Diabetes mellitus is a metabolic disease characterized by dysregulation of carbohydrate, protein, and lipid metabolism. The primary feature of this disorder is elevation in blood glucose levels (hyperglycemia), resulting from either a defect in insulin secretion from the pancreas, a change in insulin action, or both. Sustained hyperglycemia has been shown to affect almost all tissues in the body and is associated with significant complications of multiple organ systems, including the eyes, nerves, kidneys, and blood vessels. These complications are responsible for the high degree of morbidity and mortality seen in the diabetic population.

Epidemiology and Classification

About 16 million Americans have diabetes (between 6 and 7% of the total US population). Around the world, the prevalence of diabetes is expected to double between 1994 and 2010, at which time about 240 million people will have the disease. In the United States, the incidence of diabetes rises as the population ages and as the prevalence of obesity increases. Unfortunately, about half of those Americans with diabetes are presently unaware that they have the disease. Most dental practices have a significant number of diabetic patients in their population. Based on US prevalence data, an “average” practice would have between 60 and 70 diabetic individuals for every 1,000 patients, and 30 to 35 of these patients would be undiagnosed.

The American Diabetes Association provided the most recent classification of diabetes mellitus, in 1997 (Table 21-1). The most common forms of diabetes are termed type 1 and type 2. Type 1 diabetes was previously called insulin-dependent diabetes or juvenile diabetes while type 2 diabetes was formerly known as non-insulin-dependent diabetes or adult-onset diabetes. The older terminology was often confusing
since both insulin-dependent and non-insulin-dependent diabetic individuals may take insulin as part of their management regimen. The difference is that type 1 patients are truly dependent on insulin therapy whereas type 2 patients may benefit from insulin therapy but are not dependent on it for survival. The new classification system minimizes this confusion because it is based on the pathophysiology of the different disease types, rather than on the treatment methodology used.

Gestational diabetes occurs during pregnancy and usually resolves after delivery. Other types of diabetes may occur in individuals with certain genetic disorders, pancreatic diseases, infections, injuries to the pancreas, and endocrine diseases. Drug therapy with certain agents may also induce a diabetic state.

▼ PATHOPHYSIOLOGY

An understanding of the pathophysiology of diabetes rests upon knowledge of the basics of carbohydrate metabolism and insulin action. Following the consumption of food, carbohydrates are broken down into glucose molecules in the gut. Glucose is absorbed into the bloodstream elevating blood glucose levels. This rise in glycemia stimulates the secretion of insulin from the beta cells of the pancreas. Insulin is needed by most cells to allow glucose entry. Insulin binds to specific cellular receptors and facilitates entry of glucose into the cell, which uses the glucose for energy. The increased insulin secretion from the pancreas and the subsequent cellular utilization of glucose results in lowered blood glucose levels. Lower glucose levels then result in decreased insulin secretion.

If insulin production and secretion are altered by disease, blood glucose dynamics will also change. If insulin production is decreased, glucose entry into cells will be inhibited, resulting in hyperglycemia. The same effect will be seen if insulin is secreted from the pancreas but is not used properly by target cells. If insulin secretion is increased, blood glucose levels may become very low (hypoglycemia) as large amounts of glucose enter tissue cells and little remains in the bloodstream.

Following meals, the amount of glucose available from carbohydrate breakdown often exceeds the cellular need for glucose. Excess glucose is stored in the liver in the form of glycogen, which serves as a ready reservoir for future use. When energy is required, glycogen stores in the liver are converted into glucose via glycogenolysis, elevating blood glucose levels and providing the needed cellular energy source. The liver also produces glucose from fat (fatty acids) and proteins (amino acids) through the process of gluconeogenesis. Glycogenolysis and gluconeogenesis both serve to increase blood glucose levels. Thus, glycemia is controlled by a complex interaction between the gastrointestinal tract, the pancreas, and the liver.

Multiple hormones may affect glycemia (Table 21-2). Insulin is the only hormone that lowers blood glucose levels. The counter-regulatory hormones such as glucagon, catecholamines, growth hormone, thyroid hormone, and glucocorticoids all act to increase blood glucose levels, in addition to their other effects.

### Type 1 Diabetes

The underlying pathophysiologic defect in type 1 diabetes is an autoimmune destruction of pancreatic beta cells. Following this destruction, the individual has an absolute insulin deficiency and no longer produces insulin. Autoimmune beta cell destruction is thought to be triggered by an environmental event, such as a viral infection. Genetically determined susceptibility factors increase the risk of such autoimmune phenomena.

The onset of type 1 diabetes is usually abrupt. It generally occurs before the age of 30 years, but may be diagnosed at any age. Most type 1 diabetic individuals are of normal weight or are thin in stature. Since the pancreas no longer produces insulin, a type 1 diabetes patient is absolutely dependent on exogenously administered insulin for survival. People with type 1 diabetes are highly susceptible to diabetic ketoacidosis. Because the pancreas produces no insulin, glucose cannot enter cells and remains in the bloodstream. To meet cellular energy needs, fat is broken down through lipolysis, releasing glycerol and free fatty acids. Glycerol is converted to glucose for cellular use. Fatty acids are converted to ketones, resulting in increased ketone levels in body fluids and decreased hydrogen ion concentration (pH). Ketones are excreted in the urine, accompanied by large amounts of water. The accumulation of

### TABLE 21-1 Classification of Diabetes Mellitus

| Type 1 (insulin-dependent diabetes; juvenile diabetes) |
| Type 2 (non-insulin-dependent diabetes; adult-onset diabetes) |
| Gestational diabetes (pregnancy diabetes) |
| Other types of diabetes |
| Genetic defects affecting beta-cell function or insulin action |
| Pancreatic diseases or injuries (pancreatic cancer, pancreatitis, traumatic injury, cystic fibrosis, pancreatectomy) |
| Infections (congenital rubella, Cytomegalovirus infection) |
| Drug-induced diabetes (steroid hormones [glucocorticoids], thyroid hormone) |
| Endocrine disorders (hyperthyroidism, Cushing’s syndrome, glucagonoma, acromegaly, pheochromocytoma) |
| Other genetic syndromes (with associated diabetes) |

Reproduced with permission from American Diabetes Association.

### TABLE 21-2 Hormonal Regulation of Blood Glucose

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Main Site of Hormone Production</th>
<th>Effect on Blood Glucose Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Pancreas (beta cells)</td>
<td>Decrease</td>
</tr>
<tr>
<td>Glucagon</td>
<td>Pancreas (alpha cells)</td>
<td>Increase</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Pituitary gland</td>
<td>Increase</td>
</tr>
<tr>
<td>Thyroid hormone</td>
<td>Thyroid gland</td>
<td>Increase</td>
</tr>
<tr>
<td>Catecholamines (epinephrine)</td>
<td>Adrenal gland (medulla)</td>
<td>Increase</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Adrenal gland (cortex)</td>
<td>Increase</td>
</tr>
</tbody>
</table>
ketones in body fluids, decreased pH, electrolyte loss and dehydration from excessive urination, and alterations in the bicarbonate buffer system result in diabetic ketoacidosis (DKA). Untreated DKA can result in coma or death.

