



# CHAPTER 33

## Medical Nutrition Therapy for Diabetes Mellitus and Hypoglycemia of Nondiabetic Origin

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### CHAPTER OUTLINE

- Pathophysiology
- Diagnostic and Screening Criteria
- Management of Diabetes Mellitus
- Diabetes and Age-Related Issues
- Implementing Nutrition Self-Management
- Acute Complications
- Long-Term Complications
- Preventing Diabetes
- Hypoglycemia of Nondiabetic Origin

### KEY TERMS

**autonomic symptoms**—symptoms of hypoglycemia that are adrenergically based and that arise from the action of the autonomic nervous system

**combination therapy**—a form of therapy for diabetes using combinations of oral medications or a combination of oral medication(s) and insulin injection(s)

**counterregulatory (stress) hormones**—hormones, including glucagon, epinephrine (adrenaline), norepinephrine, cortisol, and growth hormone, released during stressful situations, which have the opposite effect of insulin and cause the liver to release glucose from stored glycogen (glycogenolysis) and the adipose cells to release fatty acids for extra energy (lipolysis); these hormones counterbalance declining glucose levels

**dawn phenomenon**—a natural increase in morning blood glucose levels and insulin requirements that occurs in people with and without diabetes but tends to be more marked in people with diabetes; possibly caused

by a diurnal variation in growth hormone, cortisol, or catecholamines

**Diabetes Control and Complications Trial (DCCT)**—a 10-year study in people with type 1 diabetes who were treated with either conventional therapy or intensive therapy; follow-up evaluations proved that tight blood glucose control reduces the risk of diabetic microvascular complications

**diabetic ketoacidosis (DKA)**—severe, uncontrolled diabetes, resulting from insufficient insulin, in which ketone bodies (acids) build up in the blood; if left untreated (with immediate administration of insulin and fluids), DKA can lead to coma and even death

**fasting (food-deprived) hypoglycemia**—low blood glucose concentrations in response to no food intake for 8 hours or longer

**gestational diabetes mellitus (GDM)**—glucose intolerance, the onset or first recognition of which occurs during pregnancy

**glucagon**—a hormone produced by the  $\alpha$ -cells of the pancreas that causes an increase in blood glucose levels by stimulating the release of glucose from liver glycogen stores

**glucotoxicity**—pancreatic beta cells chronically exposed to hyperglycemia become progressively less efficient in responding to a glucose challenge

**glycosylated hemoglobin**—a blood test that reflects the blood glucose concentration over the life span of red blood cells (~120 days), expressed as a percentage of total hemoglobin with glucose attached; may also be called glycated hemoglobin or glycohemoglobin. Hemoglobin A1 (HbA1) is an evaluation of a combination of all fractions of the hemoglobin molecule. Hemoglobin A1c (HbA1c) is a measurement of the glycosylation of the “c” fraction and is the recommended assay method (simplified to A1c). An A1c of 6.0% reflects an average plasma glucose level of ~120 mg/dl. In general, each 1% increase in A1c is a reflection of an increase in average glucose levels of ~30 mg/dl

**honeymoon phase**—the period after the initial diagnosis of type 1 diabetes when there may be some recovery of  $\beta$ -cell function and a temporary decrease in exogenous insulin requirement

**hyperglycemia**—an excessive amount of glucose in the blood (generally  $\geq 180$  mg/dl or above) caused by too little insulin, insulin resistance, or increased food intake; symptoms include frequent urination, increased thirst, weight loss, and often tiredness or fatigue

**hyperglycemic hyperosmolar state (HHS)**—extremely high blood glucose levels with an absence of or only slight ketosis and profound dehydration

**hypoglycemia (or insulin reaction)**—low blood glucose level (usually  $\leq 70$  mg/dl), which can be caused by the administration of excessive insulin or insulin secretagogues, too little food, delayed or missed meals or snacks, increased amounts of exercise or other physical activity, or alcohol intake without food

**hypoglycemia of nondiabetic origin**—low levels of blood glucose that lead to neuroglycopenia symptoms that are ameliorated by the ingestion of carbohydrate

**immune-mediated diabetes mellitus**—a form of type 1 diabetes resulting from autoimmune destruction of the  $\beta$ -cells of the pancreas

**impaired glucose homeostasis**—metabolic stages of impaired glucose use (between normal glucose concentrations and diabetes), which are risk factors for future diabetes and cardiovascular disease

**insulin**—a hormone released from the  $\beta$ -cells of the pancreas that enables cells to metabolize and store glucose and other fuels

**insulin resistance**—an impaired biologic response (sensitivity) to either exogenous or endogenous insulin; insulin resistance and insulin deficiencies are involved in the etiology of type 2 diabetes

**insulin secretagogues**—oral medications that stimulate insulin release from the  $\beta$ -cell of the pancreas, such as sulfonylureas and nonsulfonylurea secretagogues (i.e., repaglinide and nateglinide)

**insulin sensitizers**—oral medications that enhance insulin action and include biguanides (metformin) and thiazolidinediones

**macrovascular diseases**—diseases of the large blood vessels, including coronary artery disease, cardiovascular disease, and peripheral vascular disease

**metabolic syndrome**—characterized by central obesity and insulin resistance with increased risk for cardiovascular disease and type 2 diabetes; associated risk factors include dyslipidemia (elevated triglycerides, low high-density lipoprotein [HDL] cholesterol, and high low-density lipoprotein [LDL] cholesterol), hypertension, prothrombotic factors, and impaired glucose tolerance

**microvascular diseases**—diseases of the small blood vessels, including retinopathy and nephropathy

**neuroglycopenic symptoms**—neurologic symptoms of hypoglycemia that are related to an insufficient supply of glucose to the brain

**oral glucose-lowering medications**—drugs, administered orally, that are used to control or lower blood glucose levels, including first- and second-generation sulfonylureas, nonsulfonylureas, secretagogues, biguanides,  $\alpha$ -glucosidase inhibitors, and thiazolidinediones

**polydipsia**—excessive thirst

**polyuria**—excessive urination

**postprandial (after a meal) blood glucose**—blood glucose level 1 to 2 hours after eating

**postprandial (reactive) hypoglycemia**—low blood glucose within 2 to 5 hours after eating

**pre-diabetes**—blood glucose concentrations that are higher than normal but not yet high enough to be diagnosed as diabetes; sometimes referred to as impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), depending on which test was used to detect it

**preprandial (fasting) blood glucose**—blood glucose level before eating

**self-monitoring of blood glucose (SMBG)**—a method whereby individuals can test their own blood glucose levels using a chemically treated strip and visually comparing the strip to a color chart or by inserting the strip into a meter that measures the glucose level; most blood glucose meters automatically convert capillary whole blood glucose values to plasma glucose values

**Somogyi (rebound) effect**—an episode of hypoglycemia usually caused by excessive exogenous insulin, which stimulates the overproduction of counterregulatory hormones, resulting in an excessive release of glucose from the liver and hyperglycemia; often caused by inappropriate evening insulin doses; evening insulin doses should not be increased in an attempt to improve glucose levels

**target blood glucose goals**—levels for capillary blood glucose tests that are as near normal as possible and that can be achieved without risk of serious hypoglycemia

**type 1 diabetes**—a type of diabetes that usually occurs in persons younger than 30 years of age but can occur at any age; previously known as insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes

**type 2 diabetes**—a type of diabetes usually occurring in persons older than 30 years of age, previously known as non-insulin-dependent diabetes mellitus (NIDDM) or maturity-onset diabetes; now also frequently diagnosed in youth and young adults; formerly called *maturity onset diabetes of youth (MODY)*

## KEY TERMS—Continued

**United Kingdom Prospective Diabetes Study (UKPDS)**—a 20-year multicenter trial in the United Kingdom of subjects with **type 2 diabetes** who were randomized into intensive therapy or conventional therapy; lowering of A1c and aggressive treatment of hypertension significantly reduced

the development of microvascular complications and lowered the risk for macrovascular complications

**Whipple's triad**—a triad of clinical features that includes (1) low blood glucose levels, (2) accompanied by symptoms, which are (3) relieved by administration of glucose

**D**iabetes mellitus is a group of diseases characterized by high blood glucose concentrations resulting from defects in insulin secretion, insulin action, or both. Abnormalities in the metabolism of carbohydrate, protein, and fat are also present. Persons with diabetes have bodies that do not produce or respond to **insulin**, a hormone produced by the  $\beta$ -cells of the pancreas that is necessary for the use or storage of body fuels. Without effective insulin, **hyperglycemia** (elevated blood glucose) occurs, which can lead to both the short-term and long-term complications of diabetes mellitus.

In 2000, about 15 million U.S. adults 18 years of age or older had diagnosed diabetes (6.3 million men and 8.7 million women), representing an increase from 4.9% of the adult population in 1990 to 7.3% in 2000. If undiagnosed diabetes is considered as well, it is likely that almost 10% of U.S. adults have diabetes (Mokdad et al, 2001). Much of the increase is because type 2 diabetes is no longer a disease that affects mainly older adults. Between 1990 and 1998, the prevalence of diabetes increased by 76% among people in their thirties (Mokdad et al, 2001). Among children with newly diagnosed diabetes, the prevalence of type 2 diabetes also increased dramatically in the past decade, growing from less than 4% in the years preceding 1990 to as high as 45% in certain racial/ethnic groups in recent years (American Diabetes Association [ADA], 2000).

Diabetes prevalence increases with increasing age, affecting 18.4% of those 65 years of age or older (ADA, 2001). Diabetes is particularly prevalent in minorities; indeed, the prevalence of type 2 diabetes is highest in ethnic minorities in the United States, such as African Americans, Hispanic populations (Latinos and Mexican Americans), Native Americans and Alaska Natives, Asian Americans, and Pacific Islanders (see *Focus on: Diabetes Does Discriminate!*).

Of great concern are the more than 20 million adults reported to have impaired glucose tolerance (IGT) (2-hour postchallenge glucose of 140-199 mg/dl), the 13 to 14 million with impaired fasting glucose (IFG) (fasting plasma glucose 110-125 mg/dl), and the 40 to 50 million with **metabolic syndrome** (ADA, 2001). Persons with IGT or IFG are now classified as having **pre-diabetes**, and they are at high risk for conversion to type 2 diabetes if lifestyle prevention strategies are not used and are at higher risk of car-

diovascular disease compared with persons with normal blood glucose concentrations.

Diabetes mellitus contributes to a considerable increase in morbidity and mortality rates, which can be reduced by early diagnosis and treatment. In 2002 diabetes costs in the United States were \$132 billion. Direct medical expenditures, such as inpatient care, outpatient services, and nursing home care, totaled \$91.8 billion. Indirect costs, totaling \$39.8 billion, were associated with lost productivity, including premature death and disability. Total medical expenditures incurred by people with diabetes totaled \$91.8 billion, or an average annual total direct cost of medical care of \$13,243 per person compared with \$2560 per person without diabetes (ADA, 2003a).

## PATHOPHYSIOLOGY

In 1997 new recommendations for the classification and diagnosis of diabetes mellitus were accepted and supported by the ADA, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD), and the Centers for Disease Control and Prevention, Division of Diabetes Translation. Recommendations were also made to eliminate the terms *insulin-dependent diabetes mellitus (IDDM)* and *non-insulin-dependent diabetes mellitus (NIDDM)* and to keep the terms *type 1* and *type 2* diabetes but to use Arabic rather than Roman numerals (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997) (Table 33-1).

### Type 1 Diabetes

At diagnosis, people with **type 1 diabetes** are usually lean and are experiencing excessive thirst, frequent urination, and significant weight loss. The primary defect is pancreatic  $\beta$ -cell destruction, usually leading to absolute insulin deficiency and resulting in hyperglycemia, **polyuria** (excessive urination), **polydipsia** (excessive thirst), weight loss, dehydration, electrolyte disturbance, and ketoacidosis. The rate of  $\beta$ -cell destruction is quite variable, proceeding rapidly in some persons (mainly infants and children) and slowly in others (mainly adults). The capacity of a healthy pancreas to secrete insulin is far in excess of what is needed normally; therefore, the clinical onset

## FOCUS ON

## Diabetes Does Discriminate!

**D**iabetes strikes particularly hard at minorities. Certain environmental or lifestyle factors may increase the risk of developing type 2 diabetes in susceptible populations. For example, an increase in the prevalence is observed in populations who have migrated to more urbanized locations compared with people of the same group who remained in their traditional home. Urbanization is usually related to major changes in diet, physical activity, and socioeconomic status as well as increased obesity.

One theory that might explain the increased prevalence of diabetes and insulin resistance among Native people is the “thrifty” gene. Years of subsistence living have created a thrifty genotype that allows Native people to extract a lot of energy and fat from small amounts of food. In an era of store-bought processed food, that gene backfires to induce obesity and diabetes. Adoption of a “Western” lifestyle (which may include a diet high in fat and a sedentary way of life) has been associated with a dramatically increased rate of type 2 diabetes in the Pima Indians of Arizona (ADA, 2001). Among the Pima Indians of Arizona, about 55% of adults older than 35 years of age have type 2 diabetes. This disease is increasingly being diagnosed in Native Americans younger than 30 years of age and has been diagnosed in some as young as 7 years of age.

Ravussin and colleagues (1994) surveyed a closely related population of Pima Indians living in Maycoba, a small village in a remote, mountainous region of northwestern Mexico. They found that individuals in this com-

munity ate a diet lower in fat than is typically consumed in Arizona, and both men and women were very physically active. The men and women of Maycoba weighed, on average, 50 lb less than a comparable group of Pimas from the Phoenix area. More important, diabetes was diagnosed in about 10% of the Maycoba Pimas compared with almost 50% of the Arizona Pimas.

The main staples of the Maycoba Pimas’ diet are beans, corn (as tortillas), and potatoes. Several essential nutrients are lacking because of the relative absence of fruits and vegetables. Diet analysis reveals a diet composed of 13% protein, 23% fat, 63% carbohydrate, and less than 1% alcohol and containing more than 50 g of fiber. This is in sharp contrast to the present diet of the Arizona Pimas. Even more striking than the low-fat diet of the Maycoba population, however, was the high level of physical activity in this population; more than 40 hours a week were spent engaged in hard physical work (Ravussin et al, 1994).

Interventions involving increased physical activity and a reduced fat and energy diet slowed the progression to type 2 diabetes in high-risk populations (Diabetes Prevention Program Research Group, 2002). Health promotion activities through community-based exercise programs and a return to more traditional diets also may help to reduce the diabetes epidemic that affects many developing countries as well as the underprivileged in industrialized nations.

**TABLE 33-1** Types of Diabetes and Prediabetes

CLASSIFICATIONS	DISTINGUISHING CHARACTERISTICS
Type 1 diabetes	Affected persons are usually lean, have abrupt onset of symptoms before the age of 30 yr (although it may occur at any age), and are dependent on exogenous insulin to prevent ketoacidosis and death.
Type 2 diabetes	Affected persons are often older than 30 yr at diagnosis, although it is now occurring frequently in young adults and children. Individuals are not dependent on exogenous insulin for survival; they may require it for adequate glycemic control.
Gestational diabetes mellitus (GDM)	A condition of glucose intolerance affecting pregnant women, the onset or discovery of which occurs during pregnancy.
Other specific types	Diabetes that results from specific genetic syndromes, surgery, drugs, malnutrition, infections, or other illnesses.
Pre-diabetes or impaired glucose homeostasis	Metabolic stage of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) that is between current definitions of normal glucose values and diabetes.

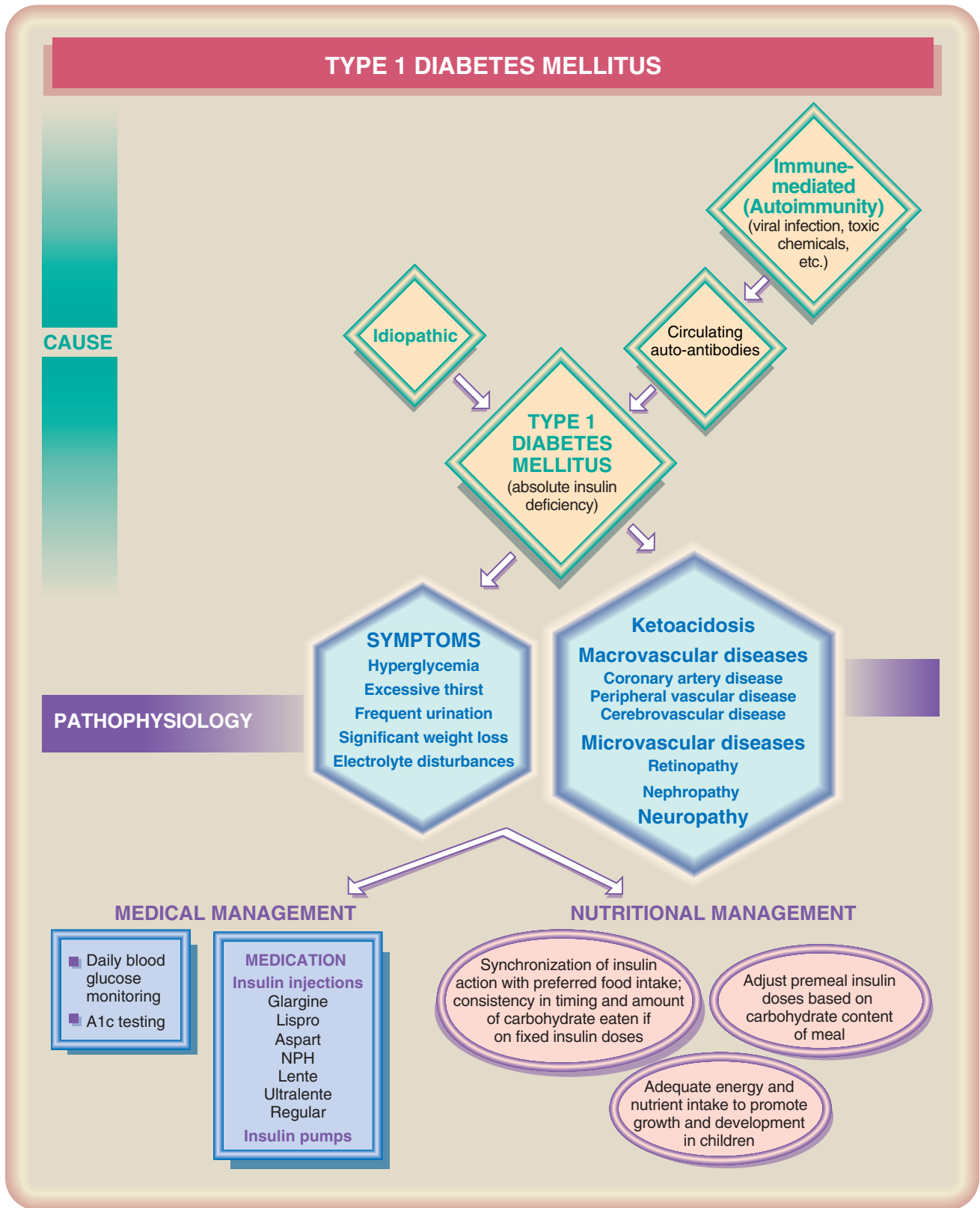
Modified from Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, *Diabetes Care* 20:1183, 1997.

of diabetes may be preceded by an extensive asymptomatic period of months to years, during which  $\beta$ -cells are undergoing gradual destruction (Figure 33-1).

Type 1 diabetes accounts for 5% to 10% of all diagnosed cases of diabetes. Persons with type 1 diabetes are dependent on exogenous insulin to prevent ketoacidosis and death. Although it may occur at any age, even in the eighth and ninth decades of life, most

cases are diagnosed in people younger than 30 years of age, with a peak incidence at around ages 10 to 12 years in girls and ages 12 to 14 years in boys.

Type 1 diabetes has two forms: immune-mediated diabetes mellitus and idiopathic diabetes mellitus. **Immune-mediated diabetes mellitus** results from an autoimmune destruction of the  $\beta$ -cells of the pancreas. *Idiopathic type 1 diabetes mellitus* refers to forms of the disease that have no known etiology. Although



**FIGURE 33-1** • Pathophysiology algorithm: type 1 diabetes mellitus. (Algorithm content developed by John Anderson, PhD, and Sanford C. Garner, PhD, 2000. Updated by Marion J. Franz, MS, RD, LD, CDE, 2002.)

only a minority of persons with type 1 diabetes fall into this category, of those who do, most are of African or Asian origin (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997).

The etiology of immune-mediated diabetes involves a genetic predisposition and an autoimmune destruction of the islet  $\beta$ -cells that produce insulin. Genetic factors involve the association between type 1 diabetes and certain histocompatibility locus antigens (HLA), with linkage to the *DQA* and *DQB* genes and influenced by the *DRB* genes. These HLA-DR/DQ alleles can be either predisposing or protective (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997).

At diagnosis, 85% to 90% of patients with type 1 diabetes have one or more circulating autoantibodies to islet cells, endogenous insulin, or other antigens that are constituents of islet cells. Antibodies identified as contributing to the destruction of  $\beta$ -cells are (1) islet cell autoantibodies (ICAs); (2) insulin autoantibodies (IAAs), which may occur in persons who have never received insulin therapy; and (3) autoantibodies to glutamic acid decarboxylase (GAD), a protein on the surface of  $\beta$ -cells. GAD autoantibodies appear to provoke an attack by the T cells (killer T lymphocytes), which may be what destroys the  $\beta$ -cells in diabetes.

Frequently, after diagnosis and the correction of hyperglycemia, metabolic acidosis, and ketoacidosis, endogenous insulin secretion recovers. During this **honeymoon phase**, exogenous insulin requirements decrease dramatically for up to 1 year; however, the need for increasing exogenous insulin replacement is inevitable, and within 8 to 10 years after clinical onset,  $\beta$ -cell loss is complete and insulin deficiency is absolute.

## Type 2 Diabetes

Type 2 diabetes may account for 90% to 95% of all diagnosed cases of diabetes and is a progressive disease that, in many cases, is present long before it is diagnosed. Hyperglycemia develops gradually and is often not severe enough in the early states for the patient to notice any of the classic symptoms of diabetes. Although undiagnosed, these individuals are at increased risk of developing macrovascular and microvascular complications.

Risk factors for type 2 diabetes include genetic and environmental factors, including a family history of diabetes, older age, obesity, particularly intraabdominal obesity, physical inactivity, a prior history of gestational diabetes, **impaired glucose homeostasis**, and race or ethnicity. Total adiposity and a longer duration of obesity are established risks factors for type 2 diabetes. Nevertheless, type 2 diabetes is found in persons who are not obese, and many obese persons never develop type 2 diabetes. Obesity combined with a genetic predisposition may be necessary for type 2 diabetes to occur. Another possibility is that a

similar genetic predisposition leads independently to both obesity and insulin resistance, which increases the risk for type 2 diabetes (ADA, 2001) (Figure 33-2).

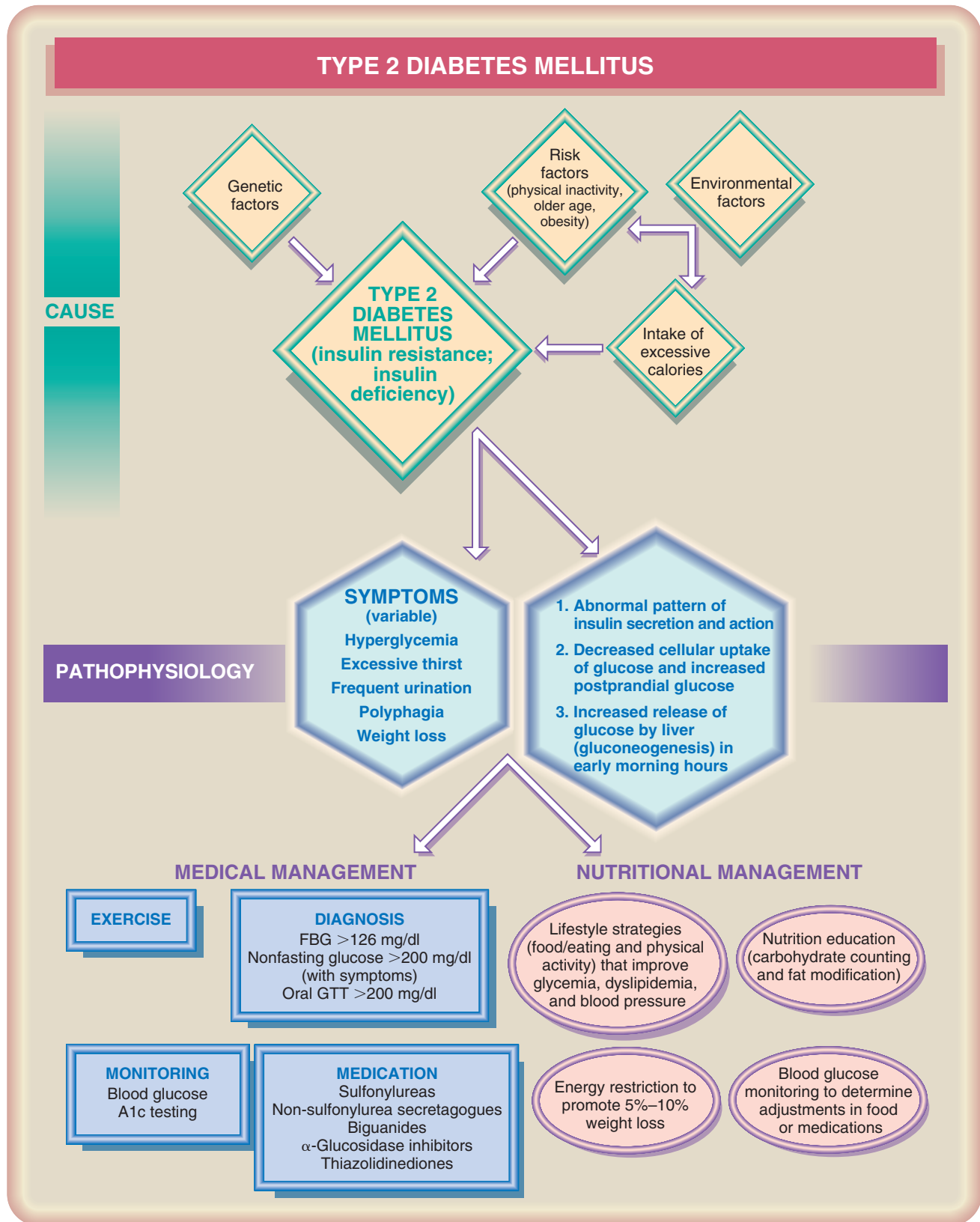
In most cases, type 2 diabetes results from a combination of insulin resistance and  $\beta$ -cell failure, but the extent to which each of these factors contributes to the development of the disease is unclear (Ferrannini, 1998). Endogenous insulin levels may be normal, depressed, or elevated, but they are inadequate to overcome concomitant **insulin resistance** (decreased tissue sensitivity or responsiveness to insulin); as a result, hyperglycemia ensues. Insulin resistance is first demonstrated in target tissues, mainly muscle and the liver. Initially, there is a compensatory increase in insulin secretion, which maintains normal glucose concentrations, but as the disease progresses, insulin production gradually decreases. Hyperglycemia is first exhibited as an elevation of **postprandial (after a meal) blood glucose** caused by insulin resistance at the cellular level and is followed by an elevation in fasting glucose concentrations. As insulin secretion decreases, hepatic glucose production increases, causing the increase in **preprandial (fasting) blood glucose** levels. Compounding the problem is the deleterious effect of hyperglycemia itself—**glucotoxicity**—on both insulin sensitivity and insulin secretion (Yki-Jarvinen, 1997), hence the importance of achieving near-euglycemia in persons with type 2 diabetes.

