Diabetes mellitus is a chronic metabolic disorder characterized by a relative or absolute lack of insulin that results in elevated blood glucose levels and produces disturbances in lipid and protein metabolism as well. Being the most common metabolic disorder, it affects 15 to 20 million Americans, roughly 2 to 4% of the population; many are yet undiagnosed. Diabetes mellitus produces multiple systemic complications, including nephropathy, retinopathy, accelerated atherosclerosis, neuropathy, delayed wound healing, and increased susceptibility to infections. It is clearly recognized for adverse effects on longevity and quality of life. With increasing disease prevalence and energized medical research initiatives, it is critical that the dental team maintain contemporary awareness.

The responsibility falls to the dental practitioner to (1) recognize signs and symptoms of diabetes, to facilitate early diagnosis and management; (2) appropriately manage oral conditions, to maximize oral function, comfort, and esthetics for the life of the patient; and (3) work in conjunction with the patient, the patient’s physician, and diabetes management team, to facilitate long-term disease control.

The two most common forms of diabetes mellitus are characterized as type 1, autoimmune, which comprises about 5% of the cases, and type 2, non-autoimmune, which accounts for roughly 85% of cases. The term type 1 diabetes mellitus is often used synonymously for insulin-dependent diabetes mellitus (IDDM), and the term type 2 is used to characterize non–insulin-dependent diabetes mellitus (NIDDM). This classification can be confusing in that patients with NIDDM may need insulin to control their disease; however, they do not develop ketoacidosis if their insulin is withdrawn. Hence they are termed non–insulin-dependent. In contrast, patients with IDDM develop ketoacidosis in the absence of insulin (ketoacidosis-sensitive) and are therefore termed insulin-dependent.

Insulin-dependent diabetes mellitus is generally found in individuals under 40 years of age. Because disease onset often occurs during adolescence, it is descriptively called “juvenile onset.” However, IDDM may occur at any age. Type 2 diabetes mellitus generally occurs in individuals over 40 years of age, and has been referred to as “adult onset.” Secondary diabetes mellitus, which applies to the development of a diabetic state that originated secondary to another disease or condition, has also been characterized. Examples include pancreatic disease from chronic alcohol intake, hormonal diseases, such as hyperthyroidism, or the administration of drugs, such as exogenous corticosteroids. All three types of diabetes may be characterized by hyperglycemia and microangiopathy. This chapter focuses on type 1, IDDM, and type 2, NIDDM.
Molecular and pathologic correlates of disease

Both IDDM and NIDDM have a genetic component involved in their etiology. Studies have shown that the concordance rate between identical twins and type 1 diabetes is 50%, as compared to 80% in identical twins with type 2 diabetes. It is believed that susceptibility to IDDM is linked to specific alleles of the class II major histocompatibility complex. However, an environmental event, such as exposure to a virus, is believed necessary to trigger the development of diabetes. Following exposure to an environmental event, an inflammatory response called “insulitis” develops in the pancreas. The cells that infiltrate the islets are activated T lymphocytes. It is not clear at this time that insulitis is central to the destructive sequence in autoimmune diabetes.

Next, the surface of the beta cell is transformed such that it is no longer recognized as “self,” but is perceived by the immune system as a foreign cell. This stimulates the development of an immune response in which cytotoxic antibodies develop and act with cell-mediated immune mechanisms to destroy the beta cells. The precise mechanism behind the autoimmune destruction is unknown. When most of the beta cells are destroyed, diabetes mellitus type 1 manifests.

Type 1 diabetics have minimal or no endogenous insulin production as a result of autoimmune destruction of insulin-producing pancreatic beta cells (Figure 9–1). These individuals require exogenous insulin for control of glycemia and, without insulin, develop serious metabolic complications leading to ketoacidosis and coma. More specifically, when ingested food is converted into glucose, insulin secretion is normally stimulated. Insulin is essential for transfer of glucose from blood into muscle, fat, and liver tissues and for preventing the liver from converting glycogen stores into glucose. If insulin is not available, glucose levels increase in the blood and tissue fluids. Blood glucose rises from underuse of blood glucose as well as overproduction owing to glycogenolysis and fat metabolism. When hyperglycemia exceeds the renal threshold (roughly 200 mg/dL) glycosuria ensues. The excessive glycosuria induces an osmotic diuresis with polyuria (passage of large volumes of urine) which results in the loss of water and electrolytes. Increased urinary output coupled with vascular hyperosmolarity tends to deplete fluid reserves. Osmoreceptors in the thirst center of the brain sense the fluid loss and polydipsia (excessive thirst) results. The lack of glucose use by insulin-dependent cells, leads to glucose-starved cells. The patient often increases the intake of food (polyphagia) but, in many cases, still loses weight. Cortisol secretion may be increased in the type 1 diabetic, in response to the stress, which leads to protein breakdown and loss of nitrogen in the urine. As the process continues, the

Figure 9–1  Hyperglycemia in both forms of diabetes leads to glycosuria with clinical signs of polydipsia, polyuria, and nocturia.
body metabolizes fat for energy, releasing free fatty acids, which are converted to harmful ketones (acetone and beta-hydroxybutyric acid) that are excreted in the urine. As this progresses, the individual develops metabolic acidosis, which can lead to coma and death if not quickly treated (Figure 9–2). Ketonic acid-buffering by sodium bicarbonate leads to generation of excess carbonic acid with increased respiratory rate (hypernea), a compensatory mechanism that attempts to raise blood pH by elimination of water and carbon dioxide.

Type 2 diabetes mellitus is the most common type of diabetes; but less is known about its etiology and onset. It is believed that genetic factors are more significant for type 2 than for type 1; but type 2 diabetes is not linked to any human leukocyte antigen (HLA) genes, being polygenic. Two metabolic defects may characterize type 2 disease: abnormal insulin secretion and inability of peripheral tissues to respond to insulin, perhaps related to a cell-surface insulin receptor defect. In early phases, glucose levels remain normal, owing to increased insulin release that balances the defective receptor-mediated insulin resistance. As insulin resistance increases, hyperglycemia develops. In the third phase, insulin resistance does not change, but insulin secretion declines, resulting in overt diabetes. It is likely that insulin secretory defects and insulin resistance are both required for diabetes to be expressed. Obesity increases an individual’s susceptibility to NIDDM. Many obese type 2 diabetics can reverse impaired glucose tolerance simply by losing weight, especially if weight is lost early in the course of their disease. Obesity may play a critical role in the development of insulin resistance, but one must remember that insulin resistance is also encountered in nonobese patients with type 2 diabetes. As the longevity of the population increases, the prevalence of NIDDM will also increase. Table 9–1 and Table 9–2 summarize the general characteristics and symptoms associated with type 1, IDDM, and type 2, NIDDM.