Many patients with type 1 diabetes are initially diagnosed with the disease following a hospital admission for DKA. In a known diabetic patient, periods of stress or infection may precipitate DKA. More often, however, DKA results from poor daily glycemic control. Patients who remain severely hyperglycemic for several days or longer due to inadequate insulin administration or excessive glucose intake are prone to developing DKA.

**Type 2 Diabetes**

About 90% of diabetic Americans have type 2 diabetes.4 The prevalence of type 2 diabetes is higher in African Americans, Native Americans, Hispanics, and Pacific Islanders than it is in Caucasians. Most type 2 diabetes patients are overweight, and most are diagnosed as adults. The genetic influence in type 2 diabetes is greater than that seen with type 1.5 While concordance rates between monozygous twins for type 1 diabetes are about 30 to 50%, the rate is approximately 90% for type 2 diabetes.4,5 Although the genetic predisposition to type 2 diabetes is strong, no single genetic defect has been found.6 In addition to genetic influences, acquired risk factors for type 2 diabetes include obesity, advancing age, and an inactive lifestyle.

The underlying pathophysiologic defect in type 2 diabetes does not involve autoimmune beta-cell destruction. Rather, type 2 diabetes is characterized by the following three disorders: (1) peripheral resistance to insulin, especially in muscle cells; (2) increased production of glucose by the liver; and, (3) altered pancreatic insulin secretion. Increased tissue resistance to insulin generally occurs first and is eventually followed by impaired insulin secretion. The pancreas produces insulin, yet insulin resistance prevents its proper use at the cellular level. Glucose cannot enter target cells and accumulates in the bloodstream, resulting in hyperglycemia. The high blood glucose levels often stimulate an increase in insulin production by the pancreas; thus, type 2 diabetic individuals often have excessive insulin production (hyperinsulinemia). Over the years, pancreatic insulin production usually decreases to below normal levels. In addition to hyperglycemia, type 2 diabetic patients often have a group of disorders that has been called “insulin resistance syndrome” or syndrome X7,8 (Table 21-3).

Obesity contributes greatly to insulin resistance, even in the absence of diabetes.9 In fact, weight loss is a cornerstone of therapy for obese type 2 diabetic patients. Insulin resistance generally decreases with weight loss. Obesity also may explain the dramatic increase in the incidence of type 2 diabetes among young individuals in the United States in the past 10 to 20 years. Once considered a disease of adults, type 2 diabetes has increased among America’s youth in direct correlation with the increase in the average weight of children and young adults during that time period.

Type 2 diabetes usually has a slow onset and may remain undiagnosed for years.5,7 Approximately half of those who have type 2 diabetes are unaware of their disease. Unfortunately, the insidious nature of the disease allows prolonged periods of hyperglycemia to begin exerting negative effects on major organ systems. By the time many type 2 diabetic patients are diagnosed, diabetic complications have already begun. Type 2 diabetic patients do not require exogenous insulin for survival since they still produce insulin. However, insulin injection is often an integral part of medical management for type 2 diabetes. Unlike type 1 diabetic patients, individuals with type 2 diabetes are generally resistant to DKA because their pancreatic insulin production is often sufficient to prevent ketone formation. Severe physiologic stress may induce DKA in those with type 2 diabetes. Long periods of severe hyperglycemia may result in hyperosmolar nonketotic acidosis. Hyperglycemia results in the urinary excretion of large amounts of glucose, with attendant water loss. If fluids are not replaced, the dehydration can result in electrolyte imbalance and acidosis.

**Gestational Diabetes**

Gestational diabetes occurs in approximately 4% of pregnancies in the United States.10 It usually develops during the third trimester and significantly increases perinatal morbidity and mortality.11 The proper diagnosis and management of gestational diabetes improves pregnancy outcomes.12 As with type 2 diabetes, the pathophysiology of gestational diabetes is associated with increased insulin resistance. Most patients with gestational diabetes return to a normoglycemic state after parturition; however, about 30 to 50% of women with a history of gestational diabetes will develop type 2 diabetes within 10 years.

**Impaired Glucose Tolerance and Impaired Fasting Glucose**

The conditions known as impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) represent metabolic states lying between diabetes and normoglycemia.7 People with IFG have increased fasting blood glucose levels but usually have normal levels following food consumption. Those with IGT are normoglycemic most of the time but can become hyperglycemic after large glucose loads. IGT and IFG are not considered to be clinical entities; rather, they are risk factors for future diabetes.13 The pathophysiology of IFG and IGT is related primarily to increased insulin resistance whereas endogenous insulin secretion is normal in most patients.

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**TABLE 21-3 Disorders Associated with Type 2 Diabetes (Insulin Resistance Syndrome or Syndrome X)**

<table>
<thead>
<tr>
<th>Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Elevated triglycerides</td>
</tr>
<tr>
<td>Decreased high-density lipoprotein</td>
</tr>
<tr>
<td>Central (abdominal) obesity</td>
</tr>
<tr>
<td>Atherosclerosis</td>
</tr>
</tbody>
</table>

---
Approximately 30 to 40% of individuals with IGT or IFG will develop type 2 diabetes within 10 years after onset.

▼ CLINICAL PRESENTATION, LABORATORY FINDINGS, AND DIAGNOSIS

The onset of type 1 diabetes is usually abrupt whereas type 2 diabetes is often present for years without overt signs or symptoms. Patients with undiagnosed diabetes may present with one or more signs and symptoms (Table 21-4). The diagnosis of diabetes is based on the presence of clinical signs and symptoms, along with specific laboratory findings. The most recent diagnostic guidelines were established by the American Diabetes Association in 1997 (Table 21-5).14 These guidelines provide for the use of fasting glucose and casual (nonfasting) glucose levels for diagnosis and restrict routine use of the oral glucose tolerance test. The diagnosis of diabetes is not made until the patient has exceeded threshold glucose levels on two separate occasions. Urinary glucose analysis is no longer used in establishing the diagnosis of diabetes.

