Section 4: Glycemic Control

<table>
<thead>
<tr>
<th>Concern</th>
<th>Care/Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycemic Control</td>
<td>▪ Check A1C; general goal: &lt; 7.0% (individualize, see Table 4-2)</td>
<td>Every 3 months if not at goal; every 6 months at goal</td>
</tr>
<tr>
<td></td>
<td>▪ Review goals, medications, side effects, and frequency of hypoglycemia</td>
<td>Each focused visit</td>
</tr>
<tr>
<td></td>
<td>▪ Assess self-blood glucose monitoring schedule</td>
<td>Each focused visit, 2 – 4 times/day, or as recommended</td>
</tr>
</tbody>
</table>

MAIN TOPICS INCLUDED IN THIS SECTION:
- General Glycemic Control Goals
- Individual and Specific Considerations for Glycemic Control Goals
- Assessment of Diabetes Control
- Hypoglycemic Agents
- Insulin Pump Therapy
- Acute Complications
- Sick Day Management
- Referral to a Diabetes Specialist
- References
Section 4: Glycemic Control

General Glycemic Control Goals

The Wisconsin Diabetes Advisory Group and a panel of experts recommend a general A1C goal of < 7.0%. Table 4-1 lists general goals for glycemic control for non-pregnant adults with diabetes.

Table 4-1: Glycemic Control Goals for Non-Pregnant Adults with Diabetes

<table>
<thead>
<tr>
<th>General A1C (%) goal</th>
<th>&lt; 7.0%*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-prandial or pre-meal goal</td>
<td>70 – 130 mg/dL</td>
</tr>
<tr>
<td>Peak post-prandial or post-meal (2 hour) goal</td>
<td>&lt; 180 mg/dL</td>
</tr>
</tbody>
</table>

*A1C is the primary target for glycemic control and referenced to a nondiabetic range of 4.0-6.0% using a DCCT-based assay.

Randomized controlled studies demonstrate reduced microvascular complications in both type 1 and type 2 diabetes with this level of control (ACCORD, 2008) (ADVANCE, 2008) (Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, 2002). It is estimated that for every one percent decrease in A1C, there is a 14-20% decrease in hospitalizations, resulting in a $4-5 billion savings in direct health care costs alone (Centers for Disease Control and Prevention Diabetes Cost-Effectiveness Group, 2002).

Although the benefits of good glycemic control on microvascular complications are well established, the benefits for macrovascular disease are less clear. The recently published Action to Control Cardiovascular Risk in Diabetes (ACCORD, 2008), Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE, 2008), and Veterans Affairs Diabetes Trial (VADT) studies did not demonstrate benefits of tight glucose control for macrovascular disease; for some people with diabetes, tight blood glucose control resulted in worse cardiovascular outcomes. Conversely, some people with short duration of diabetes and few comorbidities did show cardiovascular benefit from tight glycemic control.
Individual and Specific Considerations for Glycemic Control Goals

Although the general A1C goal of < 7.0% is applicable to most people with diabetes, experts agree that the A1C goal should be individualized. Less stringent A1C goals may be appropriate for some people with diabetes (Ismael-Beigi, Moghissi, Tiktin, Hirsch, Inzucchi & Genuth, 2011). Goals must be achievable, realistic, and safe. Health care providers should work with each person to negotiate and set glycemic goals as low as feasible to prevent microvascular complications of diabetes, while avoiding undue risk for adverse events (e.g., hypoglycemia, increased cardiovascular disease). Table 4-2 provides a list of factors that health care professionals and people with diabetes may want to consider when collaboratively setting A1C goals.

Table 4-2: Important Considerations in Individualizing Glycemic Goals

<table>
<thead>
<tr>
<th>Factors to consider when individualizing glycemic goals include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Duration of diabetes</td>
</tr>
<tr>
<td>• Comorbidities</td>
</tr>
<tr>
<td>• Complication status</td>
</tr>
<tr>
<td>(e.g., gastroparesis, chronic kidney disease)</td>
</tr>
<tr>
<td>• Known severe cardiovascular disease</td>
</tr>
<tr>
<td>• Age (e.g., children and the elderly)</td>
</tr>
<tr>
<td>• Life style, life expectancy, living status, financial status</td>
</tr>
<tr>
<td>(e.g., safety, living alone or with someone)</td>
</tr>
<tr>
<td>• History of severe and/or frequent hypoglycemia</td>
</tr>
<tr>
<td>• Increased risk for hypoglycemia or has hypoglycemia unawareness</td>
</tr>
<tr>
<td>• Planning pregnancy or during pregnancy</td>
</tr>
<tr>
<td>• Psychological/cognitive status (e.g., self-management skill, ability, and motivation)</td>
</tr>
</tbody>
</table>