Clinical features

Reports have indicated that diabetic patients are susceptible to complications that cause morbidity and premature mortality. A given patient may experience several complications simultaneously, or a single problem may dominate the clinical picture. Complications include

![Figure 9–2](image) Ketosis occurs when fatty acids are required for generation of adenosine triphosphate (ATP) in the absence of intracellular glucose.
retinopathy, nephropathy, neuropathy, macrovascular disease, and impaired wound healing (Figure 9–3). Medical complications are related to the level of hyperglycemia and pathologic changes within the vascular system and the peripheral nervous system. Hyperglycemia appears to play a major role in development of atherosclerotic plaques, which enhance development of hypertension, stroke, and myocardial infarction. Atherosclerosis develops earlier and is more prevalent and more advanced in diabetic than in nondiabetic individuals. Uncontrolled diabetics have higher levels of low-density lipoprotein (LDL) cholesterol and lower levels of high-density lipoprotein (HDL) cholesterol. Myocardial infarction is a leading cause of death in patients with NIDDM. Atherosclerotic lesions also produce intermittent claudication, poor wound healing, and gangrene.

Small-vessel changes, including thickening of the intima and lipid deposition, are especially significant in the retina of the eye and small vessels of the kidney. Diabetic retinopathy is one of the leading causes of blindness. Diabetic nephropathy progresses to end-stage renal disease in 30 to 40% of individuals with IDDM. Nearly one-fourth of individuals using renal dialysis are diabetic.

Diabetic neuropathy may affect every system, with the possible exception of the brain. It is a major cause of morbidity. Peripheral neuropathy is generally bilateral and symptoms include numbness, paresthesias, hyperesthesias, and pain.

The relation between control of glucose levels and progression of diabetic complications is becoming more clear as research continues. Microvascular-related complications can be diminished by good control of glycemia. Improved control of glycemia has also been associated with a reduction in macrovascular complications. Since hyperglycemia also plays a major role in diabetic neuropathy, improved control seems appropriate. Efforts should be made to control hyperglycemia, but such therapy should not introduce a high incidence of dangerous hypoglycemic reactions.

### Table 9–1  General Characteristics of Type 1 and Type 2 Diabetes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type 1 (IDDM)</th>
<th>Type 2 (NIDDM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>5%</td>
<td>85–90%</td>
</tr>
<tr>
<td>Clinical</td>
<td>Onset abrupt</td>
<td>Onset gradual</td>
</tr>
<tr>
<td>Age</td>
<td>Onset &lt; 20 yr of age</td>
<td>Onset &gt; 40 yr of age</td>
</tr>
<tr>
<td>Weight</td>
<td>Normal</td>
<td>Obese (80%)</td>
</tr>
<tr>
<td>Endogenous insulin</td>
<td>Inadequate or absent</td>
<td>Low, normal, or high levels</td>
</tr>
<tr>
<td>Islet cell antibodies</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Ketoacidosis</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Genetics</td>
<td>HLA-D linked</td>
<td>No HLA association</td>
</tr>
<tr>
<td>Concordance in identical twins</td>
<td>50%</td>
<td>90–100%</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>Autoimmunity to pancreatic beta cells</td>
<td>Insulin resistance</td>
</tr>
</tbody>
</table>

IDDM = insulin-dependent diabetes mellitus; NIDDM = non–insulin-dependent diabetes mellitus; HLA = human leukocyte antigen.

### Table 9–2  Symptoms of Diabetes

<table>
<thead>
<tr>
<th>Type 1 (IDDM)</th>
<th>Type 2 (NIDDM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polydipsia</td>
<td>Paresthesias</td>
</tr>
<tr>
<td>Polyuria</td>
<td>Nocturnal urination</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>Visual changes</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Weight loss or weight gain</td>
</tr>
<tr>
<td>Visual changes</td>
<td>Loss of sensation</td>
</tr>
<tr>
<td>Recurrence of bed wetting</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>Thirst or dry mouth</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td></td>
</tr>
</tbody>
</table>

Diabetic angiopathies

**Figure 9–3** Both large- and small-vessel disease are complications of diabetes.
It is uncertain if strict control of glycemia in patients with NIDDM would significantly reduce long-term complications, but improved control has been recommended by the American Diabetes Association. Management of NIDDM may require oral hypoglycemic agents as well as dietary and exercise therapy. Insulin injections may be added to the regimen.

Screening tests are available for individuals who show signs and symptoms and those in risk groups, such as individuals who are over 40 years of age, obese, have diabetic relatives, or females with gestational diabetes. A normal fasting blood glucose level ranges from 60 mg/dL to 100 mg/dL. The National Diabetes Data Groups of the National Institutes of Health, in 1979, provided revised criteria for the diagnosis of diabetes. A fasting blood glucose greater than 140 mg/dL on two occasions is generally considered diagnostic for diabetes mellitus. A 2-hour postprandial glucose assay requires the patient to ingest 75 to 100 g of glucose after a night of fasting. Blood glucose levels taken 2 hours after glucose ingestion that are greater than 200 mg/dL on two occasions are diagnostic of diabetes mellitus. These measures provide the blood glucose level at the time the blood was drawn and reflect intake from the previous 2 to 10 hours. With the availability of home monitoring equipment, many patients, especially those taking insulin, monitor their blood levels at home and are keeping a log to share with their physicians. Patients are taking a more active role in their disease management.

After the diagnosis and implementation of initial therapy, the overall goal of medical management is the prevention of diabetic complications through adequate control of glycemia. The primary assay used for assessing long-term control is the glycosylated or glycated hemoglobin assay, termed the HbA1c or HbA1 assay. This test indicates the blood glucose concentrations during the previous 6 to 8 weeks. The clinical interpretation for this assay is listed in Table 9–3. This assay is not to be used as a screening or diagnostic assay for diabetes.

