitreous "scarring," retinal detachment

GESTATIONAL DIABETES

Gestational diabetes is carbohydrate intolerance occurring (or first diagnosed) during pregnancy. Although it can be any White's classification, it normally is Class A.

Reference: Moore TR. Diabetes in Pregnancy. In Creasy RK, Resnik R, Iams JD, eds. Maternal-Fetal Medicine. Principles and Practice. 5th ed. Philadelphia: Saunders, 2004:1023-1061.

APPENDIX B
NATIONAL DIABETES DATA GROUP (NIH)
CLASSIFICATION OF DIABETES MELLITUS

Nomenclature	Old Names	Clinical Features
Type 1 (IDDM)	Juvenile-onset	Ketosis-prone Insulin deficient
Type 2 (NIDDM)	Adult-onset	Ketosis-resistant Insulin-resistant Obesity, family history, and age are common factors
Type 3	Gestational diabetes	Occurs only in pregnancy

Reference: Moore TR. Diabetes in Pregnancy. In Creasy RK, Resnik R, Iams JD, eds. Maternal-Fetal Medicine. Principles and Practice. 5th ed. Philadelphia: Saunders, 2004;1023-1061.

APPENDIX C
MATERNAL MORBIDITY ASSOCIATED WITH DIABETIC PREGNANCY BY WHITE'S CLASSIFICATION

COMPLICATION	GDM	B,C	D,F,R	TOTAL
Preeclampsia	10%	8%	16%	12%
Chronic Hypertension	10%	8%	17%	10%
All Hypertension	15%	15%	31%	18%
Ketoacidosis	8%	7%	9%	--
Polyhydramnios	5%	--	18%	18%
Preterm labor	8%	5%	10%	--
Cesarean section	12%	44%	57%	--

Reference: Moore TR. Diabetes in Pregnancy. In Creasy RK, Resnik R, Iams JD, eds. Maternal-Fetal Medicine. Principles and Practice. 5th ed. Philadelphia: Saunders, 2004:1023-1061.