

Diabetes management

INTRODUCTION

According to the Centers for Disease Control and Prevention, diabetes and associated complications cost the United States \$174 billion in direct and indirect costs in 2007.¹ Between 2009 and 2034, annual diabetes-related spending is expected to increase from \$113 billion to \$336 billion.² In 2010, 25.8 million people, or 8.3% of the U.S. population, were affected by diabetes; and 79 million, or 35% of adults older than 20 years, had pre-diabetes.¹ The number of individuals diagnosed and undiagnosed with diabetes is estimated to increase from 23.7 million to 44.1 million between 2009 and 2034.² A person with diabetes spends \$11,744 annually on healthcare costs, compared with \$5,095 for a person without diabetes.³ The Medicare eligible population with diabetes is expected to increase from 8.2 million to 14.6 million, and spending is expected to increase from \$17 billion to \$45 billion between 2009 and 2034.²

PATHOPHYSIOLOGY AND DIAGNOSTIC CRITERIA

Diabetes mellitus, a group of metabolic disorders characterized by hyperglycemia, is a result of one or a combination of the following pathophysiologic processes:

- Decreased or absent insulin secretion by the pancreas;
- Defects in insulin action; and/or

- Decreased sensitivity or resistance by body tissue to insulin.⁴

Type 1 diabetes, previously referred to as juvenile-onset diabetes or insulin-dependent diabetes, accounts for 5% to 10% of cases. Type 1 diabetes previously was associated with childhood or adolescence, but now has been identified across the lifespan. Type 1 diabetes can be caused by beta cell destruction, leading to absolute insulin deficiency as a result of cellular-mediated autoimmune destruction. Genetic predispositions and environmental factors have been linked to autoimmune destruction of beta cells. Markers of Type 1 diabetes include islet cell antibodies; autoantibodies to insulin; autoantibodies to glutamic acid decarboxylase, or GAD65; and autoantibodies to tyrosine phosphatases IA-2 and IA-2 beta. One or more antibodies are present in 85% to 90% of individuals with Type 1 diabetes. Idiopathic forms of Type 1 not associated with autoimmunity also have been identified. Plasma C-peptide levels also are used as a marker of insulin production.⁴

Type 2 diabetes, previously referred to as noninsulin-dependent diabetes or adult-onset diabetes, accounts for 90% to 95% of cases. The causes for Type 2 diabetes are multifaceted and complicated, but beta cell destruction is not the cause. Individuals with Type 2 diabetes have insulin resistance or deficiency, and un-

like Type 1 diabetes, do not always need insulin to survive. Known risk factors for development of Type 2 diabetes include increasing age, obesity, lack of physical activity, women with prior gestational diabetes, individuals with hypertension or dyslipidemia, belonging to high-risk ethnic groups (e.g., Hispanic, Native American, Asian-American, African-American, Pacific Islander) and family history.⁴

Other types of diabetes that are not generally common include:

- Genetic defects in beta cell function (e.g., MODY 1-6 and mitochondrial DNA);
- Genetic defects in insulin action (e.g., type A insulin resistance, leprechaunism, Rabson-Mendenhall syndrome, lipodystrophic diabetes);
- Diseases of the exocrine pancreas (e.g., pancreatitis, neoplasia, cystic fibrosis, hemacromatosis, fibrocalculous pancreatopathy);
- Endocrinopathies (e.g., acromegaly, cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroid, somatostatinoma, aldosteronoma);
- Drug- or chemical-induced diabetes (e.g., vacor, pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, beta adrenergics, thiazides, Dilantin, interferon-gamma);
- Infections (e.g., congenital rubella, cytomegalovirus);

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Program Goal: To improve the advanced practice clinician's ability to diagnose, treat and educate patients with diabetes based on current clinical practice recommendations.

Learning Objectives:

Upon completion of this program, the advanced practice clinician should be able to:

1. Accurately diagnose and classify the patient's type of diabetes based on pathophysiology.

2. Appropriately identify the current standards of medical care.

3. Describe pharmacologic management based on type of diabetes.

4. Discuss diabetes self-management education strategies.

5. Describe micro- and macro-vascular complications and measures to eliminate or decrease the risk of complications.

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- Immune-mediated diabetes (e.g., stiff-man syndrome, anti-insulin receptor antibodies); and
- Other genetic syndromes associated with diabetes (e.g., down syndrome, Klinefelter, Turner, Wolfram ataxia, Huntington chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome).⁴

Another form of diabetes is gestational diabetes mellitus, or GDM, which is defined as diabetes first manifesting during pregnancy. The diagnosing and management of GDM continues to evolve, and there are varying professional consensus statements on the subject. The International Association of Diabetes and Pregnancy Study Groups, or IADPSG, has issued new recommendations for the screening, diagnosis and classification of GDM.^{5,6} The American Diabetes Association, or ADA, has varying criteria for the screening, diagnosis and classification of GDM.⁷

SCREENING AND DIAGNOSIS

In January 2011, the ADA published clinical practice recommendations for the diagnosis and classification of diabetes mellitus, as well as standards of medical care in diabetes. New categories of increased risk for diabetes have been added.