The most serious consequence of insulin overdose is hypoglycemia. Drowsiness, irritability, and confusion might signal mild hypoglycemia. Coma, spasms, or seizures could develop if severe hypoglycemia develops. Of special note is the use of beta-adrenergic blockers by diabetic patients. Tachycardia often serves as a warning to patients of impending hypoglycemia. Beta-adrenergic blockers mask the tachycardia and allow hypoglycemia to progress. Long-term use of insulin can also lead to the development of insulin antibodies, requiring larger doses to compensate for antibody-mediated elimination.

Patients with NIDDM often use oral hypoglycemic or anti-hyperglycemic agents to aid control of glycemia (Table 9–5). Oral sulfonylureas represent a commonly used class in this group of medications. The first generation agents include chlorpropamide, tolbutamide, tolazamide, and acetohexamide. Second generation agents include glyburide and glipizide. These agents are commonly given to diabetics whose fasting glucose level is lower than 250 mg/dL.

Sulfonylurea agents activate beta cells to increase insulin output in patients. The second generation drugs appear to be more potent and require a lower daily dosage. In addition, they produce less displacement of endogenous insulin.

### Table 9–3 Evaluation of Diabetes: Control of Glycemia

<table>
<thead>
<tr>
<th>Glycohemoglobin Level (HbA1c)</th>
<th>Clinical Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–6%</td>
<td>Normal</td>
</tr>
<tr>
<td>Less than 7.5%</td>
<td>Good diabetes control</td>
</tr>
<tr>
<td>7.6–8.9%</td>
<td>Moderate diabetes control</td>
</tr>
<tr>
<td>&gt;9%</td>
<td>Poor diabetes control</td>
</tr>
</tbody>
</table>

### Table 9–4 Insulin Preparations

<table>
<thead>
<tr>
<th>Type</th>
<th>Time of Onset (hr)</th>
<th>Duration (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast-acting insulins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lispro</td>
<td>15 min</td>
<td>&lt; 5 hr</td>
</tr>
<tr>
<td>Insulin injection (regular)</td>
<td>30–60 min</td>
<td>6–8</td>
</tr>
<tr>
<td>Prompt insulin zinc</td>
<td>1–2</td>
<td>12–16</td>
</tr>
<tr>
<td>suspension (Semilente)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting insulins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isophane insulin suspension (NPH)</td>
<td>1–2</td>
<td>18–28</td>
</tr>
<tr>
<td>Insulin zinc suspension</td>
<td>1–3</td>
<td>18–28</td>
</tr>
<tr>
<td>(Lente)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting insulins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protamine zinc insulin</td>
<td>4–8</td>
<td>36</td>
</tr>
<tr>
<td>suspension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended insulin zinc</td>
<td>4–8</td>
<td>20–36</td>
</tr>
<tr>
<td>suspension (Ultralente)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NPH = neutral protamine hagedorn.
Table 9–5  Oral Agents for Diabetes Mellitus

<table>
<thead>
<tr>
<th>Agent</th>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylureas:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oral hypoglycemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First generation</td>
<td>Chlorpropamide</td>
<td>Diabinese</td>
</tr>
<tr>
<td>Tolbutamide</td>
<td>Orinase</td>
<td></td>
</tr>
<tr>
<td>Tolazamide</td>
<td>Tolinase</td>
<td></td>
</tr>
<tr>
<td>Acetohexamide</td>
<td>Dymelor</td>
<td></td>
</tr>
<tr>
<td>Glyburide</td>
<td>Diabeta, Micronase</td>
<td>Glucotech</td>
</tr>
<tr>
<td>Glipizide</td>
<td>Glycophage</td>
<td></td>
</tr>
<tr>
<td>Biguanides:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oral antihyperglycemic</td>
<td>Metformin</td>
<td>Glucophage</td>
</tr>
<tr>
<td>Thiazolidinediones:</td>
<td>Rosiglitazone</td>
<td>Avandia</td>
</tr>
<tr>
<td>oral antihyperglycemic</td>
<td>Pioglitazone</td>
<td>Actos</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Acarbose</td>
<td>Precose</td>
</tr>
<tr>
<td>Meglitinide: insulin enhancers</td>
<td>Repaglinide</td>
<td>Prandin</td>
</tr>
<tr>
<td></td>
<td>Nateglinide</td>
<td>Starlix</td>
</tr>
</tbody>
</table>

ment from protein binding sites and hence have less frequent interactions with other agents such as salicylates and warfarin. At high dosages, acetohexamide has been associated with additional side effects such as gastrointestinal upset and hypersensitivity to sunlight. All sulfonylurea agents are capable of producing severe hypoglycemia, and patient selection and usage in conjunction with other medications must be carefully evaluated.

Biguanides are used in the treatment of NIDDM, alone or in combination with oral sulfonylurea agents. Biguanides are not chemically or pharmacologically related to oral sulfonylureas. Unlike sulfonylureas, the biguanides do not increase secretion of insulin. They reduce hyperglycemia by improving insulin sensitivity, and enhance the glucose uptake in cells. They also inhibit gluconeogenesis and appear to reduce glucose absorption from the gut. Metformin (Glucophage) does not produce hypoglycemia and does not change insulin secretion. Metformin is contraindicated in patients with renal dysfunction and has been associated with a very low incidence of fatal lactic acidosis.

The class of drugs, thiazolidinediones, appears to heighten cellular responsiveness to insulin in muscle and adipose tissue. One of the first medications in this class, troglitazone (Rezulin) was removed from the market in 2000 because of liver toxicity and associated patient mortality. Two second generation “glitazones,” as the class is informally called, were approved in 1999. Rosiglitazone is a highly selective and potent agonist for the peroxisome proliferator-activated receptor gamma (PPAR-γ) found in tissues such as adipose, skeletal, muscle, and liver. The mechanism is thought to involve binding to nuclear receptors that regulate the transcription of a number of insulin-responsive genes critical for the control of glucose and lipid metabolism. It does not stimulate insulin release, nor does it function in the absence of circulating insulin. Rosiglitazone (Avandia) has been approved for monotherapy use or in combination with metformin in patients with Type 2 diabetes who are not able to be controlled with diet and exercise alone. Pioglitazone (Actos) also functions to decrease insulin resistance and was approved for use as monotherapy or in combination with insulin or a sulfonylurea drug such as glyburide or glipizide. These medications should be used with caution in patients with heart failure, edema, or liver disease, and they may affect ovulation. The second generation thiazolidinedione drugs appear to have less risk of liver toxicity than troglitazone, however, monitoring of liver function is recommended.