Both the fasting and casual plasma glucose tests provide a determination of glucose levels at a single moment in time, namely, at the time the blood sample is collected. It is often useful to assess the long-term control of glycemia, especially in known diabetic patients. The glycated (or glycosylated) hemoglobin assay (also called the glycohemoglobin test) allows the determination of blood glucose status over the 30 to 90 days prior to collection of the blood sample. As glucose circulates in the bloodstream, it becomes attached to a portion of the hemoglobin molecule on red blood cells. The higher the plasma glucose levels are over time, the greater is the percentage of hemoglobin that becomes glycated. There are two different glycated hemoglobin assays: the hemoglobin A1 (HbA1) test and the hemoglobin A1c (HbA1c) test. Because these tests measure two different portions of the hemoglobin molecule, the normal ranges for the test results differ.15 The normal HbA1 value is less than approximately 8% whereas the normal HbA1c value is less than 6.0 to 6.5%. These tests are not currently standardized across all laboratories; therefore, glycated hemoglobin values must be interpreted in the context of normal ranges for the specific laboratory performing the test. The American Diabetes Association recommends that individuals with diabetes attempt to achieve a target HbA1c value of less than 7% whereas an HbA1c value of more than 8% suggests that a change in patient management may be needed to improve glycemic control.16 The glycated hemoglobin assay is not currently recommended as a screening tool or as an initial test for the diagnosis of diabetes. It is used to monitor glycemic control in patients with previously diagnosed diabetes.

Another assay that can be used to determine long-term glucose control is the fructosamine test.17 This test is not used as widely as the glycated hemoglobin assay but is often helpful in managing women with gestational diabetes. The fructosamine assay assesses glycemic control over the 2 to 4 weeks preceding the test. The normal range for fructosamine is 2.0 to 2.8 mmol/L. This test may become more widely used in the future, since at-home testing is now available.

Self-blood glucose monitoring (SBGM) has revolutionized patient management of diabetes.18 The development of small handheld glucometers has allowed the diabetic individual to take much greater control of his or her disease. Glucometers use a small drop of capillary blood from a finger-stick sample to assess glucose levels within seconds. Almost all insulin-using diabetic patients (and many who are on oral agents) have glucometers. There are many different glucometers available, and the frequency with which the patient tests his or her blood glucose depends on that patient’s individual treatment regimen. Some patients test once a day or even less often. Others, especially those taking insulin, test many times each day. As a general rule, more intensively managed diabetic patients use SBGM more frequently than less intensively managed individuals.

▼ COMPLICATIONS

The major cause of the high morbidity and mortality rate associated with diabetes is a group of microvascular and macrovascular complications affecting multiple organ systems (Table 21-6).3 People with diabetes have a greatly increased risk for blindness, kidney failure, myocardial infarction, stroke, necessary limb amputation, and a host of other maladies. The onset and progression of these complications is strongly linked to the presence of sustained hyperglycemia. The complication rate and the severity of complications increase as the duration of diabetes increases. Other disorders (such as hypertension and dyslipidemia) commonly seen in people with diabetes increase the risk for microvascular and macrovascular complications. There may also be genetic determinants of risk for diabetic complications.

The vascular complications result from atherosclerosis and microangiopathy.19–21 Increased lipid deposition and atheroma formation is seen in the larger blood vessels, along with increased thickness of arterial walls. Proliferation of endothelial cells, alterations in endothelial basement mem-

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**TABLE 21-4** Signs and Symptoms of Undiagnosed Diabetes

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polydipsia (excessive thirst)</td>
</tr>
<tr>
<td>Polyuria (excessive urination)</td>
</tr>
<tr>
<td>Polyphagia (excessive hunger)</td>
</tr>
<tr>
<td>Unexplained weight loss</td>
</tr>
<tr>
<td>Changes in vision</td>
</tr>
<tr>
<td>Weakness, malaise</td>
</tr>
<tr>
<td>Irritability</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Dry mouth</td>
</tr>
<tr>
<td>Ketoacidosis*</td>
</tr>
</tbody>
</table>

*Ketoacidosis is usually associated with severe hyperglycemia and occurs primarily in type 1 diabetes.*
branes, and changes in the function of endothelial cells induce microvascular damage.

The pathophysiology of diabetic complications is complex. There is considerable heterogeneity within the diabetic population in regard to the development and progression of diabetic complications. While poor glycemic control is clearly a major risk factor for complications, not all poorly controlled diabetic patients develop complications. Conversely, some individuals develop complications despite relatively good glycemic control. Hyperglycemia plays a major role in both microvascular and macrovascular disease. Hyperglycemia dramatically alters the function of multiple cell types and their extracellular matrix. This results in structural and functional changes in the affected tissues. Research has recently focused on lipoprotein metabolism and on the glycation of proteins, lipids, and nucleic acids as possible common links between the different diabetic complications.

The function of cell membranes is determined largely by their phospholipid bilayers; thus, changes in lipid metabolism can have major effects on cell function. The oxidation of circulating low-density lipoprotein (LDL) in hyperglycemic individuals increases oxidant stress within the vasculature. This induces chemotaxis of monocytes and macrophages into the vessel walls, where oxidized LDL causes changes in cellular adhesion and increased production of cytokines and growth factors. Growth factor–induced stimulation of smooth-muscle cell proliferation increases vessel wall thickness. Other changes include increased atheroma formation and development of microthrombi in large blood vessels and alterations in vascular permeability and endothelial cell function in the microvasculature.

The glycation of proteins, lipids, and nucleic acids increases with sustained hyperglycemia. The microvasculature of the retina, renal glomerulus, and endoneurial areas, as well as the walls of the larger blood vessels, accumulate deposits of glycated proteins called advanced glycation end products (AGEs). While all people form AGEs, the accumulation of AGEs is much greater in individuals with diabetes, especially when the diabetic state is poorly controlled. AGE formation alters the structural and functional properties of the affected tissues. For example, AGE formation on collagen macromolecules impairs their normal homeostatic turnover. In the walls of the large blood vessels, accumulate deposits of glycated proteins called advanced glycation end products (AGEs), which immobilizes circulating LDL, contributing to atheroma formation. Accumulation of AGEs causes increased basement membrane thickness in the microvasculature of the retina and around the nerves and increased thickness of the mesangial matrix in the glomerulus. The cumulative effect of these changes is a progressive narrowing of the vessel lumen and decreased perfusion of affected tissues.

AGE formation also has major effects at the cellular level, causing modifications in extracellular matrix components and changes in cell-to-matrix and matrix-to-matrix interactions. The binding of AGEs to specific cellular receptors that have been identified on the surface of smooth-muscle cells, endothelial cells, neurons, monocytes, and macrophages results in increased vascular permeability and thrombus for-
mation, proliferation of smooth muscle in vessel walls, and phenotypic alteration in monocytes and macrophages. This last result causes hyper-responsiveness of monocytes and macrophages upon stimulation, with resultant increases in the production of proinflammatory cytokines and certain growth factors. These cytokines and growth factors contribute to the chronic inflammatory process in the formation of atherosclerotic lesions. They also significantly alter wound-healing events. Increased production of proinflammatory mediators results in increased tissue destruction in response to antigens such as the bacteria that cause periodontal disease.