Health care professionals must balance the potential benefits of intensive blood glucose control against the risks for each individual with diabetes. A proposed approach for considering an appropriate and safe A1C goal for each person is to use a 2-step process, which includes clinical characteristics and psychosocioeconomic conditions. The proposed framework outlined in Figure 1 offers one simple approach in determining glucose goals for people with type 2 diabetes.
Section 4: Glycemic Control

Figure 1: Framework to Assist in Determining Glycemic Treatment Targets in Patients with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Most Intensive</th>
<th>Less Intensive</th>
<th>Least Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0%</td>
<td>7.0%</td>
<td>8.0%</td>
</tr>
</tbody>
</table>

### Psychosocioeconomic Considerations

- **Highly motivated, Adherent, Knowledgeable, Excellent Self-Care Capacities, & Comprehensive Support Systems**
- **Less motivated, Non-adherent, Limited insight, Poor Self-Care Capacities, & Weak Support Systems**

### Hypoglycemia risk

- **Low**
- **Moderate**
- **High**

### Patient age, y

- 40
- 45
- 50
- 55
- 60
- 65
- 70
- 75

### Disease duration, y

- 5
- 10
- 15
- 20

### Other comorbid conditions

- None
- Few or mild
- Multiple or severe

### Established vascular complications

- None
- Early microvascular
- Advance microvascular
- Cardiovascular disease

Glycemic goals and treatment intensities are shown in terms of increasing severity or magnitude of clinical variables, as well as with limitations set by the psychosocioeconomic context. Greater height of a triangle indicates increased clinical concern about the considered variable. If a patient's position on the various triangles is widely disparate, the treatment target should be determined by the farthest-right position. As always, sound clinical judgment should prevail in these circumstances. The location of the triangles in the figure is not meant to represent their relative importance in setting glycemic targets. The depicted targets assume stable outpatient treatment protocols. Depending on the set glycemic target range for any given patient, the target range may have to be decreased (for example, for a patient in the intensive care unit with an acute infection) or increased (for example, for a patient admitted for acute renal injury) for various periods. Note that although hemoglobin A1C and mean blood glucose levels have a strong positive correlation in populations, this relationship varies substantially at an individual level and across certain populations (for various medical, nonmedical, and unknown reasons) among both glucose levels at a given hemoglobin A1C value and hemoglobin A1C values at a given average blood glucose level (30). A hemoglobin A1C value represents the mean effect of glycation reaction on hemoglobin over 2 to 3 months, whereas blood glucose levels obtained by fingersticks give a more accurate picture of glycemic control on a day-to-day basis.

Section 4: Glycemic Control

Type 1 Diabetes
The Diabetes Control and Complications Trial (DCCT) showed the significant benefits of intensive glycemic control (ADA, 2012); however, these benefits were at the expense of a three-fold increase in severe hypoglycemia. People with type 1 diabetes who are at increased risk of severe hypoglycemia (i.e., have hypoglycemia unawareness or history of severe hypoglycemia) will need to have glycemic goals moderated. An A1C goal from 7.0-8.0% may be appropriate for these people.

Type 2 Diabetes
Type 2 diabetes is a progressive disease. Beta cell loss begins almost a decade before the actual diagnosis of type 2 diabetes. (UKPDS). Beta cell function continues to decline in the years following diagnosis due to the natural progression of disease. Therefore, achieving optimal glycemic control in people with type 2 diabetes requires an understanding of the disease’s natural course. Treatment needs change over time due to one or more of the following reasons:

- Progression of type 2 diabetes
- Underlying infection, disease, or condition (including dental disease)
- The person’s dietary management and physical activity regimens
- Medication issues (discontinuation, missed doses, interference, or side effects from other medications)
- Weight change

Monotherapy alone is rarely effective over time and intensification of medications is necessary for optimal glycemic control for most people with type 2 diabetes (ADA, 2012). In the United Kingdom Prospective Diabetes Study (UKPDS) trial, monotherapy with insulin, a sulfonylurea, or metformin failed to maintain an A1C of < 7.0% after three years in approximately 50% of participants. After nine years, 75% of participants required additional therapy. The health care team should optimize glycemic control by adding medications as needed to effectively reach A1C goals in a timely manner. A recent retrospective cohort study showed all-cause mortality was greater in patients who had A1C < 7.0% or > 8.0%. For more information regarding medications to lower blood glucose, see the tool titled “Diabetes Mellitus Medications 2012” in the Tools Section.