Acarbose (Precose) is an alpha-glucosidase inhibitor for use in the management of NIDDM. It slows the digestion and uptake of carbohydrates from the gastrointestinal system, lowering the post-prandial peaks in blood glucose. It does not cause hypoglycemia, but when taken with sulfonylureas or insulin, the delay of glucose into the blood stream could lead to relative insulin excess and hypoglycemia. Acarbose is contraindicated in patients with inflammatory bowel disease and marked disorders of digestion.

The insulin enhancers are very short acting agents that stimulate the release of insulin from beta cells. Repaglinide (Prandin) and nateglinide (Starlix) are designed to be taken with each meal and skipped if a meal is omitted. These medications should be used cautiously in patients with impaired renal function or impaired liver function. The hypoglycemic action may be potentiated by nonsteroidal anti-inflammatory agents, salicylates, and several other medications that are highly protein bound.

For proper management, a thorough medication history with special attention directed at potential drug interactions is critical. New medications and contraindications with existing agents are constantly being recognized. Reference to a current pharmacology text or a recognized drug-interaction program is recommended prior to initiating therapy.

**Oral manifestations**

Diabetes is associated with several oral manifestations, primarily those related to infections, inflammations, and poor wound healing. Hyperglycemia, ketoacidosis, and vascular-wall disease contribute to the increased susceptibility of uncontrolled diabetics to infection and the decreased ability to manage infections. Hyper-
glycemia has been shown to reduce the phagocytic function of leukocytes. Associated vascular-wall changes inhibit blood flow and the transport of granulocytes to the area of injury. Xerostomia and effects associated with reduced salivary flow rates are also problematic. These conditions have significant implications for dental care.

Several studies have reported an increased incidence and severity of gingival inflammation, periodontal abscess, and chronic periodontal disease in diabetic patients (Figure 9–4). Microvascular disease in the periodontium adversely affects blood flow and leukocyte migration and predisposes to premature periodontal disease, abscess, and delayed wound healing.

Research strongly supports cessation of cigarette smoking to aid maintenance of periodontal health, especially in patients with diabetes. Data also support the concept that in diabetes-associated periodontitis, the altered host inflammatory response plays a critical role. An unexpected high level of gingival crevicular fluid mediators was found among subjects with IDDM, even in the patients with gingivitis and mild periodontitis. Diabetics had significantly higher gingival crevicular fluid levels of both prostaglandin E2 (PGE2) and interleukin (IL)-1 beta when compared to nondiabetic controls with similar periodontal status. These findings suggest that IDDM is a significant risk factor for more severe periodontal disease, because as compared to nondiabetics, diabetic subjects react with an abnormally high degree of inflammation to an equivalent bacterial burden. Other findings suggest that both hyper- and hypoglycemia might directly impair the biologic functions of periodontal connective tissues through cell–matrix interactions.

Well-controlled diabetic patients, as measured by blood glycated hemoglobin levels, have less severe periodontal disease than poorly controlled diabetics. Recent findings indicate that effective control of periodontal infection in patients with diabetes (IDDM and NIDDM) reduces the level of advanced glycosylation end-products in the serum. If this is confirmed via additional studies, periodontal infection control must be considered as an integral part of medical management of diabetic control.

Oral candidiasis occurs more frequently in diabetics than in nonaffected populations, because of altered response to infections and xerostomia and an altered oral flora (Figure 9–5). After confirmation of diagnosis, topical or systemic antifungal agents can be prescribed as appropriate (see Chapter 18).

Antral mucormycosis is a rare but serious complication associated with immunocompromised status that accompanies uncontrolled or chronic IDDM. Signs and symptoms include nasal obstruction, bloody nasal discharge, facial pain, swelling, and visual disturbances. Progression of disease leads to blindness, seizures, and death (Figure 9–6). The patient should be referred to an infectious disease specialist for appropriate management.

Burning tongue may be associated with fungal infections, such as candidiasis, or peripheral neuropathies associated with diabetes. A cytologic smear can confirm the diagnosis of oral candidiasis and proper treatment can be initiated. The diagnosis of peripheral neuropathy
should be concluded after other probable causes have been ruled out by consultation with the patient’s physician and an oral medicine specialist.

Xerostomia may result from hyperglycemia and subsequent polyuria that depletes the extracellular fluids. The overall effect is reduction in secretion of saliva. Adequate salivary flow is recognized to be an essential component for normal mastication, taste, and swallowing functions. Saliva plays a critical role in the lubrication and protection of the oral mucosa, neutralizing harmful acid that can lead to dental caries and destroying microorganisms. Diminished flow can increase susceptibility to oral ulcers, bacterial, viral or fungal infections, and dental caries.

Dental management

Dental management of the diabetic patient should include four primary areas:

1. Screening and diagnosis of previously undiagnosed patients (based upon a health history review and oral examination),
2. Proper dental management of oral manifestations,
3. Prevention of complications during procedures related to hypoglycemic shock, hyperglycemic shock, and acute cardiovascular episodes, and
4. Proper management of medical emergencies.

Screening and referral for diagnosis should be based upon a thorough review of the patient’s health history and oral examination. Chairside glucose screening might provide helpful information. Patients suspected of having diabetes should be referred to a physician for definitive diagnosis and long-term management.

An assessment of the impact of diabetes mellitus on oral health should be included in the overall patient management. All patients diagnosed with diabetes should be identified by history, type of diabetes, treatment regimen, and presence of medical complications. It is extremely beneficial to determine the severity of the disease and degree of control of glycemia. A few screening questions might assist in that process.

- When were you diagnosed?
- When did you last visit your physician and how often do you go?
- What are your current medications?
- When was your last blood glucose measurement and what was the value?
- Do you home-monitor yourself?
- When was the last time you had an insulin reaction?
- When was the last time you went to the local hospital emergency room with complications related to your diabetes?

The diabetic patient who is receiving good medical management and is well controlled without serious complications, such as renal disease, hypertension, or coronary artery disease, can safely receive any indicated dental treatment. A diabetic patient whose disease is well controlled and who is free of infection does not require prophylactic antibiotics for dental treatment. However, some consideration should be given to helping prevent unanticipated events during dental care.