These changes in protein and lipid metabolism, induced by the elevated plasma glucose levels characteristic of diabetes, may thus provide a common connection between the various diabetic complications. However, these metabolic changes vary among individuals. For example, AGEs form in both diabetic and nondiabetic people, but their accumulation is greater in those with diabetes. There is significant heterogeneity in AGE formation even within the diabetic population, and it is thought that this heterogeneity may explain (at least, in part) the variation in the incidence and progression of diabetic complications.

▼ MANAGEMENT

Primary treatment goals for diabetes patients include the achieving of blood glucose levels that are as close to normal as possible and the prevention of diabetic complications. Other goals are normal growth and development, normal body weight, the avoidance of sustained hyperglycemia or symptomatic hypoglycemia, the prevention of diabetic ketoacidosis and nonketotic acidosis, and the immediate detection and treatment of long-term diabetic complications.

Diet, exercise, weight control, and medications are the mainstays of diabetic care. Obesity is very common in type 2 diabetes and contributes greatly to insulin resistance. Weight reduction and exercise improve tissue sensitivity to insulin and allow its proper use by target tissues. The primary medication used in type 1 diabetes management is insulin, on which the type 1 diabetic patient is dependent for survival. Type 2 diabetic individuals frequently take oral medications although many also use insulin to improve glycemic control.

Medical management and the goals of therapy for diabetes have changed since the publication of the Diabetes Control and Complications Trial (DCCT) in 1993. This prospective randomized controlled multicenter clinical trial compared the effects of intensive insulin therapy aimed at achieving the near normalization of glycemia with the effects of conventional insulin therapy on the initiation and progression of complications in patients with type 1 diabetes. The conventional control group took 1 or 2 insulin injections each day while the intensive control group took 3 or 4 injections daily or used a subcutaneous insulin infusion pump. The results showed that the intensive group had much better glycemic control during the 3- to 9-year follow-up period. The risk of developing retinopathy decreased by 76% in intensively managed patients when compared to conventional control group patients. Clinical and laboratory signs and symptoms of nephropathy and neuropathy decreased by 54 to 60%. Macrovascular complications also decreased significantly. The dramatic benefits of intensive insulin therapy led the American Diabetes Association to issue a position statement declaring that the primary treatment goal in type 1 diabetes should be to attain blood glucose control “at least equal to that in the intensively treated cohort” of the DCCT.

Several recent studies have also shown reductions in diabetic complications for intensively managed type 2 diabetic patients. In one 6-year study, maintenance of near-normal glycemia resulted in a decrease of 54 to 70% in the risk of microvascular and macrovascular complications for these patients, compared to conventional controls. Since type 2 diabetic patients make up about 90% of all diabetic Americans, these studies have the potential to affect millions of people. Diabetic patients are increasingly motivated to improve their glycemic control, and physicians have intensified diabetic management in response to recent research.

Oral Agents
A number of different oral agents are available for treating diabetes; most of these are taken by those with type 2 diabetes (Table 21-7). The first-generation sulfonylureas, once the only drugs available for treating type 2 diabetes, are not used much today. They have been replaced with second-generation agents that are more potent, have fewer drug interactions, and produce less significant side effects. Sulfonylureas stimulate pancreatic insulin secretion. The increased quantity of secreted insulin helps counteract the qualitative decrease in tissue sensitivity to insulin, allowing greater glucose entry into target cells and thereby lowering blood glucose levels. Sulfonylureas generally have a relatively long duration of action of 12 to 24 hours, depending on the drug, and are taken once or twice per day.

<table>
<thead>
<tr>
<th>TABLE 21-7 Oral Agents for Management of Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sulfonylurea agents</strong></td>
</tr>
<tr>
<td>First generation:</td>
</tr>
<tr>
<td>Chlorpropamide</td>
</tr>
<tr>
<td>Tolazamide</td>
</tr>
<tr>
<td>Tolbutamide</td>
</tr>
<tr>
<td><strong>Second generation</strong></td>
</tr>
<tr>
<td>Glyburide</td>
</tr>
<tr>
<td>Glipizide</td>
</tr>
<tr>
<td>Glimepiride</td>
</tr>
<tr>
<td><strong>Nonsulfonylurea insulin secretagogues</strong></td>
</tr>
<tr>
<td>Repaglinide</td>
</tr>
<tr>
<td><strong>Biguanides</strong></td>
</tr>
<tr>
<td>Metformin</td>
</tr>
<tr>
<td><strong>Thiazolidinediones</strong></td>
</tr>
<tr>
<td>Troglitazone</td>
</tr>
<tr>
<td>Rosiglitazone</td>
</tr>
<tr>
<td>Pioglitazone</td>
</tr>
<tr>
<td>α-Glucosidase inhibitors</td>
</tr>
<tr>
<td>Acarbose</td>
</tr>
</tbody>
</table>
day. Hypoglycemia is a major side effect of sulfonylureas. In patients taking these agents, food intake must be adequate to prevent glucose levels from falling too low.

Like the sulfonylureas, repaglinide stimulates pancreatic insulin secretion. However, its pharmacodynamic properties and mechanism of action are different from those of the sulfonylureas. Repaglinide is rapidly absorbed, reaches peak plasma levels in 30 to 60 minutes, and is then rapidly metabolized. The drug is taken with meals and lowers the peaks of postprandial plasma glucose common with type 2 diabetes to a much greater degree than the sulfonylureas are able to do.

Metformin is a biguanide agent that lowers plasma glucose mainly by preventing glycogenolysis in the liver. Metformin also improves insulin use, counteracting the insulin resistance seen with type 2 diabetes. Because metformin does not stimulate increased insulin secretion, hypoglycemia is much less common with this drug.

The thiazolidinedione agents troglitazone, rosiglitazone, and pioglitazone act to increase tissue sensitivity to insulin, thus increasing glucose utilization and decreasing blood glucose levels. These drugs also decrease hepatic glucoseogenesis. Like metformin, the thiazolidinediones generally do not cause hypoglycemia.

Acarbose has a mechanism of action that is unlike that of the other agents used in diabetes management. Acarbose is taken with meals, and it slows the digestion and uptake of carbohydrates from the gut. This serves to lower postprandial plasma glucose peaks. Acarbose does not cause hypoglycemia, but if the delayed carbohydrate absorption occurs in a patient whose plasma insulin levels are increasing due to the injection of insulin or the use of a sulfonylurea, the level of glucose in the bloodstream will not be sufficient to prevent hypoglycemia.