Children and Adolescents
Special consideration must be given when identifying A1C and plasma glucose goals for toddlers, preschoolers, school-aged children, adolescents, and young adults with diabetes. The A1C goals identified for each age group serve as a guide for health care professionals as they individualize the diabetes management plan. Plasma blood glucose and A1C goals for type 1 diabetes by age group are presented in Table 4-3. For additional information about diabetes in school-aged children, see the resource Students with Diabetes: A Resource Guide for Wisconsin Schools and Families at: http://www.dhs.wisconsin.gov/diabetes/srg.HTM.
Section 4: Glycemic Control

Table 4-3: Plasma Blood Glucose and A1C Goals for Type 1 Diabetes by Age for Children and Adolescents *

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Plasma blood glucose goal range (mg/dL)</th>
<th>A1C</th>
<th>Rationale for A1C Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toddlers and preschoolers (0-6)</td>
<td>100-180</td>
<td>110-200</td>
<td>&lt; 8.5% (but &gt; 7.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- High risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Vulnerability to low blood glucose</td>
</tr>
<tr>
<td>School age (6-12)</td>
<td>90-180</td>
<td>100-180</td>
<td>&lt; 8.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Risks of low blood glucose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Relatively low risk of complications prior to puberty</td>
</tr>
<tr>
<td>Adolescents and young adults (13-19)</td>
<td>90-130</td>
<td>90-150</td>
<td>&lt; 7.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Risk of severe low blood glucose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- May have developmental and psychological issues</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- A lower goal (&lt; 7.0%) is reasonable if achieved without excessive low blood glucose</td>
</tr>
</tbody>
</table>

Adapted from: Diabetes Care (2012). 33(1), S40.
*A plasma blood glucose level is obtained by a finger stick and a home blood glucose monitor. Although there are no national recommendations for children with type 2 diabetes, using the values in this table as a guide is reasonable.

Key concepts in setting glycemic goals:
- Goals should be individualized and lower goals may be reasonable based on benefit-risk assessment.
- Blood glucose goals should be higher than those listed above in students with frequent low blood glucose or hypoglycemia unawareness (inability to sense that blood glucose is low or going low).
- Post-prandial blood glucose values should be measured when there is a discrepancy between pre-prandial blood glucose values and A1C levels and to help assess glycemia in those on basal/bolus regimens.
- During adolescence, the need for insulin will dramatically increase due to hormone changes and growth.

Pregnancy
For information specific to preconception, and pregnancy, and postpartum care, see Section 12: Preconception, Pregnancy, and Postpartum Care.

Assessment of Diabetes Control

A1C
The A1C test is the gold standard for assessing and monitoring long-term glycemic control in people with diabetes (ADA, 2012). A1C values correlate with average blood glucose levels for approximately the previous three months. A1C should be tested a minimum of two times per year for those meeting treatment goals with stable glycemic control and four times per year for those whose therapy is changing or those not meeting treatment goals.

Point-of-care A1C testing is available and provides a viable option for monitoring of A1C when the person is in the provider’s office (ADA, 2012). The immediate results allow the provider and the person with diabetes to evaluate and modify the diabetes plan of care as needed. Point-of-care A1C testing should not be used for diagnosing diabetes or monitoring during pregnancy. Point-of-care A1C testing requires proper instruction on use and adherence to strict quality control of the device.
Section 4: Glycemic Control

Accuracy of A1C

Conditions or illness that shorten erythrocyte survival or decrease mean erythrocyte age (e.g., acute blood loss, anemia, blood transfusions, hypersplenism, cirrhosis, chronic kidney disease) may affect the accuracy of the A1C. Additionally, a variety of hemoglobin disorders such as sickle cell disease can interfere with A1C assay methods, independent of shortened erythrocyte survival. Most of these conditions will give a falsely low A1C. A1C results should be continuously compared to a person’s home glucose readings. This comparison can assist in detecting discrepancies in persons with conditions known to affect the A1C but also for those whose A1C appears at goal (e.g., 7.0%) yet blood glucose readings document extreme fluctuations (e.g., 30 to 300 mg/dL).

Estimated Average Glucose

Estimated average glucose (eAG) is an alternative method of describing the results of the A1C. Health care providers can translate A1C results into an estimated average glucose (eAG), thereby using the same unit of measurement as used by an individual with their home blood glucose monitors. Table 4-4 provides a comparison of A1C and eAG levels.

The formula is: \( (28.7 \times A1C) - 46.7 = eAG \). A calculator is available to calculate eAG from A1C or A1C from eAG: http://professional.diabetes.org/GlucoseCalculator.aspx.