ADA categories of increased risk for diabetes (prediabetes) include:

- Fasting plasma glucose, or FPG, of 100 mg/dl (5.6 mmol/l) to 125 mg/dl (6.9 mmol/l) [IFG, or impaired fasting glucose]; or
- Two-hour plasma glucose, or PG, in the 75-g oral glucose tolerance test, or OGTT, of 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l) [IGT, or impaired glucose tolerance]; or
- A1C 5.7% to 6.4%.

For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range. Interventions and follow up should be the most intensive for patients with A1Cs above 6%, who should be considered at very high risk.⁷

ADA criteria for the diagnosis of diabetes indicate patients must have one of the following:

1. A1C > 6.5%, the test should be performed in a laboratory using a method that is certified by the National Glycohemoglobin Standardization Program and standardized or traceable to the Diabetes Control and Complications Trial reference assay; or
2. FPG > 126 mg/dl (7.0 mmol/l), fasting is defined as no caloric intake for at least 8 hours; or
3. Two-hour PG > 200 mg/dl (11.1 mmol/l) during an OGTT, the test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; or
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose > 200 mg/dl (11.1 mmol/l).

In the absence of unequivocal hyperglycemia, criteria 1 to 3 should be confirmed by repeat testing.⁷

The ADA also has recommendations regarding testing for diabetes in asymptomatic patients. In order to detect Type 2 diabetes and assess risk for future diabetes, testing should be considered in all adults who are overweight, which generally is classified as a body mass index, or BMI, $\geq 25 \text{ kg/m}^2$ (at-risk BMI may be lower in some ethnic groups) and have one or more additional risk factors for diabetes.⁷

The additional risk factors for diabetes include:

- Physical inactivity;
- A first-degree relative with diabetes;
- Members of a high-risk ethnic population (e.g., African-American, Latino, Native American, Asian-American or Pacific Islander);
- Women who delivered a baby weighing more than 9 lbs. or who were diagnosed with GDM;
- Hypertension ($\geq 140/90$ mmHg) or on therapy for hypertension;

- High-density lipoprotein cholesterol level < 35 mg/dl (0.90 mmol/l) and/or a triglyceride level > 250 mg/dl (2.82 mmol/l);
- Women with polycystic ovary syndrome;
- A1C $\geq 5.7\%$, IGT or IFG on previous testing;
- Other clinical conditions associated with insulin resistance (e.g., severe obesity or acanthosis nigricans); and
- History of cardiovascular disease.⁷

In the absence of the above criteria, testing for diabetes should begin at 45 years. If results are normal, testing should be repeated at least at three-year intervals, with consideration of more frequent testing depending on initial results and risk status. To test for diabetes or assess risk of future diabetes, A1C, FPG or two-hour 75-g OGTT is appropriate.⁷

ADA criteria for testing for Type 2 diabetes in asymptomatic children include overweight (BMI > 85th percentile for age and sex; weight for height > 85th percentile; or weight > 120% of ideal for height) plus any two risk factors.⁷

Risk factors include:

- Family history of Type 2 diabetes in a first- or second-degree relative;
- Race/ethnicity (e.g., Native American, African-American, Latino, Asian-American or Pacific Islander);
- Signs of insulin resistance or conditions associated with insulin resistance (e.g., acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome or small for gestational age birth weight); and
- Maternal history of diabetes or GDM during the child's gestation.⁷

Testing should be initiated at 10 years of age or at onset of puberty if puberty occurs at a younger age. Testing should be repeated with a frequency of every three years.⁷

PHARMACOLOGIC MANAGEMENT

Pharmacologic agents used as monotherapy or in combination to treat diabetes include:

- Oral medications (e.g., sulfonylureas, meglitinides, biguanides, alpha-glucosidase inhibitors, thiazolidinediones and dipeptidyl peptidase-4 inhibitors);
- Incretins (e.g., exenatide and liraglutide);
- Amylin; and
- Insulin (e.g., short- or rapid-acting insulin, intermediate-acting insulin, long-acting insulin and pre-mixed insulin).