For patients with IDDM, the following special management considerations should be reviewed:

1. Patients should be scheduled when their glucose is high and insulin activity is low—usually morning appointments.
2. Patients should be instructed to take their usual insulin dosage and to eat their normal breakfast before the dental appointment.
3. Nutritional intake and insulin levels should be reviewed with the patient prior to dental procedures.
4. Vital signs should be monitored.
5. Patients should be instructed to inform the dentist if they feel the onset of an insulin reaction.
6. The dentist should observe for signs of hypoglycemia and treat as appropriate.
   - Signs of hypoglycemia vary among individuals. The dentist should observe the patient for any of the following signs or symptoms and initiate treatment:
     a. Hunger, weakness, fast heartbeat, tingling, or altered sensations,
     b. Confusion or mood alteration,
     c. Sweating or pallor, and
     d. Disorientation
   - Treatment
     If conscious, administer glucose via beverage (cola or juice) containing glucose. If initial signs of hypoglycemia are not apparent, hypotension and a fast weak pulse may develop and the patient may become unconscious.
   - Treatment
     If unconscious, administer 50% dextrose, 30 to 50 mL, intravenously, or 1 mg glucagon, intra-muscularly.
     Any patient who has experienced unconsciousness should be taken to a hospital for further evaluation and treatment.
7. The dentist should consider factors that will contribute to development of hypoglycemia.
   - Hypoglycemia can develop if patients received their insulin injections, but failed to eat.
   - Hypoglycemia can result if patients received too much insulin or oral hypoglycemic agent.
   - Hypoglycemia can result through adverse drug interactions.
     a. Sulfonylureas and aspirin enhance the hypoglycemic effect of oral hypoglycemic agents.
     b. Sulfonylureas and fluconazole enhance the hypoglycemic effect of oral hypoglycemic agents.
8. The dentist should treat oral infections promptly and aggressively.
   - Medical consultation regarding glycemic status and insulin therapy is indicated.
   - If purulence is associated with the oral infection, culture should be obtained if possible. Penicillin or amoxicillin could be initiated until culture and sensitivity results are obtained.
   - Close follow-up should be maintained until the patient is stable and the condition has resolved.
9. The dentist should review the following considerations when planning for surgical procedures:
   - If the return to regular food intake is anticipated immediately following the procedure, no alteration in diet or insulin is necessary.
   - If the anticipated procedure will not allow the patient to return to regular food intake, consultation with physician prior to the procedure may be appropriate.
     a. For the insulin-controlled patient, the normal dose of insulin is often decreased the morning of the surgical procedure. Slight hyperglycemia during a procedure is certainly preferable to hypoglycemic shock.
   - In all cases, patients should be advised that the recommended nutritional intake is important to attain anticipated postoperative recovery.
   - Prophylactic antibiotics may be recommended to prevent infection in patients with poorly controlled diabetes and those with a history of recurrent infection.

Diabetes insipidus

Diabetes insipidus is a condition caused by a neurohypophyseal lesion, either inflammatory or neoplastic in nature, in which renal conservation of water is impaired owing to deficient antidiuretic hormone (ADH) release. Vasopressin, also called antidiuretic hormone, affects the control of water conservation and its release in coordination with the activity of the thirst center that regulates fluid intake. Via actions on receptors in the distal tubules of the kidney, ADH conserves water and concentrates the urine. This action assists in maintaining constancy of the osmolarity and volume of body fluids.

Molecular and pathologic correlates of disease

There are five primary causes for the development of diabetes insipidus, all of which result in damage, necrosis, or loss of function of the CNS cells that secrete ADH: (1) infiltrative lesions of the hypothalamus or pituitary as a result of neoplasms, leukemia, sarcoidosis, or histiocytosis (Langerhans cell histiocytosis); (2) pituitary or hypothalamic surgery; (3) severe head injuries; (4) vascular lesions; (5) idiopathic cause.

Clinical features

Polyuria, frequent urination and polydipsia, excessive thirst, are almost invariably present. Characteristically, these symptoms are sudden in onset. Urine may be pale in color and volume immense—up to 16 to 24 L per day accompanied by frequent urination, every hour, day and night. More frequently, urine volume is only moderately increased 2 to 6 L per day or even less. Diagnosis is determined by plasma or urinary ADH levels or by measuring urinary osmolality after dehydration and again after vasopressin administration.
Oral manifestations and dental management

Infiltrative lesions of the neurohypophysis as a result of Langerhans cell histiocytosis have implications for dental treatment. Histiocytes may infiltrate the posterior pituitary, resulting in decreased output of ADH, with resultant polyuria. Retro-orbital infiltrates of histiocytes may lead to exophthalmos, and osseous infiltrates are typically found in the skull and jaws. In addition, osseous infiltrates can be identified via conventional dental radiography. In addition to jaw lesions, one might observe loosening of the teeth or teeth “floating in space” (Figure 9–7). Langerhans cell histiocytosis can be treated successfully with Vinca alkaloid chemotherapy. Radiation therapy is sometimes needed. Jaw lesions are usually treated by local curettage. Extraction of involved teeth is often required.

Dental fluorosis has been reported as a complication of hereditary diabetes insipidus. Such patients demonstrate polydipsia and polyuria from early infancy. Drinking large amounts of water, even with lower than accepted fluoride content, can produce fluorosis of the teeth. In one study, six affected members from two families with hereditary diabetes insipidus were reviewed. Two children who drank water fluoridated at optimum levels developed moderate to severe fluorosis. Four affected patients who did not consume fluoridated water showed normal dentitions. In a second study, a mother and her four children presented different degrees of fluorosis directly related to the stage at which hormonal therapy was introduced.

Addison disease

Both hyperfunction and hypofunction of the adrenal glands can have profound effects on dental management of affected individuals. The following sections address primary and secondary adrenal insufficiency and hyperfunctioning of the adrenal cortex.

Molecular and pathologic correlates of disease

The adrenal glands are located on the superior aspect of each kidney and consist of two defined portions that provide several special functions. The outer portion of the gland, the adrenal cortex, produces three groups of steroid hormones: glucocorticoids, mineralocorticoids, and androgens. They are derived from cholesterol and share a common core structure. The adrenal cortex has three zones (Figure 9–8). The outermost zona glomerulosa produces mineralocorticoids, primarily aldosterone, which are critical for sodium and potassium balance and extracellular fluid volume. The zona fasciculata and the innermost zona reticularis secrete the glucocorticoid, cortisol, and androgens. Cortisol is essential for metabolism, anti-inflammatory properties, and maintenance of homeostasis during periods of physical or emotional stress. The inner portion of the gland, adrenal medulla, produces catecholamines, epinephrine (adrenalin), and norepinephrine (noradrenalin).