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>eAG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0%</td>
<td>97</td>
</tr>
<tr>
<td>5.5%</td>
<td>111</td>
</tr>
<tr>
<td>6.0%</td>
<td>126</td>
</tr>
<tr>
<td>6.5%</td>
<td>140</td>
</tr>
<tr>
<td>7.0%</td>
<td>154</td>
</tr>
<tr>
<td>7.5%</td>
<td>169</td>
</tr>
<tr>
<td>8.0%</td>
<td>183</td>
</tr>
<tr>
<td>8.5%</td>
<td>197</td>
</tr>
<tr>
<td>9.0%</td>
<td>212</td>
</tr>
<tr>
<td>9.5%</td>
<td>226</td>
</tr>
<tr>
<td>10.0%</td>
<td>240</td>
</tr>
<tr>
<td>10.5%</td>
<td>255</td>
</tr>
<tr>
<td>11.0%</td>
<td>269</td>
</tr>
<tr>
<td>11.5%</td>
<td>283</td>
</tr>
<tr>
<td>12.0%</td>
<td>298</td>
</tr>
</tbody>
</table>

Adapted from: Diabetes Care (2008). 31(8), 1473-1478.

Fructosamine

Non-hemoglobin-based methods for assessing glycemic control may be useful when the A1C is known to be unreliable (ADA, 2004). The fructosamine test, or glycated serum albumin test, reflects changes in glycemic control over a period of one to two weeks. It may also be useful in situations where information on recent glycemic control is required. Measurement of a fructosamine level, however, has not been demonstrated to correlate with the risk of development of complications, and thus should not be considered equivalent to an A1C test.
Self-Monitoring of Blood Glucose

Self-monitoring of blood glucose (SMBG) is a powerful tool that gives people with diabetes a way to check their blood glucose level at any time of day (American Association of Diabetes Educators, 2010). Studies have consistently demonstrated the benefits of SMBG in type 1 diabetes. However, similar studies in people with type 2 diabetes have not always produced consistent results. Nonetheless, SMBG is still considered the best way for people and health care providers to assess efficacy of all ongoing diabetes management regimen. Providers should review blood glucose logs and/or downloaded meter results during each diabetes-focused visit and use the results to enhance self-management skills, reinforce lifestyle modifications, and guide medical treatment changes. Many different meters are available and meter choice should match individual needs. Accuracy of the meter should be checked annually. This is most often done by comparing a meter test result to a lab test result. A lab test will be about 10-15% higher than the value given by a meter that measures whole blood. Many meters now measure plasma blood values, which means the result can be compared more directly to lab test value. More information on meters can be found at: http://www.forecast.diabetes.org/files/images/v63n01_p44v2.pdf.

Self-monitoring of blood glucose is quick and easy but can be expensive (ADA, 2012). Frequency and timing of SMBG testing depends on individual circumstances. Some common self-monitoring suggestions are listed in Table 4-5. The following factors are considerations when recommending frequency of testing:

- Type of diabetes
- Blood sugar fluctuation (i.e., degree of and number of fluctuations through the day)
- Blood glucose control
- Type of treatment (i.e., oral medication, insulin, food choices, and physical activity)
- Adjustments of medications/insulin
- Frequency of hypoglycemia
- Individual ability and willingness to test
- Insurance coverage and limits
### Table 4-5: Self-Monitoring of Blood Glucose Suggestions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Testing Amount</th>
<th>Recommended Testing Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 or Type 2: Using insulin (intensive regimen, multiple injections, or pump) or during illness</td>
<td>4 or more times/day (during illness, check urine or blood ketones with each blood glucose &gt; 250 mg/dL)</td>
<td>• Fasting, pre-meal, and bedtime  &lt;br&gt; • 1-2-hour post-meal is beneficial especially when trying to achieve tighter control by adjusting treatment for the specific grams of carbohydrates consumed before a meal and for teaching about how lifestyle choices affect glucose levels  &lt;br&gt; • If not eating, the person with diabetes should check every 4-6 hours</td>
</tr>
<tr>
<td>Type 2: Not on insulin; adding or adjusting treatment</td>
<td>2 or more times/day</td>
<td>• Fasting, pre-meal, bedtime, and/or 1-2-hour post-meal (alternate days with varied times)  &lt;br&gt; • Adjust the doses of medications to attain the goal fasting glucose level  &lt;br&gt; • 1-2-hour post-meal is beneficial especially when trying to achieve tighter control by adjusting treatment when fasting glucose is at goal and for teaching about how lifestyle choices affect glucose levels</td>
</tr>
<tr>
<td>Type 2: Stable treatment regimen; not on insulin</td>
<td>1 or more times/day</td>
<td>• Alternate fasting and 1-2-hour post-meal  &lt;br&gt; • Adjust the doses of medications to attain the goal fasting glucose level  &lt;br&gt; • 1-2-hour post-meal is beneficial for teaching about how lifestyle choices affect glucose levels</td>
</tr>
<tr>
<td>Pre-conception</td>
<td>4 or more times/day</td>
<td>• Fasting, pre-meal, and bedtime  &lt;br&gt; • 1-2-hour post-meal is beneficial especially when trying to achieve tighter control by adjusting treatment for the specific grams of carbohydrates consumed before a meal and for teaching about how lifestyle choices affect glucose levels</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>4 or more times/day</td>
<td>• Fasting, pre-meal, 1-hour or 2-hour post-meal, and bedtime</td>
</tr>
</tbody>
</table>