Insulin resistance is also demonstrated at the adipocyte level, leading to lipolysis and an elevation in circulating free fatty acids. Increased fatty acids cause a further decrease in insulin sensitivity at the cellular level, impair pancreatic insulin secretion, and augment hepatic glucose production (**lipotoxicity**) (Bergman and Adler, 2000). The above defects contribute to the development and progression of type 2 diabetes and are also primary targets for pharmacologic therapy.

Persons with type 2 diabetes may or may not experience the classic symptoms of uncontrolled diabetes, and they are not prone to develop ketoacidosis. Although persons with type 2 diabetes do not require exogenous insulin for survival, about 40% or more will eventually require exogenous insulin for adequate blood glucose control. Insulin may also be required for control during periods of stress-induced hyperglycemia, such as during illness or surgery.

## Gestational Diabetes Mellitus

**Gestational diabetes mellitus (GDM)** is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It occurs in about 7% of all pregnancies, resulting in more than 200,000 cases annually (ADA, 2001). Women with known diabetes mellitus before pregnancy are not classified as having GDM. GDM is usually diagnosed during the second or third trimester of pregnancy. At this point, insulin-antagonist hormone levels increase, and insulin resistance normally occurs.



**FIGURE 33-2** • Pathophysiology algorithm: type 2 diabetes mellitus. (Algorithm content developed by John Anderson, PhD, and Sanford C. Garner, PhD, 2000. Updated by Marion J. Franz, MS, RD, LD, CDE, 2002.)

## Other Types of Diabetes

This category includes diabetes associated with specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses. Such types of diabetes may account for 1% to 2% of all diagnosed cases of diabetes.

## Impaired Glucose Homeostasis

A stage of impaired glucose homeostasis includes IFG and IGT and is called pre-diabetes. This condition can be detected by either a fasting plasma glucose (FPG) test or an oral glucose tolerance (OGT) test. Individuals with pre-diabetes are at high risk for future diabetes and cardiovascular disease.

### DIAGNOSTIC AND SCREENING CRITERIA

Diagnostic criteria for diabetes are summarized in Table 33-2. Three diagnostic methods may be used to diagnose diabetes; however, because of the ease, acceptability to the patient, and the cost, the FPG test is recommended (ADA, 2002a). At this time, hemoglobin A1c (A1C), is not recommended for diagnosis. In pregnant women, different criteria are applied in establishing the diagnosis of gestational diabetes. One of the following three tests can be used to diagnose diabetes but must be confirmed on a subsequent day:

- ◆ An FPG value equal to or greater than 126 mg/dl
- ◆ Symptoms of diabetes and a nonfasting plasma glucose (casual) value of greater than or equal to 200 mg/dl. *Casual* refers to any time of the day, without regard to the elapsed time since one's last meal. Symptoms of diabetes include the classic ones of polyuria, polydipsia, and unexplained weight loss.
- ◆ A 2-hour postprandial glucose equal to or greater than 200 mg/dl during an OGT test involving administration of 75 g of glucose

Testing or screening for diabetes should be considered in all patients 45 years of age and older; if normal, the test should be repeated at 3-year intervals. Testing should be considered at a younger age or be carried out more frequently in patients who:

- ◆ Have a family history of diabetes (i.e., parents or siblings with diabetes)
- ◆ Are overweight with a body mass index (BMI)  $\geq 25 \text{ kg/m}^2$
- ◆ Are members of a high-risk ethnic population (e.g., African Americans, Hispanic Americans, Native Americans, Asian Americans, and Pacific Islanders)

**TABLE 33-2** Diagnosis of Diabetes Mellitus and Impaired Glucose Homeostasis

DIAGNOSIS	CRITERIA
Diabetes	FPG $\geq 126 \text{ mg/dl}$ ( $\geq 7.0 \text{ mmol/L}$ ) CPG $\geq 200 \text{ mg/dl}$ ( $\geq 11.1 \text{ mmol/L}$ ) plus symptoms 2hPG $\geq 200 \text{ mg/dl}$ ( $\geq 11.1 \text{ mmol/L}$ )
Impaired glucose homeostasis	
Impaired fasting glucose	FPG $\geq 110$ and $< 126 \text{ mg/dl}$ ( $\geq 6.1$ and $< 7.0 \text{ mmol/L}$ )
Impaired glucose tolerance	2hPG $\geq 140$ and $< 200 \text{ mg/dl}$ ( $\geq 7.8$ and $< 11.1 \text{ mmol/L}$ )
Normal	FPG $< 110 \text{ mg/dl}$ ( $< 6.1 \text{ mmol/L}$ ) 2hPG $< 140 \text{ mg/dl}$ ( $< 7.8 \text{ mmol/L}$ )

Modified from Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, *Diabetes Care* 20:1183, 1997.

FPG, Fasting plasma glucose (preferred testing method); CPG, casual plasma glucose; 2hPG, 2-hour plasma glucose level (measured 2 hours after an oral glucose tolerance test with administration of 75 g of glucose).

- ◆ Are women who have a history of GDM or a history of having infants weighing more than 9 lb at birth
- ◆ Are hypertensive (blood pressure  $\geq 140/90 \text{ mm Hg}$ )
- ◆ Have a high-density lipoprotein (HDL) cholesterol level  $\leq 35 \text{ mg/dl}$  or a triglyceride level  $\geq 250 \text{ mg/dl}$
- ◆ Had IGT or IFG on previous testing
- ◆ Have polycystic ovary syndrome

The incidence of type 2 diabetes in children and adolescents is increasing dramatically and is consistent with screening recommendations for adults: children and youth at increased risk for type 2 diabetes should be tested. Youth who are overweight (body mass index [BMI]  $> 85$ th percentile for age and sex) and who have two of the following risk factors should be screened: family history of type 2 diabetes, members of high-risk ethnic populations, signs of insulin resistance (such as acanthosis nigricans—gray-brown skin pigmentations). The age of initiation of screening is age 10 years or onset of puberty, and the frequency is every 2 years (ADA, 2002a).

Screening and diagnosis for GDM is discussed under Gestational Diabetes Mellitus in the Pregnancy section.

### MANAGEMENT OF DIABETES MELLITUS

Optimal control of diabetes requires the restoration of normal carbohydrate, protein, and fat metabolism. Insulin is both anticatabolic and anabolic and facilitates

cellular transport (Table 33-3). In general, the **counterregulatory (stress) hormones** (glucagon, growth hormone, cortisol, epinephrine, and norepinephrine) have the opposite effect of insulin.

Diabetes is a chronic disease that requires changes for a lifetime. The management of diabetes includes medical nutrition therapy (MNT), physical activity, blood glucose monitoring, medications, and self-management education. An important goal of treatment is to provide the patient with the necessary tools to achieve the best possible control of glycemia, lipidemia, and blood pressure to prevent, delay, or arrest the microvascular and macrovascular complications of diabetes while minimizing hypoglycemia and excess weight gain (ADA, 2002a).

Glycemic treatment goals for persons with diabetes are listed in Table 33-4. Achieving goals requires open communication and appropriate self-management education. Patients can assess day-to-day glycemic control by self-monitoring of blood glucose (SMBG) and measurement of urine and blood ketones.

Longer-term glycemic control is assessed from the results of **glycosylated hemoglobin** (simplified as A1C) tests. When hemoglobin and other proteins are exposed to glucose, the glucose becomes at-

tached to the protein in a slow, nonenzymatic, and concentration-dependent fashion. Measurements of A1C reflect a weighted average of plasma glucose concentration over the preceding weeks, thereby complementing day-to-day testing. In nondiabetic persons, A1C values are 4.0% to 6.0%; these values correspond to mean blood glucose levels of about 90 mg/dl (or about 5 mmol/L). Lipid levels and blood pressure must also be monitored (Table 33-5). Lipids should be measured annually, and blood pressure at every diabetes management visit (ADA, 2002a).

### Control and Outcomes

Evidence relating hyperglycemia and other metabolic consequences of insulin deficiency to the development of complications comes from a series of studies in Europe and North America; however, the **Diabetes Control and Complications Trial (DCCT)** demonstrated beyond a doubt the clear link between glycemic control and development of complications in persons with type 1 diabetes. The DCCT, sponsored by the National Institutes of Health, was a long-term, prospective, randomized, controlled, multicenter trial that studied approximately 1400 young adults (ages 13 to 39 years)

**TABLE 33-3** Action of Insulin on Carbohydrate, Protein, and Fat Metabolism

EFFECT	CARBOHYDRATE	PROTEIN	FAT
Anticatabolic (prevents breakdown)	Decreases breakdown and release of glucose from glycogen in the liver	Inhibits protein degradation, diminishes gluconeogenesis	Inhibits lipolysis, prevents excessive production of ketones and ketoacidosis
Anabolic (promotes storage)	Facilitates conversion of glucose to glycogen for storage in liver and muscle	Stimulates protein synthesis	Facilitates conversion of pyruvate to free fatty acids, stimulating lipogenesis
Transport	Activates the transport system of glucose into muscle and adipose cells	Lowers blood amino acids in parallel with blood glucose levels	Activates lipoprotein lipase, facilitating transport of triglycerides into adipose tissue

**TABLE 33-4** Recommendations for Glycemic Control\*

BIOCHEMICAL INDEX	NORMAL	GOAL
<b>Plasma Values</b>		
Average preprandial glucose (mg/dl)	<110	90-130
Peak postprandial average plasma glucose (mg/dl) (measured within 1-2 hr after eating)	<140	<180
A1c (%)	<6	<7

Modified from American Diabetes Association: Standards of medical care for patients with diabetes mellitus, *Diabetes Care* 26(suppl 1):S37, 2003. \*Values are for nonpregnant individuals. A1c, glycosylated hemoglobin, is referred to a nondiabetic range of 4.0%-6.0%.

**TABLE 33-5** Lipid and Blood Pressure Goals\*

LIPIDS (mg/dl)	BLOOD PRESSURE (mm Hg)
Cholesterol	Systolic <130
LDL Cholesterol	Diastolic <80
HDL Cholesterol	
Men	>45
Women	>55
Triglycerides	<150

Modified from American Diabetes Association: Standards of medical care for patients with diabetes mellitus [Position Statement], *Diabetes Care* 25(suppl 1):S33, 2002. \*Values are for nonpregnant adults. LDL, Low-density lipoprotein; HDL, high-density lipoprotein.

with type 1 diabetes who were treated with either intensive therapeutic regimens (multiple injections of insulin or use of insulin infusion pumps guided by blood glucose monitoring results) or conventional regimens (one or two insulin injections per day) (Diabetes Control and Complications Trial Research Group, 1995). Patients who achieved control similar to that of the intensively treated patients in the study could expect a 50% to 75% reduction in the risk of progression to retinopathy, nephropathy, and neuropathy after 8 to 9 years (DCCT Research Group, 1993).

Previously, small studies had demonstrated the relationship of blood glucose control to complications in type 2 diabetes (Kuusisto et al, 1994; Ohkubbo et al, 1995). However, the reports of the **United Kingdom Prospective Diabetes Study (UKPDS)** in 1998 demonstrated conclusively that elevated blood glucose levels cause long-term complications in type 2 diabetes just as in type 1 diabetes (UKPDS, 1998a). The UKPDS recruited and followed up on 5102 newly diagnosed type 2 diabetic patients for an average of 10 to 11 years. Subjects were randomized into a group treated conventionally, primarily with nutrition therapy, and had an average HbA1c of 7.9% compared with subjects randomized into an intensively treated group, initially treated with sulfonylureas, and who had an average HbA1c of 7.0%. In the intensive therapy group, the microvascular complications rate decreased significantly by 25% and the risk of macrovascular disease decreased by 16%. **Combination therapy** (combining insulin or metformin with sulfonylureas) was needed in both groups to meet glycemic goals as loss of glycemic control was noted over the 10-year trial. Aggressive treatment of even mild-to-moderate hypertension was also beneficial in both groups (UKPDS, 1998b).

Before randomization into intensive or conventional treatment, subjects received individualized intensive nutrition therapy for 3 months. During this run-in period, the mean A1C decreased by 1.9% (~9% to ~7%) and patients lost an average of 3.5 kg (8 lb). UKPDS researchers concluded that a reduction of energy intake was at least as important, if not more important, than the actual weight lost in determining the FPG (UKPDS, 1990).

This study clearly illustrates the progressive nature of type 2 diabetes. An important lesson learned from the UKPDS is that therapy needs to be intensified over time and that as the disease progresses, MNT alone is not enough to keep most patients' A1C level at 7%. Medication(s), and for many patients, eventually insulin, needs to be added to the treatment regimen. It is not the "diet" failing; it is the pancreas failing to secrete enough insulin to maintain adequate glucose control.

## Nutrition Therapy

Medical nutrition therapy is integral to total diabetes care and management. To integrate MNT ef-

fectively into the overall management of diabetes requires a coordinated team effort, including a dietitian who is knowledgeable and skilled in implementing current principles and recommendations for diabetes. MNT requires an individualized approach and effective nutrition self-management education. Monitoring glucose, A1C and lipid levels, blood pressure, weight, and quality-of-life issues is essential in evaluating the success of nutrition-related recommendations. If desired outcomes from MNT are not met, changes in overall diabetes care and management should be recommended (ADA, 2001).

The ADA's nutrition guidelines underscore the importance of individualizing nutrition care. Before 1994 nutrition recommendations attempted to define optimal percentages for macronutrient intake. Then, by determining a person's energy needs based on theoretic calorie requirements and using the ideal percentages for carbohydrate, protein, and fat, a nutrition prescription was developed—for example, 1800 calories, 225 g of carbohydrate (50%), 90 g of protein (20%), and 60 g of fat (30%). The problem with this approach is that the prescribed "diet" can not really be individualized, and it often lacks relevance to the patient's personal lifestyle, culture, or socioeconomic status. Furthermore, this approach is not supported by scientific evidence and usually does not produce successful outcomes. Beginning in 1994, the ADA recommended that an individualized nutrition prescription be based on metabolic profiles, treatment goals, and changes that the person with diabetes is willing and able to make, not on rigid, predetermined calorie levels and macronutrient percentages (Franz et al, 1994). This approach continues with the 2002 ADA nutrition principles and recommendations for persons with diabetes (ADA, 2002b; Franz, 2002).

## Goals and Outcomes of Medical Nutrition Therapy for Diabetes

The goals for MNT for diabetes emphasize the role of lifestyle in improving not only glucose control but also lipid and lipoprotein profiles and blood pressure. Improving health through food choices and physical activity is the basis of all nutrition recommendations for the treatment and prevention of diabetes (Box 33-1).

Besides being skilled and knowledgeable in regard to assessing and implementing MNT, dietitians must also be aware of expected outcomes from nutrition therapy, when to assess outcomes, and what feedback, including recommendations, should be given to referral sources. Research supports MNT as an effective therapy in reaching diabetes treatment goals. Outcomes studies demonstrate that MNT provided by a registered dietitian

## Box 33-1. Goals of Medical Nutrition Therapy for Diabetes Mellitus

### Goals of Medical Nutrition Therapy That Apply to All Persons With Diabetes

1. Attain and maintain optimal metabolic outcomes including:
  - Blood glucose levels in the normal range or as close to normal as is safely possible to prevent or reduce risk or complications of diabetes.
  - A lipid and lipoprotein profile that reduces the risk for cardiovascular disease.
  - Blood pressure levels that reduce the risk for vascular disease.
2. Prevent and treat the chronic complications: Modify nutrient intake as appropriate for the prevention and treatment of obesity, cardiovascular disease, hypertension, and nephropathy.
3. Improve health through healthy food choices and physical activity.
4. Address individual nutritional needs, taking into consideration personal and cultural preferences and lifestyle while respecting the individual's needs and willingness to change.

### Goals of Nutrition Therapy That Apply to Specific Situations

1. For youth with type 1 diabetes, provide adequate energy to ensure normal growth and development; integrate insulin regimen into usual eating and exercise habits.
2. For youth with type 2 diabetes, facilitate changes in eating and exercise habits that reduce insulin resistance and improve metabolic status.
3. For pregnant and lactating women, provide adequate energy and nutrients needed for successful outcomes.
4. For older adults, provide for the nutritional needs of an aging individual.
5. For individuals treated with insulin or insulin secretagogues, provide information on prevention and treatment of hypoglycemia and exercise-related blood glucose problems and how to manage acute illness.
6. For individuals at risk for diabetes, decrease risk by increasing physical activity and promoting food choices that facilitate moderate weight loss or at least prevent weight gain.

From American Diabetes Association: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications [Position Statement], *Diabetes Care* 25:202, 2002.

(RD) is associated with a decrease of about 1.0% of A1C in patients with newly diagnosed type 1 diabetes (Kulkarni et al, 1998), a decrease of about 2.0% of A1C in patients with newly diagnosed type 2 diabetes (Franz et al, 1995; UKPDS Group, 1990), and a decrease of about 1.0% of A1C in patients with an average 4-year duration of type 2 diabetes (Franz et al, 1995). These outcomes are similar to those from oral glucose-lowering medications. Furthermore, the effect of MNT on A1C will be known by 6 weeks to 3 months, at which time the RD must assess whether the goals of therapy have been met by changes in lifestyle and whether changes or additions of medications are needed (ADA, 2001).

### Prioritizing Nutrition Therapy for Type 1 Diabetes

The priority for anyone who requires insulin therapy is first to determine a food and meal plan and then to integrate an insulin regimen into his or her usual eating habits and physical activity schedule. With the many insulin options now available (new rapid-acting and long-acting insulins), an insulin regimen usually can be developed that will conform to an individual's preferred meal routines and food choices

(ADA, 2002b; Franz et al, 2002). It is no longer necessary to create unnatural or artificial divisions of meals and snacks.

Flexible insulin regimens involve multiple injections (three or more insulin injections per day) or use of an insulin infusion pump. Half of the required insulin dose is given as a basal or background insulin, and the other half is divided and given before meals (bolus or premeal insulin). These types of insulin regimens allow increased flexibility in choosing when and what to eat. The total carbohydrate content of meals is the major determinant of the mealtime rapid-acting insulin dose and postprandial glucose response (Rabasa-Lhoret et al, 1999). Thus, individuals can be taught how to adjust mealtime insulin doses based on the carbohydrate content of the meal and how to delay mealtime insulin for late meals. Even with flexible insulin regimens, however, consistency in food intake facilitates improved glycemic control (Delahanty and Halford, 1993). For persons who receive fixed insulin regimens, such as with the use of premixed insulins, or those who do not adjust their mealtime insulin doses, day-to-day consistency in the timing and amount of carbohydrate eaten is recommended (Wolever et al, 1999).

### Prioritizing Nutrition Therapy for Type 2 Diabetes

The priority for individuals with type 2 diabetes is to adopt lifestyle strategies that improve the associated metabolic abnormalities of glycemia, dyslipidemia, and hypertension (ADA, 2002b; Franz et al, 2002). Lifestyle strategies independent of weight loss that can improve glycemia include reducing energy intake, monitoring carbohydrate servings, limiting consumption of saturated fats, and increasing physical activity. These strategies should be implemented as soon as the diagnosis of diabetes (or prediabetes) is made.

In the short-term, small amounts of weight loss may improve insulin resistance and glycemia, but, because of the difficulty in maintaining weight loss long term, it is unknown whether this benefit continues. Short-term studies lasting 6 months or less demonstrate that modest amounts of weight loss improve metabolic abnormalities in many persons with type 2 diabetes (Markovic et al, 1998a; Wing et al, 1987) but not in all (Watts et al, 1990). Weight loss, especially of intraabdominal fat, reduces insulin resistance and helps to correct dyslipidemia (Markovic et al, 1998b); however, long-term data assessing the extent to which these improvements can be maintained in persons with diabetes are not available, probably because long-term weight loss is difficult to achieve. Long-term weight loss of 5% to 7% from baseline weight requires frequent, regular, and long-term follow-up of patients (Diabetes Prevention Program Research Group, 2002; Tuomilehto et al, 2001).

An energy-restricted diet, however, can have an important regulatory effect on glucose control in persons with type 2 diabetes, independent of any effects from weight loss (Kelley et al, 1993; Wing et al, 1994). When energy intake is restricted, hyperglycemia improves more rapidly than with weight loss. Furthermore, when calories are increased after weight reduction, glucose levels increase despite no regain of weight. This suggests that energy intake is more important than weight loss.

Physical activity improves insulin sensitivity, can acutely lower blood glucose in diabetic persons, and may also improve cardiovascular status; but by itself it has only a modest effect on weight. Physical activity is useful as an adjunct to other weight loss strategies and is essential for long-term maintenance of weight loss (Albright et al, 2000). It should be noted, however, that cardiorespiratory fitness appears to be more important than thinness in relation to all-cause and cardiovascular mortality (Lee et al, 1999). During an 8-year study of about 25,000 men, fit men had greater longevity than unfit men regardless of their body composition or risk factor status. No elevated mortality risk was observed in obese men if they were physically fit, and obese fit men had a lower risk of all-cause and cardiovascular mortality than lean unfit men.

Teaching which foods are carbohydrates (fruits, grains, starchy vegetables, milk, sweets), average portion sizes, how many servings to select at meals (and snacks, if desired), and how to limit fat and especially saturated fat intake; encouraging physical activity; and using blood glucose monitoring to adjust food and eating patterns and medications are important components of successful MNT for type 2 diabetes (Rickheim et al, 2002). Frequent follow-up with a dietitian as outlined in nutrition practice guidelines for type 2 diabetes can provide the problem-solving techniques, encouragement, and support that lifestyle changes require (Monk et al, 1995).

### Carbohydrate

*Sugars, starch, and fiber* are the preferred terms for carbohydrates (Report of a Joint FAO/WHO Expert Consultation, 1998). Foods that contain carbohydrate from whole grains, fruits, vegetables, and low-fat milk are important components of a healthy diet for all Americans, including those with diabetes. They are excellent sources of vitamins, minerals, dietary fiber, and energy. Historically it was a long-held belief that sucrose must be restricted based on the assumption that sugars, such as sucrose, are more rapidly digested and absorbed than starches and thus aggravate hyperglycemia; however, scientific evidence does not justify restricting sugars or sucrose based on this belief. In approximately 20 studies in which sucrose was substituted for other carbohydrates, sucrose did not increase glycemia to a greater extent than isocaloric amounts of starch (Bantle et al, 1993; Peterson et al, 1986; Rickard et al, 1998). The glycemic effect of carbohydrate foods cannot be predicted based on their structure (i.e., starch versus sugar) owing to the efficiency of the human digestive tract in reducing starch polymers to glucose. Starches are rapidly metabolized into 100% glucose during digestion, in contrast to sucrose, which is metabolized into glucose and fructose. Fructose has a lower glycemic index, which has been attributed to its slow rate of absorption and its storage in the liver as glycogen (Nuttall et al, 1992) (see Chapters 3, 12, and 26).

Numerous factors influence glycemic responses of foods, including the amount of carbohydrate, type of sugar (glucose, fructose, sucrose, lactose), nature of the starch (amylose, amylopectin, resistant starch), cooking and food processing, particle size, and food form as well as the fasting and preprandial glucose concentrations, severity of the glucose intolerance, and the second meal or lente effect of carbohydrates. There is, however, strong evidence to state that the total amount of carbohydrate is more important than the source (sugar or starch) or the type (glycemic index) of carbohydrate. Numerous studies have reported that when subjects are allowed to choose from a variety of starches and sugars, the glycemic re-

sponse is identical if the total amount of carbohydrate is similar (ADA, 2002b). Therefore, the first priority for food and meal planning is the total amount of carbohydrate that the person with diabetes chooses to have for meals or snacks. This is the basis of carbohydrate counting, whereby food portions contributing 15 g of carbohydrate (regardless of the source) are considered to be one carbohydrate serving.

