Diabetes Mellitus, Type 2

Description/Etiology
Diabetes mellitus, type 2 (DM2)—formerly known as non-insulin dependent diabetes and adult-onset diabetes—is a chronic, multisystem, metabolic syndrome of gradual onset characterized by an insufficient body tissue response to insulin (i.e., insulin resistance) and impaired pancreatic production of insulin. Subsequent hyperglycemia (i.e., increased blood sugar) is typically detected incidentally during routine examinations because symptoms are usually mild, develop over several years, and mimic age-related health changes. Longstanding diabetic complications (e.g., eye disease, peripheral neuropathy, diabetic nephropathy, cardiovascular disease [CVD]) are commonly present at diagnosis. DM2 is thought to be caused by genetic, behavioral, and environmental factors, including the synergistic effects of genetic susceptibility and obesity.

Diagnosis of DM2 is based on findings of abnormally high blood glucose from two tests on different days (see Assessment, below). Tests that measure C-peptide levels or detect the presence of pancreatic islet cell autoantibodies can be used to differentiate between DM2 and diabetes mellitus, type 1 (DM1), in which an autoimmune reaction causes the destruction of the insulin-producing cells of the pancreas. (For more information on DM1, see Quick Lesson About … Diabetes Mellitus, Type 1).

Although a treatment regimen of appropriate nutrition, regular physical activity (i.e., at least 150 minutes per week of moderate-intensity aerobic exercise[e.g., walking], or vigorous-intensity aerobic activity for 75 minutes per week, as well as resistance exercise 3 times per week), and desirable body weight maintenance is important in order to attain blood glucose control and reduce the risk of complications or their progression, the addition of a glucose-lowering oral drug therapy is necessary for optimal DM2 control in the majority of patients. Temporary insulin therapy is commonly combined with oral agents during periods of illness or extreme stress, and many patients routinely require insulin during late-stage DM2. Bariatric surgery can be considered in patients with DM2 whose body mass index (BMI) exceeds 35 kg/m². The long-term quality of blood glucose control plays a major role in determining the onset and severity of complications. Strict adherence to the multidisciplinary treatment regimen and routine screening examinations of the skin, eyes, and feet are essential to optimize quality of life and maximize life expectancy.

Facts and Figures
About 30 million Americans—23 million diagnosed plus 7 million undiagnosed—have diabetes, and DM2 accounts for 90–95% of diabetes cases. Another 86 million people in the United States, or 37% of adults, have prediabetes (i.e., elevated levels of blood glucose that are not high enough to meet the diagnostic criteria for diabetes). Although it can occur at any age, DM2 is most commonly diagnosed after age 40; however, the recent increase in prevalence of obesity in children and adolescents in the U.S. has led to a corresponding increase in the diagnosis of DM2 in a younger population. Rates of diabetes vary widely among racial and ethnic groups in the U.S.; the prevalence of diagnosed diabetes in adults is 7.4% for Whites, 8.0% for Asians, 12.1% for Hispanics, 12.7% for Blacks, and 15.1% for American Indians/Alaska Natives. Because of the long presymptomatic phase, DM2 is typically diagnosed 4–7 years after onset. Among adults with diabetes, 74% have hypertension and 66% have dyslipidemia. Neuropathy affects 70–80% of patients with DM2 and ~29% of adults 40 years and older with DM2 have retinopathy. DM2 accounts for 44%
of cases of end-stage renal disease and 60% of nontraumatic lower limb amputations. DM2 is associated with a 1.8-fold increased risk of myocardial infarction and a 1.5-fold increased risk of stroke.

**Risk Factors**

Risk factors for DM2 include family history (i.e., DM in a first-degree relative), previous gestational diabetes (i.e., onset during pregnancy), obesity, sedentary lifestyle, age > 45 years, hypertension (blood pressure ≥ 140/90), polycystic ovary syndrome, prediabetes, metabolic syndrome, and dyslipidemia.

**Signs and Symptoms/Clinical Presentation**

Approximately 87% of patients with DM2 are obese. Patients most commonly experience gradually increasing symptoms of fatigue, recurrent infections, prolonged wound healing, and vision changes. Presentation may also include such classic symptoms as polyuria (i.e., increased urination), polydipsia (i.e., increased thirst), unexplained changes in weight, and polyphagia (i.e., increased appetite). Macro- and microvascular complications that may be present at diagnosis or develop over the disease course include renal dysfunction, eye disease, atherosclerotic cardiovascular and peripheral vascular disease, peripheral neuropathy, bowel and bladder dysfunction, dry pruritic skin, and infection or gangrene of the extremities. Diabetic ketoacidosis (DKA; i.e., metabolic acidosis caused by insulin deficiency) is uncommon in DM2 but may occur during severe illness; other conditions associated with DM2 include hypertension, sexual dysfunction, hyperlipidemia (i.e., increased blood fat levels), and hyperglycemic hyperosmolar nonketotic syndrome (HHNS; i.e., a life-threatening hyperglycemia-driven metabolic imbalance characterized by inability to replace fluids, polyuria, aphasia, seizures, paralysis, decreased mentation, and rarely, coma).