Insulin

All type 1 diabetic patients use exogenous insulin, as do many with type 2 diabetes. Insulin is taken via subcutaneous injection, most often with a syringe. Insulin infusion pumps deliver insulin through a subcutaneous catheter. There are a variety of insulin preparations available; they vary in their onset, peak, and duration of activity and are classified as long-, intermediate-, short-, or rapid-acting (Table 21-8). Although beef and pork insulin species are still available, most individuals use human insulin preparations today.

Ideally, the use of exogenous insulin provides an insulin profile similar to that seen in a nondiabetic individual, with a continuous basal level of insulin availability augmented by increased availability following each meal. There is no single insulin preparation that can achieve this goal with only one or two injections per day. Combinations of different insulin preparations taken three or more times daily or the use of a subcutaneous infusion pump more closely approximate the ideal profile, but even with such regimens, blood glucose levels are often unstable.

Ultralente insulin is the longest-acting insulin. Commonly called “peakless” insulin, Ultralente has a very slow onset of action, minimal peak activity, and a long duration of action. It is usually taken to mimic the basal metabolic rate of insulin secreted from a normally functioning pancreas. The intermediate-acting insulins (lente and neutral protamine Hagedorn [NPH]) take several hours after injection to begin having an effect. Peak activity varies among individuals and sites of injection but generally occurs between 4 and 10 hours after injection. Thus, a patient who injects intermediate-acting insulin in the early morning will reach peak plasma insulin levels at about lunchtime. Regular insulin is short acting, with an onset of activity at about 30 minutes to 1 hour after injection and a peak activity at 2 to 3 hours. The rapid-acting insulin called lispro insulin is rapidly absorbed, becomes active about 15 minutes after injection, and is at peak activity at 30 to 90 minutes. Rapid- and short-acting insulins are usually taken just prior to or during meals. Thus, regular insulin taken prior to breakfast will peak at about midmorning; when taken prior to lunch, it will peak during the midafternoon. Some examples of common insulin regimens are given in Table 21-9.

The most common complication of insulin therapy is hypoglycemia, a potentially life-threatening emergency. While hypoglycemia may occur in patients who are taking oral agents such as sulfonylureas, it is much more common in those who are using insulin. Intensified treatment regimens for diabetes increase the risk of hypoglycemia. Thus, the long-term benefit of reduced diabetic complications seen with intensive treatment must be weighed against the increased risk of symptomatic low blood glucose. In the DCCT, the incidence of severe hypoglycemic events in which the patient became unconscious or required the assistance of another person was three times greater in the intensively

### Table 21-8 Types of Insulin

<table>
<thead>
<tr>
<th>Type</th>
<th>Classification</th>
<th>Onset of Activity (h)</th>
<th>Peak Activity (h)</th>
<th>Duration of Activity (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultralente</td>
<td>Long acting</td>
<td>6–10</td>
<td>12–16</td>
<td>20–30</td>
</tr>
<tr>
<td>Lente</td>
<td>Intermediate acting</td>
<td>3–4</td>
<td>4–12</td>
<td>16–20</td>
</tr>
<tr>
<td>NPH</td>
<td>Intermediate acting</td>
<td>2–4</td>
<td>4–10</td>
<td>14–18</td>
</tr>
<tr>
<td>Regular</td>
<td>Short acting</td>
<td>0.5–1.0</td>
<td>2–3</td>
<td>4–12</td>
</tr>
<tr>
<td>Lispro</td>
<td>Rapid acting</td>
<td>0.25</td>
<td>0.5–1.5</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

NPH = neutral protamine Hagedorn.
managed cohort than in the conventional control group.\textsuperscript{35,36} One-third of the severe hypoglycemic episodes resulted in seizure or loss of consciousness. In addition, 36% of the episodes occurred with no warning symptoms for the patient.

The phenomenon known as “hypoglycemia unawareness” is more common in diabetic patients with good glycemic control than in those with poor control.\textsuperscript{35} Hypoglycemia unawareness is characterized by an inability to perceive the warning symptoms of hypoglycemia until the blood glucose drops to very low levels. Signs and symptoms of hypoglycemia are most common when blood glucose levels fall to < 60 mg/dL, but they may occur at higher levels in diabetic patients with chronic poor metabolic control.\textsuperscript{18} In people with hypoglycemia unawareness, glucose levels can fall to 40 mg/dL or lower before an individual “feels” hypoglycemic.

\textbf{\textit{Principles of Medicine}}

\textbf{ORAL DISEASES AND DIABETES}

Oral conditions that are seen in individuals with diabetes may include burning mouth, altered wound healing, and an increased incidence of infection. Enlargement of the parotid glands and xerostomia can occur; both are conditions that may be related to the metabolic control of the diabetic state.\textsuperscript{37} Medications that diabetic patients often take for related or unrelated systemic conditions may have significant xerostomic effects. Thus, the xerostomia seen in individuals with diabetes may result more from medications than from the diabetic condition itself.

Neuropathy of the autonomic system can also cause changes in salivary secretion since salivary flow is controlled by the sympathetic and parasympathetic pathways.\textsuperscript{38} Dry mucosal surfaces are easily irritated and are associated with

<table>
<thead>
<tr>
<th>Description</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single injection of intermediate-acting insulin (early morning)</td>
<td>Peak insulin activity at midday Can provide enough insulin for midday meals only Hyperglycemia common upon rising and following breakfast and dinner</td>
</tr>
<tr>
<td>Single injection of mixture of intermediate-acting and regular or lispro insulin (early morning)</td>
<td>Peak insulin activity at both midmorning (from regular or lispro insulin) and midday (from intermediate-acting insulin) Can provide enough insulin for breakfast and midday meals Hyperglycemia common upon rising and from late afternoon until next morning</td>
</tr>
<tr>
<td>Twice-daily injection of intermediate-acting insulin (prior to breakfast and dinner)</td>
<td>Peak insulin activity at both midday (from morning injection) and late evening (from dinner injection) Can provide enough insulin for lunch and sometimes dinner; often prevents early-morning high blood glucose levels Hyperglycemia common after breakfast and shortly after dinner</td>
</tr>
<tr>
<td>Twice-daily injection of mixture of intermediate-acting insulin and regular or lispro insulin (prior to breakfast and dinner)</td>
<td>Peak insulin activity after breakfast (from morning regular or lispro insulin), after lunch (from morning intermediate-acting insulin), after dinner (from dinnertime regular or lispro insulin), and late evening or early morning (from dinnertime intermediate-acting insulin) Can provide enough insulin for all meals; often prevents early-morning high blood glucose levels</td>
</tr>
<tr>
<td>Three daily injections of regular or lispro insulin (prior to each main meal) and one injection of intermediate-acting insulin (bedtime)</td>
<td>Peak insulin activity after breakfast, lunch, and dinner (from regular or lispro insulin before each meal), and late evening or early morning (from dinnertime intermediate-acting insulin) Can provide enough insulin for all meals; often prevents early-morning high blood glucose levels Often provides better glycemic control than once- or twice-daily injection regimens</td>
</tr>
<tr>
<td>Three daily injections of regular or lispro insulin (prior to each main meal) and one injection of Ultralente insulin (morning)</td>
<td>Peak insulin activity after breakfast, lunch, and dinner (from regular or lispro insulin before each meal); insulin activity in late evening or early morning (from dinnertime Ultralente insulin) Can provide enough insulin for all meals; often prevents early-morning high blood glucose levels Often provides better glycemic control than once- or twice-daily injection regimens</td>
</tr>
<tr>
<td>Use of insulin infusion pump with regular or lispro insulin; basal metabolic rate set to provide continuous delivery of small amounts of insulin (bolus of insulin programmed prior to each meal)</td>
<td>Provides on-demand insulin with meals Basal metabolic rate most closely mimics normal pancreatic function Often (but not always) provides better glycemic control than any injection regimen</td>
</tr>
</tbody>
</table>