Emerging therapies also will be discussed.

Sulfonylureas

Second-generation sulfonylureas, or SUs, available in the United States include glimepiride, glipizide, glyburide and micronized glyburide. Sulfonylureas work by sensitizing the pancreatic beta cells to release insulin after meal ingestion. Common side effects include hypoglycemia and weight gain. Hypoglycemia is more likely to occur with such long-acting SUs as glyburide.⁸ Glipizide is the shortest-acting SU and is preferred in the elderly and those with chronic kidney disease (Table 1). A decrease of 1% to 2% reduction in A1C is observed with SUs.⁹

Meglitinides

Meglitinides also stimulate the release

of insulin from beta cells and are considered nonsulfonylurea secretagogues. These drugs are taken with meals, which makes compliance difficult for some patients. Nateglinide and repaglinide are the two meglitinides available. Unlike SUs, meglitinides have a rapid onset of action and short duration, thus reducing postprandial hyperglycemia and decreasing the risk of hypoglycemia.⁸ A reduction of 1% to 2% in A1C is observed with meglitinides.⁹

Biguanides

Biguanides lower fasting plasma glucose by decreasing hepatic gluconeogenesis, improving peripheral tissue insulin sensitivity and decreasing intestinal absorption of glucose. Common side effects include nausea and modest weight loss.¹⁰ Gastrointestinal symptoms can be minimized by switching patients to the extended-release forms. A reduction of 1% to 2% in A1C is observed with biguanides.⁹

Alpha-glucosidase inhibitors

Alpha-glucosidase inhibitors decrease postprandial glucose by decreasing the rate of carbohydrate absorption in the small intestine. Common side effects are gastrointestinal in nature, including diarrhea and flatulence.^{10,11} Dosing usually is three times a day before meals, which is a common reason for missed doses. A

reduction of 0.5% to 0.8% in A1C is observed with alpha-glucosidase inhibitors.⁹

Thiazolidinediones

The two thiazolidinediones, or TZDs, available in the United States are pioglitazone and rosiglitazone. TZDs improve adipose and muscle sensitivity to insulin and decrease hepatic glucose production. Common side effects include weight gain and leg edema.¹⁰ On Sept. 23, 2010, the Food and Drug Administration announced the restricted use of rosiglitazone due to data suggesting elevated risk of cardiovascular events, including myocardial infarctions and cerebrovascular accidents. Rosiglitazone is recommended to be used with patients who are unable to take pioglitazone and are unable to achieve glucose control on other medications. Healthcare prescribers will have to attest and document patients' eligibility, review the cardiovascular risks with patients and have them acknowledge their understanding.¹² On Sept. 17, 2010, the FDA announced it was reviewing data to evaluate a link between the use of pioglitazone and an increased incidence of bladder cancer, but has not found a statistically significant association.¹³ A reduction of 0.5% to 1.4% in A1C is observed with TZDs.⁹

DDP-4 inhibitors

Glucagon-like peptide 1, or GLP-1, and

TABLE 1

Second-generation sulfonylureas⁹

Generic name	Brand name	Duration	Common dose and available strengths
Glimepiride	Amaryl®	24 hours	1 mg to 2 mg, to 8 mg daily <i>Tabs: 1 mg, 2 mg, 4 mg</i>
Glipizide	Glucotrol®	12 to 18 hours	2.5 mg to 5 mg, to 40 mg daily
	Glucotrol XL®	24 hours	Max 20 mg with XL daily <i>Tabs: 5 mg, 10 mg XL: 2.5 mg, 5 mg, 10 mg</i>
Glyburide	DiaBeta®	24 hours	2.5 mg to 20 mg daily
	Micronase	12 to 24 hours	<i>Tabs: 1.25 mg, 2.5 mg, 5 mg</i>
Micronized glyburide	Glynase®	12 to 24 hours	1.5 mg to 3 mg, to 12 mg daily <i>Tabs: 1.5 mg, 3 mg, 4.5 mg, 6 mg</i>

glucose-dependent insulinotropic peptide, or GIP, are gut-derived hormones that play a role in glycemic control through insulin secretion, inhibition of glucagon secretion and stimulation of beta cell proliferation.¹¹ Dipeptidyl peptidase-4, or DDP-4, is a gut enzyme that inactivates GLP-1 and GIP, thus affecting glycemic control in individuals with Type 2 diabetes.¹² DDP-4 inhibitors are classified as incretin enhancers that affect fasting and postprandial plasma glucose by inhibiting the degradation of GLP-1.¹⁴⁻¹⁶ DDP-4 inhibitors generally are well tolerated and are not associated with delayed gastric emptying, nausea, vomiting or weight loss.¹⁷ Dosing has to be adjusted based on renal function. DDP-4 inhibitors enhance insulin secretion, inhibit glucagon secretion, do not slow gastric emptying, do not induce satiety or weight loss and improve beta cell function.¹⁸ A reduction of 0.5% to 1% in A1C is observed with DDP-4 inhibitors.⁹