### Glycemic Index and Glycemic Load

Although different carbohydrates do have different glycemic responses (*glycemic index*), there is limited evidence to show long-term benefit when low glycemic index diets are compared with high glycemic index diets in studies lasting 2 weeks or longer. In subjects with type 1 diabetes (five studies in total,  $n = 48$ ), no studies in which low versus high glycemic index diets are compared show a beneficial effect of the low glycemic index diet on A1c; three studies report the low glycemic index diet improved fructosamine (a short-term measure of overall control), whereas one study reported no improvement in fructosamine. In subjects with type 2 diabetes (nine studies in total,  $n = 129$ ), one study reported beneficial effects of the low glycemic index diet on A1c, whereas four studies reported no beneficial effects on A1c. Three studies reported improvement in fructosamine from the low glycemic index diet, whereas three studies reported no improvement. FPG is reported in all studies; however, no studies in persons with type 1 or type 2 diabetes report improvements in FPG from the low glycemic index diets (Franz, 2001). Therefore, there is insufficient evidence to recommend low glycemic index diets as the primary strategy in food and meal planning for individuals with diabetes (ADA, 2002b). The concept of the glycemic index is perhaps best used for fine-tuning postprandial responses after focusing on total carbohydrate.

The glycemic load is a newer concept and incorporates both the number of grams of carbohydrate in a usual food serving or meal and the glycemic index (see Appendix 54). At this time, however, no intervention studies have been done that show benefit from using this technique in persons with diabetes.

### Fiber

Early short-term studies using large amounts of fiber (>30 g daily) in small numbers of subjects suggested a positive effect on glycemia; however, results from later studies have shown mixed effects. In subjects with type 1 diabetes, a high-fiber diet (56 g daily) had no beneficial effects on glycemic control (Lafrance et al, 1998). Another study of subjects with type 1 diabetes showed positive effects from 50 g of fiber on glucose concentrations but no beneficial effects on lipids (Giacco et al, 2000). In persons with type 2 dia-

betes, increasing fiber from 11 to 27 g/1000 kcal did not improve glycemia, insulinemia, or lipemia (Hollenbeck et al, 1986), whereas another study comparing 24 g of fiber per day with 50 g of fiber reported improved glycemic control, reduced hyperinsulinemia, and decreased plasma lipids (Chandalia et al, 2000). Therefore, it appears that ingestion of large amounts of fiber (~50 g/day) is necessary to have beneficial effects on glycemia, insulinemia, and lipemia. It is unknown whether free-living individuals can maintain such high levels of fiber and whether this amount would be acceptable to most people (ADA, 2002b). Although the consumption of fiber is to be encouraged, just as it is for the general public, there is no reason to recommend that persons with diabetes eat a greater amount of fiber than other Americans.

### Sweeteners

Even though sucrose restriction cannot be justified on the basis of its glycemic effect, it is still good advice to suggest that persons with diabetes be careful in their consumption of foods containing large amounts of sucrose. Besides often being high in total carbohydrate content, these foods may also contain significant amounts of fat. If sucrose is included in the food and meal plan, it should be substituted for other carbohydrate sources or, if added, be adequately covered with insulin or other glucose-lowering medications. Sucrose and sucrose-containing foods also should be eaten in the context of a healthy diet (ADA, 2002b).

There appears to be no significant advantage of alternative nutritive sweeteners over sucrose. Fructose provides 4 kcal/g, as do other carbohydrates, and even though it does have a lower glycemic response than sucrose and other starches, large amounts (15%-20% of daily energy intake) of fructose have an adverse effect on plasma lipids (Bantle et al, 1992, 2000). There is no reason, however, to recommend that persons with diabetes avoid fructose, which occurs naturally in fruits and vegetables as well as in foods sweetened with fructose (ADA, 2002b).

Sorbitol, mannitol, xylitol, isomalt, lactitol, and hydrogenated starch hydrolysates are common sugar alcohols that also have a lower glycemic response and lower caloric content than sucrose and other carbohydrates. Because they are not soluble in water, they are often combined with fat; therefore, foods sweetened with sugar alcohols may have a caloric content that is similar to that of the foods they are replacing. It is unlikely, however, that sugar alcohols in the amounts likely to be ingested in individual food servings or meals will contribute to significant reduction in total energy or carbohydrate intake (ADA, 2002b). Some patients report gastric discomfort after eating foods sweetened with these products, and consuming large quantities may cause diarrhea.

Saccharin (Sweet'N Low), aspartame (Equal and NutraSweet), acesulfame K, and sucralose are noncaloric sweeteners currently approved for use in the United States. Approval of the U.S. Food and Drug Administration (FDA) is being sought for alitame and cyclamates. All such products must undergo rigorous testing by the manufacturer and scrutiny from the FDA before they are approved and marketed to the public. For all food additives, including nonnutritive sweeteners, the FDA determines an acceptable daily intake (ADI), defined as the amount of a food additive that can be safely consumed on a daily basis over a person's lifetime without risk (see Chapter 14). The ADI includes a 100-fold safety factor and greatly exceeds average consumption levels. For example, aspartame actual daily intake in persons with diabetes is 2 to 4 mg per kilogram of body weight daily, well below the ADI of 50 mg/kg daily (Butchko and Stargel, 2001). All FDA-approved nonnutritive sweeteners can be used by persons with diabetes, including pregnant women (ADA, 2002b).

### Protein

The rate of protein degradation and conversion of protein to glucose in type 1 diabetes depends on the state of insulinization and the degree of glycemic control. With less than optimal insulinization, conversion of protein to glucose can occur rapidly, adversely influencing glycemic control. In poorly controlled type 2 diabetes, gluconeogenesis is also accelerated and may account for most of the increased glucose production in the postabsorptive state (Henry, 1994). In those with controlled type 2 diabetes Gannon et al, 2001a; Nuttall et al, 1984) and well-controlled type 1 diabetes (Peters and Davidson, 1993), ingested protein did not increase plasma glucose concentrations. Although nonessential amino acids undergo gluconeogenesis, it is unclear why the glucose produced does not appear in the general circulation after ingestion of protein (Franz, 2000). Furthermore, protein does not slow the absorption of carbohydrate (Nordt et al, 1991; Nuttall et al, 1984), and adding protein to the treatment of hypoglycemia does not prevent subsequent hypoglycemia (Gray et al, 1996). In type 2 diabetic patients who are still able to produce insulin, ingested protein is just as potent a stimulant of insulin secretion as carbohydrate.

There is evidence that moderate hyperglycemia in persons with type 2 diabetes (Gougeon et al, 1994) and uncontrolled diabetes in persons with type 1 diabetes (Lariviere et al, 1994) cause increased protein catabolism. Protection against increased protein catabolism requires near-normal glycemia and an adequate protein intake (Brodsky and Devlin, 1996; Gougeon et al, 2000). Therefore, for persons with diabetes, the protein requirement may be greater than the recommended dietary allowance (RDA) but not

greater than typical intake in the United States. No evidence has been found to suggest that typical protein intake (15%-20% of total daily energy) must be modified if renal function is normal (ADA, 2002b). In studies in which protein intake was in the range of usual intake and rarely exceeded 20% of energy intake, dietary protein intake was not associated with the development of diabetic nephropathy. In a cross-sectional study (Toeller et al, 1997), patients in whom protein intakes were 20% or greater of daily energy had a higher incidence of albuminuria. This finding suggests that it may be prudent to avoid protein intake that is more than 20% of total daily energy.

The long-term effects of weight-loss diets high in protein and low in carbohydrate are unknown. Although initially blood glucose levels may improve and weight may be lost, it is unknown whether weight loss is maintained better with these diets than with other low-calorie diets. Furthermore, protein is just as potent a stimulant of insulin as is carbohydrate. Because these diets are usually high in saturated fat, the long-term effect on LDL cholesterol is also a concern (ADA, 2002b) (see Chapters 24 and 35).

### Dietary Fat

In all persons with diabetes, less than 10% of energy intake should be derived from saturated fats, and dietary cholesterol intake should be less than 300 mg daily. Some persons (i.e., those with LDL cholesterol  $\geq 100$  mg/dl) may benefit from lowering saturated fat intake to less than 7% of energy intake and dietary cholesterol to less than 200 mg daily. To lower plasma LDL cholesterol, saturated fat can be reduced if concurrent weight loss is desirable or replaced with carbohydrate or monounsaturated fat if weight loss is not a goal. Intake of *trans*-fatty acids should also be minimized (see Chapter 35).

If saturated fat contributes less than 10% of total daily energy, if about 10% of energy is from polyunsaturated fat, and if protein contributes 15% to 20% of energy, then 60% to 70% of total energy intake remains to be distributed between carbohydrate and monounsaturated fat. Diets high in monounsaturated fat or low in fat and high in carbohydrate result in improvement in glucose tolerance and lipids compared with diets high in saturated fat. Diets enriched with monounsaturated fats may also reduce insulin resistance (Parillo et al, 1992); however, other studies have reported high total dietary fat (regardless of the type of fat) to be associated with insulin resistance (Lovejoy and DiGirolamo, 1992). In metabolic studies in which energy intake is maintained so that subjects do not lose weight, diets high in either carbohydrate or monounsaturated fat lower LDL cholesterol equivalently, but the concern has been the potential of a high-carbohydrate diet (greater than 55% of energy intake) to increase triglycerides and postprandial

glucose compared with a high-monounsaturated fat diet (Garg et al, 1994). If energy intake is reduced and a low-fat, high-carbohydrate diet is compared with a high-monounsaturated fat diet, no detrimental effects on triglycerides result from the high-carbohydrate diet (Heilbronn et al, 1999). Energy intake, therefore, appears to be a factor in determining the effects of a high-carbohydrate versus high-monounsaturated fat diet.

Low-fat, high-carbohydrate diets over long periods have not been shown to increase triglycerides and have been shown to lead to modest weight loss (Kendall et al, 1991) and weight-loss maintenance (Carmichael et al, 1998). Thus, a person's metabolic profile and need to lose weight will determine nutrition recommendations. For persons who need to lose weight, a lower energy intake and a low-fat, moderate-carbohydrate approach can be used. For persons who do not need to lose weight, a high-monounsaturated fat approach may be recommended to improve triglycerides or postprandial glycemia (ADA, 2002b).

There is evidence from the general population that foods containing omega-3 fatty acids are beneficial, and two to three servings of fish per week are recommended. Although most studies in persons with diabetes have used omega-3 supplements and show beneficial lowering of triglycerides, an accompanying rise in LDL cholesterol also has been noted (Montori et al, 2000). If supplements are used, the effects on LDL cholesterol should be monitored. The omega-3 supplements may be most beneficial in the treatment of severe hypertriglyceridemia (Patti et al, 1999).

### Fiber and Phytosterols

Evidence for the effects of fiber on lipids is provided by a metaanalysis of 67 controlled trials (Brown et al, 1999). Within the practical range of intake, the authors concluded that the effect of soluble fiber on total and LDL cholesterol is small. For example, daily intake of 3 g of soluble fiber from oats (three servings of oatmeal, 28 g each) or three apples can decrease total cholesterol by about 5 mg/dl, an approximate 2% reduction.

Intake of 2 to 3 g of plant stanols or sterols per day are reported to decrease total and LDL cholesterol levels by 9% to 20% (Hallikainen et al, 1999). Use of low-fat food and fat replacers or substitutes approved by the FDA are safe for use and may reduce total fat and energy intake.

### Energy Balance and Obesity

Improved glycemic control with intensive insulin therapy is often associated with increases in body weight. Because of the potential for weight gain to affect lipids and blood pressure adversely, prevention of weight gain is desirable; however, the benefits of improved blood glucose control outweigh concerns about weight gain, at least initially (Chaturvedi et al,

1995). To prevent weight gain, insulin therapy should be integrated into usual eating and exercise habits and insulin doses adjusted accordingly. Overtreatment of hypoglycemia should be avoided; total protein, fat, and calories ingested must be accounted for; and adjustments in insulin should be made for exercise.

Many individuals with type 2 diabetes are overweight, with about 36% having a BMI of 30 kg/m<sup>2</sup> or greater (Cowie and Harris, 1995). The risk of obesity and excess mortality is controversial. Obesity in persons with type 2 diabetes was not related to mortality (Chaturvedi and Fuller, 1995) or to the long-term incidence of microvascular and macrovascular complications (Klein et al, 1997). Short-term studies that lasted 6 months or less, however, demonstrated that weight loss in subjects with type 2 diabetes is associated with improvement in insulin resistance, glycemia, serum lipids, and blood pressure. Long-term data assessing the extent to which these improvements can be maintained in people with type 2 diabetes are scarce, as already mentioned.

A genetic predisposition to obesity and possible impaired metabolic and appetite regulation as well as environmental factors make it difficult to lose and, more important, to maintain weight loss. Because of the psychological and physiologic impact of dieting, encouragement to attain and maintain a reasonable body weight is crucial. Emphasis should be on blood glucose control, improved food choices, increased physical activity, and moderate energy restriction rather than weight loss alone.

Standard weight-reduction diets, when used alone, are unlikely to produce long-term weight loss. Structured, intensive lifestyle programs are necessary to produce long-term weight loss of 5% to 7% of starting weight (Diabetes Prevention Program Research Group, 2002; Tuomilehto et al, 2001). Currently available weight-loss drugs have a modest beneficial effect in persons with diabetes and should be used only in people with a BMI greater than 27. Gastric reduction surgery can be an effective weight-loss treatment for severely obese patients with type 2 diabetes; however, it should be considered only in patients with a BMI greater than 35 because long-term data comparing the benefits and risks of gastric reduction surgery with medical therapy are not available (ADA, 2002b) (see Chapter 24).

### Alcohol

The same precautions that apply to alcohol consumption for the general population apply to persons with diabetes. The effect of alcohol on blood glucose levels depends not only on the amount of alcohol ingested but also on its relationship to food intake. In the fasting state, alcohol may cause hypoglycemia in persons using exogenous insulin or insulin secretagogues. Alcohol is used as a source of energy, but it is not converted to glucose. It is metabolized in a manner similar to fat. It also blocks gluconeogenesis and aug-

ments or increases the effects of insulin by interfering with the counterregulation response to insulin-induced hypoglycemia. All these factors contribute to the development of hypoglycemia when alcohol is consumed without food (Franz, 1999).

If individuals choose to drink alcohol, daily intake should be limited to one drink for adult women and two drinks for adult men (1 drink = 12 oz beer, 5 oz of wine, or 1½ oz of distilled spirits [15 g alcohol]). For most persons, blood glucose levels are not affected by moderate use of alcohol when diabetes is well controlled (Koivisto et al, 1993). Alcoholic beverages should be considered an addition to the regular food and meal plan for all persons with diabetes. No food should be omitted given the possibility of alcohol-induced hypoglycemia and the fact that alcohol does not require insulin to be metabolized. Pregnant women and patients with medical problems such as pancreatitis, advanced neuropathy, severe hypertriglyceridemia, or alcohol abuse should avoid alcohol (ADA, 2002b).

Epidemiologic evidence in nondiabetic individuals suggests that light to moderate alcohol ingestion in adults is associated with decreased risk of type 2 diabetes and stroke and improved insulin resistance. In adults with type 2 diabetes, light to moderate alcohol ingestion is associated with decreased risk of coronary heart disease, perhaps because of the concomitant increase in HDL cholesterol. Long-term, prospective studies are needed to confirm these observations (ADA, 2002b) (see Chapter 35). Ingestion of light to moderate amounts of alcohol does not raise blood pressure, whereas excessive, chronic ingestions of alcohol does raise blood pressure and may be a risk factor for stroke (Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, 1997).

### Micronutrients

No clear evidence has been established of benefits from routine vitamin or mineral supplements in persons with diabetes who do not have underlying deficiencies. Exceptions include folate for the prevention of birth defects and calcium for prevention of bone disease. Routine supplementation of the diet with antioxidants is not advised because of uncertainties related to long-term efficacy and safety (ADA, 2002b). Observational studies and several placebo-controlled clinical trials with small subject numbers have found beneficial effects of antioxidants, especially vitamin E, on physiologic and biochemical end points. Large placebo-controlled clinical trials have failed to show benefit from antioxidants and, in some instances, have suggested adverse effects (Omenn et al, 1996). Of interest is the Heart Outcomes Prevention Evaluation Trial, which included 9541 subjects, 38% of whom had diabetes (Yusuf et al, 2000). Supplementation with 400 IU daily of vitamin E for 4.5 years did not result in any significant benefit on cardiovascular outcomes.

Because the response to supplements is determined largely by a person's nutritional status, persons with micronutrient deficiencies are most likely to respond favorably. Although difficult to ascertain, if deficiencies of vitamins or minerals are identified, supplementation can be beneficial. Those at greatest risk of deficiency who may benefit from prescription of vitamin and mineral supplements include patients who consume extreme calorie-restricted diets, strict vegetarians, older adults, pregnant or lactating women, those taking medication known to alter micronutrient metabolism (see Chapter 19), patients in poor metabolic control (glycosuria), and patients in critical care environments.

Chromium deficiency in animal models is associated with elevated blood glucose, cholesterol, and triglyceride levels. It is unlikely, however, that most persons with diabetes are chromium deficient. In three double-blind crossover studies of chromium supplementation in individuals with diabetes, no improvement in blood glucose control was noted (Mooradian et al, 1994). In a randomized, placebo-controlled study in Chinese subjects with diabetes, chromium supplementation did have beneficial effects on glycemia (Anderson et al, 1997; Cheng et al, 1999); however, the study population may have had marginal baseline chromium status because the chromium status was not evaluated either at baseline or after supplementation. Therefore, before chromium supplementation can be recommended, placebo-controlled clinical trials need to be undertaken in which people with diabetes with known dietary intakes of chromium use chromium supplements that may be better absorbed than older supplements.

### Exercise

Exercise should be an integral part of the treatment plan for persons with diabetes. Exercise helps all persons with diabetes improve insulin sensitivity, reduce cardiovascular risk factors, control weight, and bring about a healthier mental outlook. Given appropriate guidelines, people with diabetes can exercise safely. The exercise plan will vary depending on interest, age, general health, and level of physical fitness.

Despite the increase in glucose uptake by muscles during exercise, glucose levels change little in individuals without diabetes. Muscular work causes insulin levels to decline while counterregulatory hormones (primarily glucagon) rise. In this way, increased glucose utilization by the exercising muscle is matched precisely with increased glucose production by the liver. This balance between insulin and counterregulatory hormones is the major determinant of hepatic glucose production, underscoring the need for insulin adjustments in addition to adequate carbohydrate intake during exercise for people with diabetes.

In persons with type 1 diabetes, the glycemic response to exercise varies depending on overall diabetes control, plasma glucose, and insulin levels at the start of exercise; timing, intensity and duration of the exercise; previous food intake; and previous conditioning. An important variable is the level of plasma insulin during and after exercise. Hypoglycemia can occur because of insulin-enhanced muscle glucose uptake by the exercising muscle. In contrast, insulin deficiency in a poorly controlled (underinsulinized) exerciser results in increases in glucose concentrations and free fatty acids release continues with minimal uptake. This can result in large increases in plasma glucose and ketone levels (Wasserman and Zinman, 1994).

In persons with type 2 diabetes, blood glucose control can improve with exercise, largely because of decreased insulin resistance and increased insulin sensitivity, which results in increased peripheral use of glucose not only during but also after the activity. This exercise-induced enhanced insulin sensitivity occurs without changes in body weight. Exercise also decreases the effects of counterregulatory hormones; this, in turn, reduces the hepatic glucose output, contributing to improved glucose control. Exercise regimens at an intensity of 50% to 80%  $\text{VO}_{2\text{max}}$  three to four times a week for 30 to 60 minutes a session can result in a 10% to 20% baseline improvement in A1c and are most beneficial in persons with mild type 2 diabetes and in those who are likely to be the most insulin resistant. Regular exercise also has consistently been shown to be effective in reducing triglyceride levels in persons with type 2 diabetes; however, the effect of exercise on HDL cholesterol levels is unclear. Reductions in blood pressure and improvements in impaired fibrinolysis have also been noted (ADA, 2002c).

### Potential Problems With Exercise

Hypoglycemia is a potential problem associated with exercise in persons taking insulin or insulin secretagogues. Hypoglycemia can occur during, immediately after, or many hours after exercise. Hypoglycemia has been reported to be more common after exercise, especially after exercise of long duration, after strenuous activity or play, or after sporadic exercise, than during exercise (MacDonald et al, 1987). This is because of increased insulin sensitivity after exercise and the need to replete liver and muscle glycogen, which can take up to 24 to 30 hours (see Chapter 26). Hypoglycemia can also occur during or immediately after exercise. Blood glucose levels before exercise reflect only the value at that time, and it is unknown if this is a stable blood glucose level or a blood glucose level that is dropping. If blood glucose levels are dropping before exercise, adding exercise can contribute to hypoglycemia during exercise. Furthermore, hypoglycemia on the day before exercise is reported to increase the risk of hypoglycemia on the day of exercise as well (Davis et al, 2000).

Hyperglycemia can also result from exercise. When a person exercises at what for him or her is a high

level of exercise intensity, there is a greater than normal increase in counterregulatory hormones. As a result, hepatic glucose release exceeds the rise in glucose utilization. The elevated glucose levels may also extend into the postexercise state (Mitchell et al, 1988; Purdon et al, 1993). Although not as likely, hyperglycemia and worsening ketosis can also result from insulin deficiency if exercise is done when fasting blood glucose levels are higher than 250 to 300 mg/dl. With elevated fasting blood glucose and ketones, exercise should be postponed until control improves (ADA, 2002b). The latter cause of hyperglycemia is not as likely to occur as the first.

### Exercise Guidelines

The variability of glucose responses to exercise contributes to the difficulty in giving precise nutrition (and insulin) guidelines. Frequent blood glucose monitoring before, during, and after exercise helps individuals identify their response to physical activities. To meet their individual needs, patients must modify general guidelines to ingest carbohydrate after (or before) and to reduce insulin doses before (or after) exercise.

### Carbohydrate for Insulin Users

During moderate-intensity exercise, glucose uptake is increased by 8 to 13 g per hour, and this is the basis for the recommendation to add 15 g carbohydrate for every 30 to 60 minutes of activity (depending on the intensity) over and above normal routines. Moderate exercise for less than 30 minutes rarely requires any additional carbohydrate or insulin adjustment; however, a small snack may be needed if the blood glucose level is less than 100 mg/dl (Franz, 2002).

In all persons, blood glucose levels decline gradually during exercise, and ingesting a carbohydrate feeding during prolonged exercise can improve performance by maintaining the availability and oxidation of blood glucose. For the exerciser with diabetes whose blood glucose levels may drop sooner and lower than the exerciser without diabetes, ingesting carbohydrate after 40 to 60 minutes of exercise is important and may also assist in preventing hypoglycemia. Drinks containing 6% or less of carbohydrate empty from the stomach as quickly as water and have the advantage of providing both needed fluids and carbohydrate (see Chapter 26). Consuming carbohydrate immediately after exercise optimizes repletion of muscle and liver glycogen stores. For the exerciser with diabetes, this takes on added importance because of increased risk for late-onset hypoglycemia (Franz, 2002).

### Insulin Guidelines

It is often necessary to adjust the insulin dosage to prevent hypoglycemia. This occurs most often with moderate to strenuous activity lasting more than 45 to 60 minutes. For most persons, a modest decrease

(of about 1 to 2 U) in the rapid- or short-acting insulin during the period of exercise is a good starting point. For prolonged vigorous exercise, a larger decrease in the total daily insulin dosage may be necessary. After exercise, insulin may also need to be decreased. In addition to these acute reductions in insulin dosages, individuals who participate in a regular, long-term fitness program often find their usual total dosage of insulin decreasing by as much as 15% to 20% (Waserman and Zinman, 1994).

Insulin doses should be reduced in anticipation of exercise after a meal, depending on the duration and intensity of the exercise. In persons with type 1 diabetes, Rabasa-Lhoret and colleagues validated that exercise at 25%  $VO_{2max}$  for 60 minutes required a 50% reduction in mealtime rapid-acting insulin, and exercise at 50%  $VO_{2max}$  for 30 and 60 minutes required a 50% and 75% reduction in mealtime rapid-acting insulin, respectively. Such reductions in mealtime rapid-acting insulin for postprandial exercise resulted in a 75% decrease in exercise-induced hypoglycemia (Rabasa Lhoret et al, 2001).

### Precautions for Persons With Type 2 Diabetes

Persons with type 2 diabetes may have a lower  $VO_{2max}$  and therefore need a more gradual training program. Rest periods may be needed; this does not impair the training effect from physical activity. Autonomic neuropathy or medications, such as for blood pressure, may not allow for increased heart rate, and individuals must learn to use perceived exertion as a means of determining exercise intensity. Blood pressure may also increase more in persons with diabetes than in those who do not have diabetes, and exercise should not be undertaken if systolic blood pressure is greater than 180 to 200 mm Hg.

### Exercise Prescription

The type of exercise one chooses to perform should be tailored to his or her physical capacity and interests. A complete exercise program includes warm-up and cool-down periods. This not only prepares muscles for an aerobic workout, but it also improves range of motion. Cardiovascular conditioning is also helpful. Most people can at least undertake a walking program safely. Those with type 2 diabetes should strive to achieve a minimum cumulative total of 1000 kcal per week from physical activities, which equates to walking about 10 miles per week; 1 mile = ~100 kcal expenditure (Albright et al, 2000). Ideally, the aerobic portion of an exercise session should last a minimum of 20 minutes, with a goal of 30 to 40 minutes; however, even three sessions of 10 minutes of activity during the day can improve physical fitness (Pate et al, 1995). Muscle-strengthening exercises, such as lifting light weights, are also an important component of an exercise session. Because muscles dispose of glucose, this type of exercise can also improve glucose control.