\textbf{\textit{TABLE 21-9 Common Insulin Regimens}}
“burning mouth” syndrome; they also provide a favorable environment for the growth of fungal organisms. Some studies have shown an increased incidence of oral candidiasis in patients with diabetes whereas other studies have not.39,40

The effect of diabetes on the dental caries rate is unclear. Some studies have demonstrated increased caries in people with diabetes, which has been associated with xerostomia or increased gingival crevicular fluid glucose levels.41 Other studies have shown similar or decreased caries rates in people with diabetes.42,43 Since most diabetic individuals limit their intake of fermentable carbohydrates, the less cariogenic diet may limit caries incidence. In recent studies of type 2 diabetic patients and nondiabetic control subjects, no differences were seen in salivary flow rates, organic constituents of saliva, salivary counts of acidogenic bacteria, salivary counts of fungal organisms, or coronal and root caries rates.38,44 These findings suggest that diabetic individuals as a group are similar to nondiabetic people in regard to these oral conditions.

**Periodontal Health and Diabetes**

Strong evidence suggests that, unlike the conditions discussed above, diabetes is a risk factor for the prevalence and severity of gingivitis and periodontitis.45,46 Diabetes is associated with increased gingival inflammation in response to bacterial plaque, but the degree of glycemic control is an important variable in this relationship. In general, well-controlled diabetic individuals and nondiabetic people have similar degrees of gingivitis, with the same level of plaque. Conversely, poorly controlled diabetic subjects have significantly increased gingivitis, compared to either well-controlled diabetic or nondiabetic individuals.47-49

In large epidemiologic studies, diabetes has been shown to significantly increase the risk of attachment loss and alveolar bone loss approximately threefold when compared to nondiabetic control subjects.50,51 These findings have been confirmed in meta-analyses of multiple studies in various diabetic populations.45 Diabetes increases not only the prevalence and severity of periodontitis but also the progression of bone loss and attachment loss over time.52

Periodontitis is similar to the classic complications of diabetes in its variation among individuals. Just as retinopathy, nephropathy, and neuropathy are more likely to be seen in diabetic patients with poor glycemic control, progressive destructive periodontitis is also more common in those with poor control.53,54 However, some poorly controlled diabetic patients do not develop significant periodontal destruction, just as some do not develop the classic diabetic complications. Conversely, well-controlled diabetes places the person at a lower risk for periodontal disease, similar to the risk of nondiabetic individuals; yet, well-controlled diabetic patients may still develop periodontitis, just as nondiabetic individuals do. Other risk factors for periodontitis, such as poor oral hygiene and smoking, play a similar deleterious role in both diabetic and nondiabetic individuals.

The mechanisms by which diabetes influences the periodontium are similar in many respects to the pathophysiology of the classic diabetic complications. There are few differences between the subgingival microbiota of diabetic patients with periodontitis and nondiabetic patients with periodontitis.55,56 This lack of significant differences in the primary bacteriologic agents of periodontal disease suggests that differences in host response may play a role in the increased prevalence and severity of periodontal destruction seen in patients with diabetes.

Hyperglycemia results in increased gingival crevicular fluid glucose levels, which may significantly alter periodontal wound-healing events by changing the interaction between cells and their extracellular matrix within the periodontium.57,58 Vascular changes seen in the retina, glomerulus, and perineural areas also occur in the periodontium.59,60 The formation of AGEs results in collagen accumulation in the periodontal capillary basement membranes, causing membrane thickening.61 AGE-stimulated smooth-muscle proliferation increases the thickness of vessel walls. These changes decrease tissue perfusion and oxygenation. AGE-modified collagen in gingival blood vessel walls binds circulating LDL, which is frequently elevated in diabetes, resulting in atheroma formation and further narrowing of the vessel lumen.62 These changes in the periodontium may dramatically alter the tissue response to periodontal pathogens, resulting in increased tissue destruction and diminished repair potential.

Diabetes results in changes in the function of host defense cells such as polymorphonuclear leukocytes (PMNs), monocytes, and macrophages. PMN adherence, chemotaxis, and phagocytosis are impaired.63,64 Defects in this first line of defense against periodontopathic microorganisms may significantly increase periodontal destruction. Monocytes and macrophages in diabetic individuals are often hyper-responsive to bacterial antigens.65 This up-regulation results in a significantly increased production of proinflammatory cytokines and mediators.66,67 The net effect of these host defense alterations is an increase in periodontal inflammation, attachment loss, and bone loss.

Collagen is the primary structural protein in the periodontium. Changes in collagen metabolism in diabetic individuals contribute to wound-healing alterations and periodontal destruction.68 The production of matrix metalloproteinases (MMPs) such as collagenase is increased in many diabetic patients. Increased collagenase production readily degrades newly formed collagen. Conversely, AGE modification of existing collagen decreases its solubility. The result of these changes in collagen metabolism is a rapid dissolution of recently synthesized collagen by host collagenase and a preponderance of older AGE-modified collagen. Thus, diabetes induces a shift in the normal homeostatic mechanism by which collagen is formed, stabilized, and eventually turned over; this shift alters healing responses to physical or microbial wounding of the periodontium. Tetracycline antibiotics and chemically modified tetracycline agents reduce host collagenase production and collagen degradation through mechanisms that are independent of their antimicrobial activity.69 These drugs may have benefits in managing conditions such as
periodontitis, arthritis, diabetes, osteoporosis, and others in which collagen metabolism is altered.