Incretins

Exenatide and liraglutide are the two current glucagon-like peptide-1 receptor, or GLP-1R, agonists available for the treatment of Type 2 diabetes. Incretin hormones increase glucose-dependent insulin secretion, slow the rate of gastric emptying, decrease plasma glucose, decrease food intake and weight, and have

an effect of beta cell apoptosis and increase beta cell hypertrophy.¹⁹ Exenatide is administered twice daily before meals and liraglutide is administered once daily. Common side effects include nausea and vomiting, which diminishes over time and gradual increases in dosing. These drugs are not associated with hypoglycemia unless used with sulfonylureas.

A reported side effect of exenatide is pancreatitis, but concomitant use of more than 200 drugs might play a role. Additionally, when pancreatitis has occurred, it usually is evident within a few days after initiating exenatide.¹⁷ Studies with liraglutide reported C-cell hyperplasia and medullary thyroid cancer, or MTC, and should be avoided in patients with a family or personal history of MTC.¹⁷ GLP-1 receptor agonists enhance insulin secretion, inhibit glucagon secretion, slow gastric emptying, induce satiety and weight loss, and improve beta cell function.¹⁸ A reduction of 0.5% to 1% in A1C is observed with GLP-1R agonists.⁹

Amylin

Amylin, or islet amyloid polypeptide, is an amino acid peptide co-secreted with insulin from the beta cells. Amylin levels increase in response to food intake, glucagon stimulation, GLP-1 and cholinergic agonists, and are inhibited by somatostatin and insulin. Common side effects include nausea and weight loss, as well as

hypoglycemia with concomitant use of insulin.¹⁸ Amylin is approved for use in patients with Type 1 or Type 2 diabetes and is administered three times a day with meals. Amylin does not enhance insulin secretion or improve beta cell function, but does inhibit glucagon secretion, slows gastric emptying and induces satiety and weight loss.¹⁸ A reduction of 0.25% to 5% in A1C is observed with amylin.⁹

Insulin

Table 2 lists the current insulin types available on the market. Regular human insulin and NPH insulin no longer are recommended for use since the development of insulin analogues. Insulin is necessary in individuals with Type 1 diabetes and can be used in combination with oral agents in those with Type 2 diabetes. The reduction in A1C is limitless. Insulin delivery methods include subcutaneous injections through the use of needles or prefilled insulin pens, or with the use of continuous subcutaneous insulin injection or CSII through the use of insulin pumps.^{8,9} Dosing is based on body weight or based on carbohydrate ratios.

Emerging therapies

The cycloset safety trial — a 52-week, randomized, double-blind, multicenter trial with 3,070 individuals with Type 2 diabetes — evaluated the cardiovascular

TABLE 2

Insulin^{8,9}

Type	Onset	Peak	Duration	Frequency
Rapid-acting insulin analogue Aspart (NovoLOG [®]) Lispro (HumaLOG [®]) Glulisine (Apidra [®])	15 minutes	0.5 to 1.5 hours	3 to 4 hours	Three times a day with meals, or four times a day with basal-bolus injections or with continuous subcutaneous insulin injection
Premixed insulin/protamine Aspart+ aspart-protamine (NovoLOG [®] Mix 70/30) Lispro + lispro-protamine (HumaLOG [®] Mix 50/50 [™])	15 minutes	1.5 hours	10 to 16 hours	Twice a day
Long-acting insulin analogues Glargine (Lantus [®]) Detemir (Levemir [®])	1 to 4 hours	No peak	24 hours 12 to 20 hours	Once or twice a day

safety of a quick-release bromocriptine, or bromocriptine-QR. Bromocriptine-QR is a D2 dopamine receptor agonist indicated for the treatment of Type 2 diabetes.²⁰ Bromocriptine-QR is administered in the morning to provide a timed pulse of dopamine activity centrally. Nausea, the most common side effect, is more common during the initial titration and usually lasts less than two weeks.²⁰ A 42% reduction in the combination of myocardial infarction, or MI; stroke; coronary revascularization; and hospitalization for angina or CHF, as well as a 55% reduction in the combination of MI, stroke or death, was observed.²¹

