patients with CHF, thiazolidinediones should not be used (Chap. 418). However, metformin can be used in patients with stable CHF if the renal function is normal.

Antiplatelet therapy reduces cardiovascular events in individuals with DM who have CHD and is recommended. Current recommendations by the ADA include the use of aspirin for primary prevention of coronary events in diabetic individuals with an increased 10-year cardiovascular risk >10% (at least one risk factor such as hypertension, smoking, family history, albuminuria, or dyslipidemia in men >50 years or women >60 years of age). ASA is not recommended for primary prevention in those with a 10-year cardiovascular risk <10%. The aspirin dose is the same as in nondiabetic individuals.

Cardiovascular Risk Factors • ***DYSLIPIDEMIA*** Individuals with DM may have several forms of dyslipidemia (Chap. 421). Because of the additive cardiovascular risk of hyperglycemia and hyperlipidemia, lipid abnormalities should be assessed aggressively and treated as part of comprehensive diabetes care (Chap. 418). The most common pattern of dyslipidemia is hypertriglyceridemia and reduced high-density lipoprotein (HDL) cholesterol levels. DM itself does not increase levels of low-density lipoprotein (LDL), but the small dense LDL particles found in type 2 DM are more atherogenic because they are more easily glycated and susceptible to oxidation.

Almost all treatment studies of diabetic dyslipidemia have been performed in individuals with type 2 DM because of the greater frequency of dyslipidemia in this form of diabetes. Interventional studies have shown that the beneficial effects of LDL reduction with statins are similar in the diabetic and nondiabetic populations. Large prospective trials of primary and secondary intervention for CHD have included some individuals with type 2 DM, and subset analyses have consistently found that reductions in LDL reduce cardiovascular events and morbidity in individuals with DM. No prospective studies have addressed similar questions in individuals with type 1 DM. Because the frequency of CVD is low in children and young adults with diabetes, assessment of cardiovascular risk should be incorporated into the guidelines discussed below.

Based on the guidelines provided by the ADA, priorities in the treatment of dyslipidemia are as follows: (1) lower the LDL cholesterol, (2) raise the HDL cholesterol, and (3) decrease the triglycerides. A treatment strategy depends on the pattern of lipoprotein abnormalities. Initial therapy for all forms of dyslipidemia should include dietary changes, as well as the same lifestyle modifications recommended in the nondiabetic population (smoking cessation, blood pressure control, weight loss, increased physical activity). The dietary recommendations for individuals with DM include increased monounsaturated fat and carbohydrates and reduced saturated fats and cholesterol (Chap. 421). According to guidelines of the ADA, the target lipid values in diabetic individuals (age >40 years) without CVD should be as follows: LDL <2.6 mmol/L (100 mg/dL); HDL >1 mmol/L (40 mg/dL) in men and >13 mmol/L (50 mg/dL) in women; and triglycerides <1.7 mmol/L (150 mg/dL). In patients >40 years, the ADA recommends addition of a statin, regardless of the LDL level, in patients with CHD and those without CHD who have CHD risk factors. Recently released guidelines by the American College of Cardiology (ACC) and American Heart Association (AHA) differ slightly and recommend that diabetic individuals aged 40–75 without CHD and a LDL of 70–189 mg/dl receive "moderate" intensity statin therapy (Chap. 291e). Improvement in glycemic control will lower triglycerides and have a modest beneficial effect by raising HDL.

If the patient is known to have CHD, the ADA recommends an LDL goal of <18 mmol/L (70 mg/dL) as an "option" (in keeping with evidence that such a goal is beneficial in nondiabetic individuals with CHD [Chap. 421]). The ACC/AHA guidelines do not advocate a specific LDL for statin therapy. HMG-CoA reductase inhibitors are the agents of choice for lowering LDL. Combination therapy with an HMG-CoA reductase inhibitor and a fibrate or another lipid-lowering agent (ezetimibe, niacin) may be considered but increases the possibility of side effects such as myositis and has not been shown to be beneficial. Nicotinic acid effectively raises HDL and can be used in patients with diabetes, but may worsen glycemic control and increase insulin resistance and has not been shown to provide additional benefit beyond statin therapy alone. Bile acid–binding resins should not be used if hypertriglyceridemia is present. In large clinical trials, statin usage is associated with a mild increase in the risk of developing type 2 DM. This risk is greatest in individuals with other risk factors for type 2 DM (Chap. 417). However, the cardiovascular benefits of statin use outweigh the mildly increased risk of diabetes.

HYPERTENSION Hypertension can accelerate other complications of DM, particularly CVD, nephropathy, and retinopathy. In targeting a goal of blood pressure of <140/80 mmHg, therapy should first emphasize lifestyle modifications such as weight loss, exercise, stress management, and sodium restriction. The BP goal should be individualized. In some younger individuals, the provider may target a blood pressure of <130/80 mmHg. Realizing that more than one agent is usually required to reach the blood pressure goal, the ADA recommends that all patients with diabetes and hypertension be treated with an ACE inhibitor or an ARB. Subsequently, agents that reduce cardiovascular risk (beta blockers, thiazide diuretics, and calcium channel blockers) should be incorporated into the regimen. ACE inhibitors and ARBs are likely equivalent in most patients with diabetes and renal disease. Serum potassium and renal function should be monitored.

Because of the high prevalence of atherosclerotic disease in individuals with type 2 DM, the possibility of renovascular hypertension should be considered when the blood pressure is not readily controlled.

LOWER EXTREMITY COMPLICATIONS

DM is the leading cause of nontraumatic lower extremity amputation in the United States. Foot ulcers and infections are also a major source of morbidity in individuals with DM. The reasons for the increased incidence of these disorders in DM involve the interaction of several pathogenic factors: neuropathy, abnormal foot biomechanics, PAD, and poor wound healing. The peripheral sensory neuropathy interferes with normal protective mechanisms and allows the patient to sustain major or repeated minor trauma to the foot, often without knowledge of the injury. Disordered proprioception causes abnormal weight bearing while walking and subsequent formation of callus or ulceration. Motor and sensory neuropathy lead to abnormal foot muscle mechanics and to structural changes in the foot (hammer toe, claw toe deformity, prominent metatarsal heads, Charcot joint). Autonomic neuropathy results in anhidrosis and altered superficial blood flow in the foot, which promote drying of the skin and fissure formation. PAD and poor wound healing impede resolution of minor breaks in the skin, allowing them to enlarge and to become infected.

Many individuals with type 2 DM develop a foot ulcer (great toe or metatarsophalangeal areas are most common), and a significant subset who develop an ulceration will ultimately undergo amputation (14–24% risk with that ulcer or subsequent ulceration). Risk factors for foot ulcers or amputation include male sex, diabetes for >10 years, peripheral neuropathy, abnormal structure of foot (bony abnormalities, callus, thickened nails), PAD, smoking, history of previous ulcer or amputation, visual impairment, and poor glycemic control. Large calluses are often precursors to or overlie ulcerations.

TREATMENT LOWER EXTREMITY COMPLICATIONS

The optimal therapy for foot ulcers and amputations is prevention through identification of high-risk patients, education of the patient, and institution of measures to prevent ulceration. High-risk patients should be identified during the routine, annual foot examination performed on all patients with DM (see "Ongoing Aspects of Comprehensive Diabetes Care" in Chap. 418). If the monofilament test or one of the other tests is abnormal, the patient is diagnosed with loss of protective sensation (LOPS; Chap. 417). Providers should consider screening for asymptomatic PAD in individuals >50 years of age who have diabetes and other risk factors using ankle-brachial index testing in high-risk individuals (Chap. 302). Patient