## Medications

### Oral Glucose-Lowering Medications

The use of the newer oral glucose-lowering medications, alone or in combination, provides numerous options for achieving euglycemia in persons with type 2 diabetes. Some persons with hyperglycemia that is not adequately controlled by MNT alone can be treated with MNT, and oral medications—frequently combination therapy using two, and occasionally even three, oral medications may be needed. If glycemic control cannot be attained with MNT and oral medications, insulin, either alone or in combination with oral medications, is required. The transition to insulin often begins with an intermediate or long-acting insulin given at bedtime to control fasting glucose levels and oral medications given in the morning are to control daytime glucose levels. Eventually, however, many patients with type 2 diabetes will require two or more insulin injections daily to achieve control. If large doses of insulin are required, oral medications, such as insulin sensitizers, are often combined with the insulin regimen.

Currently, four classes of oral medications exist: (1) insulin secretagogues, which include the sulfonylureas (first and second generation) and the meglitinides (repaglinide and nateglinide); (2) biguanides (metformin); (3) thiazolidinediones (TZD; e.g., pioglitazone, rosiglitazone); and (4)  $\alpha$ -glucosidase inhibitors (acarbose, miglitol). Each class has a different mechanism of action—in the pancreas, insulin secretion is stimulated; at the cellular level (muscle and adipose tissue), insulin resistance is decreased and glucose uptake enhanced; in the liver, hepatic glucose output is decreased, especially overnight, improving fasting glucose levels; or in the intestine, glucose absorption is slowed, improving postprandial glucose concentrations (Table 33-6). Because of the different sites of action, the medications can be used alone or in combination.

**Insulin secretagogues** (*sulfonylureas* and *meglitinides*) promote insulin secretion by the  $\beta$ -cells of the pancreas. First- and second-generation sulfonylurea drugs differ from one another in their potency, pharmacokinetics, and metabolism. Disadvantages of their use include weight gain and the potential to cause hypoglycemia. The meglitinides differ from the sulfonylureas in that they have short metabolic half-lives, which result in brief episodic stimulation of insulin secretion. As a result, a frequent dosing schedule is required with meals, postprandial glucose excursions are less, and because less insulin is secreted several hours after a meal, there is a decreased risk of hypoglycemia between meals and overnight. Nateglinide only works in the presence of glucose and is a somewhat less potent secretagogue (Inzucchi, 2002).

Insulin sensitizers enhance insulin action and include biguanides (metformin) and TZD. Both classes require the presence of insulin, exogenous or endogenous, to be effective. Metformin (Glucophage) sup-

**TABLE 33-6** Oral Glucose-Lowering Medications for Type 2 Diabetes

CLASS AND GENERIC NAMES	RECOMMENDED DOSE	PRINCIPAL ACTION	MEAN DECREASE IN A1c
<b>Sulfonylureas (Second Generation)</b>		Stimulate insulin secretion from the $\beta$ -cells	1%-2%
Glipizide (Glucotrol)	2.5-20 mg single or divided dose; single dose for XL		
Glipizide (Glucotrol XL)			
Glyburide (Glynase Prestabs)	12 mg once daily		
Glimepiride (Amaryl)	4 mg once daily		
<b>Meglitinides</b>		Stimulate insulin secretion from $\beta$ -cells	1%-2%
Repaglinide (Prandin)	0.4-4.0 mg before meals		
Nateglinide (Starlix)	120 mg before meals		
<b>Biguanides</b>		Decrease hepatic glucose production	1.5%-2%
Metformin (Glucophage)	500-850 mg tid or 1000 mg bid		
Metformin Extended Release (Glucophage XR)	500-2000 mg once daily		
Metformin Glyburide (Glucovance) [1.25/250 mg]	2.5/500 mg to 5.0/500 mg once daily	Also increases insulin secretion	
Metformin/glipizide (Metaglip) [2.5 to 5.0/250 to 500 mg]	2.5/250 mg to 5.0/500 mg	Also increases insulin secretion	$\approx$ 2%
Metformin/rosiglitazone (Avandamet) [1 to 4/500 mg]	2.5/250 mg to 2.5/500 mg	Improves insulin sensitivity and reduces hepatic glucose production	Unknown; no clinical trials yet
<b>Thiazolidinediones</b>		Improve peripheral insulin sensitivity	1%-2%
Pioglitazone (Actos)	15-45 mg daily		
Rosiglitazone (Avandia)	4-8 mg daily		
<b>Alpha Glucosidase Inhibitors</b>		Delay carbohydrate absorption	0.5%-1%
Acarbose (Precose)	25-100 mg tid		
Miglitol (Glyset)	25-100 mg tid		

From Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association. *bid*, Twice daily; *tid*, three times daily.

presses hepatic glucose production and lowers insulin resistance, but it does not stimulate insulin secretion. It is not associated with hypoglycemia, may cause small weight losses when therapy begins, and improves lipid levels. Adverse effects include gastrointestinal distress, such as abdominal pain, nausea, and diarrhea, in up to 50% of patients. The frequency of these adverse effects can be minimized with food consumption and slow titration of dose. A rare side effect is severe lactic acidosis, which can be fatal. Acidosis usually occurs in patients who use alcohol excessively, have renal dysfunction, or have liver impairments (Inzucchi, 2002). Biguanides can be used alone or in combination with other diabetes medications. Other available agents include metformin extended release (Glucophage XR) and glyburide/metformin (Glucovance).

The TZDs decrease insulin resistance in peripheral tissues and thus enhance the ability of muscle and fat cells to take up glucose. TZDs also have certain lipid benefits. HDL cholesterol increases and triglycerides frequently decrease with TZD therapy. Although LDL cholesterol may increase because of a shift from small and dense to large and buoyant LDL particles, these types of particles are less atherogenic, and thus the increase in LDL cholesterol may not be a concern (Inzucchi, 2002). Adverse effects include weight gain and edema, and these effects are more common in pa-

tients who receive TZDs along with insulin. Patients with advanced forms of congestive heart disease or hepatic impairment should not receive TZDs. Troglitazone (Rezulin), the first approved TZD, was removed from the market because of hepatocellular injury. Rosiglitazone (Avandia) and pioglitazone (Actos) are the two TZD drugs currently available and have not been associated with liver injury.

$\alpha$ -Glucosidase inhibitors work in the small intestine to inhibit enzymes that digest carbohydrates, thereby delaying carbohydrate absorption and lowering postprandial glycemia. Acarbose (Precose) and miglitol (Glyset) are competitive inhibitors of intestinal brush-border  $\alpha$ -glucosidases required for the breakdown of starches, dextrans, maltose, and sucrose to absorbable monosaccharides. They do not cause hypoglycemia or weight gain when used alone, but they can frequently cause flatulence, diarrhea, cramping, or abdominal pain. Symptoms may be alleviated by initiating therapy at a low dose and gradually increasing the dose to therapeutic levels (Coniff, 1995).

## Insulin

Persons with type 1 diabetes depend on insulin to survive. In persons with type 2 diabetes, insulin may be needed to restore glycemia to near normal. Circumstances that require the use of insulin in type 2

**TABLE 33-7** Action Times of Human Insulin Preparations

TYPE OF INSULIN	ONSET OF ACTION	PEAK ACTION	USUAL EFFECTIVE DURATION	MONITOR EFFECT IN:
Rapid-acting Lispro Aspart	<15 min	0.5-1.5 hr	2-4 hr	2 hr
Short-acting Regular	0.5-1 hr	2-3 hr	3-6 hr	4 hr
Intermediate-acting NPH Lente	2-4 hr 3-4 hr	6-10 hr 6-12 hr	10-16 hr 12-18 hr	8-12 hr 8-12 hr
Long-acting Ultralente Glargine (Lantus)	6-10 hr 1.1 hr	10-16 hr —	18-20 hr 24 hr	10-12 hr 10-12 hr
Mixtures 70/30 (70% NPH, 30% regular) 50/50 (50% NPH, 50% regular) 75/25 (75% neutral protamine lispro [NPL], 25% lispro) 70/30 (75% neutral protamine aspart [NPA], 30% aspart)	0.5-1 hr	Dual	10-16 hr	

From Franz MJ, Reader D, Monk D: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association. NPH, Neutral protamine Hagedorn.

diabetes include the failure to achieve adequate control with administration of oral medications; periods of acute injury, infection, or surgery; pregnancy; and allergy or serious reactions to sulfonyleurea agents.

Insulin has four properties: action, concentration, purity, and source. These properties determine its onset, peak, and duration (Table 33-7). Most insulin now is made biosynthetically, purified, and then treated enzymatically to yield human insulin (Burge and Schade, 1997). A major advantage of human insulin is that it produces fewer antibodies and, as a result, can also be used for intermittent periods of insulin treatment, such as during surgery and pregnancy. U-100 is the concentration of insulin available in the United States. This refers to insulin activity per milliliter of insulin; therefore, U-100 means 100 U/ml of insulin. Pen injectors are now being used more frequently as an alternative to the traditional syringe-needle units.

*Rapid-acting insulins* include insulin lispro (Humalog) and insulin aspart (Novolog) and are used as bolus (mealtime) insulins. They are insulin analogs that differ from human insulin in amino acid sequence but bind to insulin receptors and thus function in a manner similar to human insulin. Both lispro and aspart have an onset of action within 15 minutes, a peak in activity at 60 to 90 min, and a duration of action of 3 to 5 hours. Both result in fewer hypoglycemic episodes compared with regular insulin. In the future, insulin administered via the pulmonary route (inhaled insulin) also may be used as bolus insulin.

Regular is a *short-acting* insulin with an onset of action 15 to 60 minutes after injection and a duration of action ranging from 5 to 8 hours. For best results, the slow onset of regular insulin requires it to be taken 30 to 60 minutes before meals.

*Intermediate-acting* insulins include NPH and lente. Their appearance is cloudy, and their onset, peak,

and duration are similar. Their onset of action is about 2 hours after injection, and their peak effect is from 6 to 10 hours

*Long-acting* insulins are ultralente and glargine (Lantus). Ultralente has its peak activity 8 to 10 hours after injection and a duration of about 18 to 20 hours. Insulin glargine is the newest insulin on the market and is also an insulin analog. Slow dissolution of glargine at the site of the injection results in a relatively constant and peakless delivery over 24 hours. Glargine is clear in solution, similar to lispro, aspart, and regular, whereas NPH, lente, and ultralente are cloudy. Patients need to be sure they have their vial marked clearly. Glargine cannot be mixed with other insulins and is usually given at bedtime. However, glargine can also be given before any meal, but whichever time is chosen, glargine must be given consistently at that time. Clinical trials have demonstrated lower fasting glucose levels and less hypoglycemia with glargine than with NPH (Vajo et al, 2001). Detemir is a long-acting insulin still under development.

Premixed insulins are also available: 70/30, which is 70% NPH and 30% regular, and 50/50, which is 50% NPH and 50% regular. The addition of neutral protamine to lispro creates an intermediate-acting insulin that has been used in 75/25 combinations with lispro. Similarly, the addition of neutral protamine to aspart creates an immediate-acting insulin that has been used in 10/30 combination with aspart.

All persons with type 1 diabetes and those with type 2 diabetes who no longer produce adequate endogenous insulin need replacement of insulin that mimics normal insulin action. After individuals without diabetes eat, their plasma glucose and insulin concentrations increase rapidly, peak in 30 to 60 minutes, and return to basal concentrations within 2 to 3 hours. To mimic this, rapid-acting (or short-acting) insulin is given before meals, and this is referred to

as *bolus* or *mealtime insulin*. Mealtime insulin doses are adjusted based on the amount of carbohydrate in the meal. An insulin-to-carbohydrate ratio can be established for an individual that will guide decisions on the amount of mealtime insulin to inject.

*Basal* or *background insulin* dose is that amount of insulin required in the postabsorptive state to restrain endogenous glucose output primarily from the liver. Basal insulin also limits lipolysis and excess flux of free fatty acids to the liver.

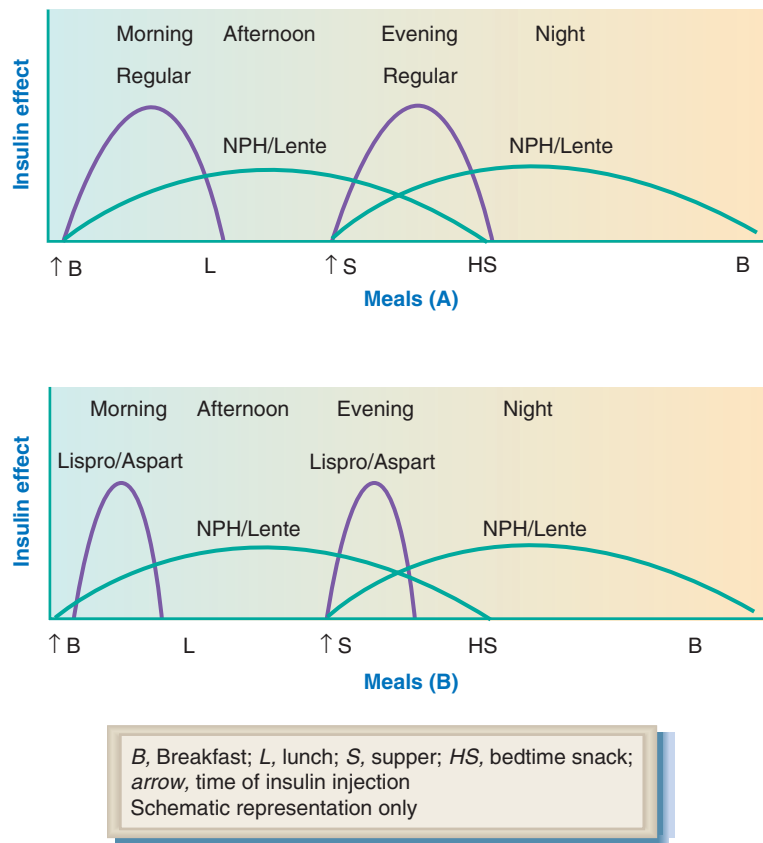
The type and timing of insulin regimens should be individualized, based on eating and exercise habits and blood glucose concentrations. For normal-weight persons with type 1 diabetes, the required insulin dosage is about 0.5 to 1.0 U per kilogram of body weight per day. About 50% of the total daily insulin dose is used to provide for basal or background insulin needs (such as NPH or glargine). The remainder (rapid-acting insulins, such as lispro or aspart) is divided among the meals either proportionate to the carbohydrate content or by giving about 1.0 to 1.5 U insulin per 10 g carbohydrate consumed. The larger amount is usually needed to cover breakfast carbohydrate as a result of the presence in the morning of higher levels of counterregulatory hormones (Rabasa-Lhoret et al, 1999). Persons with type 2 diabetes may require insulin doses in the range of 0.5 to 1.2 U per kilogram of body weight daily. Large doses, even >1.5 U/kg of

body weight daily, may be required at least initially to overcome prevailing insulin resistance.

A single dose of insulin is seldom effective for optimal blood glucose control in either type of diabetes, although occasionally insulin is added at bedtime to suppress nocturnal hepatic glucose production and to normalize fasting glucose concentrations and oral medications are continued during the day (Yki-Jarvinen et al, 1992).

The administration of basal insulin twice a day may suffice for persons with type 2 diabetes who still have significant endogenous insulin production. A commonly used insulin regimen combines a short-acting (such as regular) or a rapid-acting (such as lispro or aspart) insulin and a basal insulin (such as NPH) given twice a day. The prebreakfast dose consists of about one third regular and two thirds NPH. The presupper dose is usually divided into equal amounts of NPH and regular insulin (Figure 33-3). Another option is to combine regular (or lispro or aspart) and NPH before breakfast, regular (or lispro or aspart) before supper, and NPH or ultralente at bedtime. The NPH (or ultralente) is administered at bedtime to control the early morning surge in blood glucose levels (**dawn phenomenon**).

For persons with type 1 diabetes and many patients with type 2 diabetes a *flexible insulin regimen* is preferred. Basal insulin, such as NPH, may be adminis-

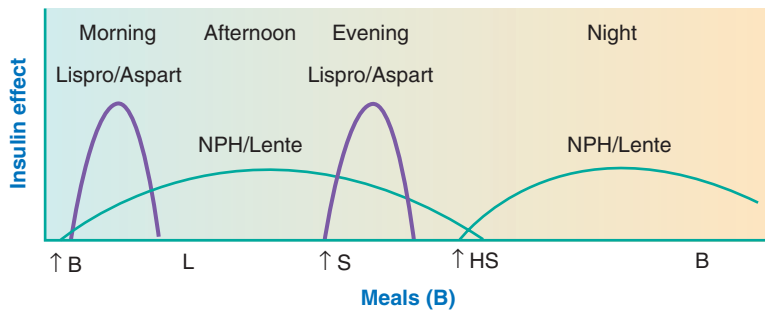
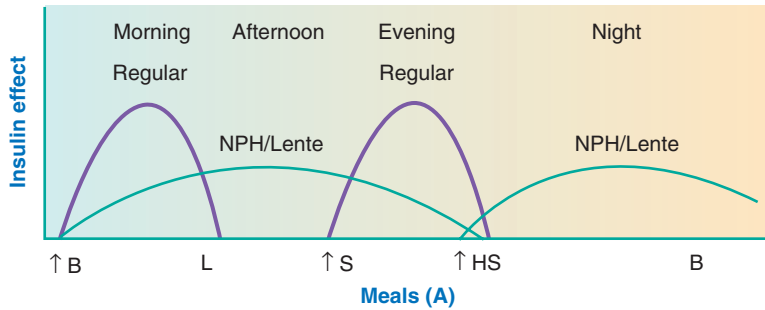


**FIGURE 33-3** • Time actions of two-injection insulin regimens. (Modified from Skyler US: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.)

tered twice a day, before breakfast and at bedtime. Meal insulin is provided by rapid-acting (lispro or aspart) insulin administered with each meal (Figure 33-4). Because of the peaking action of NPH, this regimen often results in erratic glucose levels. The introduction of glargine has provided a solution to many of these problems. With glargine as basal insulin at bedtime and rapid-acting insulin as bolus for meals, in-

ulin doses can be identified more accurately, and initial dosing is simplified (Figure 33-5). These types of insulin regimens allow increased flexibility in the type and timing of meals.

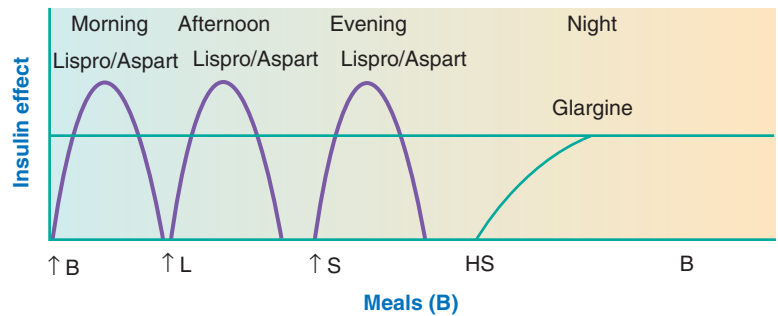
*Insulin pump* therapy provides basal rapid-acting or short-acting insulin pumped continuously by a mechanical device in micro amounts through a subcutaneous catheter that is monitored 24 hours a day.



**FIGURE 33-4** • Time actions of multiple-action insulin regimens. (Modified from Skyler US: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.)

B, Breakfast; L, lunch; S, supper; HS, bedtime snack; arrow, time of insulin injection  
Schematic representation only

**FIGURE 33-5** • Time actions of flexible insulin regimens. (Modified from Skyler US: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.)



B, Breakfast; L, lunch; S, supper; HS, bedtime snack; arrow, time of insulin injection  
Schematic representation only

Both lispro and aspart work well in insulin pumps, resulting in improved glycemia and less hypoglycemia than with regular insulin (Bode and Strange, 2001). Boluses of the insulin are given before meals. Pump therapy requires a committed and motivated person who is willing to do a minimum of four blood glucose tests per day, to keep blood glucose and food records, and to learn the technical features of pump use.

## Blood Glucose Monitoring

**Self-monitoring of blood glucose (SMBG)** is used on a day-to-day basis to manage diabetes effectively and safely; however, laboratory measurement of glycated hemoglobin provides the best available index of overall diabetes control.

The health care team, including the individual with diabetes, should work together to implement blood glucose monitoring and establish individual **target blood glucose goals** (see Table 33-4 for a listing of these goals). The frequency of monitoring depends on the type of diabetes and overall therapy.

Patients can perform SMBG up to eight times per day—before breakfast, lunch, and dinner; at bedtime; 1 to 2 hours after meals; and during the night or whenever needed to determine causes of hypoglycemia or hyperglycemia. For most patients with type 1 diabetes, SMBG is recommended four or more times a day, before each meal and at bedtime. SMBG in patients with type 2 diabetes should be sufficient to facilitate reaching glucose goals and is often performed one to four times a day, often before breakfast and before and 2 hours after the largest meal but only 3 or 4 days per week. When adding to or modifying therapy, type 1 and type 2 patients with diabetes should test more often than usual (ADA, 2002d).

Because the accuracy of SMBG is instrument and user dependent, it is important for health care providers to evaluate each patient's monitoring techniques, both initially and at regular intervals thereafter. Comparisons between results from patient self-testing in the clinic and simultaneous laboratory testing are useful to assess the accuracy of patient results. Most meters now automatically convert the capillary whole-blood test to plasma glucose values so comparisons can readily be made with laboratory values.

It is important that the results of SMBG be written in a record book and that patients be taught how to adjust their management program based on these results. The first step in using such records is to learn how to identify patterns in blood glucose levels and how to adjust basic insulin doses. For example, if blood glucose levels are consistently (generally 3 days in a row) elevated at a specific testing time, adjustments are made in the insulin or medication acting at that time. After pattern management is mastered, algorithms for insulin dose changes to compensate for an elevated or low glucose value can be added.

In using blood glucose monitoring records, it should be remembered that factors other than food affect blood glucose concentrations. An increase in blood glucose can be the result of insufficient insulin or insulin secretagogue, too much food, or increases in glucagon and other counterregulatory hormones as a result of stress, illness, or infection. Factors that contribute to hypoglycemia include too much insulin or insulin secretagogue, not enough food, unusual amounts of exercise, and skipped or delayed meals. Urine glucose testing, frequently used in the past, has so many limitations that it should not be used.

It is now possible to do continuous ambulatory blood glucose monitoring to determine 24-hour blood glucose patterns and to detect unrecognized hypoglycemia. One such system consists of a subcutaneous sensor that monitors interstitial glucose levels for up to 72 hours. Data can be downloaded in the physician's office after completion of the prescribed cycle. Another device is worn on the wrist and can provide up to three glucose readings each hour for a maximum of 12 hours. It works through a process called *reverse iontophoresis*, in which a low-level electric current passes through intact skin and extracts glucose molecules.

Urine or blood testing can be used to detect ketones. Testing for ketonuria or ketonemia should be performed regularly during periods of illness and when blood glucose levels consistently exceed 240 mg/dl. The presence of persistent, moderate, or large amounts of ketones, along with elevated blood glucose levels, requires insulin adjustments. Persons with type 2 diabetes rarely have ketosis; however, ketone testing should be done when the person is seriously ill.

## Self-Management Education

Diabetes management is a team effort. Persons with diabetes must be at the center of the team because they have the responsibility for day-to-day management. Dietitians, nurses, physicians, and other health care providers contribute their expertise to developing therapeutic regimens that help the person with diabetes achieve the best metabolic control possible. The goal is to provide patients with the knowledge, skills, and motivation to incorporate self-management into their daily lifestyles.

For newly diagnosed patients, a staged approach to education should be used. Education initially focuses on the needed basic skills (Box 33-2). Optimal self-management of diabetes requires changes in existing behaviors in addition to the adoption of new ones. Successful behavioral change requires comprehensive education, skill development, and motivation (see Chapter 22). The knowledge and skills needed to implement nutritional recommendations cannot be acquired in one session; therefore, continued nutrition education is essential and must be an ongoing component of diabetes care (Box 33-3).

### Box 33-2. Medical Nutrition Therapy Basic Self-Management Education Skills for Persons With Diabetes

- Basic food and meal planning guidelines
- Physical activity guidelines
- Self-monitoring of blood glucose levels
- For insulin or insulin secretagogue users, signs, symptoms, treatment, and prevention of hypoglycemia
- For insulin or insulin secretagogue users, guidelines for managing short-term illness
- Plans for follow-up and ongoing education

Modified from American Dietetic Association: *Medical nutrition therapy evidence-based guides for practice: nutrition practice guidelines for type 1 and type 2 diabetes*, CD-Rom, Chicago, Ill, 2001, American Dietetic Association.

## DIABETES AND AGE-RELATED ISSUES

### Children and Adolescents

Involvement of a multidisciplinary team, including a physician, dietitian, nurse, and behavioral specialist, all trained in pediatric diabetes, is the best means of achieving optimal diabetes management in youth. The most important team members, however, are the child or adolescent and his or her family.

A complete nutrition assessment, which is the basis for the food and meal plan for youth with diabetes, includes anthropometric measurements, nutrition assessment and food history, biochemical indices, assessment of feelings and family concerns related to nutrition and diabetes, and typical activity patterns (see Chapters 17 and 18).

A major nutrition goal for children and adolescents with type 1 diabetes is maintenance of normal growth and development. Possible causes of poor weight gain and linear growth include poor glycemic control, inadequate insulin, and overrestriction of calories. The last may be a consequence of the common erroneous belief that restricting food, rather than adjusting insulin, is the way to control blood glucose. Other reasons unrelated to diabetes management include thyroid abnormalities and malabsorption syndromes. Excessive weight gain can be due to excessive caloric intake, overtreatment of hypoglycemia, or overinsulinization. Other causes include low physical activity levels and hypothyroidism (accompanied by poor linear growth) (Drash, 1993).

