DM or individuals with type 2 DM taking multiple insulin injections each day should routinely measure their plasma glucose three or more times per day to estimate and select mealtime boluses of short-acting insulin and to modify long-acting insulin doses. Most individuals with type 2 DM require less frequent monitoring, although the optimal frequency of SMBG has not been clearly defined. Individuals with type 2 DM who are taking insulin should use SMBG more frequently than those on oral agents. Individuals with type 2 DM who are on oral medications should use SMBG as a means of assessing the efficacy of their medication and the impact of diet. Because plasma glucose levels fluctuate less in these individuals, one to two SMBG measurements per day (or fewer in patients who are on oral agents or are diet-controlled) may be sufficient. Most measurements in individuals with type 1 or type 2 DM should be performed prior to a meal and supplemented with postprandial measurements to assist in reaching postprandial glucose targets (Table 418-2).

Devices for continuous glucose monitoring (CGM) have been approved by the U.S. Food and Drug Administration (FDA), and others are in various stages of development. These devices do not replace the need for traditional glucose measurements and require calibration with SMBG. This rapidly evolving technology requires substantial expertise on the part of the diabetes management team and the patient. Current CGM systems measure the glucose in interstitial fluid, which is in equilibrium with the blood glucose. These devices provide useful short-term information about the patterns of glucose changes as well as an enhanced ability to detect hypoglycemic episodes. Alarms notify the patient if the blood glucose falls into the hypoglycemic range. Clinical experience with these devices is rapidly growing, and they are most useful in individuals with hypoglycemia unawareness, individuals with frequent hypoglycemia, or those who have not achieved glycemic targets despite major efforts. The utility of CGM in the intensive care unit (ICU) setting remains to be determined.

Assessment of Long-Term Glycemic Control Measurement of glycated hemoglobin (HbA_{1c}) is the standard method for assessing long-term glycemic control. When plasma glucose is consistently elevated, there is an increase in nonenzymatic glycation of hemoglobin; this alteration reflects the glycemic history over the previous 2–3 months, because erythrocytes have an average life span of 120 days (glycemic level in the preceding month contributes about 50% to the HbA_{1c} value). Measurement of HbA_{1c} at the "point of care" allows for more rapid feedback and may therefore assist in adjustment of therapy.

HbA_{1c} should be measured in all individuals with DM during their initial evaluation and as part of their comprehensive diabetes care. As the primary predictor of long-term complications of DM, the HbA_{1c} should mirror, to a certain extent, the short-term measurements of SMBG. These two measurements are complementary in that recent intercurrent illnesses may impact the SMBG measurements but not the HbA_{1c}. Likewise, postprandial and nocturnal hyperglycemia may not be detected by the SMBG of fasting and preprandial capillary plasma glucose but will be reflected in the HbA_{1c}. In standardized assays, the HbA_{1c} approximates the following mean plasma glucose values: an HbA_{1c} of 6% = 7.0 mmol/L (126 mg/dL), 7% = 8.6 mmol/L (154 mg/dL), 8% = 10.2 mmol/L (183 mg/dL), 9% = 11.8 mmol/L (212 mg/dL), 10% = 13.4 mmol/L (240 mg/dL), 11% = 14.9 mmol/L (269 mg/dL), and 12% = 16.5 mmol/L (298 mg/dL). In patients achieving their glycemic goal, the ADA recommends measurement of the HbA_{1c} at least twice per year. More frequent testing (every 3 months) is warranted when glycemic control is inadequate or when therapy has changed. Laboratory standards for the HbA_{1c} test have been established and should be correlated to the reference assay of the Diabetes Control and Complications Trial (DCCT). Clinical conditions such hemoglobinopathies, anemias, reticulocytosis, transfusions, and uremia may interfere with the HbA_{1c} result. The degree of glycation of other proteins, such as albumin, can be used as an alternative indicator of glycemic control when the HbA_{1c} is inaccurate. The fructosamine assay (measuring glycated albumin) reflects the glycemic status over the prior 2 weeks.