**Assessment**

› **Laboratory Tests That May Be Ordered**
  * Diagnosis is based on any of the following tests drawn on different days:
    – Fasting plasma glucose levels of 126 mg/dL (7.0 mmol/L) or higher. (Note: Fasting plasma glucose < 100 is considered normal; 100–125 is considered prediabetes)
    – Two-hour postprandial plasma glucose readings of 200 mg/dL (11.1 mmol/L) or higher after a glucose load of 75 g
    – Nonfasting blood glucose level of 200 mg/dL (11.1 mmol/L) or higher in a symptomatic patient
    – Glycosylated hemoglobin (HbA1c) level, a measure of long-term glycemic exposure, of 6.5% or higher
  * UA may show abnormal levels of acetone or glucose
  * Tests may be ordered to differentiate between DM1 and DM2
    – Islet cell autoantibodies will be present in early-stage DM1 but not in DM2
    – C-peptide levels are decreased in DM1 and normal or elevated in DM2
  * Additional tests may be required to evaluate the extent of complications. Testing for DM2 and prediabetes should be implemented in children and adolescents with 2 or more risk factors in addition to obesity

**Treatment Goals**

› **Stabilize Diabetic Symptoms and Reduce Risk of Complications**
  * Assess status of eyes, skin, extremities, lungs, heart, kidneys, neurological system, and electrolytes by physical assessment, monitoring of vital signs, and review of laboratory values and diagnostic studies, per facility protocol
  * Administer prescribed antidiabetic medications (e.g., metFORMIN, sulfonylureas) and/or exogenous insulin or insulin analogues to treat hyperglycemia; monitor for adverse effects of antidiabetic medications (e.g., hypoglycemia with sulfonylureas, thiazolidinediones, and secretagogues; diarrhea, nausea, and vomiting with metformin and alpha-glucosidase inhibitors; peripheral edema with thiazolidinediones)
  * Monitor and treat hyperglycemia (i.e., abnormally low blood sugar) with oral glucose
  * Monitor for and treat HHNS or DKA by correcting dehydration, nutrition imbalance, electrolyte loss, and acidosis to prevent subsequent coma and death, as ordered
  * Follow facility pre- and postsurgical protocols if patient becomes a candidate for surgery (e.g., bariatric surgery, debridement or amputation); reinforce pre- and postsurgical education and verify completion of facility informed consent documents
  * Request patient referral to an ophthalmologist upon diagnosis of DM2 and subsequently annually for recommended dilated fundoscopic eye exam and/or laser therapy
• Request patient referral upon initial DM2 diagnosis, then annually, to a neurologist for distal symmetric polyneuropathy (DPN) screening

Educate on Monitoring and Assessment of all Body Systems, Self-Care, and Prevention of Complications
• Supervise self-monitoring of blood glucose to adjust insulin treatment regimen for optimal control, especially during illness or other periods of stress, and self-administration of glucose-lowering oral agents and/or insulin, as ordered
• Emphasize that all patients diagnosed with DM2 should use a glucometer as directed by their physician for consistent blood glucose monitoring and monitoring during acute episodes of hyper- or hypoglycemia or illness
• Provide ongoing instruction, assessment and consistent evaluation (e.g., the teach-back method) for patients/patient’s family who are monitoring blood glucose levels at home
• Supervise self-monitoring of urine ketones, if recommended by the treating clinician
• Reinforce education regarding the disease and treatment of DM2, including foot, eye, oral, and skin care, and ways to reduce the risk of complications, such as infection, amputation, and blindness
• Provide resources for information on nutrition, exercise, weight control, and stress reduction; as appropriate, request referral to a dietitian, social worker, and/or mental health clinician

Food for Thought
› To prevent or delay the onset of DM2 in patients with prediabetes, the American Diabetes Association recommends referral to a support program targeting weight loss of 7% and increased physical activity to at least 150 minutes per week of moderate activity; the group advises that metformin therapy should be considered in patients with prediabetes, especially those with BMI > 35 kg/m², age < 60 years, and history of gestational diabetes (in women)
› Although researchers have reported links between DM2 and numerous types of cancer, investigators who performed an umbrella review of meta-analyses of observational studies found robust evidence supporting a link between DM2 and only four types of cancer: breast, intrahepatic cholangiocarcinoma, colorectal, and endometrial cancers (Tsilidis et al., 2015)
› Researchers who analyzed administrative data from more than 800,000 U.S. veterans from 2000 to 2010 determined that, among patients with DM2 not controlled with metformin, initiation of sulfonylureas was associated with a 50% increased risk of all-cause mortality and a 68% increased risk of avoidable hospitalization compared to initiation of thiazolidinediones (Prentice et al., 2014)
› Results from numerous clinical trials have demonstrated that metabolic surgery provides excellent glycemic control and decreases cardiovascular risk factors and should be recommended to treat DM2 in patients with severe obesity and uncontrolled hyperglycemia (Rubino et al., 2016)
› Following numerous clinical trials which showed a reduction in the risk of cardiovascular death, The American Diabetes Association standards of care now recommend clinicians to consider empagliflozin or liraglutide for long-standing DM2 patients with atherosclerotic cardiovascular disease (Thrasher, 2017)

Red Flags
› Clinicians must be knowledgeable about potential complications and factors that contribute to hyper- and hypoglycemia, HHNS, and DKA in patients who are receiving inpatient treatment unrelated to DM2 (e.g., physiologic nondiabetic disease alterations, altered diet and exercise, nondiabetic medication influence on blood sugar levels, and timing issues with food)
› Obstructive sleep apnea in patients with DM2 is associated with poorer glucose control

What Do I Need to Tell the Patient/Patient’s Family?
› Explain that treatment involves lifelong medical surveillance, education, physical self-assessment, and lifestyle modification, and periodic alteration of the therapeutic plan
› Instruct patient/patient’s family how to identify signs and symptoms of hyper- or hypoglycemic reactions, and appropriate interventions to normalize blood glucose levels. Advise patient to seek medical attention for new or worsening symptoms
› Emphasize the importance and utility in following the prescribed blood glucose monitoring schedule using a glucometer, writing down the readings, and bringing the glucometer and readings to each appointment with the doctor

References