### Box 33-3. Essential Self-Management Nutrition Education Skills\*

- Sources of carbohydrate, protein, fat
- Understanding nutrition labels
- Modification of fat intake
- Alcohol consumption guidelines
- Use of blood glucose monitoring data for problem solving related to food choices and physical activity options
- Use of blood glucose monitoring data to identify blood glucose patterns and need for medication changes
- Adjustments in carbohydrate or insulin for exercise
- Grocery shopping guidelines
- Guidelines for eating out: restaurant, cafeteria, school lunch
- Snack choices
- Mealtime adjustments
- Use of sugar-containing foods and nonnutritive sweeteners
- Recipes, menu ideas, cookbooks
- Behavior modification techniques
- Problem-solving tips for birthdays, special occasions, holidays
- Travel, schedule changes
- Vitamin, mineral, and botanical supplements
- Work shift rotation, if needed

Modified from American Dietetic Association: *Medical nutrition therapy evidence-based guides for practice: nutrition practice guidelines for type 1 and type 2 diabetes*, CD-Rom, Chicago, Ill, 2001, American Dietetic Association.

\*Topics emphasized based on patient's lifestyle, level of nutrition knowledge, and experiences in planning, purchasing, and preparing food and meals.

The nutrition prescription is based on the nutrition assessment. Newly diagnosed children often present with weight loss and hunger; as a result, the initial meal plan must be based on adequate calories to restore and maintain appropriate body weight. In about 4 to 6 weeks, the initial caloric level may need to be modified to meet more usual caloric requirements. Children have a natural ability to know how much to eat for normal growth and development. Table 33-8 lists a formula that can be used to confirm that a child or adolescent is receiving the minimum number of calories necessary for growth and development. Height and weight should be recorded on growth charts every 3 to 6 months to make sure children are growing normally. If not, the overall diabetes management plan needs to be assessed. For growth charts see Appendixes 6 to 11, 18, and 19. Caloric needs in children change continuously, and so food intake should be evaluated every 3 to 6 months.

Individualized food and meal plans, insulin regimens using basal (background) and bolus (mealtime) insulins, and insulin algorithms can provide flexibility for children with type 1 diabetes and their families. This approach accommodates irregular meal times and schedules and varying appetites and activity levels (ADA, 2002b).

Daily eating patterns in young children generally include three meals and two or three snacks, depending on the length of time between meals and the child's physical activity level. Children often prefer smaller meals and snacks. Snacks can prevent hypoglycemia between meals and provide adequate calories. Older children and teens may prefer only three meals. Blood glucose monitoring data are then used to integrate an insulin regimen into the meal, snack, and exercise schedules.

Realistic blood glucose goals should be determined and discussed with the youth and family. Youth with diabetes are also more likely than their age- and sex-matched nondiabetic peers to be at risk for cardiovascular disease. It is therefore essential to reduce the risk factors in youth with type 1 diabetes. Lipid levels should be monitored regularly, and National Cholesterol Education Program treatment guidelines for children and adolescents should be followed (ADA, 2003b) (see Chapter 35).

After the appropriate nutrition prescription has been determined, the meal planning approach can be selected. Most pediatric educators agree that it is better to start with a more precise meal plan and then teach flexibility than to start with flexibility and try to teach precise planning later. A number of meal planning approaches can be used. Carbohydrate counting for food planning provides youth and their families with guidelines that facilitate glycemic control while

still allowing the choice of many common foods that children and adolescents enjoy. Whatever approach to food planning is used, however, the youth and family must find it understandable and applicable to their lifestyle. Blood glucose records are essential to assist the dietitian and other team members in making appropriate changes in insulin regimens.

### Type 2 Diabetes in Youth

Childhood obesity has been accompanied by an increase in the prevalence of type 2 diabetes among children and adolescents. Impaired glucose tolerance has been shown to be highly prevalent in obese youth, irrespective of ethnic group, and is associated with insulin resistance. Once type 2 diabetes develops,  $\beta$ -cell failure is also a factor (Sinha et al, 2002). Thus, type 2 diabetes in youth appears to follow a progressive pattern similar to type 2 diabetes in adults.

Successful lifestyle treatment of type 2 diabetes in children and adolescents involves cessation of excessive weight gain, promotion of normal growth and development, and the achievement of blood glucose and A1C goals (ADA, 2000). Nutrition guidelines should also address comorbidities, such as hypertension and dyslipidemia. Behavior modification strategies to decrease intake of high-caloric, high-fat food while encouraging healthy eating habits and regular physical activity for the entire family should be considered. Unfortunately, successful lifestyle treatment regimens for youth with type 2 diabetes have not been defined (ADA, 2002b). Metformin is often used when lifestyle strategies alone have not achieved target glucose goals and has been shown to be safe and effective for the treatment of pediatric type 2 diabetes (Jones et al, 2002). Some youth may also require insulin therapy to achieve adequate glycemic control.

### Pregnancy

Normalization of blood glucose levels during pregnancy is very important for women who have preexisting diabetes or who develop GDM. MNT goals are to assist in achieving and maintaining optimal blood glucose control, to provide adequate maternal and fetal nutrition, to supply energy intake for appropriate maternal weight gain, and to provide necessary vitamin and mineral supplements (ADA, 2002b).

### Preexisting Diabetes and Pregnancy

Preconception counseling and the ability to achieve near-normal blood glucose levels before pregnancy have been shown to be effective in reducing the incidence of anomalies in infants born to women with preexisting diabetes to nearly that of the general population (Kitzmilller et al, 1996). Normal blood glucose levels are lower during pregnancy. Table 33-9 outlines blood glucose goals during pregnancy for preexisting diabetes and for GDM (ADA, 2002e; Jovanovic, 2000).

**TABLE 33-8** Estimating Minimum Energy Requirements for Youth

Base energy requirements on food and nutrition assessment  
Validate energy needs

AGE	ENERGY REQUIREMENTS
1 yr	1000 kcal for the first year
<b>Toddler</b>	
2-11 yr	Add 100 kcal/yr to 1000 kcal; up to 2000 kcal at age 10
<b>Girls</b>	
12-15 yr	2000 kcal plus 50-100 kcal/yr per year after age 10
>15 yr	Calculate as for an adult
<b>Boys</b>	
12-15 yr	2000 kcal plus 200 kcal/yr per year after age 10
>15 yr	Sedentary: 16 kcal/lb (30-35 kcal/kg) Moderate physical activity: 18 kcal/lb (40 kcal/kg) Very physically active: 23 kcal/lb (50 kcal/kg)

Modified from Franz MJ, Reader D, Monk D: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.

As a result of hormonal changes during the first trimester, blood glucose levels are often erratic. Although caloric needs do not differ from those preceding pregnancy, the meal plan may need to be adjusted to accommodate the metabolic changes. Women should be educated about the increased risk of hypoglycemia during pregnancy and cautioned against overtreatment.

The need for insulin increases during the second and third trimesters of pregnancy. This is the reason why screening for GDM is done between weeks 24 and 28 of pregnancy. At 38 to 40 weeks' postconception, insulin needs and levels peak at two to three times prepregnancy levels. Pregnancy-associated hormones that are antagonistic to the action of insulin lead to an elevation of blood glucose levels. For women with pre-existing diabetes, this increased insulin need must be met with increased exogenous insulin.

Meal plan adjustments are necessary to provide the additional calories required to support fetal growth. Weight gain should be monitored, and guidelines for appropriate weight gain that apply to women without diabetes also apply to women with diabetes. Regular follow-up visits are needed to also monitor caloric and nutrient intake, blood glucose control, and whether there is starvation ketosis. Urine or blood ketones during pregnancy may signal starvation ketosis that can be caused by inadequate energy or carbohydrate intake, omission of meals or snacks, or prolonged intervals between meals (e.g., more than 10 hours between the bedtime snack and breakfast). Ketonemia during pregnancy has been associated with reduced IQ scores in children (Rizzo et al, 1991). Women should be instructed to test for ketones periodically before breakfast.

Nutrition therapy is individualized according to the food and nutrition history, prepregnancy weight, and physical activity levels. Generally, an additional 100 to 300 kcal daily is added to the meal plan at the beginning of the second trimester. The increased caloric requirement can be met easily by the addition

of one or two cups of reduced-fat or skim milk and 1 to 2 oz of meat or meat substitute. This also provides adequately for the increased protein need. Smaller meals and more frequent snacks are often needed to prevent hypoglycemia. A late-evening snack is especially important to decrease the likelihood of overnight starvation ketosis. Records of food intake and blood glucose values are essential for determining whether glycemic goals are being met and for preventing and correcting ketosis.

### Gestational Diabetes Mellitus

About 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually (ADA, 2002e). After delivery, about 90% of all women with GDM become normoglycemic but are at increased risk of developing GDM earlier in subsequent pregnancies and are at increased risk for developing type 2 diabetes. Although estimates vary, within 4 years after pregnancy, about 30% to 40% of women with GDM who are obese will develop type 2 diabetes (ADA, 2001). Avoidance of obesity in women before and after pregnancy reduces the risk of subsequent type 2 diabetes.

Because fetal morbidity may be increased, a risk assessment for GDM should be done at the first prenatal visit and for women at high risk (those with marked obesity, previous history of GDM, glycosuria, or a strong family history of diabetes) as soon as possible. An FPG of 126 mg/dl or higher or a casual PG of 200 mg/dl meets the threshold for the diagnosis of diabetes and, if confirmed on a second day, requires no further testing (ADA, 2002a). High-risk women not found to have GDM at the initial screening and average risk women (a few women can be classified as low-risk) should be tested between 24 to 28 weeks' gestation. An oral glucose challenge (which does not have to be preceded by fasting) with a 50-g glucose load is performed, and an elevated plasma glucose level ( $\geq 140$  mg/dl) 1 hour later is considered an indication of the need for diagnostic testing. The criteria for the diagnosis of GDM based on a 100-g oral glucose tolerance test (OGTT) are listed in Table 33-10. Low-risk women who do not need to be screened must meet all the following criteria: younger than 25 years of age; normal body weight; no family history of diabetes; no history of abnormal glucose tolerance; and not a member of an ethnic or racial group with a high prevalence of diabetes (ADA, 2002a).

Limited research has been done to determine the ideal diet for GDM. In general, the overall nutrition recommendations for preexisting diabetes also apply to GDM, although the diagnosis is generally not made before the second or third trimester. The goal of nutrition therapy is to provide adequate energy levels for appropriate gestational weight gain, achievement and maintenance of normoglycemia, and absence of ketones. Individualization of the meal plan

**TABLE 33-9** Plasma Glucose Goals During Pregnancy

TEST	PREEXISTING DIABETES (mg/dl)	GESTATIONAL DIABETES (mg/dl)
Fasting plasma glucose	65-100	80-110
Premeal	65-110	
1 hr postprandial	<145	<155
2 hr postprandial	<135	<130
2 to 6 hr postprandial	65-135	
Normal values during pregnancy		
Fasting plasma glucose:	70-105	
1-2 hr postprandial:	$\leq 140$	

Modified from Jovanovic L, editor: *Medical management of pregnancy complicated by diabetes*, ed 3, Alexandria, Va, 2000, American Diabetes Association, and American Diabetes Association: Gestational diabetes mellitus [Position Statement], *Diabetes Care* 25(suppl 1):S94, 2002.

**TABLE 33-10** Diagnosis of Gestational Diabetes Mellitus (GDM)

TYPE OF TEST	RESULTS
Screening during pregnancy—a 50-g oral glucose challenge (does not have to be fasting) at 24 to 28 wk gestation	A plasma glucose level $\geq 140$ mg/dl ( $\geq 7.8$ mmol/L) 1 hr later indicates the need for further diagnostic testing.
Oral glucose tolerance test with an abnormal screen	After a 100-g oral glucose load, GDM may be diagnosed if two plasma glucose values equal or exceed: <b>Fasting:</b> $\geq 95$ mg/dl <b>1 hr:</b> $\geq 180$ mg/dl <b>2 hr:</b> $\geq 155$ mg/dl <b>3 hr:</b> $\geq 140$ mg/dl

Modified from American Diabetes Association: Standards of medical care for patients with diabetes mellitus [Position Statement], *Diabetes Care* 25(suppl 1):S33, 2002.

is recommended, as the ideal percentage and type of carbohydrate is controversial. Monitoring blood glucose, urine and blood ketones, appetite, and weight gain can aid in developing an appropriate, individualized meal plan and in adjusting the meal plan throughout pregnancy (ADA, 2002b).

Nutrition practice guidelines for gestational diabetes have been developed and field-tested (Reader and Sipe, 2001). With input from patients, the dietitian designs a food and meal plan; however, without blood glucose monitoring data, it is impossible to assess its effectiveness. Food and blood glucose records guide nutrition therapy, and alterations to food plans are used to assess outcomes of therapy and, along with weight changes, determine whether insulin therapy is needed. Insulin therapy is added if glucose goals exceed target range (see Table 33-9) on two or more occasions in a 1- to 2-week period without some obvious explanation from food records or if glucose levels are consistently elevated because of patients' dietary indiscretions after MNT intervention. Weight gain or lack of weight gain and ketone testing can be useful in determining whether patients are undereating to keep glucose levels within target range to avoid insulin therapy.

Medical nutrition therapy involves developing a carbohydrate-controlled, consistent food and meal plan. Generally, 40% to 45% of total energy intake will be from carbohydrate, which is distributed throughout the day in three small to moderate-sized meals and two to four snacks. An evening snack is usually needed to prevent accelerated ketosis overnight. Carbohydrate is not as well tolerated at breakfast as it is at other meals because of increased levels of cortisol and growth hormones. To compensate for this, the initial food plan may have 30 to 45 g of carbohydrate at breakfast. To satisfy hunger, protein foods, because they do not affect blood glucose levels, can be added.

Although caloric restriction must be viewed with caution, in obese women with GDM, a 30% caloric restriction (an intake of about 1700 to 1800 kcal daily) can reduce hyperglycemia with no increase in ketonuria (Knopp et al, 1991). Intake below these levels is not advised. The pattern of weight gain during pregnancy for women with GDM should be similar to that of women without diabetes.

Exercise can also assist in overcoming peripheral resistance to insulin and in controlling postprandial hyperglycemia. It may be used as an adjunct to nutrition therapy to improve maternal glycemia. The ideal form of exercise is unknown, but a brisk walk after meals is often recommended.

## Older Adults

The prevalence of diabetes and IGT increases dramatically as people age. Many factors predispose older adults to diabetes: age-related decreases in insulin production and increases in insulin resistance, adiposity, decreased physical activity, multiple prescription medications, genetics, and coexisting illnesses. A major factor appears to be insulin resistance. Controversy persists as to whether the insulin resistance is itself a primary change or whether it is attributable to reduced physical activity, decreased lean body mass, and increased adipose tissue, which are all frequently seen in older adults. Abdominal obesity also correlates with insulin resistance in older adults (Kohrt et al, 1993). Furthermore, medications used to treat coexisting diseases may complicate diabetes therapy in older persons.

Despite the increase in glucose intolerance with age, aging per se should not be a reason for suboptimal control of blood glucose. Even if it is incorrectly assumed that preventing long-term diabetic complications is not relevant to the care of older adults, persistent hyperglycemia has deleterious effects on the body's defense mechanisms against infection. It also increases the pain threshold by exacerbating neuropathic pain, and it has a detrimental effect on the outcome of cerebrovascular accidents.

Exercise training can significantly reduce the decline in aerobic capacity that occurs with age, improve risk factors for atherosclerosis, slow the decline in age-related lean body mass, decrease central adiposity, and improve insulin sensitivity.

A daily multivitamin supplement may be appropriate for older adults, especially those with reduced energy intake. All older adults should have a calcium intake of at least 1200 mg daily and a vitamin D intake of 15  $\mu$ g or 600 IU per day.

Malnutrition, not obesity, is often the more prevalent nutrition-related problem of older adults. It often remains subclinical or unrecognized because the result of malnutrition—excessive loss of lean body mass—resembles the signs and symptoms of the aging process. Until a primary disease develops or chronic problems are exacerbated by illness or some

other stress, malnutrition may remain unrecognized. Both malnutrition and diabetes adversely affect wound healing and defense against infection, and malnutrition is associated with depression and cognitive deficits. The most reliable indicator of poor nutritional status in older adults is probably a change in body weight. In general, involuntary weight gain or loss of more than 10 pounds or 10% of body weight in less than 6 months indicates a need to evaluate whether the reason is nutrition related (ADA, 2002b).

Because of concern over malnutrition, it is essential that older adults, especially those in long-term care settings, be provided a diet that meets their nutritional needs, enables them to attain or maintain a reasonable body weight, helps control blood glucose, and is palatable. The imposition of dietary restriction on older residents in long-term health facilities is not warranted. Residents should be served the regular (unrestricted) menu with consistency in the amount and timing of carbohydrate (ADA, 2002f).

In older adults, acute hyperglycemia and dehydration can lead to a serious complication of diabetes: the **hyperglycemic hyperosmolar state (HHS)**. Patients with HHS have a very high blood glucose level (ranging from 400 to 2800 mg/dl, with an average of 1000 mg/dl) without ketones. Patients are markedly dehydrated, and mental status often ranges from mild confusion to hallucinations or coma. Treatment includes provision of adequate fluids as well as blood glucose control.

## IMPLEMENTING NUTRITION SELF-MANAGEMENT

Medical nutrition therapy begins with developing rapport with the patient, and whether provided individually or in groups, MNT involves a common process—assessment (evaluation at follow-up visits), intervention including self-management education, goal setting, and communication (documentation) (see Chapter 21). If MNT is to be implemented individually, the intervention is then individualized based on the needs of the patient and whether the intervention is for initial, continuing, or intensive care.

Providing MNT in groups is becoming increasingly more important, since reimbursement criteria for diabetes self-management education and for MNT recommend that when possible group sessions are preferable. It is helpful if the group participants are similar in their stage of diabetes management and if they all speak and understand the same language. Group education shifts more responsibility to the patient to provide the needed initial assessment information, to evaluate outcomes, and to decide about therapy changes (Franz, Reader, and Monk, 2002). Group interventions for diabetes self-management education, when compared with individual interventions, have produced similar positive outcomes (Rickheim et al,

### Box 33-4. Food/Nutrition Assessment

- *Minimum referral data:* age, diagnosis of diabetes and other pertinent medical history, diabetes and other pertinent medications, laboratory data (A1C, cholesterol fractionation, albumin-to-creatinine ratio, and blood pressure), and clearance for exercise
- *Diabetes history:* previous diabetes education, use of blood glucose monitoring, diabetes problems/concerns (hypoglycemia, hyperglycemia, fear of insulin)
- *Food/nutrition history:* current eating habits with beginning modifications
- *Social history:* occupation, hours worked/away from home, living situation, financial issues
- *Medications/supplements:* medications taken, vitamin/mineral/supplement use, herbal supplements

Modified from Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.

2002). Implementation of group MNT is covered in *Implementing Group and Individual Medical Nutrition Therapy for Diabetes* (Franz, Reader, and Monk, 2002).

### Assessment

To develop an individualized nutrition care plan, the following parameters are assessed: anthropometric measures (height, weight, BMI), laboratory data, food and nutrition history, learning style, cultural heritage, and socioeconomic status. Box 33-4 provides a summary of such assessment data. Food and eating histories can be done several ways, with the objective being to determine a schedule and pattern of eating that will be the least disruptive to the lifestyle of the individual with diabetes and, at the same time, will facilitate improved metabolic control. With this objective in mind, asking the individual either to record or report what, how much, and when he or she typically eats during a 24-hour period may be the most useful.

Another approach is to ask the patient to keep and bring with him or her a 3-day or 1-week food intake record. This request can be made when an appointment with the dietitian is scheduled. Assessment of the most typical daily pattern can then be made. The history can also reveal other useful information, including (1) usual caloric intake; (2) quality of the usual diet; (3) times, sizes, and contents of meals and snacks; (4) food idiosyncrasies; (5) frequency with which meals are eaten in restaurants; (6) who usually prepares food;

(7) eating problems (e.g., as related to dental, gastrointestinal or other problems); (8) alcoholic beverage intake; and (9) supplements used (see Chapter 17).

It is also essential to learn about the patient’s daily routine and schedule. The following information is needed: (1) time of waking; (2) usual meal and eating times; (3) work schedule or school hours; (4) type, amount, and timing of exercise; and (5) usual sleep habits.

Using the assessment data and food and nutrition history information, a preliminary food and meal plan can then be designed and, if the patient desires, sample menus provided. Developing a food and meal plan does not begin with a set calorie or macronutrient prescription; instead, it is determined by modifying the usual food intake as necessary. The worksheet in Figure 33-6 can be used to record the usual foods eaten and to modify the usual diet as necessary. The macronutrient and caloric values for the exchange lists are listed on the form and in Table 33-11. See Appendix 33 for portion sizes of the foods on the exchange lists. These tools are useful in evaluating nutrition assessments. Using the form in Figure 33-6, the dietitian begins by totaling the number of exchanges from each list and multiplying this number by the grams of carbohydrate, protein, and fat contributed by each. Next

the grams of carbohydrate, protein, and fat are totaled from each column; the grams of carbohydrate and protein are then multiplied by 4 (4 kcal/g of carbohydrate and protein), and the grams of fat are multiplied by 9 (9 kcal/g of fat). Total calories and percentage of calories from each macronutrient can then be determined. Numbers derived from these calculations are then rounded off. Figure 33-7 provides an example of a preliminary food and meal plan. In this example, the nutrition prescription would be the following:

1900-2000 calories  
 230 g of carbohydrate (50%)  
 90 g of protein (20%)  
 65 g of fat (30%)

The number of carbohydrate choices for each meal and snack is the total of the starch, fruit, and milk servings. Vegetables, unless starchy or eaten in very large amounts (three or more servings per meal), are generally considered “free foods.” The carbohydrate choices are circled under each meal and snack column. Table 33-12 is an example of a sample meal plan and menu based on Figure 33-7.

The next step is to evaluate the preliminary meal plan. First and foremost, does the patient with diabetes think it is feasible to implement the meal plan

		Meal/Snack/Time										
Food Group	Breakfast	Snack	Lunch	Snack	Dinner	Snack	Total servings/day	CHO (g)	Protein (g)	Fat (g)	Calories	
Starches								15	3	1	80	
Fruit								15			60	
Milk								12	8	1	90	
Vegetables								5	2		25	
Meats/ Substitutes									7	5(3)	75(55)	
Fats										5	45	
CHO Choices							Total grams					
							Calories/gram	X4=	X4=	X9=	Total calories	
							Percent calories					

Calculations are based on medium-fat meats and skim/very low-fat milk. If diet consists predominantly of low-fat meats, use the factor 3 g instead of 5 g fat; if predominantly high-fat meats, use 8 g fat. If low-fat (2%) milk is used, use 5 g fat; if whole milk is used, use 8 g fat.

**FIGURE 33-6** • Worksheet for assessment and design of a meal or food plan. CHO, Carbohydrate.

into his or her lifestyle? Second, is it appropriate for diabetes management? Third, are the calories appropriate? Fourth, does it encourage healthful eating?

To answer the first question concerning the feasibility of the food plan, the food and meal plan is re-

viewed with the patient in terms of general food intake. Timing of meals and snacks and approximate portion sizes and types of foods are discussed. Later, a meal-planning approach can be selected that will assist the patient in making his or her own food

**TABLE 33-11** Macronutrient and Caloric Values for Exchange Lists\*

GROUPS/LISTS	CARBOHYDRATE (g)	PROTEIN (g)	FAT (g)	CALORIES
<b>Carbohydrate Group</b>				
Starch	15	3	0-1	80
Fruit	15	—	—	60
Milk				
Skim	12	8	0-3	90
Reduced-fat	12	8	5	120
Whole	12	8	8	150
Other carbohydrates	15	Varies	Varies	Varies
Vegetables	5	2	—	25
<b>Meat and Meat Substitute Group</b>				
Very lean	—	7	0-1	35
Lean	—	7	3	55
Medium-fat	—	7	5	75
High-fat	—	7	8	100
<b>Fat Group</b>				
	—	—	5	45

From American Diabetes Association and American Dietetic Association: *Exchange lists for meal planning*, Alexandria, Va, 1995, American Diabetes Association. \*See Appendix 53.

Food Group	Meal/Snack/Time						Total servings/day	CHO (g)	Protein (g)	Fat (g)	Calories
	Breakfast 7:30 AM	Snack 10:00	Lunch 12:00	Snack 3:00	Dinner 6:30	Snack 10:00					
Starches	2	1	2-3	1	2-3	1-2	10	150	30	10	80
Fruit	1		1		1	0-1	3	45			60
Milk	1				1		2	24	16	2	90
Vegetables			✓		✓			5	2		25
Meats/ Substitutes			2-3		3-4		6		7	5(3)	75(55)
Fats	1	0-1	1-2	0-1	1-2	0-1	5			5	45
CHO Choices	3-4 CHO	1 CHO	3-4 CHO	1 CHO	4-5 CHO	1-2 CHO	Total grams	229	92	67	
1900-2000 calories 230 g CHO-50% 90 g protein-20% 65 g fat-30%							Calories/gram	X4= 916	X4= 368	X9= 603	Total calories
							Percent calories	50	19	30	1900-2000

Calculations are based on medium-fat meats and skim/very low-fat milk. If diet consists predominantly of low-fat meats, use the factor 3 g, instead of 5 g fat; if predominantly high-fat meats, use 8 g fat. If low-fat (2%) milk is used, use 5 g fat; if whole milk is used, use 8 g fat.

**FIGURE 33-7** • An example of a completed worksheet from the assessment, the nutrition prescription, and a sample 1900- to 2000-calorie meal plan. CHO, Carbohydrate.