*All people with diabetes must be instructed to test their glucose when experiencing symptoms of hypoglycemia or when at risk of hypoglycemia. These testing schedules and recommendations are intended to serve as a guide for health care providers. They are not intended to replace or preclude clinical judgment.  
†1-hour or 2-hour recommendation will be determined by provider  
‡ACOG and ADA have different recommendations for testing freq and targets during pregnancy. Providers caring for pregnant women with diabetes should be familiar with recommendations and treat accordingly. Pregnant women with diabetes should be cared for by an experienced provider in diabetes management.

### Alternate Site Testing

Many blood glucose meters provide the ability to measure blood glucose using blood from a location other than a finger, such as the forearm, upper arm, base of the thumb, or thigh (Johnson & Hinnen (2001). Typically, alternate site testing utilizes a specific lancet device (or device tip) to obtain an adequate blood specimen. Alternate site blood glucose results differ from finger stick results when blood glucose levels are changing rapidly, such as after a meal, after taking insulin, during physical activity, or during illness/stress. A finger stick test is advised:

- If alternative site test results are not consistent with how the person is feeling
- When hypoglycemia is suspected and symptoms are present
- Within two hours after a meal
- During/after physical activity
- During illness or stress

When possible, fingerstick testing is preferred. Providers caring for people asking to do alternate site testing may consider referring to a diabetes educator in order to troubleshoot testing technique. In most cases people can modify fingerstick testing technique to minimize pain and monitor effectively without use of alternate site testing.
Section 4: Glycemic Control

Continuous Glucose Monitors

Continuous Glucose Monitors (CGM), sometimes called sensors, are devices that continuously measure glucose levels in the interstitial fluid of the skin (National Diabetes Information Clearinghouse, 2008). CGMs provide an additional method of evaluating glucose control as the CGM tracks glucose levels and trends throughout the day for 3 or 7 days depending on the monitor. CGM is not intended to be a replacement for finger stick testing. CGM may be used for a variety of reasons:

- To augment insulin therapy with the goal of optimizing glycemic control
- To identify erratic blood glucose fluctuations
- To serve as a warning tool for those with frequent, severe hypoglycemia or hypoglycemia unawareness
- To identify previously undetected hyperglycemia and hypoglycemia
- For optimal glucose control during pregnancy

CGM systems are programmed to alert for hyperglycemia and hypoglycemia, as well as rapidly changing glucose levels (either rising or falling). CGM systems may not alert for all high or low blood glucose levels. **A CGM reading should never be used to determine treatment.** In the presence of CGM, blood glucose monitoring by finger stick is still essential with any symptoms of hyperglycemia or hypoglycemia and high or low alerts.

Calibration of a CGM is essential and is best done when glucose levels are stable. Various types of continuous glucose monitors are available as shown in Table 4-6. More information on CGMs can be found at: http://www.forecast.diabetes.org/files/images/v63n01_p44v2.pdf.

An office-based continuous glucose monitor (Medtronics iPRO) is also available for professional use. This device is inserted in the office, worn for 3 days, then removed and downloaded. People may need prior authorization for use of this device. It can be helpful to determine:

- Daily glucose patterns
- Otherwise unidentified hyperglycemia and hypoglycemia
- Discordance between A1C and SMBG monitoring

<table>
<thead>
<tr>
<th>Table 4-6: Continuous Glucose Monitors for Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Name</strong></td>
</tr>
<tr>
<td>Seven Plus ☀</td>
</tr>
<tr>
<td>Guardian Real-Time ✦</td>
</tr>
<tr>
<td>MiniMed Paradigm Real-Time ✦</td>
</tr>
</tbody>
</table>


- ☀ FDA approved for adults 18 years and older
- ✦ FDA approved for children 7 years and older

Hypoglycemic Agents

Oral Glucose-Lowering Medications

Many oral medications are available for treatment of type 2 diabetes. These can effectively reduce fasting plasma glucose (FPG) or post-prandial glucose to achieve optimal glycemic control. For a comprehensive list of oral glucose-lowering medications see the tool titled “Diabetes Mellitus Medications 2012” in the Tools Section.
Injectable Glucose-Lowering Agents

Incretin mimetics are glucagon-like peptide 1 (GLP-1) agonists. These agents can effectively reduce post-prandial, and to a lesser extent, fasting glucose levels. For a comprehensive list of injectable non-insulin glucose-lowering agents see the tool titled “Diabetes Mellitus Medications 2012” in the Tools Section.