Colesevelam HCL, a bile acid sequestrant, demonstrated improved glycemic control and reduced LDL cholesterol in patients with Type 2 diabetes in a 26-week, randomized, double-blind, placebo-controlled, parallel group multicenter study. A decrease of 0.32% in A1C and 16.1% in LDL was observed from baseline to week 26.²² Colesevelam also has been shown to decrease glucose in combination with insulin, metformin and sulfonylureas. Common side effects include constipation, upper respiratory infection and urinary tract infection.²³

TREATMENT OF HYPOGLYCEMIA

Hypoglycemia, defined as plasma glucose < 70 mg/dl, is a common yet preventable and manageable complication in individuals with diabetes, likely to occur with use of sulfonylureas or insulin when inadequate calories are consumed. Over-treatment of hyperglycemia often is common, and the role of healthcare providers is to educate individuals on the adequate treatment to avoid hyperglycemia. Fifteen to 20 g of glucose given orally or any form of carbohydrate is the preferred treatment for a conscious person with hypoglycemia. Wait 15 minutes and retreat if the person continues to experience hypoglycemia. Once the person's blood glucose level is normalized, the individual should eat a snack or meal to prevent hypoglycemia. For the unconscious individual, glucagon should be administered to reverse the hypoglycemia. Hypoglycemia unawareness is a serious consequence resulting from

the autonomic dysfunction accompanied by diabetes. Individuals should be monitored closely and glycemic targets should be higher in such individuals.⁷

NONPHARMACOLOGIC MANAGEMENT

Lifestyle modification, including medical nutrition therapy, or MNT, and physical activity, is the cornerstone of diabetes self-management. The ADA recommends saturated fat intake should be less than 7% of total calories, and individuals should limit the amount of saturated fatty acids, trans fatty acid and cholesterol to reduce cardiovascular disease risk. Carbohydrate intake can be monitored with the use of carbohydrate counting or exchanges, but these techniques require education and an understanding by the patient. The recommended daily allowance for digestible carbohydrate is 130 g/day to ensure delivery of fuel for central nervous system function.⁷ A registered dietitian can assist with individualization of meal plans.

Bariatric surgery should be considered for adults with Type 2 diabetes and a body mass index, or BMI, greater than 35 kg/m². Many insurance providers now cover the cost of the procedure due to the long-term benefits and cost-effectiveness related to the decrease in complications. Studies have demonstrated 55% to 95% of patients with Type 2 diabetes who undergo bariatric surgery have near or complete normalization of glycemia, depending on the procedure performed.⁷ The types of bariatric surgery most commonly studied include gastric bypass and gastric banding.²⁴

DIABETES SELF-MANAGEMENT EDUCATION

Diabetes self-management education, or DSME, is a collaborative process through which people with or at risk for developing diabetes gain the knowledge and skills necessary to perform self-care behaviors needed to manage the disease and/or minimize or prevent diabetes complications.²⁵ DSME incorporates the needs, goals and life experiences of the person. The objectives of DSME are to support informed decision-making, self-care behaviors, problem solving and active collaboration with healthcare providers to improve clinical outcomes,

health status and quality of life.^{26,27}

A program that is accredited by the ADA, AADE and the Indian Health Services can bill Medicare for 10 hours of initial diabetes self-management training, or DSMT, in a 12-month period and for no more than two hours of follow-up training for each subsequent year. The Healthcare Common Procedure Coding System, or HCPCS, codes used are G0108 for 30 minutes of individual DSMT or G0109 for 30 minutes of DSMT conducted in group sessions.²⁸ Some private payers have adopted Medicare's HCPCS codes to provide reimbursement for DSMT. Another option is to check with private insurance carriers to determine which use the Current Procedural Terminology, or CPT, codes 98960, 98961 and 98962 for DSMT. Currently, billing codes do not exist for healthcare providers who conduct DSMT as part of routine encounters. Evaluation and Management, or E&M, codes 99211-99215 (established patients) and 99201-99205 (new patients) often are used by primary care providers when providing counseling or educations as part of the routine encounter.²⁹

CLINICAL PRACTICE RECOMMENDATIONS: GOALS AND TREATMENT

The current clinical practice recommendations for outcome measures include A1C ≤ 7%, blood pressure < 130/80 mmHg and LDL < 100 mg/dl. Treatment recommendations include yearly influenza immunization for people ≥ 6 months; pneumococcal vaccine for patients ≥ 2 years of age; a onetime pneumococcal vaccination for individuals > 64 years of age who previously were immunized when they were < 65 years, or if the vaccine was administered more than five years prior; antiplatelet treatment with aspirin 75 mg/day to 162 mg/day or clopidogrel 75 mg/day if allergic to aspirin; and smoking-cessation counseling.

