TABLE 66-6 SCREENING CRITERIA FOR DIABETES IN ASYMPTOMATIC ADULTS

1. Testing for diabetes should be considered in all persons ≥45 yr of age; if normal, the test should be repeated at 3-yr intervals.
2. Testing should be considered at a younger age (<30 yr) or performed more frequently in individuals who
   a. Are overweight (BMI ≥25) or who have central obesity with normal BMI (18.5-24.9)
   b. Have an habitually sedentary lifestyle
   c. Have a first-degree relative with diabetes (i.e., parent or sibling)
   d. Are members of a high-risk ethnic population (e.g., African American, Latino/Hispanic American, Native American, Asian American, Pacific Islander)
   e. Have delivered a baby weighing >9 lb (4 kg), have experienced unexplained perinatal death of a child, or have been diagnosed with gestational diabetes
   f. Are hypertensive (≥140/90 mm Hg)
   g. Have an HDL cholesterol level <35 mg/dL (0.9 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   h. Had, on previous testing, impaired glucose tolerance (plasma glucose ≥140 mg/dL [7.8 mmol/L] but <200 mg/dL [11.1 mmol/L] 2 hr after 75-g oral glucose tolerance test), impaired fasting glucose (plasma glucose 100-125 mg/dL [5.6-6.9 mmol/L]), or HbA_{1C} ≥5.7%
   i. Have other clinical conditions associated with insulin resistance (e.g., PCOS, acanthosis nigricans)
   j. Have a history of cardiovascular disease

Modified from the American Diabetes Association Clinical Practice Recommendations 2013, Diabetes Care 36(Suppl 1):S11–S66, 2013.

BMI, Body mass index (weight [kg]/height [m^2]); HbA_{1C}, glycosylated hemoglobin; HDL, high-density lipoprotein; PCOS, polycystic ovary syndrome; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

Depending on initial blood glucose levels, the presence or absence of symptoms related to hyperglycemia, and the presence of other complicating medical conditions, a decision can be made on whether to treat the patient initially with diet alone or to also start medication. Patients with marked hyperglycemia, fluid deficits, altered mental status related to hyperosmolar state, and DKA should be hospitalized for acute treatment (see later discussion).

For most patients, treatment of T2DM can be conducted on an outpatient basis. Useful and frequently updated guidelines are available on line from the ADA and the European Association for the Study of Diabetes. Most expert panels recommend starting with one or two oral glucose-lowering medications (depending on the degree of hyperglycemia) with progression to a third oral agent or insulin if this proves ineffective. In patients with marked hyperglycemia (>300 mg/dL or HbA_{1c} >9.0% to 9.5%), consideration should be given to starting insulin from the outset. There typically is gradually progressive loss of beta cell function in T2DM, extending sometimes over many years, and this results in a need over time for increased doses or additional glucose-lowering agents and often, ultimately, the use of insulin. As for T1DM, the overall management of T2DM should include not only the treatment of hyperglycemia but also interventions that assess, decrease the risks for, and treat long-term microvascular and macrovascular complications.

Blood Glucose Control

The United Kingdom Prevention of Diabetes Study (UKPDS) and other randomized, controlled trials have established that improved blood glucose control lowers the risk of microvascular long-term complications (retinopathy, nephropathy, and neuropathy) in T2DM. The risk appears to increase progressively, starting with any increment above normoglycemia. Randomized clinical trial data have not convincingly demonstrated improved macrovascular (i.e., cardiovascular disease) outcomes in T2DM. HbA_{1c} goals therefore should be developed on an individualized basis, such that the benefits of improving microvascular complications are balanced against the risks of hypoglycemia. T2DM patients, particularly those who are older or have complicating comorbid conditions, may have limited capacity to manage a tight blood glucose control regimen and also increased susceptibility to adverse effects of hypoglycemia. Whereas an HbA_{1c} of 7.0% or less is an appropriate target for younger T2DM patients, 8.0% or less may be an acceptable and safer target for older patients with complicating medical conditions and limited life expectancy. Patients or their caregivers should perform regular glucose monitoring (SMBG) to assess ongoing blood glucose control, identify potential hypoglycemia, and detect marked increases in blood glucose that may occur during an intercurrent illness. HbA_{1c} determinations provide important supplemental information about blood glucose control and should be performed at intervals of 3 to 6 months.

Non-Insulin Pharmacologic (Antidiabetic) Agents in T2DM

Non-insulin pharmacological agents from many different drug classes are available for treatment of T2DM, some taken orally and others by injection (Table 66-7). When non-insulin pharmacologic agents are appropriate, metformin is first-line therapy because of its glucose-lowering efficacy, absence of weight gain and hypoglycemia, favorable safety and tolerability profile based on many years of clinical experience, and low cost. For patients who are unable to tolerate metformin, a sulfonylurea is a reasonable choice, again based on efficacy, tolerability, and low cost. Sulfonylureas have the disadvantages of inducing modest weight gain in many patients, and they carry a risk of causing hypoglycemia. Agents in other drug classes can be considered for first-line therapy, but there is less knowledge or more concern about their long-term safety profiles, and they have higher cost.

If a single drug is tolerated but does not adequately control blood glucose levels, the usual practice is to continue that drug and add a second. Drug combinations often are selected from classes with complementary mechanisms of actions. For example, the combination of an insulin sensitizer such as metformin and an insulin secretagogue such as a sulfonylurea has theoretical appeal in providing greater potential for additive or synergistic actions. Patients with marked hyperglycemia that is not judged severe enough to merit insulin treatment may be started on two agents from the outset. This has the potential advantage of more rapidly achieving blood glucose control but the disadvantage of exposing patients to the potential side effects of taking two drugs simultaneously. Many combination preparations are available for administration of more than one drug; these are more convenient for patients and sometimes less expensive than taking the multiple drugs separately.

Available non-insulin antidiabetic agents are summarized here and in Table 66-7. Current manufacturer information should be