Effects of Periodontal Infection on Glycemic Control

Not only does diabetes affect the periodontium, but evidence also suggests that periodontal infection may adversely affect glycemic control of diabetes. Diabetic subjects with severe periodontal disease often have a worsening of glycemic control over time, compared to diabetic subjects without periodontitis. Periodontal infection increased the risk of poor glycemic control by sixfold in one study. Periodontitis is also associated with an increased risk for other diabetic complications, such as nephropathy and macrovascular disease. In one study, 82% of diabetic patients with severe periodontitis had at least one major cardiovascular, cerebrovascular, or peripheral vascular event during the 1- to 11-year study period, compared to only 21% of diabetic subjects with little or no periodontal disease.

In diabetic patients with periodontitis, periodontal treatment may have beneficial effects on glycemic control. Several well-controlled studies of diabetic subjects with severe periodontal disease have shown improvements in glycemic control following a combination of mechanical débridement (scaling and root planing) and systemic doxycycline antibiotic therapy. Other studies in which patients received only mechanical therapy or in which the subject population already had good glycemic control prior to periodontal treatment showed no significant effect on glycemic control. The mechanisms by which adjunctive systemic antibiotics, when combined with subgingival mechanical débridement, may induce positive changes in glycemic control are presently unclear. Changes may result from more complete elimination of the subgingival pathogens in patients receiving antibiotics or from the suppression of collagenase production and AGE formation.

▼ DENTAL MANAGEMENT OF THE DIABETIC PATIENT

General Dental Treatment

Overall, diabetic patients respond to most dental treatments similarly to the way nondiabetic patients respond. Responses to therapy depend on many factors that are specific to each individual, including oral hygiene, diet, habits such as tobacco use, proper dental care and follow-up, overall oral health, and metabolic control of diabetes. For example, the diabetic patient with poor oral hygiene, a history of smoking, infrequent dental visits, and a high fermentable-carbohydrate intake is more likely to experience oral diseases such as caries and periodontitis and to respond poorly to dental treatment than a diabetic patient without these factors. Glycemic control appears to play an important role in the response to periodontal therapy. Well-controlled diabetic patients with periodontitis have positive responses to nonsurgical therapy, periodontal surgery, and maintenance that are similar to those of people without diabetes. However, poorly controlled diabetic patients respond much less favorably, and short-term improvements in periodontal health are frequently followed by regression and by recurrence of disease. It is imperative that the dental practitioner have a clear understanding of each diabetic patient’s level of glycemic control prior to initiating treatment.

Patients may present to the dental office with oral conditions that suggest an undiagnosed diabetic state. An example is severe rapidly progressing periodontitis that exceeds what would be expected given the patient’s age, habit history, oral hygiene, and level of local factors (plaque, calculus) (Figures 21-1 and 21-2). Other findings seen in some undiagnosed diabetic patients include enlarged gingival tissues that bleed easily upon manipulation and the presence of multiple periodontal abscesses (Figures 21-3, 21-4, and 21-5).

If the clinician suspects an undiagnosed diabetic state, the patient should be questioned to elicit a history of polydipsia, polyuria, polyphagia, or unexplained weight loss (see Table 21-4). The patient should be questioned about a family history of diabetes. If diabetes is suspected, laboratory evaluation and physician referral are indicated (see Table 21-5). A patient with previously diagnosed but poorly controlled diabetes may present with oral findings similar to those of the undiagnosed diabetic individual. The dental practitioner must establish the level of glycemic control early in the treatment process; this can be done by physician referral or by a review of the patient’s medical records. Patients who perform SBGM may be asked to bring their glucose log to the dental office for review by the dental team.

The clinician should determine the patient’s recent glycated hemoglobin values since this test provides a measure of glycemic control over the preceding 2 to 3 months. HbA1c values of less than 8% indicate relatively good glycemic control; values greater than 10% indicate poor control. Physician
referral is appropriate any time glycemic control is in question. The issue of glycemic control should be addressed often by the dental team since dental treatment outcomes may be dependent partly on good metabolic control of the underlying diabetic state. Other key dental treatment considerations for diabetic patients include stress reduction, treatment setting, the use of antibiotics, diet modification, appointment timing, changes in medication regimens, and the management of emergencies.

Endogenous production of epinephrine and cortisol increase during stressful situations. These hormones elevate blood glucose levels and interfere with glycemic control. Adequate pain control and stress reduction are therefore important in treating diabetic patients. Profound anesthesia reduces pain and minimizes endogenous epinephrine

release. The small amounts of epinephrine in dental local anesthetics at 1/100,000 concentration have no significant effect on blood glucose. Conscious sedation should be considered for extremely anxious patients. Most practitioners who use intravenous sedation elect to use fluids without dextrose, such as normal saline. However, fluids such as D5W (a 5% solution of dextrose in water) in small amounts should not produce wide fluctuations in glycemia in most patients.

Most diabetic patients can easily be managed on an outpatient basis in the dental office. Patients with very poor glycemic control, severe head and neck infections, other systemic diseases or complications, and dental-treatment needs that will require long-term alteration of medication regimens or diet may be considered for treatment in a more controlled medical environment.

![Figure 21-2](image21-2.png) Radiograph of area 18-19 in the same patient shown in Figure 21-1 at 39 years of age and with an 8-year history of poorly controlled type 1 diabetes (HbA1c values were 10.2 to 11.3%). There is a rapid progression of bone loss, the severity of which exceeds that expected from plaque and calculus levels.

![Figure 21-3](image21-3.png) Lingual view of mandibular incisors of a 60-year-old female with poorly controlled type 2 diabetes. The HbA1c value at initial examination was 13.9%. Multiple periodontal abscesses (teeth 22, 23, 25, 26, and 27) with severe inflammation and bone loss can be seen.

![Figure 21-4](image21-4.png) Palatal view of the maxillary right sextant in the same patient shown in Figure 21-3. An abscess can be noted on the palatal aspect of tooth 2.

![Figure 21-5](image21-5.png) Radiograph of the same sextant shown in Figure 21-4. Severe bone loss can be noted on tooth 2.
The use of systemic antibiotics for routine dental treatment is not necessary for most diabetic patients. Antibiotics may be considered in the presence of acute infection. Some clinicians prefer to prescribe prophylactic antibiotic coverage prior to surgical therapy if the diabetic patient’s glycemic control is poor. This usually applies to emergency situations since elective procedures are generally deferred until glycemic control improves. In patients with severe periodontitis, adjunctive use of tetracycline antibiotics in conjunction with mechanical periodontal therapy may have beneficial effects on glycemic control as well as on periodontal status.