**TABLE 33-12** Sample Menu for 1900-2000 Kilocalorie Meal Plan

MEAL/TIMING	FOOD SELECTIONS
<b>Breakfast—7:30 AM</b>	
3-4 Carbohydrate choices (i.e., 2 starch, 1 fruit, 1 milk)	Raisin bran cereal, ½ c Bagel, ¼ (1 oz) Cantaloupe (5-inch), ⅓ Skim milk, 1 c
1 Fat	Reduced-fat cream cheese, 1 tbsp
<b>Snack—10:00 AM</b>	
1 Carbohydrate choice (i.e., 1 starch or fruit)	Bagel, ¼ (1 oz)
0-1 Fat	Reduced-fat cream cheese, 1 tbsp
<b>Lunch—Noon</b>	
3-4 Carbohydrate choices (i.e., 2-3 starches, 1 fruit)	Whole-wheat bread, 2 slices Vegetable-beef soup, 1 c Apple, 1 small
Vegetable	Lettuce and tomato slices
2-3 Meats	Turkey, 2 oz
1-2 Fats	Reduced-fat mayonnaise, 1 tbsp
<b>Snack—3:00 PM</b>	
1 Carbohydrate choice (i.e., 1 starch or fruit)	Pretzels, ¾ oz
0-1 Fat	
<b>Dinner—6:30 PM</b>	
4-5 Carbohydrate choices (i.e., 2-3 starch, 1 fruit, 1 milk)	Baked potato, 1 medium Dinner roll, 1 Mandarin oranges, ¾ c Skim milk, 1 c
Vegetables	Broccoli spears, ½ c Dinner salad, 1 small
3-4 Meats	Chicken breast, baked, 3 oz
1-2 Fats	Sour cream, regular, 2 tbsp Reduced-fat salad dressing, 2 tbsp
<b>Snack—10:00 PM</b>	
1-2 Carbohydrate choices (i.e., 1-2 starches, 0-1 fruit)	Ice cream, light, ½ c Strawberries, 1¼ c
0-1 Fat	

choices. At this point, it needs to be determined whether this meal plan is reasonable for the patient with diabetes. To determine the appropriateness of the meal plan for diabetes management involves assessing both distribution of the meals (and snacks, if desired) and the macronutrient percentages. Appropriateness is based on the types of medications prescribed as well as treatment goals.

For patients receiving MNT alone, often the food and meal plan begins with three or four carbohydrate servings per meal for women and four or five for men, and, if desired, one or two for a snack. Blood glucose monitoring before the meal and 2 hours after the meal is recommended, with the plasma glucose goal being premeal values below 130 mg/dl and 2-hour postprandial values below 160 to 180 mg/dl.

Patients on oral glucose-lowering medications often do better with smaller meals and snacks, especially if they are taking an insulin secretagogue. Persons with type 2 diabetes, however, generally have

### Box 33-5. Estimating Approximate Energy Requirements for Adults

• Obese or very inactive persons and chronic dieters	10-12 kcal/lb (20 kcal/kg)
• Persons >55 yr, active women, sedentary men	13 kcal/lb (25 kcal/kg)
• Active men, very active women	15 kcal/lb (30 kcal/kg)
• Thin or very active men	20 kcal/lb (40 kcal/kg)

Data from Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.

fewer problems with hypoglycemia and do not need snacks unless this is their choice. If they choose to have snacks, this cannot be in addition to the usual meals. A portion of the meal should be saved to be eaten as a snack between meals.

For patients who require insulin, the timing of eating is extremely important. Food consumption must be synchronized with the time actions of insulin (see previous section on medications). If the eating pattern is determined first, an insulin regimen can be selected that will fit with it. To prevent overnight hypoglycemia, many patients require a bedtime snack. Often individuals who use morning intermediate-acting insulins (NPH or lente) also require an afternoon snack. Individuals using rapid-acting insulin (lispro or aspart) do not need a snack.

The next step is to determine whether the number of calories is appropriate or realistic for the individual patient. Energy requirements depend on several factors, such as age, gender, height, weight, and activity level. Box 33-5 outlines a simple method for determining approximate caloric requirements based on actual weight. Many dietitians use handheld calculators to determine caloric requirements, and the Harris Benedict equation, with modifications, is generally used in their calculations. The determination of a caloric level for a child or adolescent is also based on the nutrition assessment. Table 33-18 can be used to confirm that the child is receiving the minimum necessary calories.

Methods for determining caloric requirements are only approximate. On a practical basis, they do provide a starting point for evaluating the caloric adequacy of the meal plan. Adjustments in calories can be made during follow-up visits. Parameters that should be taken into consideration are weight

changes, feelings of satiety and hunger, and concerns about palatability.

The best way to ensure that the meal plan encourages healthful eating is to encourage patients to eat a variety of foods from all the food groups. The Food Guide Pyramid, with its suggested number of servings from each food group, can be used to compare the patient's meal plan with the nutrition recommendations for all Americans (see Chapter 15).

## Intervention and Self-Management Education

This step involves selecting an appropriate meal-planning approach and identifying strategies for behavioral change that enhance motivation and adherence to necessary lifestyle changes. A number of meal-planning approaches are available, ranging from simple guidelines or menus to more complex counting methods (Table 33-13). No single meal-planning approach has been shown to be more effective than any other, and the meal-planning approach selected should allow individuals with diabetes to select appropriate foods for meals and snacks.

A popular approach to meal planning is carbohydrate counting. It can be used as a basic meal-planning approach or for more intensive management. Carbohydrate-counting educational tools are based on the concept that after eating, it is the carbohydrate in foods that is the major predictor of postprandial blood glucose levels. One carbohydrate serving contributes 15 g of carbohydrate.

## Facilitating Behavioral Changes

The transtheoretic model was proposed by Prochaska as a general model of intentional behavior change (Prochaska et al, 1994). It includes a sequence of stages along a continuum of behavioral change. Different intervention strategies may be needed for individuals at different stages of the change process. Motivational interventions may work best with patients in the earlier contemplative stages, whereas specific skill-training interventions may be most appropriate for persons who have decided to change. Relapse and recycling through the stages occur quite frequently as patients attempt to modify behaviors (see Chapter 22).

## Goal Setting

*Short-term goals* (days or weeks) are often behavioral goals and relate to lifestyle changes. Common self-management behavioral goals are consistent and include appropriate carbohydrate servings, regular physical activity, correct medication dosage (if needed), and blood glucose monitoring as determined to be needed. Goals should be specific, written in behavioral language, and realistic for the patient.

Before the patient leaves the initial session, plans and an appointment for a follow-up session should be identified. In making plans for follow-up, the patient is asked to keep a 3-day or weekly food record with blood glucose-monitoring data.

## Evaluation and Documentation

Outcomes must be identified, and the effectiveness of nutrition interventions must be documented. Monitoring of medical and clinical outcomes should be done after the second or third visit to determine whether the patient is making progress toward established goals. If no progress is evident, the individual and dietitian need to reassess and perhaps revise the nutritional care plan. If altering food intake alone is not achieving metabolic target ranges, the dietitian should recommend that medications be added or adjusted.

Finally, documentation is essential for communication and reimbursement. Box 33-6 lists the areas of the nutrition intervention that require documentation.

## Follow-Up and Continuing Medical Nutrition Therapy

Successful nutrition therapy involves a process of assessment, problem solving, adjustment, and readjustment. Food records can be compared with the meal plan, which will help to determine whether the initial meal plan needs changing and can be integrated with the blood glucose-monitoring records to determine changes that can lead to improved glycemic control. For patients receiving oral medications or insulin, it can then be determined whether blood glucose values that are outside target ranges can be corrected with adjustments in the meal plan or whether adjustments in medications are needed.

After the basic food and nutrition strategies have been mastered, other aspects of nutrition education should be presented to increase flexibility in food choices and lifestyle while still maintaining glucose control. Of particular importance is information about eating out and the use of information from food labels. Persons using insulin also need information about how to make adjustments in food intake or insulin when schedules are disrupted.

Nutritional follow-up visits should provide encouragement and ensure realistic expectations for the patient. A change in eating habits is not easy for most people, and they become discouraged without appropriate recognition of their efforts. Patients should be encouraged to speak freely about problems they are having with food and eating patterns. Furthermore, there may be major life changes that require changes in the meal plan. Job and schedule changes, travel, illness, and other factors all have an impact on the meal plan.

**TABLE 33-13** Food-Planning Approaches for Diabetes

APPROACH	PUBLICATION	DESCRIPTION
<b>Diabetes nutrition guidelines</b>	<i>The First Step in Diabetes Meal Planning</i> (American Diabetes Association and American Dietetic Association)	A pamphlet that provides general guidelines for meal planning based on the Food Guide Pyramid. Designed to be given to patients to use until an individualized meal plan can be implemented; however, for some individuals there may be no need to advance to more complex meal-planning approaches.
	<i>Healthy Food Choices</i> (American Diabetes Association and American Dietetic Association)	A pamphlet that promotes healthy eating. It is divided into two sections: (1) guidelines for making healthy food choices and (2) simplified exchanges lists.
	<i>Healthy Eating for People With Diabetes</i> (International Diabetes Center, Minneapolis, Minn.)	Based on the <i>plate method</i> , which visualizes kinds and amounts of food and is used to illustrate portions of common foods in relation to plate size. General guidelines for choosing healthy foods, lowering fat intake, and timing of meals and snacks are included.
	<i>Eating Healthy With Diabetes Easy Reading Guide</i> (American Diabetes Association and American Dietetic Association)	A booklet designed specifically for persons with minimal reading skills. The amount of text is limited, symbols and color codes are used, and concepts and foods are presented visually.
<b>Menu approaches</b>	<i>Month of Meals: Classic Cooking, Old-Time Favorites, Meals in Minutes, Vegetarian Pleasures, and Ethnic Delights</i> (American Diabetes Association)	Separate books with each book containing 28 days of complete menus for breakfast, lunch, dinner, and snacks. Designed to help patients who need help in planning basic menus for their diabetes.
<b>Carbohydrate counting</b>	<i>Basic Carbohydrate Counting</i> (American Diabetes Association and American Dietetic Association)	A pamphlet that outlines what foods are carbohydrates, and average portions sizes. It can be used as a basic meal-planning approach for anyone with diabetes and is based on the concept that after eating, carbohydrate in foods has the major impact on blood glucose levels. One carbohydrate serving = 15 g of carbohydrate.
	<i>Advanced Carbohydrate Counting</i> (American Diabetes Association and American Dietetic Association)	A booklet for individuals who have chosen flexible insulin regimens or an insulin pump. The relationship between carbohydrate eaten and insulin injected can be shown as an insulin-to-carbohydrate ratio. This ratio gives the individual a good guide to how much bolus rapid-acting insulin is needed when eating more or less carbohydrate than usual; however, before insulin ratios can be established, blood glucose levels must be under good control and the usual dose of both the basal and rapid-acting (bolus) insulin determined. The grams of carbohydrate consumed at a meal are divided by the number of units of insulin needed to maintain target glucose goals. This is called an <i>insulin-to-carbohydrate ratio</i> . For example, 75 g of carbohydrate may require 8 units of rapid-acting insulin and the insulin-to-carbohydrate ratio would be 1:10. Therefore, for each anticipated addition of 10 g of carbohydrate an additional 1 unit of rapid-acting insulin is needed (or for 10 g less of carbohydrate, 1 less unit of rapid-acting insulin is needed).
	<i>My Food Plan</i> (International Diabetes Center, Minneapolis, Minn.)	A pamphlet that combines both carbohydrate counting and calorie control in a simplified approach. It groups carbohydrate, meat, and fat choices by approximate portion sizes. A form for filling in an individualized meal plan is included.
<b>Exchange list approaches</b>	<i>Exchange Lists for Meal Planning</i> (American Diabetes Association and American Dietetic Association) (See Appendix 53.)	A booklet that contains lists that group foods in measures that contribute approximately the same number of calories, carbohydrate, protein, and fat. Foods are divided into three basic lists: carbohydrates, meat and meat substitutes, and fat. An individualized food plan that outlines the number of servings from each list for each meal and for snacks is included.

Modified from Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.

### Box 33-6. Nutrition Care Documentation

Documentation of each MNT visit must include:

- Patient name and identification information
- Date of MNT visit and amount of time spent with patient
- Reason for visit
- Patient's current diagnosis (and relevant past diagnoses)
- Pertinent test results and current medications (name, dose)
- Names of others present during MNT
- Physician's referral for MNT (if billing Medicare)

Summaries of:

- Histories: nutrition, medical, social and family
- Nutrition risk factor assessment
- Nutrition problem list
- MNT intervention provided
  - Food and meal plan
  - Short- and long-term goals
  - Educational topics covered
- Short- and long-term goals
- RD's impressions, patient progress
  - Patient acceptance and understanding
  - Anticipated compliance
  - Successful behavior changes
- Plan of care
  - Additional needed skills or information
  - Additional recommendations
  - Plans for ongoing care

From Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.

MNT, Medical nutrition therapy; RD, registered dietitian.

## ACUTE COMPLICATIONS

Hypoglycemia, diabetic ketoacidosis, and hyperglycemic hyperosmolar state (HHS) are acute complications related to diabetes.

### Hypoglycemia

**Hypoglycemia (or insulin reaction)** is a common side effect of insulin therapy, although patients taking insulin secretagogues can also be affected. **Autonomic symptoms** are often the first signs of mild hypoglycemia and include shakiness, sweating, palpitations, and hunger. **Neuroglycopenic symptoms** can also occur at similar glucose levels as autonomic symptoms but with different manifestations. The earliest signs of neuroglycopenia include a slowing down in performance and difficulty concentrating and reading. As blood glucose levels drop further, the following symptoms occur: frank mental confusion

### Box 33-7. Common Causes of Hypoglycemia

- Medication errors
  - Excessive insulin or oral medications
  - Inadvertent or deliberate errors in insulin doses
  - Improper timing of insulin in relation to food intake
- Intensive insulin therapy
- Inadequate food intake
- Omitted or inadequate meals or snacks
- Delayed meals or snacks
- Increased exercise or activity
- Unplanned activities
- Prolonged duration or increased intensity of exercise
- Alcohol intake without food

Modified from Skyler JS, editor: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.

and disorientation, slurred or rambling speech, irrational or unusual behaviors, extreme fatigue and lethargy, seizures, and unconsciousness.

Several common causes of hypoglycemia are listed in Box 33-7. In general, a glucose of 70 mg/dl or lower should be treated immediately (Cryer et al, 1994). Even a level of 60 to 80 mg/dl may require a management decision (e.g., carbohydrate ingestion, deferral of exercise, change in insulin dosage). Treatment of hypoglycemia requires ingestion of glucose or carbohydrate-containing food. Although any carbohydrate will raise glucose levels, glucose is the preferred treatment. Commercially available glucose tablets have the advantage of being premeasured to help prevent overtreatment. Ingestion of 15 to 20 g of glucose is an effective but temporary treatment. Initial response to treatment should be seen in about 10 to 20 minutes; however, blood glucose should be evaluated again in about 60 minutes because additional treatment may be necessary (Box 33-8). The form of carbohydrate—liquid or solid—used to treat does not make a difference. Furthermore, adding protein to the carbohydrate does not assist in treatment or prevent subsequent hypoglycemia (Gray et al, 1996). If patients are unable to swallow, administration of subcutaneous or intramuscular glucagon may be needed. Parents, roommates, and spouses should be taught how to mix, draw up, and administer glucagon so that they are properly prepared for emergency situations. Kits that include a syringe pre-filled with diluting fluid are available.

Self-monitoring of blood glucose is essential for prevention and treatment of hypoglycemia. Changes in insulin injections, eating, exercise schedules, and travel routines warrant increased frequency of monitoring (Cryer et al, 2003). Some patients experience hypoglycemia unawareness, which means that they

### Box 33-8. Treatment of Hypoglycemia

- Immediate treatment with carbohydrate is essential.
  - If the blood glucose level falls below 70 mg/dl (3.9 mmol/L), treat with 15 g of carbohydrate, which is equivalent to:
    - 3 glucose tablets
    - Fruit juice or regular soft drinks, ½ c
    - Saltine crackers, 6
    - Sugar or honey, 1 tbsp
- Wait 15 minutes and retest. If the blood glucose level remains  $\leq 70$  mg/dl ( $\leq 3.9$  mmol/L), treat with another 15 g of carbohydrate.
- Repeat testing and treatment until the blood glucose level returns to within normal range.
- Evaluate the time to the next meal or snack to determine the need for additional food. If it is more than an hour to the next meal, add an additional 15 g of carbohydrate.

Modified from Skyler JS, editor: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.

do not experience the usual symptoms. Patients need to be reminded of the need to treat hypoglycemia, even in the absence of symptoms. Patients with recurrent hypoglycemia may not be good candidates for intensive insulin therapy.

## Hyperglycemia and Diabetic Ketoacidosis

Hyperglycemia can lead to **diabetic ketoacidosis (DKA)**, a life-threatening but reversible complication characterized by severe disturbances in carbohydrate, protein, and fat metabolism. DKA is always the result of inadequate insulin for glucose utilization. As a result, the body depends on fat for energy, and ketones are formed. Acidosis results from increased production and decreased utilization of acetoacetic acid and 3- $\beta$ -hydroxybutyric acid from fatty acids. These ketones spill into the urine, hence the reliance on testing for ketones.

Diabetic ketoacidosis is characterized by elevated blood glucose levels ( $\geq 250$  mg/dl but generally  $< 600$  mg/dl) and the presence of ketones in the blood and urine. Symptoms include polyuria, polydipsia, hyperventilation, dehydration, the fruity odor of ketones, and fatigue. SMBG, testing for ketones, and medical intervention can all help prevent DKA. If left untreated, DKA can lead to coma and death. Treatment includes supplemental insulin, fluid and electrolyte replacement, and medical monitoring. Acute illnesses, such as flu, colds, vomiting, and diarrhea, if not managed appropriately, can lead to the development of DKA. Patients need to know the steps to take during acute illness to prevent DKA

### Box 33-9. Sick-Day Guidelines for Persons With Diabetes

1. During acute illnesses, take usual doses of insulin. The need for insulin continues, or may even increase, during periods of illness. Fever, dehydration, infection, or the stress of illness can trigger the release of counterregulatory or “stress” hormones, causing blood glucose levels to become elevated.
2. Monitoring of blood glucose levels and urine or blood testing for ketones should be done at least four times daily (before each meal and at bedtime). Blood glucose readings exceeding 240 mg/dl and ketones are danger signals indicating that additional insulin is needed.
3. If regular foods are not tolerated, liquid or soft carbohydrate-containing foods (such as regular soft drinks, soup, juices, and ice cream) should be eaten. At least 50 g of carbohydrate (3 to 4 carbohydrate choices) should be consumed every 3 to 4 hr in small, frequent feedings.
4. Ample amounts of liquid should be consumed every hour. If nausea or vomiting occurs, small sips—1 or 2 tbsp every 15 to 30 min—should be consumed. If vomiting continues, the health care team should be notified.
5. The health care team should be called if illness continues for more than 1 day.

Modified from Franz MJ, Joynes JO: *Diabetes and brief illness*, Minneapolis, 1993, International Diabetes Center.

(Box 33-9). During acute illness, oral ingestion of about 150 to 200 g of carbohydrate per day should be sufficient, along with medication adjustments, to keep glucose in the goal range and to prevent starvation ketosis (ADA, 2002b).

## Fasting Hyperglycemia

The possible reasons for fasting hyperglycemia include waning of insulin action, the dawn phenomenon, and the **Somogyi (rebound) effect** (phenomenon). The first situation is due to an inadequate insulin dose overnight and requires an adjustment in insulin doses.

The amount of insulin required to normalize blood glucose levels during the night is less in the predawn period (from 1:00 to 3:00 AM) than at dawn (4:00 to 8:00 AM). This rise in fasting blood glucose levels is referred to as the **dawn phenomenon** and may result if insulin levels decline between predawn and dawn or if overnight hepatic glucose output becomes excessive as is common in type 2 diabetes. Blood glucose level is monitored at bedtime and at 2:00 to 3:00 AM to identify the dawn phenomenon. With the dawn

phenomenon, predawn blood glucose levels will be in the low range of normal but not in the hypoglycemic range. For patients with type 2 diabetes, metformin is often used because of its effect on hepatic glucose output. For persons with type 1 diabetes, administering insulin that does not peak at 1:00 to 3:00 AM should be considered. Taking intermediate-acting insulin at bedtime or substituting a peakless, long-acting insulin, such as glargine, is often effective.

Hypoglycemia followed by “rebound” hyperglycemia is called the Somogyi effect. This phenomenon originates during hypoglycemia with the secretion of counterregulatory hormones (glucagon, epinephrine, growth hormone, and cortisol) and is usually caused by excessive exogenous insulin doses. Hepatic glucose production is stimulated, thus raising blood glucose levels. If rebound hyperglycemia goes unrecognized and insulin doses are increased, a cycle of overinsulinization may result. Decreasing evening insulin doses or, as for the dawn phenomenon, taking intermediate-acting insulin at bedtime or substituting a long-acting insulin should be considered.

### Hyperosmolar Hyperglycemic State

*Hyperosmolar hyperglycemic state* is defined as an extremely high blood glucose level, the absence of or the presence of only small amounts of ketones, and profound dehydration. Glucose levels generally range from greater than 600 to 2000 mg/dl. Patients who have HHS have sufficient insulin to prevent lipolysis and ketosis. This condition occurs rarely, usually in older patients with type 2 diabetes. Treatment consists of hydration and small doses of insulin to correct the hyperglycemia.

## LONG-TERM COMPLICATIONS

Long-term complications of diabetes include macrovascular diseases, microvascular diseases, and neuropathy. **Macrovascular diseases** involve diseases of large blood vessels; **microvascular diseases** associated with diabetes involve the small blood vessels and include nephropathy and retinopathy. In contrast, diabetic neuropathy is a condition characterized by damage to the nerves.

Medical nutrition therapy is important in managing several long-term complications of diabetes. Nutrition therapy is also a major component in reducing risk factors for chronic complications, especially those related to macrovascular disease. The DCCT and the UKPDS provided convincing evidence for the relationship between improved control of blood glucose and decreased risk of microvascular complications (DCCT Research Group, 1993; UKPDSG, 1998a). Although improved glycemic control has not been absolutely proven to reduce macrovascular complications, accumulating evidence is quite sug-

gestive of such a benefit. Blood pressure control is definitely of benefit.

### Macrovascular Diseases

Insulin resistance, which may precede the development of type 2 diabetes and macrovascular disease by many years, induces numerous metabolic changes, known as the *metabolic syndrome* or the *insulin resistance syndrome*. It is characterized by intraabdominal obesity or the android distribution of adipose tissue (waist circumference greater than 102 cm [ $>40$  in] in men and greater than 88 cm [ $>35$  inches] in women) and is associated with dyslipidemia, hypertension, glucose intolerance, and increased prevalence of macrovascular complications. Other risk factors include genetics, smoking, sedentary lifestyle, high-fat diet, renal failure, and microalbuminuria.

Macrovascular diseases—including coronary heart disease (CHD), peripheral vascular disease (PVD), and cerebrovascular disease (CVD)—are more common, tend to occur at an earlier age, and are more extensive and severe in people with diabetes. Furthermore, in women with diabetes, the increased risk of mortality from heart disease is greater than in men, in contrast to the nondiabetic population, in which heart disease mortality is greater in men than in women (ADA, 2001).

### Dyslipidemia

Lipid abnormalities occur in 11% to 44% of adults in the United States with diabetes. In type 2 diabetes, the prevalence of an elevated cholesterol level is about 28% to 34%, and about 5% to 14% have high triglyceride levels; also, lower HDL cholesterol levels are common. Furthermore, patients with type 2 diabetes typically have smaller, denser LDL particles, which increases atherogenicity even if the total LDL cholesterol level is not significantly elevated. Primary therapy is directed first at lowering LDL cholesterol levels with the goal being to reduce LDL cholesterol concentrations to 100 mg/dl or lower. Lifestyle interventions should be intensified at LDL cholesterol concentrations greater than 100 mg/dl, and pharmacologic therapy with a statin (HMG-CoA reductase inhibitors) should be initiated at LDL cholesterol concentrations of 130 mg/dl or greater. In addition, if the HDL cholesterol is less than 40 mg/dl, a fibric acid such as fenofibrate can be used (ADA, 2002g). Aspirin therapy should be used in all adult patients with diabetes and macrovascular disease and for primary prevention in patients 40 years of age or older with diabetes and one or more cardiovascular risk factors (ADA, 2002a).

### Medical Nutrition Therapy for Dyslipidemia

For individuals with elevated LDL cholesterol, saturated fatty acids and trans fatty acids should be limited to less than 10% of energy and perhaps to less than 7% of energy and, if replaced, can be substituted

with carbohydrates or monounsaturated fats (ADA, 2002b).

For patients with the metabolic syndrome, improved glycemic control, modest weight loss, restricted intake of saturated fats, increased physical activity, and if weight is not an issue incorporation of monounsaturated fats may be beneficial (ADA, 2002b). In addition, triglyceride lowering can be achieved with very-high-dose statins (for subjects with both high LDL cholesterol and triglyceride levels) or fibric acid derivatives (gemfibrozil or fenofibrate).

Individuals with triglyceride measurements of 1000 mg/dl should restrict all types of dietary fat (except omega-3 fatty acids) and be treated with medication to reduce triglycerides. Supplementation with fish oils may benefit those with resistant hypertriglyceridemia (ADA, 2002b).

### Hypertension

Hypertension is a common comorbidity of diabetes, affecting 20% to 60% of persons with diabetes, depending on the person's age, obesity, and ethnicity. Treatment of hypertension in persons with diabetes should also be vigorous to reduce the risk of macrovascular and microvascular disease. Blood pressure should be measured at every routine visit with a goal for blood pressure control of less than 130/80 mm Hg. Patients with a systolic blood pressure of 130 to 139 mm Hg or a diastolic pressure of 80 to 89 mm Hg should be treated with MNT alone for a maximum of 3 months. Patients with a systolic blood pressure of 140 mm Hg or greater or a diastolic pressure of 90 mm Hg or greater should receive drug therapy in addition to MNT. Initial drug therapy may be with angiotensin-converting enzyme (ACE) inhibition, angiotensin receptor blockers (ARBs),  $\beta$ -blockers, or diuretics. Additional drugs may be chosen from these classes or another drug class if necessary to achieve target goals (ADA, 2002a).