Insulin

Insulin is essential for the treatment of type 1 diabetes and is frequently necessary for people with type 2 diabetes to achieve optimal blood glucose levels. Insulin provides benefit for lowering both fasting and post-prandial glucose. For detailed information on the types of insulin, insulin regimens, and tips for using insulin, see the tool titled “Insulin Therapy 2012” in the Tools Section.

U-500

For persons whose insulin needs exceed 200 IU to 300 IU daily due to insulin resistance, U-500 insulin may be an option. Advantages are a lower quantity of fluid injected into the subcutaneous tissue, resulting in less discomfort, potentially increased medication adherence and improved glycemic control (Garg et al 2007, Dailey 2010). Disadvantages of U-500 insulin are due to safety concerns. There is no increase in hypoglycemia as compared to U-100 insulin when appropriate safety precautions are present for U-500 use (Garg et al 2007, Quinn 2011), however, three publications have reported clinically significant hypoglycemia during U-500 use (Dailey 2010, Boldo 2012, Ziesmer 2012). No dedicated insulin syringes exist for U-500, so careful instruction is needed for either a U-100 insulin or tuberculin syringes for U-500 insulin administration (Garg 2007). The Institute for Safe Medication Practices (ISMP) recommends use of a tuberculin syringe with doses expressed both in units and volume (Pena et al, Cochran et al, Lane, et al). For more information on ISMP go to: http://www.ismp.org/Newsletters/ambulatory/archives/200708_2.asp. U-500 insulin must be stored away from U-100 insulin to avoid an error in giving the wrong strength of insulin. A referral to an endocrinologist is recommended for those considering use and or using U-500 insulin.

Insulin Pump Therapy

Insulin pump therapy is also known as continuous subcutaneous insulin infusion (CSII) (Grunberger, G. et al., 2010) (Cummins, E. et al., 2010). The use of an insulin pump is one way to deliver insulin with more flexibility and convenience than multiple daily injections. Candidates for CSII are people with type 1 diabetes, type 2 diabetes, and gestational diabetes. It is estimated that in 2010, approximately 20-30% of people with type 1 diabetes and less than 1% of people with type 2 diabetes are currently managing their diabetes with CSII (ACCORD, 2008). The National Institute for Health and Clinical Excellence (NICE) issued guidelines in 2002 on appropriate initiation of CSII in patients with diabetes (ADVANCE, 2008). The guideline recommended CSII in people with type 1 diabetes whose diabetes is not sufficiently controlled including, but not limited to, people who have large fluctuations in blood glucose levels despite multiple adjustments of multiple daily insulin regimens. A systematic review conducted by NICE in 2010 revealed potential benefits of CSII in children and adult people with type 1 diabetes such as improved control of hemoglobin A1C, less hypoglycemic episodes, and increased quality of life with greater lifestyle flexibility. Few studies were conducted in people with type 2 diabetes and gestational diabetes to recommend CSII in such populations (ACCORD, 2008). In one study in the United States, CSII did not significantly improve hemoglobin A1C compared to the multiple daily insulin injections; however, CSII demonstrated a non-statistically significant trend in decreasing the amount of insulin demand in persons with type 2 diabetes.
Currently in the United States, there is no official requirement for medical supervision for persons with diabetes using CSII for glycemic control (ACCORD, 2008). As a result, adverse events can occur often with CSII due to inappropriate candidates, inadequate training on self-management, and limited expert guidance. Therefore, people wishing to use CSII must be willing to invest time and energy into learning a new insulin delivery approach and be able to fulfill follow-up responsibilities to ensure positive outcomes. Manufacturer resources exist for pump therapy. All the insulin pump companies have various resources and educational tools that are available free of charge. A compressive listing of insulin pumps and infusion sets can be found in the American Diabetes Association: January 2012 Diabetes Forecast Consumer Guide at: http://forecast.diabetes.org/magazine/features/2012-insulin-pumps. More information on CGMs can be found at: http://forecast.diabetes.org/magazine/features/2012-continuous-glucose-monitors.

### Acute Complications

#### Hypoglycemia

Hypoglycemia is defined as a blood glucose less than 70 mg/dL (Briscoe, V., & Davis, S. 2006). People with diabetes on glucose-lowering agents with the exceptions of metformin, thiazolidinediones and DPP-4 Inhibitors are at risk of hypoglycemia. The risk of hypoglycemia increases as the blood glucose levels approach euglycemia. Some of the most common causes of hypoglycemia in people taking certain glucose-lowering agents are:

- Skipping or delaying meals or snacks, or eating less than usual
- More than the usual amount of physical activity without carbohydrate compensation
- Taking glucose lowering agents incorrectly (wrong dose, wrong medication, or wrong time)
- Ingesting alcohol
- Renal insufficiency
- Taking oral medications or injecting insulin too far in advance of eating
- Taking the wrong dose of rapid- or short-acting insulin (regular, aspart, lispro, or glulisine) before a meal (either calculating too much for the amount eaten or failing to correct for a low blood sugar first)
- Overcorrecting for high blood glucose by taking too much medication

The symptoms of hypoglycemia vary in characteristics, pattern, and intensity between individuals (McAulay, V., Deary, I, & Frier, B., 2001). It is important for people receiving glucose lowering agents with the potential of causing hypoglycemia to be familiar with their own individualized hypoglycemic symptoms. Although no single symptom is universally applicable to all people, some symptoms are more common than others, such as:

- Sweating, shaking, trembling
- Overall body weakness
- Visual disturbances and difficulty speaking
- Hunger
- Dizziness and headache
- Difficulty concentrating and confusion
- Anxiety
- Tingling in the mouth
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Common symptoms can differ greatly in people from different age groups (McAulay et al., 2001). Children are more likely to have asymptomatic hypoglycemic episodes. Some common symptoms of hypoglycemia in children include weakness, sleepiness, tremor, hunger, and behavioral changes. The warning symptoms of hypoglycemia are less apparent in elderly people. People from this age group are more prone to severe hypoglycemic attacks. Children and the elderly may require modification of their glycemic goals to less intensified diabetes control due to safety concerns. Refer to the tool titled “Signs and Symptoms of Low Blood Glucose (Hypoglycemia)” in the Tools Section.

To prevent an accident because of hypoglycemia, blood glucose testing is recommended before and during any potentially dangerous activity (Briscoe & Davis, 2006). For example, blood glucose levels should be tested at least every two hours during prolonged use of motorized or moving vehicles or heavy machinery. Hypoglycemia can impair a person’s ability to:

- Operate motorized or moving vehicles (e.g., car, motorcycle, lawn mower, scooter, bike)
- Operate equipment or machinery (e.g., power tools, firearms)
- Be aware of potential dangers during physical activities (e.g., swimming, diving, skiing)

Glucagon kits should be prescribed for any person taking glucose lowering agents with potential of causing hypoglycemia (Briscoe & Davis, 2006). Glucagon is used when the hypoglycemic person is unconscious or unable to take oral carbohydrates. Oral carbohydrates should be avoided in anyone that is unconscious as this practice is neither safe nor effective in treating severe hypoglycemia. It is important that the glucagon injection is available for use and that the person’s family member(s) or caregivers are knowledgeable in its use. While glucagon is given to a person Emergency Medical Services (e.g., 9-1-1) should be called.

Glucagon injections should be given to a hypoglycemic person under the following conditions:

- Unable to safely take liquids or solids by mouth
- Confused or unable to follow commands or directions
- Unresponsive or unconscious
- Having a seizure or convulsion

Glucagon will not be effective if glycogen stores are depleted in the liver. Other instances that can reduce the effectiveness of glucagon are: a prolonged fasting state, low levels of adrenaline, chronic hypoglycemia, or hypoglycemia caused by drinking too much alcohol.

Emergency identification in the form of a bracelet or necklace noting that the person has diabetes is also recommended for anyone taking oral hypoglycemic agents and/or insulin (Briscoe & Davis, 2006) (McAulay, 2001).

The health care provider/educator should evaluate people’s hypoglycemic episodes and develop a specific plan for treating hypoglycemia in a variety of settings (Briscoe & Davis, 2006). Table 4-7 presents the “Rule of 15” with a list of some common treatment options that are safe and effective for treating hypoglycemia. Over treatment of hypoglycemia with an inappropriate carbohydrate source (e.g., candy bar) is common and may cause significant rebound hyperglycemia. For additional information, go to: http://www.diabetesnet.com/diabetes-control/low-blood-sugars/treatment.
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### Table 4-7: Treatment of Hypoglycemia – Rule of 15

<table>
<thead>
<tr>
<th>If awake and able to swallow:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Give 15 grams carbohydrate such as:</td>
</tr>
<tr>
<td>- 3-4 glucose tablets</td>
</tr>
<tr>
<td>- 1 tube of glucose gel (one tube may not always be 15 grams)</td>
</tr>
<tr>
<td>- 8-12 oz of milk</td>
</tr>
<tr>
<td>- 4 oz of any juice without sugar added</td>
</tr>
<tr>
<td>- 4-6 oz of regular soda pop</td>
</tr>
<tr>
<td>- 3 sugar packets</td>
</tr>
<tr>
<td>2. Wait 15 minutes. Recheck blood glucose; if still less than 70 mg/dL, repeat 15 gram carbohydrate oral feeding.</td>
</tr>
<tr>
<td>3. Recheck blood glucose every 15 minutes, repeat “Rule of 15” as necessary until no longer hypoglycemic. If the blood glucose is still low after two attempts to treat, one should consider obtaining assistance from a health care professional.</td>
</tr>
<tr>
<td>4. Rule of thumb: approximately 15 grams of carbohydrate will raise blood glucose about 50-60 mg/dL.</td>
</tr>
<tr>
<td>5. Always troubleshoot for the cause of the hypoglycemic episode. Common reasons for hypoglycemic episodes include too much medication, extra activity, medication taken/given at wrong time, or delaying a meal.</td>
</tr>
</tbody>
</table>

Never give glucose gel to a person that is unconscious.