COMPLICATIONS

Macrovascular complications

Diabetes-related macrovascular complications include coronary artery disease, cerebrovascular disease and peripheral arterial disease.⁷ Cardiovascular

conditions that co-exist with diabetes are hypertension and dyslipidemia. Lifestyle modification along with the use of either an angiotensin converting enzyme inhibitor, or ACEI, an angiotensin II receptor blocker, or ARB, a thiazide diuretic or multiple-drug treatment have been efficacious in maintaining blood pressure at goal. Renal function and serum potassium need to be monitored with the use of ACEI and ARB, and lipid levels with thiazide use. Calcium channel blockers and beta-blockers are additional therapies to be considered to further decrease blood pressure or in those unable to tolerate ACEI or ARBs.⁷ Direct renin inhibitors, or DRIs, are a new class of drugs that work by blocking the renin-angiotensin system. DRIs block the conversion of angiotensin I from angiotensinogen, thus blocking the generation of angiotensin II. DRIs can be added to an ACEI or ARB to provide additional blood pressure-lowering effects.³⁰

Lifestyle modification, weight loss, reduction in saturated fat consumption, increased omega-3 fatty acids and physical activity are recommended in the treatment of dyslipidemia. Statins should be initiated regardless of lipid levels in individuals with overt cardiovascular disease, or CVD; LDL greater than 100 mg/dl; or with CVD risk factors (e.g., family history of CVD, HTN, smoking, dyslipidemia, albuminuria). Aspirin, or ASA, therapy (75 mg/day to 162 mg/day) should be initiated in men older than 50 years and women older than 60 years, or in individuals with risk factors for CVD. Individuals with ASA allergy can take clopidogrel 75 mg/day. Screening for CAD is not recommended in asymptomatic patients. Cardiac testing is indicated in individuals with typical or atypical cardiac symptoms and an abnormal resting electrocardiogram.⁷

Microvascular complications

Diabetes-related microvascular complications include retinopathy, nephropathy and neuropathy.⁷ Diabetes is the leading cause of new cases of blindness among adults ages 20 years to 74 years and the leading cause of kidney failure in 2005, accounting for 44% of new cases.¹ Adults and

children 10 years or older diagnosed with Type 1 diabetes should have an initial dilated and comprehensive eye exam within five years after the onset of diabetes. Individuals with Type 2 diabetes should have an initial dilated and comprehensive eye exam at the time of diagnosis. Eye exams should be repeated at least annually. Laser photocoagulation therapy is indicated in proliferative diabetic retinopathy and nonproliferative diabetic retinopathy. Optimal glycemic and blood pressure control can reduce the risk or slow the progression of retinopathy.⁷

An annual urine albumin excretion test should be performed in individuals to identify microalbuminuria (30 $\mu\text{g}/\text{mg}$ to 299 $\mu\text{g}/\text{mg}$ creatinine) or macroalbuminuria ($\geq 300 \mu\text{g}/\text{mg}$ creatinine). Serum creatinine also should be measured annually to estimate the glomerular filtration rate and stage the level of chronic kidney disease regardless of urine albumin excretion. Screening for microalbuminuria is performed by measuring the albumin-to-creatinine ratio in a random spot urine collection. Two or three specimens collected within a three- to six-month period should be abnormal before diagnosing microalbuminuria since exercise, infection, fever, CHF, hyperglycemia and HTN may elevate urinary albumin excretion values.^{7,31}

ACEI have been shown to delay the progression of nephropathy in individuals with Type 1 diabetes, HTN and any degree of albuminuria. In individuals with Type 2 diabetes, HTN and microalbuminuria, and both ACEI and ARBs have been shown to delay the progression to macroalbuminuria. ARBs have been shown to delay the progression of nephropathy in individuals with Type 2 diabetes, HTN, macroalbuminuria and serum creatinine $> 1.5 \text{ mg}/\text{dl}$. Optimal glucose and blood pressure control can reduce the risk or progression of nephropathy.⁷ DRIs can be added to an ACEI or ARB in patients with Type 1 and Type 2 diabetes and nephropathy.³⁰