### Medical Nutrition Therapy for Hypertension

Although blood pressure response varies widely, the lower the sodium intake, the greater the lowering of blood pressure (Sacks et al, 2001). Responses to sodium may be greater in subjects who are "sodium sensitive," a characteristic of many individuals with diabetes. Therefore, in normotensive and hypertensive persons, the goal should be to reduce sodium intake to 2400 mg of sodium or 6000 mg of sodium chloride (salt) per day. A modest amount of weight loss and a low-fat diet that includes fruits and vegetables (five to nine servings per day) and low-fat dairy products (two to four servings per day) will be rich in potassium, magnesium, and calcium and will beneficially affect blood pressure. Drinking small to moderate amounts of alcohol will not adversely affect blood pressure; however, large alcohol intakes (more than three drinks per day) are related to an elevation in blood pressure (ADA, 2002b).

## Microvascular Diseases

### Nephropathy

In the United States, diabetic nephropathy accounts for about 40% of new cases of end-stage renal disease (ESRD). About 20% to 30% of patients with type 1 or type 2 diabetes develop evidence of nephropathy, but in type 2 diabetes, a considerably smaller number will progress to ESRD; however, because of the greater prevalence of type 2 diabetes, such patients constitute more than half of the patients with diabetes currently starting on dialysis (ADA, 2002h).

The earliest clinical evidence of nephropathy is the appearance of low but abnormal urine albumin levels ( $>30$  mg daily or  $20 \mu\text{g}$  per minute), referred to as *microalbuminuria* or *incipient nephropathy*. Without specific interventions, progression to overt nephropathy or clinical albuminuria ( $\geq 300$  mg daily or  $200 \mu\text{g}$  per minute) with hypertension and a gradual decline in glomerular filtration rate (GFR) can occur, leading to the development of ESRD in both patients with type 1 diabetes and type 2 diabetes. An annual test for microalbuminuria should be performed in patients who have had type 1 diabetes for more than 5 years and in all patients with type 2 diabetes starting at diagnosis (ADA, 2002h).

Although diabetic nephropathy cannot be cured, persuasive data indicate that the clinical course of the disease can be modified. To reduce the risk or slow the progression of nephropathy, glucose and blood pressure control should be optimized. In hypertensive and nonhypertensive patients with type 1 diabetes, ACE inhibitors are the initial agents of choice. In hypertensive patients with type 2 diabetes, angiotensin receptor blockers (ARBs) are the initial agents of choice. If one class is not tolerated, the other should be substituted and their combination will decrease albuminuria more than use of either agent alone (ADA, 2002h).

### Medical Nutrition Therapy for Nephropathy

With the onset of nephropathy, restricted-protein diets may modify the underlying glomerular injury and, along with control of hypertension and hyperglycemia, delay the progression of renal failure (Pedrini et al, 1996; Zeller et al, 1991). Several studies that attempted to reduce protein intake in persons with type 1 or type 2 diabetes and microalbuminuria achieved a protein reduction to about 1.0 g per kilogram of body weight. In a dose-response analysis (Pijs et al, 1999), a 0.1 g per kilogram of body weight per day decrease in the intake of protein was related to an improvement of 11.1% in albuminuria. In studies conducted in subjects with type 1 diabetes and macroalbuminuria (overt nephropathy), the achieved protein restriction was for about 0.8 g per kilogram of body weight daily, which slowed the rate of decline in the GFR significantly over 32 to 35 months (Walker et al, 1989; Zeller et al, 1991). In patients with microalbuminuria, a limit of protein to 0.8 to 1.0 g per

kilogram of body weight daily and for patients with overt nephropathy, limiting protein to 0.8 g per kilogram of body weight daily is recommended (ADA, 2002b).

A few studies have explored the potential benefit of plant protein rather than animal protein (Kontesis et al, 1995). In general, the subjects have been normoalbuminuric, normotensive, and not hyperfiltering so that benefits may not have been expected. Furthermore, when plant protein is substituted for animal protein, the amount of protein consumed was also reduced and the beneficial effect may have been from a reduction in protein content or from the change in protein source. Long-term clinical trials are needed to determine whether reductions in animal protein or changes in plant or animal protein will have a beneficial effect on diabetic nephropathy (ADA, 2002b).

### Retinopathy

Diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults 20 to 74 years of age. After 20 years of diabetes, nearly all patients with type 1 diabetes and more than 60% of patients with type 2 diabetes have some degree of retinopathy. Laser photocoagulation surgery can reduce the risk of further vision loss but generally is not beneficial in reversing already diminished acuity—thus the importance for a screening program to detect diabetic retinopathy. An initial dilated and comprehensive eye examination should be done in patients 10 years of age and older with type 1 diabetes and in patients with type 2 diabetes shortly after the diagnosis of diabetes. Subsequent examinations for both groups should be done annually (ADA, 2002i).

There are three stages of diabetic retinopathy. The early stages of nonproliferative diabetic retinopathy (NPDR) are characterized by microaneurysms; a pouchlike dilation of a terminal capillary; lesions that include cotton-wool spots (also referred to as *soft exudates*); and the formation of new blood vessels as a result of the retina's great metabolic need for oxygen and other nutrients supplied by the bloodstream. As the disease progresses to the middle stages of moderate, severe, and very severe NPDR, gradual loss of the retinal microvasculature occurs, resulting in retinal ischemia. Extensive intraretinal hemorrhages and microaneurysms are common reflections of increasing retinal nonperfusion.

The most advanced stage—termed *proliferative diabetic retinopathy (PDR)*—is the final and most vision-threatening stage of diabetic retinopathy. It is characterized by the onset of ischemia-induced new vessel proliferation at the optic disk or elsewhere in the retina. The new vessels are fragile and prone to bleeding, resulting in vitreous hemorrhage. With time, the neovascularization tends to undergo fibrosis and contraction, resulting in retinal traction, retinal tears, vitreous hemorrhage, and retinal detachment. *Diabetic macular edema*, which involves thickening of the cen-

tral (macular) portion of the retina, and glaucoma, in which fibrous scar tissue increases intraocular pressure, are other clinical findings in retinopathy (Aiello et al, 1998).

### Neuropathy

Chronic high levels of blood glucose are also associated with nerve damage and affects 60% to 70% of patients with both type 1 and type 2 diabetes (ADA, 2001). Peripheral neuropathy usually affects the nerves that control sensation in the feet and hands. Autonomic neuropathy affects nerve function controlling various organ systems. Cardiovascular effects include postural hypotension and decreased responsiveness to cardiac nerve impulses, leading to painless or silent ischemic heart disease. Sexual function may be affected, with impotence the most common manifestation. Damage to nerves innervating the gastrointestinal tract can cause a variety of problems. Neuropathy can be manifested in the esophagus as nausea and esophagitis, in the stomach as unpredictable emptying, in the small bowel as loss of nutrients, and in the large bowel as diarrhea or constipation. Intensive treatment of hyperglycemia reduces the risk of developing diabetic neuropathy.

### Gastroparesis

Gastroparesis (impaired gastric motility) affects about 25% of this population and is perhaps the most frustrating condition that patients and dietitians experience. It results in delayed or irregular contractions of the stomach, leading to various gastrointestinal symptoms, such as feelings of fullness, bloating, nausea, vomiting, diarrhea, or constipation. It can cause detrimental effects on blood glucose control.

### Medical Nutrition Therapy for Gastroparesis

Treatment involves minimizing abdominal stress. Small, frequent meals may be better tolerated than three full meals a day, and these meals should be low in fiber and fat. If solid foods are not well tolerated, liquid meals may need to be recommended. As much as possible, the timing of insulin administration should be adjusted to match the usually delayed nutrient absorption. This may even require insulin injections after eating. Frequent blood glucose monitoring is important to determine appropriate insulin therapy.

## PREVENTING DIABETES

The development of type 2 diabetes is strongly related to lifestyle factors, thus suggesting to researchers that it might be a preventable disease. Supporting evidence comes from both observational and interven-

tion studies. Observational studies addressing physical activity, weight loss, and dietary intake, including whole grains and fiber and dietary fat, provided evidence for factors that might delay or prevent type 2 diabetes (Wing, 1999). Early intervention trials also provided support for the benefits of lifestyle interventions, but all had methodologic limitations. Based on these observational and intervention studies, the Finnish Diabetes Prevention Study (Tuomilehto et al, 2001) and the Diabetes Prevention Program (Diabetes Prevention Program Research Group, 2002) were designed to investigate the effects of lifestyle interventions on prevention of diabetes in those at high risk (IGT).

In the Finnish study, 522 middle-aged, overweight subjects with IGT were randomized to receive either brief diet and exercise counseling (control group) or intensive individualized instruction on how to reduce weight (goal of 5% weight reduction), total intake of fat (goal of <30% of energy intake), and saturated fat (goal of <10% of energy intake) and how to increase fiber intake (goal of  $\geq 15$  g/1000 kcal) and physical activity (goal of >150 minutes weekly). After an average follow-up of 3.2 years, there was a 58% reduction in the incidence of type 2 diabetes in the intervention group compared with the control group. The reduction in the incidence of diabetes was directly associated with the ability of the subjects to achieve one or more of the lifestyle strategies.

The Diabetes Prevention Program (DPP) randomized 3234 persons (45% from minority groups) with IGT to placebo, metformin, or a lifestyle intervention. Subjects in the placebo and medication arms received standard lifestyle recommendations that included written information and an annual 20- to 30-minute individual session. Subjects in the lifestyle arm were expected to achieve and maintain a weight loss of at least 7% and to perform 150 minutes of physical activity per week. Subjects were seen weekly for the first 24 weeks, followed by monthly sessions. After an average follow-up of 2.8 years, a 58% decrease in the progression to diabetes was observed in the lifestyle group and a 31% relative reduction was observed in the metformin group. On average, 59% of the lifestyle group achieved the goal of 7% or greater weight reduction and 74% maintained at least 150 minutes per week of moderately intense activity.

The greater benefit of weight loss and physical activity over medication strongly suggests that lifestyle modification should be the first choices to prevent or delay diabetes. Modest weight loss (5%-10% of body weight) and modest physical activity (30 minutes daily) are the recommended goals (ADA, 2002j). Structured programs that emphasize lifestyle changes are necessary to accomplish these objectives.

No nutritional recommendations can be made for the prevention of type 1 diabetes. Breast-feeding may be of benefit. Although increased obesity in youth may be related to an increased prevalence of type 2

diabetes, research supporting lifestyle interventions is not available. Increased physical activity, reduced energy and fat intake, and resultant weight management may be beneficial.

## HYPOGLYCEMIA OF NONDIABETIC ORIGIN

**Hypoglycemia of nondiabetic origin** has been defined as a clinical syndrome with diverse causes in which low levels of plasma glucose eventually lead to neuroglycopenia (Service, 1995). Hypoglycemia literally means low (hypo) blood glucose (glycemia). Normally, the body is remarkably adept at maintaining fairly steady blood glucose levels—usually between 60 and 100 mg/dl (3.3 to 5.6 mmol/L), despite the intermittent ingestion of food. Maintaining normal levels of glucose is important because body cells, especially the brain and central nervous system, must have a steady and consistent supply of glucose to function properly. Under physiologic conditions, the brain depends almost exclusively on glucose for its energy needs. Even with hunger, either because it is many hours since food was eaten or because the last meal was small, blood glucose levels remain fairly consistent.

### Pathophysiology

In a small number of people, however, blood glucose levels become too low. If the brain and nervous system are deprived of the glucose they need to function, symptoms, such as sweating, shaking, weakness, hunger, headaches, and irritability, can develop. Hypoglycemia can be difficult to diagnose because these typical symptoms can be caused by many different health problems besides hypoglycemia. For example, adrenaline (epinephrine), released as a result of anxiety and stress, can trigger the symptoms of hypoglycemia. The only way to determine whether hypoglycemia is causing these symptoms is to measure blood glucose levels while an individual is experiencing the symptoms (Brun, Fedou, and Mercier, 2000). Hypoglycemia, therefore, can best be defined by the presence of three features known as **Whipple's triad**: (1) a low plasma or blood glucose level; (2) symptoms of hypoglycemia at the same time as the low blood glucose values; and (3) amelioration of the symptoms by correction of the hypoglycemia (Prince, 1997). A fairly steady blood glucose level is maintained by the interaction of several mechanisms. After eating, food is broken down into glucose and enters the bloodstream. As blood glucose levels rise, the pancreas responds by releasing the hormone insulin, which allows glucose to leave the bloodstream and enter various body cells where it fuels the body's activities. Glucose is also taken up by the liver and

stored as glycogen for later use. When glucose concentrations from the last meal decline, the body goes from a “fed” to a “fasting” state. Insulin levels decrease, which keeps the blood glucose levels from falling too low. In addition, stored glucose is released from the liver back into the bloodstream with the help of *glucagon*, a hormone that is also released from the pancreas. Normally, the body’s ability to balance glucose, insulin, and glucagon (and other counter-regulatory hormones) keeps glucose levels within the normal range. Glucagon provides the primary defense against hypoglycemia; without it full recovery does not occur. Epinephrine is not necessary for counterregulation when glucagon is present. In the absence of glucagon, however, epinephrine has an important role (Cryer, 1993).

Symptoms of hypoglycemia have been recognized at plasma glucose levels of about 60 mg/dl, and impaired brain function has occurred at levels of about 50 mg/dl (Mitrakou et al, 1991). Symptoms are classified into two major groups: those that arise from the action of the autonomic nervous system (adrenergic symptoms) and those related to an insufficient supply of glucose to the brain (neuroglycopenic symptoms). Adrenergic symptoms include sweating, trembling, feelings of warmth, anxiety, and nausea. Symptoms of neuroglycopenia include dizziness, confusion, tiredness, difficulty speaking, headaches, and inability to concentrate. Hunger, blurred vision, drowsiness, and weakness are other symptoms some people experience. Symptoms differ for different people but are consistent from episode to episode for any one person. Furthermore, there is not a consistent chronologic order to the evolution of symptoms; autonomic symptoms do not always precede neuroglycopenic ones. In many persons, neuroglycopenic symptoms are the only ones observed. Hypoglycemia is the cause for any of these symptoms only if blood glucose levels are determined to be below normal at the time the symptoms occur.

## Types of Hypoglycemia

If blood glucose levels fall below normal limits within 2 to 5 hours after eating, this is often referred to as reactive hypoglycemia (named because the body is reacting to food) or **postprandial (reactive) hypoglycemia**. Postprandial hypoglycemia can be caused by an exaggerated insulin response caused by either insulin resistance or elevated glucagon-like-peptide-1 (GLP-1), alimentary hyperinsulinism, renal glycosuria, defects in glucagon response, high insulin sensitivity, or rare syndromes, such as hereditary fructose intolerance, galactosemia, leucine sensitivity, or a rare  $\beta$ -cell pancreatic tumor (insulinoma) (Brun, Fedou, and Mercier, 2000).

*Alimentary hyperinsulinism* is the most common type of documented postprandial hypoglycemia and is seen in patients who have undergone gastric sur-

gery or some other type of gastric surgery (Gebhard et al, 2001) (see Chapter 29). These procedures are associated with rapid delivery of food to the small intestine, rapid absorption of glucose, and exaggerated insulin response. These patients respond best to multiple, frequent feedings (Prince, 1997).  $\alpha$ -Glucosidase inhibitors such as acarbose may also be helpful because they decrease the absorption of carbohydrates (Hasler, 2002).

The ingestion of alcohol after a prolonged fast, or the ingestion of large amounts of alcohol and carbohydrate on an empty stomach (“gin-and-tonic” syndrome) may also cause hypoglycemia within 3 to 4 hours in some healthy persons.

*Idiopathic reactive hypoglycemia* is characterized by normal insulin secretion but increased insulin sensitivity and, to some extent, reduced response of glucagon to acute hypoglycemia symptoms (Brun, Fedou, and Mercier, 2000). The increase in insulin sensitivity associated with a deficiency of glucagon secretion leads to hypoglycemia late postprandially (Leonetti et al, 1996). Idiopathic reactive hypoglycemia has been inappropriately overdiagnosed by both physicians and patients, to the point that some physicians doubt its existence. Although rare, it does exist but can be documented only in persons with hypoglycemia that occurs spontaneously and who meet the criteria of Whipple’s triad.

**Fasting (food-deprived) hypoglycemia** may occur in response to having gone without food for 8 hours or longer; however, generally, fasting hypoglycemia is the result of a serious underlying medical condition. Causes of fasting hypoglycemia include hormone deficiency states (e.g., hypopituitarism, adrenal insufficiency, catecholamine or glucagon deficiency), acquired liver disease, renal disease, certain drugs (e.g., alcohol, propranolol, salicylate), insulinoma (of which most are benign, but 6% to 10% can be malignant), and other nonpancreatic tumors. Factitious hypoglycemia, or self-administration of insulin or sulfonylurea in persons who do not have diabetes, is a common cause as well (Prince, 1997). Symptoms related to fasting hypoglycemia tend to be particularly severe and can include a loss of mental acuity, seizures, and unconsciousness. If the underlying problem can be resolved, hypoglycemia is no longer a problem.

## Diagnostic Criteria

One of the criteria used to confirm the presence of hypoglycemia is a blood glucose level of less than 50 mg/dl (<2.8 mmol/L). Previously, the oral glucose tolerance test was the standard test for this condition; however, this test is not helpful because it involves a nonphysiologic stimulus and because results show little correlation with persons who later are documented to have hypoglycemia. Recording fingerstick blood glucose measurements during spontaneously

occurring symptomatic episodes at home is a method that is often used to establish the diagnosis. An alternative method is to perform a glucose test in a medical office setting, in which case the patient is given a typical meal that has been documented in the past to lead to symptomatic episodes; Whipple's triad can be confirmed if symptoms occur (Prince, 1997). If blood glucose levels are low during the symptomatic period, and if the symptoms disappear upon eating, hypoglycemia is probably responsible. It is essential to make a correct diagnosis in patients with fasting hypoglycemia because the implications for therapy are serious.

## Management of Hypoglycemia

The management of hypoglycemic disorders involves two distinct components: (1) relief of neuroglycopenic symptoms by the restoration of blood glucose concentrations to the normal range and (2) correction of the underlying cause. The immediate treatment is to eat foods or beverages containing carbohydrate. As the glucose from the breakdown of carbohydrate is absorbed into the bloodstream, it will increase the level of glucose in the blood and relieve the symptoms. If an underlying problem is causing hypoglycemia, appropriate treatment of this disease or disorder is essential.

Almost no research has been done to determine what type of food-related treatment is best for the prevention of hypoglycemia. Traditional advice has been to avoid foods containing sugars and to eat protein- and fat-containing foods. Recent research on the glycemic index and sugars has raised questions about the appropriateness of restricting only sugars because these foods have been reported to have a lower glycemic index than many of the starches that were encouraged in the past. Restriction of sugars may contribute to a decreased intake in total carbohydrate, which may be more important than the source of the carbohydrate.

Using the following information, guidelines for the prevention of hypoglycemia have been published (International Diabetes Center, 1998). It is helpful to review metabolism of carbohydrates, protein, and fat; their effects on blood glucose levels and their relationship to insulin secretion. It should be remembered that this research has been conducted using normal subjects, not subjects who have been diagnosed with hypoglycemia.

After digestion, the major macronutrients absorbed are glucose, fructose, galactose, amino acids, and fatty acids that are reconstituted into triglycerides in chylomicrons. Glucose, fructose, and galactose are the major absorbed products of carbohydrate-containing foods, with about 75% being glucose, 22% being fructose and 3% as galactose. The effect of these absorbed sugars on plasma glucose levels and insulin response is different for each (Nuttall and Gannon, 1991a). Fructose ingestion in normal subjects results

in little increase in glucose concentrations and little or no change in insulin concentrations. Ingestion of galactose (initially lactose) results in only a modest increase in peripheral glucose concentrations and a modest rise in insulin, which is attributable to the rise in glucose. Fructose and galactose appear to be used primarily for glycogen synthesis in the liver (Gannon et al, 2001). Blood glucose levels generally return to premeal levels after about 4 hours; with smaller amounts of carbohydrate, this time span is shortened.

The amount of insulin secreted after glucose ingestion depends more on the amount of glucose ingested than on the magnitude of the glucose increase (Castro et al, 1970). Quantitatively, the increase in insulin concentration greatly exceeds the increase in glucose concentration. For example, the maximal glucose concentration typically does not exceed 50% of the premeal value, whereas the increase in insulin concentration is commonly 800% to 900%.

Overall, the system is designed to maintain the circulating glucose concentration in the nonfed state within narrowly defined limits. It is also designed to allow only a modest rise in glucose after carbohydrate-containing meals and to return glucose concentrations rapidly to the nonfed state. Most of the insulin secreted during a 24-hour period is secreted during times of the day when ingested food is not being assimilated, that is, as basal insulin secretion (Nuttall and Gannon, 1991a).

Ingested protein does not raise the plasma glucose concentrations in normal subjects, even when ingested in large amounts, although 50% to 70% of the ingested protein can be accounted for by deaminated amino acids and urea synthesis in the liver. Presumably, most deaminated amino acids are converted to glucose (Nuttall and Gannon, 1991b).

Although fat does not independently stimulate insulin secretion, it also does not affect the circulating glucose concentration. However, when fat is ingested with carbohydrate, the plasma glucose and insulin responses are modified. This is an area that requires additional research. Preliminary evidence also suggests that a high fat intake may contribute to insulin resistance.

The goal of treatment is to adopt eating habits that will keep blood glucose levels as static as possible. Recommended guidelines are listed in Box 33-10. Patients with hypoglycemia may also benefit from learning carbohydrate counting and limiting carbohydrate servings (15 g of carbohydrate per serving) to two to four at a meal and one to two for snacks (see Appendix 53). Foods containing protein that are also low in fat can be eaten at meals or with snacks. These foods would be expected to have minimal effect on blood glucose levels and can add extra food for satiety and calories. Because protein as well as carbohydrate stimulates insulin release, however, a moderate intake may be advisable.

### Box 33-10. Guidelines for Avoiding Hypoglycemic Symptoms

1. Eat small meals, with snacks interspersed between meals and at bedtime. This means eating five to six small meals rather than two to three large meals to steady the release of glucose into the bloodstream.
2. Spread the intake of carbohydrate foods throughout the day. Eating large amounts of carbohydrate at one time produces increased amounts of glucose and stimulates the release of increased amounts of insulin, which can cause blood glucose levels to drop. Most individuals can eat two to four servings of carbohydrate foods at each meal and one to two servings at each snack. Furthermore, if carbohydrate is removed from the diet, the body loses its ability to handle carbohydrate properly. Carbohydrate foods include starches, fruits and fruit juices, milk and yogurt, and foods containing sugar.
3. Avoid foods that contain large amounts of carbohydrate. Examples of these foods are regular soft drinks, syrups, candy, regular fruited yogurts, pies, and cakes.
4. Avoid beverages and foods containing caffeine. Caffeine can cause the same symptoms as hypoglycemia and make the individual feel worse (Kerr et al, 1993).
5. Limit or avoid alcoholic beverages. Drinking alcohol on an empty stomach and without food can lower blood glucose levels by interfering with the liver's ability to release stored glucose (gluconeogenesis) (Franz, 1999). If an individual chooses to drink alcohol, it should be done in moderation (one or two drinks no more than twice a week), and food should always be eaten along with the alcoholic beverage.
6. Decrease fat intake. A high-fat diet, especially saturated fat, has been shown to affect the body's ability to use insulin (insulin resistance). Decreasing fat intake can also help with weight loss, if weight is a problem. Excess weight also interferes with the body's ability to use insulin.

Modified from International Diabetes Center: *Reactive and fasting hypoglycemia*, Minneapolis, 1998, International Diabetes Center.

## SUMMARY

In summary, nutrition is a challenging aspect of the management of diabetes and hypoglycemia of nondiabetic origin. Attention to nutrition and meal-planning principles is essential for glycemic control

and overall good health. A registered dietitian who is knowledgeable and skilled in implementing current nutrition principles and making recommendations for diabetes or hypoglycemia of nondiabetic origin is the medical team member who should plan, implement, and evaluate MNT. Outcomes must be identified, and the effectiveness of nutrition interventions continually documented.

### Clinical Scenario 1: Type 1 Diabetes

Ellen is a 15-year-old girl with newly diagnosed type 1 diabetes. She is 5 ft 2 in. tall, weighs 115 lb, and is active in cheerleading and basketball in high school. Her physician will be regulating the dosage and timing of her insulin regimen.

Her grandmother has diabetes and is supportive of Ellen's need for education. Ellen's parents are divorced, and she now lives with her grandmother. What steps should you, as her nutrition counselor, take?

1. What food and meal-planning information needs to be shared with the health care team as insulin therapy is integrated into Ellen's normal eating and exercise habits?
2. What guidance should you offer regarding Ellen's sports activities?
3. Ellen is worried about keeping up with her peers. How will you help her adapt to the possible need for snacks during exercise and during a busy school day or during activities with her friends?
4. When Ellen travels on field trips or vacations, what types of food can she pack to take along?
5. What signs and symptoms of lack of diabetes control must Ellen understand to manage her disease? Which problem is she more likely to experience—hyperglycemia or hypoglycemia?

### Clinical Scenario 2: Type 2 Diabetes

Debra is a 45-year-old woman with a known diagnosis of type 2 diabetes for 3 years. She has not had a medical check-up for 2 years. She returns at this time with a primary complaint of chronic fatigue. Her laboratory test results show the following: HbA1c 8.3%; serum cholesterol 214 mg/dl; triglycerides 275 mg/dl. Her current weight is 175 lb., and her height is 64 in. (BMI = 30). She states she hasn't returned for any follow-up visits because the only advice she gets is to lose weight and not to eat sugar, neither of which she is able to do.