PHARMACOLOGIC TREATMENT OF DIABETES

Comprehensive care of type 1 and type 2 DM requires an emphasis on nutrition, exercise, and monitoring of glycemic control but also usually involves glucose-lowering medication(s). This chapter discusses classes of such medications but does not describe every glucose-lowering agent available worldwide. The initial step is to select an individualized, glycemic goal for the patient.

ESTABLISHMENT OF TARGET LEVEL OF GLYCEMIC CONTROL

Because the complications of DM are related to glycemic control, normoglycemia or near-normoglycemia is the desired, but often elusive, goal for most patients. Normalization or near-normalization of the plasma glucose for long periods of time is extremely difficult, as demonstrated by the DCCT and United Kingdom Prospective Diabetes Study (UKPDS). Regardless of the level of hyperglycemia, improvement in glycemic control will lower the risk of diabetes-specific complications (Chap. 419).

The target for glycemic control (as reflected by the HbA_{1c}) must be individualized, and the goals of therapy should be developed in consultation with the patient after considering a number of medical, social, and lifestyle issues. The ADA calls this a *patient-centered approach*, and other organizations such as the IDF and American Association of Clinical Endocrinologists (AACE) also suggest an individualized glycemic goal. Important factors to consider include the patient's age and ability to understand and implement a complex treatment regimen, presence and severity of complications of diabetes, known cardiovascular disease (CVD), ability to recognize hypoglycemic symptoms, presence of other medical conditions or treatments that might affect survival or the response to therapy, lifestyle and occupation (e.g., possible consequences of experiencing hypoglycemia on the job), and level of support available from family and friends.

In general, the ADA suggests that the goal is to achieve an HbA_{1c} as close to normal as possible without significant hypoglycemia. In most individuals, the target HbA_{1c} should be <7% (Table 418-2) with a more stringent target for some patients. For instance, the HbA_{1c} goal in a young adult with type 1 DM may be 6.5%. A higher HbA_{1c} goal may be appropriate for the very young or old or in individuals with limited life span or comorbid conditions. For example, an appropriate HbA_{1c} goal in elderly individuals with multiple, chronic illnesses and impaired activities of daily living might be 8.0 or 8.5%. A major consideration is the frequency and severity of hypoglycemia, because this becomes more common with a more stringent HbA_{1c} goal.

More stringent glycemic control (HbA_{1c} of ≤6%) is not beneficial, and may be detrimental, in patients with type 2 DM and a high risk of CVD. Large clinical trials (UKPDS, Action to Control Cardiovascular Risk in Diabetes [ACCORD], Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation [ADVANCE], Veterans Affairs Diabetes Trial [VADT]; Chap. 419) have examined glycemic control in type 2 DM in individuals with low risk of CVD, with high risk of CVD, or with established CVD and have found that more intense glycemic control is not beneficial and, in some patient populations, may have a negative impact on some outcomes. These divergent outcomes stress the need for individualized glycemic goals based on the following general guidelines: (1) early in the course of type 2 diabetes when the CVD risk is lower, improved glycemic control likely leads to improved cardiovascular outcome, but this benefit occurs more than a decade after the period of improved glycemic control; (2) intense glycemic control in individuals with established CVD or at high risk for CVD is not advantageous, and may be deleterious, over a follow-up of 3–5 years; an HbA_{1c} goal <7.0% is not appropriate in this population; (3) hypoglycemia in such high-risk populations (elderly, CVD) should be avoided; and (4) improved glycemic control reduces microvascular complications of diabetes (Chap. 419) even if it does not improve macrovascular complications like CVD.

TYPE 1 DIABETES MELLITUS

General Aspects The ADA recommendations for fasting and bedtime glycemic goals and HbA_{1c} targets are summarized in Table 418-2.