Diabetic neuropathies are classified into peripheral neuropathic pain and diabetic autonomic neuropathy. Peripheral neuropathic pain symptoms include distal, symmetrical prickling, deep ach-

ing, sharp and burning, which tend to occur more frequently during the night.³² First-line therapies available for the treatment of neuropathic pain include tricyclic antidepressant, duloxetine, pregabalin or gabapentin. Diabetic autonomic neuropathy is a disorder of the autonomic nervous system and includes cardiovascular and gastrointestinal autonomic neuropathy, erectile, bladder and sudomotor dysfunction.³² In individuals with diabetes, 60% to 70% have mild to severe forms of neuropathy, and 30% ages 40 years or older have impaired sensation in the feet and account for more than 60% of nontraumatic lower extremity amputations.¹

SPECIAL CONSIDERATIONS FOR RETAIL CLINIC SETTINGS

Advanced practice clinicians in retail clinic settings are managing chronic conditions, including diabetes. Controversy exists whether comprehensive diabetes care can be provided in retail clinics.^{33,34} Retail clinics have demonstrated a cost savings in the treatment of patients.³⁵ Advanced practice clinicians who have received education and training in the management of patients with diabetes can care for these patients. Keeping up to date with the latest clinical practice recommendations and knowing when to refer a patient to a qualified provider is crucial in the delivery of competent care. Protocols and checklists for screenings, tests and procedures are one way to ensure emerging complications are identified and proper referrals are made. Consumers have identified the convenience, affordability and timeliness of care provided in retail clinics, and as the incidence and prevalence of diabetes increases, advanced practice clinicians must be prepared to care for a growing patient population.

Guidelines require coding to the highest level of specificity. Table 3 lists common diabetes, manifestation and complication codes. The reader is referred to a current ICD-9 code book for a complete list of codes. An example of coding follows: for a patient with an A1C of 9.2% and a urine albumin level of 50 $\mu\text{g}/\text{ml}$ creatinine, the following diagnoses codes would be listed:

250.02 (uncontrolled Type 2 diabetes), 250.42 diabetic renal manifestations in uncontrolled Type 2 diabetes) and 583.81 (diabetic nephropathy).

TREATMENT MODALITIES

New modalities in the management of diabetes have evolved, including the

use of continuous glucose monitoring, or CGM. CPT code 95250 is used to bill for the sensor placement, hook up, calibration, patient training, sensor removal and printing of data. CPT code 95251 is used to bill for the interpretation of the data printout.²⁹ A caveat to using these codes is that a provider cannot use evalu-

ation and management codes along the CGM CPT codes. The patient does not have to be present when interpreting the data. However, the evaluation and management code can be used when the patient returns to discuss the results along with any changes that might be needed in the treatment.²⁹

TABLE 3
Common diabetes codes and manifestations^{29,36}

Type 2	Type 1
Controlled or unspecified 250.00	Controlled 250.01
Uncontrolled 250.02 (A1C >9 %)	Uncontrolled 250.03 (A1C > 9%)

	Diagnosis code	Manifestations
Diabetes with neurological manifestations	250.6x	
DM with neuropathy		357.2
DMN with ulcers		707.1, 8
DMN with impotence		607.84
DMN with foot drop		736.79
DMN with gastroparesis or gastroparalysis		536.3
Autonomic neuropathy		337.1
Amyotrophy		358.1
Diabetes with ophthalmic manifestations	250.5x	
Retinopathy		362.0x
Blindness		369.00 - 369.9
Cataracts		366.41
Glaucoma		365.44
Macular edema		362.07 + 362.0x
Diabetic peripheral/circulatory disorders	250.7x	
DM peripheral vascular disease, or PVD		443.81
DM PVD with ulcers		443.81 + 707.1, .8
DM gangrene		785.4
Diabetic renal manifestations	250.4x	
DM nephropathy		583.81
DM nephropathy with renal insufficiency		593.91
DM nephropathy with renal failure		585, 586
DM nephropathy with nephrotic syndrome		581.81
Other manifestations	250.8x	
Diabetic ulcers (not PVD or neuropathy)		707.1, .8
Diabetic bone change		731.8
Diabetic osteomyelitis		731.8 + 730.x
Diabetic impotence (not neuropathy)		607.84
Diabetes with unspecified complications		250.9

SPECIAL PATIENT POPULATIONS

Children, pregnant patients and older adults are special patient populations that still need the current practice recommendations, but require additional considerations. Historically, Type 1 diabetes was diagnosed in children. Current trends in increasing obesity have led to the onset of Type 2 diabetes in children. Growth and development need to be taken into account when managing diabetes. Additionally, children with Type 2 diabetes often experience HTN and dyslipidemia, but clinical trials are lacking on the safety and efficacy of pharmacologic treatment for these conditions.