Cortisol secretion is regulated by the hypothalamic-pituitary-adrenal axis. The circadian rhythm, mediated by the CNS, and responses to stress stimulate the hypothalamus to release corticotropin-releasing hormone (CRH), which stimulates the production and secretion of adrenocorticotropic hormone (ACTH) by the anterior pituitary. The adrenal cortex is stimulated by ACTH to produce and secrete cortisol. Circulating plasma cortisol levels are elevated within minutes after stimulation in a normally functioning gland. The increased levels of cortisol act to inhibit the production of CRH and ACTH, and thereby decrease the output of cortisol. This process constitutes the negative feedback loop of cortisol.
regulation. The normal pattern of cortisol secretion usually peaks about the time of awakening in the morning and is lowest in the afternoon and evening. During a 24-hour period, approximately 20 mg of cortisol are secreted. Stress from trauma, illness, and emotional concerns can enhance this secretion.

Aldosterone secretion is regulated by the renin-angiotensin system, ACTH, sodium, and potassium levels (see Chapter 4). When renal blood pressure decreases, renin is released, which stimulates release of angiotensin and activates the secretion of aldosterone via a negative feedback loop.

Clinical features

Primary adrenocortical insufficiency, known as Addison disease, is an uncommon endocrine condition attributable to a progressive destruction of the adrenal cortex. The gland destruction may be the result of an autoimmune process, an infectious disease, such as tuberculosis, or a malignancy. Autoimmune disease has surpassed tuberculosis as the primary cause of Addison disease, but tuberculosis still accounts for a significant proportion of cases. As cortisol and aldosterone are primary hormones produced by the adrenal cortex, Addison disease may manifest by a variety of nonspecific symptoms, such as malaise, anorexia, and nausea, related to inadequate levels of these hormones.

The clinical manifestations of Addison disease do not begin to appear until at least 90% of the glandular tissue has been destroyed. The clinical picture is a reflection of the deficiency of cortisol and aldosterone. A lack of cortisol produces altered glucose, fat, and protein metabolism, resulting in weakness, fatigue, weight loss, inability to tolerate stress, and hypotension. This may develop over a period of months. The individual may complain of anorexia, nausea, diarrhea, weight loss, and sometimes a craving for salt. Aldosterone deficiency
leads to sodium imbalance, hypovolemia, hyperkalemia, and acidosis. A generalized hyperpigmentation of the skin occurs, classically described as “bronzing,” which may be more pronounced on sun-exposed skin. It is caused by increased levels of ACTH, which stimulate melanocytes to increase melanin production.

Secondary adrenocortical insufficiency results from the administration of exogenous corticosteroids. As the plasma cortisol level increases, from exogenous sources, the production of ACTH decreases via the negative feedback system. Inhibition of ACTH production results in suppression of the production of cortisol, but the production of aldosterone is not significantly affected. In general, patients with secondary adrenal insufficiency do not present with symptoms unless the patient is severely stressed. However, they may not have adequate circulating cortisol to manage a stressful event.

The diagnosis of Addison disease may be confirmed by rapid ACTH stimulation test measurement of plasma ACTH levels. A 24-hour urine collection to evaluate the level of 17-hydroxycorticosteroids, and other stimulation and suppression tests may be employed.

**Oral manifestations and dental management**

The oral manifestations include diffuse patchy brown macular pigmentation of the oral mucosa. Oral mucosal changes may be the first manifestations of the disease, with skin hyperpigmentation following. Patients demonstrating diffuse oral pigmentation should be questioned regarding onset.

Medical management of a patient with Addison disease includes glucocorticoid replacement, usually with daily cortisone or prednisone. The need for glucocorticoid augmentation during times of stress remains for a lifetime. If a patient with Addison disease is suddenly stressed, for example by dental infection or surgery, an adrenal crisis can be precipitated. Although this can occur even in the presence of supplementation, the probability is reduced. Acute adrenal insufficiency can be associated with high morbidity and mortality if allowed to progress unrecognized. The symptoms include extreme weakness, headache, and dehydration. The index of suspicion should be particularly high if the patient also has a history of an autoimmune disease (hypothyroidism, diabetes) or recent prior use of exogenous steroids. Hypotension, fever, and decreasing mental status, should initiate aggressive treatment. Immediate therapy would include injection of glucocorticoid and fluid replacement.

The ongoing concern regarding dental management for secondary adrenal cortical insufficiency is focused on when and to what degree to supplement patients who are on routine steroid regimens. Judgments based on duration and dosage are not always dependable. Studies have demonstrated a lack of correlation between suppression level and clinical reaction to a stressful event. Based on clinical evidence and reports, it appears that patients with secondary adrenal insufficiency undergoing routine dental care (including dental extractions) with local anesthesia do not require supplementation. This recommendation assumes adequate postoperative pain management and blood pressure monitoring. In some situations, however, patients exhibiting extreme dental anxiety may benefit from special anxiety management or supplementation.

When extensive procedures are planned for these patients, especially when the patient exhibits anxiety, doubling the normal amount on the day of the dental procedure is recommended. If postoperative pain is anticipated, a prudent recommendation would be to double the dose on the first postoperative day. Some literature states that the adrenal suppression from exogenous glucocorticosteroids lasts for 12 months. However, the stress response will return in 2 to 4 weeks. Therefore, if less than 30 days have passed since the last dose and extensive procedures are planned, the maintenance dose should be doubled on the day of the procedure.

Patients with adrenal insufficiency for whom dental procedures require general anesthesia should be treated in a hospital setting. Steroid augmentation may include 100 mg of hydrocortisone the morning of the procedure, 100 mg 1 hour before and/or after the procedure and doubled maintenance dose the first postoperative day. Appropriate management of pain and infection should be applied.

Patients with adrenal insufficiency should be monitored for possible hypotension and observed for signs of hypoglycemia. A medical consultation regarding steroid supplementation may be helpful.

**Cushing disease**

Cushing syndrome is a condition that results from a sustained increase in glucocorticoid levels. In most cases, the increase is attributable to exogenous corticosteroid therapy prescribed for treatment of medical disorders, such as autoimmune conditions and organ transplants. When the excess glucocorticoid is from an endogenous source, such as a functional adrenal cortical tumor or an ACTH-secreting pituitary tumor, the condition is known as Cushing disease. This condition is rare and generally affects young adult females.