- If initial blood glucose is < 50 mg/dL, consider using 30 grams of carbohydrate initially.
- If, after a hypoglycemic episode, blood glucose is > 70 mg/dL, and risk for low blood sugar remains (e.g., person will be physically active, next meal is more than one hour away, person is going to drive or operate a motorized vehicle or machinery, or is otherwise at higher risk for inability to detect or treat low blood sugar), consider an additional snack with 15 grams of carbohydrate and a protein (e.g., cheese, meat).
- Many over-the-counter products exist for treating low blood glucose such as glucose tablets and gels. The grams of carbohydrates vary for these products, so read labels carefully.

Hyperglycemia

Severe, uncontrolled hyperglycemia can lead to the short-term complications of diabetic ketoacidosis (DKA) in type 1 diabetes or Hyperosmolar Hyperglycemia State (HHS) in type 2 diabetes (Kitabchi & Nyenwe, 2006). Prolonged hyperglycemia increases the risks of both short-term and long-term diabetes complications. People with diabetes need to be instructed on proper management of severe hyperglycemia. Persistent high blood glucose should be shared with the health care provider so adjustments to the treatment regimen can be made. For more information, refer to the tool titled “Signs and Symptoms of High Blood Glucose (Hyperglycemia)” in the Tools Section.

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a dangerous life-threatening condition that may occur when blood glucose levels are high (usually ≥ 250 mg/dL) and ketones are present (Kitabchi & Nyenwe, 2006). A single high blood glucose reading of ≥ 250 mg/dL without the presence of ketones should be monitored, but is not considered an emergency. DKA is a medical emergency. DKA is caused by lack of enough insulin to meet the body’s requirements. It is often seen during another illness that increases insulin needs in the body. DKA primarily occurs in type 1 diabetes, but can occur in type 2 diabetes. Common symptoms/signs associated with DKA include:

- Nausea and/or vomiting
- Stomach cramps/pain
- Sweet/fruity odor to breath
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- Sleepiness and/or lethargy, weakness
- Confusion, inattentiveness, or other behavior change
- Thirst/dry mouth
- Deep, fast, labored breathing

Hyperosmolar Hyperglycemic State

Hyperosmolar Hyperglycemic State (HHS) is an acute, life-threatening condition seen in type 2 diabetes (Kitabchi & Nyenwe, 2006). Previously termed Hyperosmolar Hyperglycemic Nonketotic Coma (HHNC), this condition occurs less frequently than DKA and typically occurs in people with type 2 diabetes over age 50. Features of HHS include hyperglycemia (often above 600 mg/dL), elevated serum osmolality, profound dehydration, and alterations in consciousness. Coma occurs in less than 20% of cases. Mortality rates can be as high as 10-40% for people with HHS.

Sick Day Management

During illness, the body releases stress hormones that contribute to hyperglycemia (by opposing the action of insulin) and to the formation of ketones (Kitabchi & Nyenwe, 2006). Any person with diabetes who is ill is at higher risk of dehydration, ketosis, DKA, or HHS, any of which can lead to hospitalization. Managing diabetes during illness often requires special care to achieve and maintain euglycemia, maintain fluid and electrolyte balance, provide adequate nutrition, and prevent further complications. Testing for urine ketones is recommended during periods of illness, infections, injury, or when blood glucose levels are ≥ 250 mg/dL to assist with early detection of DKA. Sick day management is a survival skill and all people with diabetes require detailed sick day instructions. For additional information, refer to the tool titled “Diabetes Sick Days Plan” in the Tools Section.

Referral to a Diabetes Specialist

Referral to a diabetologist, endocrinologist, or other health care provider with diabetes certification or who specializes in diabetes is valuable in the following circumstances:

- For clinical expertise in diabetes management
- For intensive insulin management
- For insulin pump or continuous glucose monitor initiation or adjustment
- For clients with hypoglycemia unawareness
- For clients with advanced diabetes complications
- For clients with complex diabetes regimens
- For clients requiring use of U500 insulin
- For clients with uncontrolled blood glucose despite multiple medication adjustments and/or who require the addition of insulin and/or experience frequent hypoglycemia
References


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