In pregnant women, the use of most oral agents for the treatment of diabetes and dyslipidemia, as well as ACEI and ARBs, are contraindicated. Regular insulin, metformin and the DDP-4I are category B and approved for use in pregnancy. Glycemic targets in older adults need to be adjusted according to co-existing co-morbidities, functional and cognitive abilities, and the risk for hypoglycemic unawareness.

PROFESSIONAL RESOURCES AVAILABLE

The CDC, FDA, American Association of Diabetes Educator, ADA and American Association of Clinical Endocrinologists provide information on education materials, clinical and practice guidelines, and current research findings on the science of diabetes management. There are a variety of resources that provide information on diabetes management, but advanced practice clinicians should be aware and become acquainted with reputable sources to ensure delivery of evidence-based practice.

CONCLUSION

Diabetes mellitus is a complex, multi-

factorial chronic condition requiring healthcare providers to keep up to date with the latest treatment modalities. This lesson was a summary of current clinical standards and treatment options to provide healthcare providers the information needed to screen, diagnose, manage and treat patients with diabetes. Diabetes is a chronic condition that continues to increase in prevalence and incidence. Improvement in outcomes in patient populations with chronic conditions has been the focus of current demonstration projects. Advanced practice clinicians working in retail clinics can play a pivotal role in providing data to demonstrate that comprehensive diabetes care can be provided in retail clinics.

PRACTICE POINTS

- Advanced practice clinicians need to be aware of the current screening and diagnosing guidelines for diabetes.
- Lifestyle modification, pharmacologic and nonpharmacologic interventions are needed to prevent and treat diabetes and complications.
- Caring for patients with chronic conditions continues to grow in retail clinics, and providers need to be able to manage patients with diabetes.

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Diabetes management

Learning Assessment

Successful completion of "Diabetes management" is accredited for 1.25 (one and one-quarter) hours of continuing education credit, of which 0.90 hours is accredited for pharmacology by Partners in Healthcare Education LLC, an approved provider of nurse practitioner continuing education by the American Academy of Nurse Practitioners, provider No. 031206. To obtain credit, answer the following questions and complete the evaluation online at RetailClinician.com.

1. **Type 2 diabetes mellitus pathology is characterized by:**
 - a. Decrease in insulin secretion
 - b. Insulin resistance
 - c. Complete lack of insulin secretion
 - d. A and B
2. **Type 1 diabetes previously was associated with childhood or adolescence but now has been identified across the lifespan.**
 - a. True
 - b. False
3. **Which of the following is a risk factor for developing Type 2 diabetes?**
 - a. Obesity
 - b. History of hypertension or dyslipidemia
 - c. Women with prior gestational diabetes
 - d. All of the above
4. **The current diabetes clinical practice recommendations for outcome measures include all of the following EXCEPT:**
 - a. $A1C \leq 7\%$
 - b. Blood pressure $< 130/80$ mmHg
 - c. $LDL < 130$ mg/dl
 - d. Yearly influenza immunization for people ≥ 6 months
5. **Which of the following needs to be monitored with the use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers?**
 - a. Renal function
 - b. Serum potassium
 - c. Lipid levels
 - d. A & B
 - e. All of the above
6. **Which of the following is a long-acting insulin?**
 - a. Aspart
 - b. Glargine
 - c. Lispro
 - d. All of the above
7. **Hypoglycemia is defined as a blood glucose level of which of the following, along with clinical symptoms of hypoglycemia?**
 - a. < 50 mg/dl
 - b. < 70 mg/dl
 - c. < 100 mg/dl
 - d. > 126 mg/dl
8. **_____ have been shown to delay the progression of nephropathy in individuals with Type 1 diabetes, HTN and any degree of albuminuria.**
 - a. Angiotensin converting enzyme inhibitors
 - b. Angiotensin II receptor blockers
 - c. Direct renin inhibitors
 - d. All of the above
9. **Individuals with Type 2 diabetes should have:**
 - a. An initial dilated and comprehensive eye exam at the time of diagnosis
 - b. An initial dilated and comprehensive eye exam within five years after the onset of diabetes
 - c. Eye exams that should be repeated at least annually
 - d. A & C
10. **Which of the following is an amino acid peptide co-secreted with insulin from the beta cells?**
 - a. Amylin
 - b. Exenatide
 - c. Liraglutide
 - d. Pioglitazone