**Clinical features**

Excessive corticosteroid therapy can produce signs and symptoms of hyperadrenalism or Cushing syndrome. The onset is generally slow, with weight gain in the central body area being the most obvious clinical manifest-
A “buffalo hump” may result from the accumulation of fat in the dorsal cervical spine area. Fat deposition in the face results in the rounded facial appearance or moon-shaped facies. In addition, a patient may develop hypertension, osteoporosis, diabetes mellitus, delayed wound healing, and depression. Females may demonstrate hirsutism.

Dental management

Owing to exogenous steroid therapy, the patient with Cushing syndrome is susceptible to an adrenal crisis during stressful events, as previously discussed. The clinician must be aware of the possible complications and plan the patient’s dental care appropriately.

Hyperthyroidism

Obtaining an understanding of thyroid dysfunction is of significant importance to the dentist for two reasons. First, the dentist may be the first to suspect a serious thyroid disorder and aid in early diagnosis. The second reason is to avoid possible dental complications resulting from treating patients with poorly controlled hyperthyroid conditions. Although a rare occurrence, a thyrotoxic crisis—a true medical emergency—can occur associated with hyperthyroidism and dental procedures. The patient with hypothyroidism presents risks less critical in nature, but a few precautions are noteworthy. This section reviews hyperthyroidism and pertinent dental management considerations.

Hyperthyroidism is a condition caused by excess levels of circulating triiodothyronine (T3) and thyroxine (T4). The increased levels of these hormones may be a result of Graves disease, multinodular goiter, a functional thyroid adenoma, ectopic thyroid tissue, or disease involving the anterior portion of the pituitary gland. The most common cause of hyperthyroidism is Graves disease, which is the focus of this discussion. Graves disease is thought to be triggered by autoantibodies directed against thyroid-stimulating hormone (TSH) receptors on the surface of the thyroid cells. When the autoantibodies attach to these surface receptors, they stimulate the thyroid cells to release excessive thyroid hormone. The onset is unclear but may be associated with severe emotional trauma or infection.

Molecular and pathologic correlates of disease

The thyroid gland is a butterfly-shaped gland located in the anterior portion the neck just below the thyroid cartilage, and consists of two lateral lobes connected by an isthmus (Figure 9–9). Manual palpation of the thyroid gland should be a routine part of all new patient examinations and annual health updates. The normal thyroid tissue is soft and smooth. The thyroid should move upward during swallowing. The dentist may discover diffuse enlargement, indicative of thyroid hyperfunctioning, or a solitary nodule, suggesting a neoplasm.

To gain an understanding of the manifestations of thyroid hyperfunctioning (thyrotoxicosis) or hypofunctioning (myxedema or cretinism), a review of the hormones produced by the thyroid is appropriate. The thyroid gland secretes three hormones: thyroxine and triiodothyronine, which regulate growth and metabolism, and calcitonin, which regulates serum calcium levels, in conjunction with parathyroid hormone and vitamin D (see Chapter 10).

Circulating levels of T4 and T3 are controlled through a negative feedback mechanism mediated by the hypothalamic-pituitary-thyroid axis. Under steady-state conditions, thyrotropin-releasing hormone (TRH) is released by the hypothalamus in response to external stimuli, such as stress, illness, metabolic demand, and low levels of T3 and T4. Thyrotropin-releasing hormone stimulates the pituitary to release TSH, which causes the thyroid gland to secrete T4 and T3. In addition, high circulating levels of T4 and T3 diminish the release of TSH, and low levels of T4 and T3 increase the release of TSH from the pituitary.

Clinical features

Common manifestations of thyrotoxicosis include nervousness, emotional instability, inability to sleep, tremors, and excessive sweating. Weight loss is usual despite an adequate diet. In older patients, cardiovascular manifestations may predominate, such as exacerbation of angina pectoris.

The primary manifestations of Graves disease include hyperthyroidism with diffuse goiter, ophthalmopathy, and dermopathy (Figure 9–10). All components may manifest, or they may do so independently. Graves disease is 5 to 10 times more common in females than in males and affects nearly 2% of women. It is generally diagnosed during the third and fourth decades of life but may develop at puberty, pregnancy, or menopause. Most patients with Graves disease present with diffuse thyroid enlargement and have complaints associated with excessive thyroid hormones. Weight loss and increased appetite are commonly found owing to increased metabolic rate. Palmar erythema and a rosy complexion may be found. Hair may become fine, and the nails may soften. Skin manifestations are characterized by thickening of the dermis, which is infiltrated with lymphocytes and mucopolysaccharides. The skin change
Hyperthyroidism during development and eruption of primary teeth can lead to early exfoliation of primary teeth and early eruption of permanent teeth. One may observe a tremor of the tongue.

A small number of patients may exhibit a raised, reddish asymptomatic mass in the dorsal posterior tongue area, near the foramen cecum. This is called lingual thyroid and represents a mass of normal thyroid tissue left along the path of the thyroglossal duct. This appears in females more commonly than in males. Before removal or biopsy of this mass, it should be confirmed that the thyroid gland is present and functional. In many cases, the lingual thyroid is the only functional thyroid tissue present.

The major treatments are focused on limiting the quantity of thyroid hormones produced by the gland. One major approach is to limit hormone production by surgical removal of a portion of the gland or by the use of radioactive iodine. Radioactive iodine is one of the

is often found on the dorsum of the legs and may be pruritic and hyperpigmented with a raised “orange peel” appearance. Hyperpigmentation of the oral mucosa has not been reported. Some patients complain of anxiety, nervousness, heart palpitations, heat intolerance, emotional instability, and muscle weakness. Profuse sweating is common. Patients may demonstrate widened pulse pressure, with an elevated systolic pressure. Another prominent feature is ocular manifestations. In early stages of hyperthyroidism, patients demonstrate a wide stare with eyelid retraction and lid lag. Sometimes jerky movements of the lids are present. If the exophthalmos, protrusion of the eyes, begins unilaterally, it usually progresses to be bilateral. The globe protrusion is attributable to the accumulation of glycosaminoglycans in connective tissues behind the eyes. Corneal ulceration and ocular muscle weakness may develop.