1. What advice will you offer to improve Debra's metabolic parameters and, in particular, to improve her blood glucose control?
2. What guidelines for carbohydrate intake can help Debra improve her glycemia?
3. What suggestions will you have about fat intake?
4. What information will you share about exercise?
5. What meal-planning method do you suggest for her?
6. What will you recommend regarding her sugar intake?

### Clinical Scenario 3: Type 2 Diabetes

John is a moderately obese (BMI = 29) 49-year-old man who complains of increased thirst, polyuria, and fatigue. His family history includes his mother and an older brother with type 2 diabetes. A random (casual) plasma glucose test shows a level of 480 mg/dl. His serum electrolyte level and anion gap are normal.

He reports finding it difficult to control his eating during the evening and because of his long working hours finds it difficult to work in an hour for exercise most days. When asked what he is interested in learning about, he replies that he would like to learn how to control his eating because he is always hungry.

1. What type of diabetes does John likely have? Is it likely to be controlled by nutrition therapy alone?
2. Given the symptoms of hyperglycemia, is it more likely that an oral agent or insulin therapy will be recommended?
3. If John is started on medication, are lifestyle strategies still important?
4. What advice can you give to John to help him with his eating problems?
5. What other lifestyle strategies will be helpful?

### Relevant Web Sites

#### American Association of Diabetes Educators

[www.aadenet.org](http://www.aadenet.org)

#### American Diabetes Association

[www.diabetes.org](http://www.diabetes.org)

#### American Dietetic Association, Diabetes Care and Education Practice Group

[www.dce.org](http://www.dce.org)

#### Children With Diabetes

[www.childrenwithdiabetes.com](http://www.childrenwithdiabetes.com)

#### Coverage for Medical Nutrition Therapy

[www.eatright.org/gov/reimbursement.html](http://www.eatright.org/gov/reimbursement.html)

#### Healthy Weight Network

[www.healthyweight.net](http://www.healthyweight.net)

#### International Diabetes Center, Minneapolis, Minnesota

[www.idcdiabetes.org](http://www.idcdiabetes.org)

#### Lifestyle Manuals Used in the Diabetes Prevention Program

[www.bsc.gwu.edu/dpp](http://www.bsc.gwu.edu/dpp)

#### National Institute of Diabetes and Digestive Kidney Diseases

[www.niddk.nih.gov](http://www.niddk.nih.gov)

### Cited References

- Aiello LP et al: Diabetic retinopathy [Technical Review], *Diabetes Care* 21:143, 1998.
- Albright A et al: American College of Sports Medicine position stand: exercise and type 2 diabetes, *Med Sci Sports Exerc* 32:1345, 2000.
- American Diabetes Association: Type 2 diabetes in children and adolescents [Consensus Statement], *Diabetes Care* 23:381, 2000.
- American Diabetes Association: *Diabetes 2001 vital statistics*, Alexandria, Va, 2001, American Diabetes Association.
- American Diabetes Association: Standards of medical care for patients with diabetes mellitus [Position Statement], *Diabetes Care* 25(suppl 1):S33, 2002a.
- American Diabetes Association: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications [Position Statement], *Diabetes Care* 25:202, 2002b.
- American Diabetes Association: Diabetes mellitus and exercise [Position Statement], *Diabetes Care* 25(suppl 1):S64, 2002c.
- American Diabetes Association: Tests of glycemia in diabetes [Position Statement], *Diabetes Care* 25(suppl 1):S97, 2002d.
- American Diabetes Association: Gestational diabetes mellitus [Position Statement], *Diabetes Care* 25(suppl 1):S94, 2002e.
- American Diabetes Association: Translation of the diabetes nutrition recommendations for health care institutions, *Diabetes Care* 25(suppl 1):S61, 2002f.
- American Diabetes Association: Management of dyslipidemia in adults [Position Statement], *Diabetes Care* 25(suppl 1):S74, 2002g.
- American Diabetes Association: Diabetic nephropathy [Position Statement], *Diabetes Care* 25(suppl 1):S90, 2002h.
- American Diabetes Association: Diabetic retinopathy [Position Statement], *Diabetes Care* 25(suppl 1):S90, 2002i.
- American Diabetes Association: The prevention or delay of type 2 diabetes [Position Statement], *Diabetes Care* 25:2002j.
- American Dietetic Association: *Medical nutrition therapy evidence-based guides for practice: nutrition practice guidelines for type 1 and type 2 diabetes*, CD-Rom, Chicago, 2001, American Dietetic Association.
- American Diabetes Association and American Dietetic Association: *Exchange lists for meal planning*, Alexandria, Va, 2003, American Diabetes Association.
- American Diabetes Association: Economic costs of diabetes in the U.S. in 2002, *Diabetes Care* 26:917, 2003a.
- American Diabetes Association: Management of dyslipidemia in children and adolescents with diabetes [Consensus Statement], *Diabetes Care*, 26:2194, 2003b.
- Anderson RA et al: Beneficial effects of chromium for people with diabetes, *Diabetes* 46:1786, 1997.
- Bantle JP et al: Metabolic effects of dietary fructose in diabetic subjects, *Diabetes Care* 15:1468, 1992.
- Bantle JP et al: Metabolic effects of dietary sucrose in type II diabetic subjects, *Diabetes Care* 16:1301, 1993.
- Bantle JP et al: Effects of dietary fructose on plasma lipids in healthy subjects, *Am J Clin Nutr* 72:1128, 2000.
- Bergman RN, Adler M: Free fatty acids and pathogenesis of type 2 diabetes mellitus, *Trends Endocr Metab* 11:351, 2000.
- Bode BW, Strange P: Efficacy, safety, and pump compatibility of insulin aspart use in continuous subcutaneous insulin infusion therapy in patients with type 1 diabetes, *Diabetes Care* 24:69, 2001.
- Brodsky IG, Devlin JT: Effects of dietary protein restriction on regional amino acid metabolism in insulin-dependent diabetes mellitus, *Am J Physiol* 270:E148, 1996.
- Brown L et al: Cholesterol-lowering effects of dietary fiber: a meta-analysis, *Am J Clin Nutr* 69:30, 1999.
- Brun JF, Fedou C, Mercier J: Postprandial reactive hypoglycemia, *Diabetes Metab* 26:337, 2000.
- Burge MR, Schade DS: Insulins, *Endocrinol Metab Clin North Am* 26:575, 1997.
- Butchko HH, Stargel WW: Aspartame: scientific evaluation in the postmarketing period, *Regul Toxicol Pharmacol* 34:221, 2001.
- Carmichael HE et al: Lower fat intake as a predictor of initial and sustained weight loss in obese subjects consuming an otherwise ad libitum diet, *J Am Diet Assoc* 98:35, 1998.
- Castro A et al: Plasma insulin and glucose responses of healthy subjects to varying glucose loads during three-hour oral glucose tolerance tests, *Diabetes* 19:842, 1970.
- Chandalia M et al: Beneficial effects of a high dietary fiber intake in patients with type 2 diabetes, *N Engl J Med* 342:1392, 2000.
- Chaturvedi N, Fuller JH: The WHO Multinational Study of vascular disease in diabetes: mortality risk in body weight and weight change in people with NIDDM, *Diabetes Care* 18:766, 1995.

- Chaturvedi N et al: The WHO Multinational Study of vascular disease in diabetes: mortality and morbidity associated with body weight in people with IDDM, *Diabetes Care* 18:761, 1995.
- Cheng N et al: Follow-up survey of people in China with type 2 diabetes mellitus consuming supplemental chromium, *J Trace Elem Exp Med* 12:55, 1999.
- Coniff RF et al: Reduction of glycosylated hemoglobin and postprandial hyperglycemia by acarbose in patients with NIDDM, *Diabetes Care* 18:817, 1995.
- Cowie CC, Harris MI: Physical and metabolic characteristics of persons with diabetes. In National Diabetes Data Group, editors: *Diabetes in America*, ed 2, Bethesda Md, National Institutes of Health, NIDDK, 1995 (NIH publ No. 95-1468).
- Cryer PE: Glucose counterregulation: the physiological mechanisms that prevent or correct hypoglycemia. In Frier BM, Fisher BS, editors: *Hypoglycemia and diabetes: clinical and physiological aspects*, London, 1993, Edward Arnold.
- Cryer PE et al: Hypoglycemia in diabetes [Technical review], *Diabetes Care* 26:1902, 2003.
- Davis SN et al: Effects of antecedent hypoglycemia on subsequent counterregulatory responses to exercise, *Diabetes* 49:73, 2000.
- Delahanty LM, Halford BN: The role of diet behaviors in achieving improved glycemic control in intensively treated patients in the Diabetes Control and Complications Trial, *Diabetes Care* 16:1453, 1993.
- Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, *N Engl J Med* 339:977, 1993.
- Diabetes Control and Complications Trial Research Group: Implementation of treatment protocols in the Diabetes Control and Complications Trial, *Diabetes Care* 18:36, 1995.
- Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin, *N Engl J Med* 346:393, 2002.
- Drash A: The child, the adolescent and the Diabetes Control and Complications Trial, *Diabetes Care* 16:1515, 1993.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, *Diabetes Care* 20:1183, 1997.
- Ferrannini E: Insulin resistance versus insulin deficiency in noninsulin-dependent diabetes mellitus: problems and prospects, *Endocr Rev* 19:477, 1998.
- Franz MJ: Alcohol and diabetes. In Franz MJ, Bantle JP, editors: *American Diabetes Association guide to medical nutrition therapy for diabetes*, Alexandria, Va, 1999, American Diabetes Association.
- Franz MJ: Protein controversies in diabetes, *Diabetes Spect* 13:132, 2000.
- Franz MJ: Carbohydrate and diabetes: is the source or the amount of more importance *Curr Diabetes Rep* 1:177, 2001.
- Franz MJ: Nutrition, physical activity, and diabetes. In Ruderman N, editor: *Handbook of exercise in diabetes*, Alexandria, Va 2002, American Diabetes Association.
- Franz MJ, Joynes JO: *Diabetes and brief illness*, Minneapolis, 1993, International Diabetes Center.
- Franz MJ, Reader D, Monk A: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.
- Franz MJ et al: Nutrition principles for the management of diabetes and related complications [Technical Review], *Diabetes Care* 17:490, 1994.
- Franz MJ et al: Nutrition practice guidelines and basic care by dietitians for persons with non-insulin-dependent diabetes mellitus: medical and clinical outcomes, *J Am Diet Assoc* 95:1009, 1995.
- Franz MJ et al: Evidence-based nutrition principles and recommendations for treatment and prevention of diabetes and related complications [Technical Review], *Diabetes Care* 25:148, 2002.
- Gannon MC et al: Effect of protein ingestion on the glucose appearance rate in people with type 2 diabetes, *J Clin Endocrinol Metab* 86:1040, 2001a.
- Gannon MC et al: Glucose appearance rate after the ingestion of galactose, *Metabolism* 50:93, 2001b.
- Garg A et al: Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus, *JAMA* 271:1421, 1994.
- Gebhard B et al: Postprandial GLP-1, norepinephrine, and reactive hypoglycemia in dumping syndrome, *Dig Dis Sci* 46:1915, 2001.
- Giacco R et al: Long-term dietary treatment with increased amounts of fiber-rich low-glycemic index natural food improves blood glucose control and reduces the number of hypoglycemic events in patients with type 1 diabetes, *Diabetes Care* 23:1451, 2000.
- Gougeon R et al: Effect of NIDDM on the kinetics of whole-body protein metabolism, *Diabetes* 43:318, 1994.
- Gougeon R et al: Effects of oral hypoglycemic agents and diet on protein metabolism in type 2 diabetes, *Diabetes Care* 23:21, 2000.
- Gray RO et al: Comparison of the ability of bread versus bread plus meat to treat and prevent subsequent hypoglycemia in patients with insulin-dependent diabetes, *J Clin Endocrinol Metab* 81:1508, 1996.
- Hallikainen MA et al: Effects of 2 low-fat stanols ester-containing margarines on serum cholesterol concentrations as part of a low-fat diet in hypercholesterolemic subjects, *Am J Clin Nutr* 69:403, 1999.
- Hasler WL: Dumping syndrome, *Curr Treat Options Gastroenterol* 5(2):139, 2002.
- Heilbronn L et al: Effect of energy restriction, weight loss, and diet composition on plasma lipids and glucose in patients with type 2 diabetes, *Diabetes Care* 22:889, 1999.
- Henry RR: Protein content of the diabetic diet [Technical Review], *Diabetes Care* 17:1502, 1994.
- Hollenbeck CG et al: To what extent does increased dietary fiber improve glucose and lipid metabolism in patients with noninsulin-dependent diabetes mellitus (NIDDM)? *Am J Clin Nutr* 43:16, 1986.
- International Diabetes Center: *Reactive and fasting hypoglycemia*, Minneapolis, 1998, International Diabetes Center.
- Inzucchi SE: Oral antihyperglycemic therapy for type 2 diabetes [Scientific Review], *JAMA* 287:360, 2002.
- Joint National Committee on Prevention, Detection, Evaluation and Treatment of Hypertension: The sixth report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, *Arch Intern Med* 157:2413, 1997.
- Jones KL et al: Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial, *Diabetes Care* 25:89-94, 2002.
- Jovanovic L, editor: *Medical management of pregnancy complicated by diabetes*, ed 3, Alexandria, Va, 2000, American Diabetes Association.
- Kelley DE et al: Relative effects of caloric restriction and weight loss in non-insulin-dependent diabetes mellitus, *J Clin Endocrinol Metab* 77:1287, 1993.
- Kendall A et al: Weight loss on a low-fat diet: consequence of the imprecision of the control of food intake in humans, *Am J Clin Nutr* 53:1124, 1991.
- Kerr D et al: Effect of caffeine on the recognition of and responses to hypoglycemia in humans, *Ann Intern Med* 119:799, 1993.
- Kitzmiller JL et al: Preconception care of diabetes, congenital malformations, and spontaneous abortions [Technical Review], *Diabetes Care* 19:514, 1996.
- Klein R et al: Is obesity related to microvascular complications of diabetes? *Arch Int Med* 157:650, 1997.
- Knopp RH et al: Metabolic effects of hypocaloric diets in management of gestational diabetes, *Diabetes* 40(suppl 2):165, 1991.
- Kohrt WM et al: Insulin resistance in aging is related to abdominal obesity, *Diabetes* 42:273, 1993.
- Koivisto VA et al: Alcohol with a meal has no adverse effects on postprandial glucose homeostasis in diabetic patients, *Diabetes Care* 16:1612, 1993.
- Kontessis PS et al: Renal, metabolic, and hormonal responses to protein of different origin in normotensive, nonproteinuric type 1 diabetic subjects, *Diabetes Care* 18:1233, 1995.
- Kulkarni K et al: Nutrition practice guidelines for type 1 diabetes positively affect dietitian practices and patient outcomes, *J Am Diet Assoc* 98:62, 1998.

- Kuusisto JL et al: NIDDM and its metabolic control predict coronary heart disease in elderly subjects, *Diabetes* 43:960, 1994.
- Lafrance L et al: The effects of different glycaemic index food and dietary fibre intakes on glycaemic control in type 1 patients with diabetes on intensive insulin therapy, *Diabet Med* 15:972, 1998.
- Lariviere FJ et al: Effects of dietary protein restriction on glucose and insulin metabolism in normal and diabetic humans, *Metabolism* 43:462, 1994.
- Lee DC et al: Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men, *Am J Clin Nutr* 69:373, 1999.
- Leonetti F et al: Increased nonoxidative glucose metabolism in idiopathic reactive hypoglycemia, *Metabolism* 45:606, 1996.
- Lovejoy JG, DiGirolamo M: Habitual dietary intake and insulin sensitivity in lean and obese adults, *Am J Clin Nutr* 55:1174, 1992.
- MacDonald MJ: Postexercise late-onset hypoglycemia in insulin-dependent diabetic patients, *Diabetes Care* 10:584, 1987.
- Markovic TP et al: The determinants of glycemic responses to diet restriction and weight loss in obesity and NIDDM, *Diabetes Care* 21:687, 1998a.
- Markovic TP et al: Beneficial effect on average lipid levels from energy restriction and fat loss in obese individuals with or without type 2 diabetes, *Diabetes Care* 21:695, 1998b.
- Mitchell TH et al: Hyperglycemia after intense exercise in IDDM subjects during continuous subcutaneous insulin infusion, *Diabetes Care* 11:311, 1988.
- Mitrakou A et al: Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction, *Am J Physiol* 260:E67, 1991.
- Mokdad AH et al: The continuing epidemics of obesity and diabetes in the United States, *JAMA* 286:1195, 2001.
- Monk A et al: Practice guidelines for medical nutrition therapy for dietitians for persons with non-insulin-dependent diabetes mellitus, *J Am Diet Assoc* 95:999, 1995.
- Montori VM et al: Fish oil supplementation in type 2 diabetes: a quantitative systematic review, *Diabetes Care* 23:1407, 2000.
- Mooradian AD et al: Selected vitamins and minerals in diabetes mellitus [Technical Review], *Diabetes Care* 17:464, 1994.
- Nordt TK et al: Influences of breakfasts with different nutrient contents on glucose, C peptide, insulin, glucagon, triglycerides, and GIP in non-insulin-dependent diabetics, *Am J Clin Nutr* 53:155, 1991.
- Nuttall FQ, Gannon MC: Plasma glucose and insulin responses to macronutrients in nondiabetic and NIDDM subjects, *Diabetes Care* 14:824, 1991a.
- Nuttall FQ, Gannon MC: Metabolic responses to dietary protein in persons with and without diabetes mellitus, *Diabetes Nutr Metab Clin Exp* 4:71, 1991b.
- Nuttall FQ et al: Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load, *Diabetes Care* 7:465, 1984.
- Nuttall FQ et al: The metabolic responses to various doses of fructose in type II diabetic subjects, *Metabolism* 41:510, 1992.
- Ohkubo Y et al: Intensive therapy prevents the progression of diabetic complications in Japanese patients with non-insulin diabetes mellitus: a randomized prospective 6-year study, *Diabetes Res Clin Pract* 28:103, 1995.
- Omenn GS et al: Risk factors for lung cancer and for intervention effects in CARET: the Beta Carotene and Retinol Efficacy Trial, *J Natl Cancer Inst* 88:1350, 1995.
- Parillo M et al: A high-monounsaturated fat/low carbohydrate diet improves peripheral insulin sensitivity in non-insulin-dependent diabetic patients, *Metabolism* 41:1373, 1992.
- Pate RR et al: Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine, *JAMA* 273:402, 1995.
- Patti L et al: Long-term effects of fish oil on lipoprotein subfractions and low density lipoprotein size in non-insulin-dependent diabetic patients with hypertriglyceridemia, *Atherosclerosis* 146:361, 1999.
- Pedrin MT et al: The effect of protein restriction on the progression of diabetic and nondiabetic renal diseases: a meta-analysis, *Ann Intern Med* 124:627, 1996.
- Peters AL, Davidson MB: Protein and fat effects on glucose response and insulin requirements in subjects with insulin-dependent diabetes mellitus, *Am J Clin Nutr* 58:555, 1993.
- Peterson DB et al: Sucrose in the diet of patients with diabetes—just another carbohydrate? *Diabetologia* 29:216, 1986.
- Pijls LJ et al: The effect of protein restriction on albuminuria in patients with type 2 diabetes mellitus: a randomized trial, *Nephrol Dial Transplant* 14:1445, 1999.
- Prince MJ: Hypoglycemia of nondiabetic origin, *Curr Ther Endocrinol Metab* 6:454, 1997.
- Prochaska JO et al: *Changing for good*, New York, 1994, Morrow Press.
- Purdon C et al: The roles of insulin and catecholamines in the glucoregulatory response during intense exercise and early recovery in insulin-dependent diabetic and control subjects, *J Clin Endocrinol Metab* 76:566, 1993.
- Rabasa-Lhoret R et al: The effects of meal carbohydrate content on insulin requirements in type 1 diabetic patients treated intensively with the basal bolus (ultralente-regular) insulin regimen, *Diabetes Care* 22:667, 1999.
- Rabasa-Lhoret R et al: Guidelines for premeal insulin dose reduction for postprandial exercise of different intensities and durations in type 1 diabetic subjects treated intensively with a basal-bolus insulin regimen (ultralente-lispro), *Diabetes Care* 24:625, 2001.
- Ravussin E et al: Effects of a traditional lifestyle on obesity in Pima Indians, *Diabetes Care* 17:1067, 1994.
- Reader D, Sipe M: Key components of care for women with gestational diabetes, *Diabetes Spectrum* 14:188, 2001.
- Report of a Joint FAO/WHO Expert Consultation: *Carbohydrates in human nutrition*, Rome, Italy, 1998, Food and Agriculture Organization of the United Nations and World Health Organization.
- Rickard KA et al: Lower glycemic response to sucrose in the diets of children with type 1 diabetes, *J Pediatr* 133:429, 1998.
- Rickheim P et al: Assessment of group versus individual diabetes education: a randomized study, *Diabetes Care* 25:269, 2002.
- Rizzo T et al: Correlations between antepartum maternal metabolism and intelligence of offspring, *N Engl J Med* 335:911, 1991.
- Sacks FM et al: Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet, *N Engl J Med* 344:3, 2001.
- Service FJ: Hypoglycemic disorders, *N Engl J Med* 17:1144, 1995.
- Sinha R et al: Prevalence of impaired glucose tolerance among children and adolescents with marked obesity, *N Engl J Med* 346:802, 2002.
- Skyler JS editor: *Medical management of type 1 diabetes*, ed 3, Alexandria, Va, 1998, American Diabetes Association.
- Toeller M et al: Protein intake and urinary albumin excretion rates in the EURODIAB IDDM Complications Study, *Diabetologia* 40:1219, 1997.
- Tuomilehto J et al: Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance, *N Engl J Med* 344:1390, 2001.
- United Kingdom Prospective Diabetes Study Group: UK Prospective Diabetes Study 7: Response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients, *Metabolism* 39:905, 1990.
- United Kingdom Prospective Diabetes Study Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 34), *Lancet* 352:854, 1998a.
- United Kingdom Prospective Diabetes Study Group: Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes (UKPDS 38), *BMJ* 317:703, 1998b.
- Vajo Z et al: Recombinant DNA technology in the treatment of diabetes: insulin analogs, *Endocr Rev* 22:706, 2001.
- Walker JD et al. Restriction of dietary protein and progression of renal failure in diabetic nephropathy, *Lancet* 2:1411, 1989.
- Wasserman DH, Zinman B: Exercise in individuals with IDDM (Technical Review), *Diabetes Care* 17:924, 1994.

- Watts NB et al: Prediction of glucose response to weight loss in patients with non-insulin-dependent diabetes mellitus, *Arch Intern Med* 150:803, 1990.
- Wing RR: Lifestyle and the prevention of diabetes. In Franz MJ, Bantle JP, editors: *American Diabetes Association guide to medical nutrition therapy for diabetes*, Alexandria, Va, 1999, American Diabetes Association.
- Wing RR et al: Long-term effects of modest weight loss in type II diabetic patients, *Arch Intern Med* 147:1749, 1987.
- Wing RR et al: Caloric restriction per se is a significant factor in improvements in glycemic control and insulin sensitivity during weight loss in obese NIDDM patients, *Diabetes Care* 17:30, 1994.
- Wolever TMS et al: Day-to-day consistency in amount and source of carbohydrate intake associated with improved glucose control in type 1 diabetes, *J Am Coll Nutr* 18:242, 1999.
- Yki-Jarvinen H: Acute and chronic effects of hyperglycaemia on glucose metabolism, implications for the development of new therapies, *Diabet Med* 14(suppl 3):S32, 1997.
- Yki-Jarvinen H et al: Comparison of insulin regimens in patients with non-insulin-dependent diabetes mellitus, *N Engl J Med* 337:1426, 1992.
- Yusuf S et al: Vitamin E supplementation and cardiovascular events in high-risk patients: the Heart Outcomes Prevention Evaluation Study Investigators, *N Engl J Med* 342:154, 2000.
- Zeller K et al: Effect of restricting dietary protein and progression of renal failure in patients with insulin-dependent diabetes mellitus, *N Engl J Med* 324:778, 1991.
- American Diabetes Association: The prevention or delay of type 2 diabetes [Position Statement], *Diabetes Care* 26:(suppl 1):S62, 2003.
- American Dietetic Association: *Nutrition practice guidelines for type 1 and type 2 diabetes*, CD-Rom, Chicago, 2001, American Dietetic Association.
- American Dietetic Association: *Nutrition practice guidelines for gestational diabetes*, CD-Rom, Chicago, 2001, American Dietetic Association.
- Anderson BJ, Rubin RR, editors: *Practical psychology for diabetes clinicians*, Alexandria, Va, 1996, American Diabetes Association.
- Franz MJ, section editor: Nutritional treatment of type 2 diabetes mellitus and obesity, *Curr Diabetes Rep* 1:159, 2001.
- Franz MJ, Bantle JP, editors: *American Diabetes Association guide to medical nutrition therapy for diabetes*, Alexandria, Va, 1999, American Diabetes Association.
- Franz MJ et al, editors: *A core curriculum for diabetes educators*, ed 4, Chicago, 2001, American Association of Diabetes Educators.
- Franz MJ et al: *Implementing group and individual medical nutrition therapy for diabetes*, Alexandria, Va, 2002, American Diabetes Association.
- Rickheim P et al: Type 2 diabetes BASICS. In *A complete curriculum for diabetes education*, Minneapolis, 2000, International Diabetes Center.
- Ruderman N et al, editors: *Handbook of exercise in diabetes*, Alexandria, Va, 2002, American Diabetes Association.
- Schafer RG et al: Translation of the diabetes nutrition recommendations for health care institutions [Technical Review], *Diabetes Care* 20:96, 1997.
- Virally ML, Guillausseau PJ: Hypoglycemia in adults, *Diabetes Metab* 25:477, 1999.

## ■ Additional References

American Diabetes Association: Consensus development conference on insulin resistance [Consensus Report], *Diabetes Care* 21:310, 1998.