Dental treatment can result in postoperative discomfort. This may necessitate changes in the diet, especially in cases of extensive dental therapy. Because diet is a major component of diabetes management, diet alterations that are made because of dental treatment may have a major impact on the patient. Whereas some patients are very knowledgeable about their diabetic condition and can adjust for changes in diet, this may not be the case with others. The clinician may need to consult the patient’s physician prior to therapy, to discuss diet modifications and required changes in medication regimens. Another diet change occurs when patients are placed on orders to take nothing by mouth (NPO) before dental treatment, a common recommendation before conscious sedation. Consultation with the patient’s physician may be needed to adjust the dose of insulin or oral agents in this situation; however, some patients are able to make these adjustments themselves. Physicians often recommend reducing the insulin dose that immediately precedes lengthy or extensive dental procedures.

Appointment timing for the diabetic patient is often determined by the individual’s medication regimen. Conventional wisdom holds that diabetic patients, like other medically compromised individuals, should receive dental treatment in the morning. While this may be true for some patients, it is not true for others. It is generally best to plan dental treatment to occur either before or after periods of peak insulin activity. This reduces the risk of perioperative hypoglycemic reactions, which occur most often during peak insulin activity. For those who take insulin, the greatest risk of hypoglycemia will thus occur about 30 to 90 minutes after injecting lispro insulin, 2 to 3 hours after regular insulin, and 4 to 10 hours after NPH or Lente insulin (see Table 21-8). For those who are taking oral sulfonylureas, peak insulin activity depends on the individual drug taken. Metformin and the thiazolidinediones rarely cause hypoglycemia.

The main factor to consider in determining appointment times is the peak action of insulin and the amount of glucose being absorbed from the gut following the last food intake. Questions such as those listed in Table 21-10 allow the clinician to assess the risk of hypoglycemia. The greatest risk would occur in a patient who has taken the usual amount of insulin or oral agent but has reduced or eliminated a meal prior to dental treatment. For example, if the patient takes the usual dose of regular insulin before breakfast but then fails to eat or eats less than the usual amount, the patient will be at increased risk for hypoglycemia during a morning dental appointment. Patients with good long-term glycemic control and patients with a previous history of severe hypoglycemic episodes are at greater risk for future hypoglycemia.

Often, it is not possible to plan dental treatment so as to avoid peak insulin activity. This is particularly true for patients who take frequent insulin injections (see Table 21-9). In these instances, the clinician must be aware that the patient is at risk for perioperative hypoglycemia. It is helpful to check the pretreatment blood glucose level (using the patient’s glucometer) and to have a source of carbohydrates readily available. When treating patients with a history of asthma or angina, dentists usually have the patients bring their inhaler or nitroglycerine with them to dental appointments. In the same way, diabetic patients should be encouraged to bring their glucometer with them to the dental office. Before dental treatment begins, the patient may check his or her blood glucose. If the level is near the lower end of the normal range, a small amount of pretreatment carbohydrate may prevent hypoglycemia during the appointment. Having the glucometer available also allows rapid determination of blood glucose levels should the patient experience signs and symptoms of hypoglycemia.

### Diabetic Emergencies in the Dental Office

The most common diabetic emergency in the dental office is hypoglycemia (Table 21-11), a potentially life-threatening complication that must be managed accordingly. Signs and symptoms include confusion, sweating, tremors, agitation, anxiety, dizziness, tingling or numbness, and tachycardia. Severe hypoglycemia may result in seizures or loss of consciousness.

As soon as a patient experiences signs or symptoms of possible hypoglycemia, he or she should check the blood glucose with a glucometer. If a glucometer is unavailable, the condition should be treated presumptively as a hypoglycemic episode. The dental practitioner should give the patient approximately 15 g of oral carbohydrate in a form that will be absorbed rapidly (Table 21-12). If the patient is unable to

### TABLE 21-10 Determining Risk of Hypoglycemia: Questions to Patient

1. Have you ever had a severe hypoglycemic reaction before?
2. How often do you have hypoglycemic reactions?
3. How well controlled is your diabetes? What was your last glycated hemoglobin* level?
4. What diabetic medication(s) do you take?
   - Did you take them today?
   - When did you take them? Is that the same time as usual?
   - How much of each medication did you take?
   - Is this the same amount you normally take?
5. What did you eat today before you came to the dental office?
   - What time did you eat? Is that when you normally eat?
   - Did you eat the same amount you normally eat for that meal?
   - Did you skip a meal?

*Hemoglobin A1 or A1c.
Because hyperglycemic emergencies develop more slowly than does hypoglycemia, they are less likely to be encountered in the dental office. Diabetic ketoacidosis and hyperosmolar nonketotic acidosis require immediate medical evaluation and treatment. In the dental office, care is limited to activating the emergency medical system, opening the airway and administering oxygen, evaluating and supporting circulation, and monitoring vital signs. The patient should be transported to a hospital as soon as possible.

\section*{CONCLUSION}

Diabetes mellitus is a metabolic condition affecting multiple organ systems. The oral cavity frequently undergoes changes that are related to the diabetic condition, and oral infections may adversely affect metabolic control of the diabetic state. The mechanisms underlie the oral effects of diabetes share many similarities with the mechanisms that are responsible for the classic diabetic complications. The intimate relationship between oral health and systemic health in individuals with diabetes suggests a need for increased interaction between the dental and medical professionals who are charged with the management of these patients. Oral health assessment and treatment should become as common as the eye, foot, and kidney evaluations that are routinely performed as part of preventive medical therapies. Dental professionals with a thorough understanding of current medical treatment regimens and the implications of diabetes on dental care are able to help their diabetic patients achieve and maintain the best possible oral health.

\section*{REFERENCES}


\begin{table}[h]
\centering
\caption{Factors That Increase Risk of Hypoglycemia}
\begin{tabular}{|l|}
\hline
Skipping or delaying food intake \\
Injection of too much insulin \\
Injection of insulin into tissue with high blood flow (eg, injection into thigh after exercise such as running) \\
Increasing exercise level without adjusting insulin or sulfonylurea dose \\
Alcohol consumption \\
Inability to recognize symptoms of hypoglycemia \\
Anxiety, stress \\
Denial of warning signs or symptoms \\
Past history of hypoglycemia \\
Hypoglycemia unawareness \\
Good long-term glycemic control \\
\hline
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\begin{table}[h]
\centering
\caption{Treatment of Hypoglycemia}
\begin{tabular}{|l|}
\hline
1. If patient is awake and able to take food by mouth, give 15 g oral carbohydrate in one of the following forms: \\
- 4–6 oz fruit juice or soda \\
- 3–4 tsp table sugar \\
- hard candy \\
- cake frosting \\
2. If patient is unable to take food by mouth and IV line is in place, give 25–30 mL D50 or 1 mg glucagon. \\
3. If patient is unable to take food by mouth and IV line is not in place, give 1 mg glucagon subcutaneously or intramuscularly. \\
\hline
D50 = 50% dextrose solution; IV = intravenous; oz = ounce; tsp = teaspoon.
\end{tabular}
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