Diagnosis of hyperthyroidism from Graves disease includes characteristic clinical manifestations and laboratory findings. Laboratory examinations include elevated levels for T3, T4, and thyroid-binding globulin (TBG) levels with minimal or undetectable TSH levels.

Figure 9–9  Thyroid hormone regulation. TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone.
most effective therapeutic strategies for patients with Graves disease. The radioactive iodine is taken up by the gland, destroying the hyperactive thyroid tissue. Thyroid hormone levels should return to normal. Patients may also be treated via partial or total thyroidectomy. These therapies may lead to hypothyroidism, which can generally be managed with hormone-replacement therapy.

Antithyroid agents, propylthiouracil and methimazole chemically block hormone synthesis by blocking iodine uptake. These agents may cause mild leukopenia. Beta-adrenergic blocking agents, such as propranolol, may alleviate sweating, tremor, and tachycardia.

Medications most useful for treatment of hyperthyroidism include thionamides, iodine, and radioactive isotopes of iodine. The thionamides (propylthiouracil and methimazole [Tapazole]), inhibit oxidation of iodide and coupling reactions to inhibit thyroid hormone formation. Non-radioactive iodides are used to temporarily suppress the gland prior to surgery. Iodides may also produce altered taste sensations, excessive salivation, and enlargement of the parotid and submandibular glands.

Thionamides may be used to control hyperthyroidism before surgery or while the therapeutic effects of radioactive iodide are realized. Thionamides may cause bone marrow suppression, resulting in greater susceptibility to infection, gingival bleeding, or delayed healing. Oral manifestations of agranulocytosis have been reported to have developed in a hyperthyroid patient 2 months after administration of methimazole. These manifestations included fever, sore throat, profound leukopenia, gingival necrosis and mucosal ulceration. When taken during pregnancy, thionamides can cross the placenta and cause fetal hypothyroidism. Thionamides may also cause rash, nausea, and headache. Hepatic toxicity and allergic hepatitis are occasionally associated with thionamides.

Radioactive sodium iodide is used in diagnosis and treatment of hyperthyroidism, and at higher concentrations, the isotope destroys thyroid cells. This treatment can result in myxedema. Radioactive sodium iodide is contraindicated during pregnancy.

**Dental management**

Patients with uncontrolled hyperthyroidism require special dental management. They are sensitive to epinephrine and pressor amines in local anesthetics and gingival retraction cords. These agents should not be administered until hyperthyroidism is controlled.

Patients with undiagnosed or poorly controlled thyrotoxicosis may develop thyrotoxic crisis, a serious complication with an abrupt onset. Most patients who develop thyrotoxic crisis have a goiter, wide pulse pressure, eye signs, and a long history of thyrotoxicosis. Precipitating factors are infections, trauma, surgical emergencies, and surgery. Symptoms are extreme restlessness, nausea, vomiting, and abdominal pain. Coma and severe hypotension may develop. Immediate treatment consists of anti-hyperthyroid therapies to include propylthiouracil, potassium iodide, propranolol, hydrocortisone, and ice packs or cooling blankets; CPR may be needed until medical help arrives.

Long-term follow-up is necessary for patients with Graves disease and should include an annual physical examination and measurement of serum concentrations of thyrotropin and free thyroxine. These should be maintained in the normal range. After the thyrotoxic patient is well controlled, the dental treatment plan will be unaffected. If acute infections develop, the patient’s physician should be consulted.

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**Hypothyroidism**

Acute hypothyroidism (myxedema) is more common in females and occurs between the ages of 30 and 60 years. Childhood hypothyroidism is termed cretinism. Hypothyroidism may be congenital or acquired.

**Clinical features**

Neonatal cretinism is characterized by dwarfism, a broad flat nose, thick lips, large protruding tongue, poor muscle tone, pale skin, retarded bone age, delayed eruption of teeth, and malocclusions. The long-term effects of severe hypothyroidism on craniofacial growth and dental development have also included impaction of the mandibular second molars, owing to failure of normal resorption of the internal aspect of the ramus. Hypothyroidism in older children and adults is characterized by a dull expression; puffy eyelids, face, and hands; rough skin and brittle, coarse hair; enlarged tongue; slurred speech; and increased sensitivity to cold. Juvenile hypothyroidism has been reported to include evidence of delays in shedding of deciduous teeth, root development, and eruption of permanent teeth as well as retarded skeletal growth. Two years of treatment with L-thyroxine results in dental and skeletal changes.

Hypothyroidism may occur from Hashimoto thyroiditis. This disorder is a chronic inflammatory disease of the thyroid in which autoimmune factors play a prominent role. It occurs in females during middle age and is the most common cause of sporadic goiter in children. Autoantibodies are indicative of disease but cytotoxic T cells probably destroy parenchyma. The most prominent feature is a diffuse goiter, which may be symmetrical or asymmetrical. The gland may feel rub-
Hashimoto thyroiditis may coexist with other diseases that are autoimmune in nature, such as pernicious anemia, Sjögren syndrome, systemic lupus erythematosus, diabetes mellitus, and Graves disease. Thyroid failure is manifested first by a rise in TSH concentration. As the condition progresses, serum T4 level declines, then T3 also declines, resulting in hypothyroidism. Autoimmune thyroiditis accounts for a significant percentage of adult hypothyroidism.

**Dental management**

Detection of hypothyroidism requires medical referral of the patient prior to dental treatment. Patients with hypothyroidism are usually treated with synthetic hormone replacement containing levothyroxine sodium (Levothroid, Levoxine, Synthroid) until normal functional levels are achieved. Unless the hypothyroid condition is transient, patients generally maintain replacement therapy for a lifetime. Levothyroxine should be used with caution in patients with cardiovascular disorders. Hypothyroid patients who are receiving warfarin or other oral anticoagulants along with levothyroxine may have prolonged prothrombin times and could be at risk for hemorrhage. Stressful situations, such as cold, surgery, or trauma, may precipitate a hypothyroid (myxedema) coma in the undiagnosed severely hypothyroid patient. This condition is treated by parenteral T3, steroids, and artificial respiration.

In general, patients with mild symptoms of untreated hypothyroidism are not in danger when receiving dental therapy. However, depressants, sedatives, or narcotic analgesics may produce an exaggerated response in patients with mild to severe hypothyroidism. These medications should be avoided in patients with severe hypothyroidism and minimized for those with mild disease. When the hypothyroid patient is under effective medical care, regular dental care can be provided.

**Suggested reading**