Diabetes Mellitus, Type 1

Description/Etiology
Diabetes mellitus, type 1 (DM1; formerly known as insulin-dependent diabetes and juvenile-onset diabetes) is a life-threatening, multisystem, metabolic disease of abrupt onset characterized by severe insulin deficiency as a result of autoimmune destruction of insulin-producing pancreatic β-cells. The disease generally occurs in individuals younger than 30 years of age and demands lifelong insulin therapy to avoid life-threatening complications.

Several genes of the HLA system that encode proteins of the major histocompatibility complex (MHC) have been associated with DM1. The MHC is a group of proteins that are expressed on the surface of normal cells to present foreign antigens from pathogens to the cells of the immune system for destruction. In addition to the HLA system, other genes involved in regulation of the immune response seem to play a role in the pathogenesis of DM1. The synergistic effects of genetic susceptibility, certain environmental factors (e.g., viral infections, toxins), and a dysfunctional immune process trigger the production of autoantibodies against self-antigens (i.e., proteins that are normally produced by pancreatic islet β-cells) and selective destruction of β-cells. The deficient production of insulin disrupts the normal regulation of carbohydrates, lipids, and proteins metabolism, which leads to chronic hyperglycemia (i.e., increased levels of blood glucose), systemic acid-base imbalance, and insufficient glucose delivery to the tissues. Macrovascular complications associated with DM1 include myocardial infarction and stroke. Microvascular complications include retinopathy, nephropathy, and neuropathy.

Diagnosis of DM1 is based on clinical presentation and results of laboratory studies demonstrating elevated fasting glucose levels and presence of autoimmune biomarkers. Management of DM1 requires self-monitoring of blood glucose levels, administration of exogenous insulin, and patient/family education regarding lifestyle changes in exercise and diet. Strict adherence to an intensive treatment regimen of 3–4 insulin injections/day or continuous subcutaneous insulin infusion is essential to prevent acute complications (e.g., diabetic ketoacidosis [DKA; i.e., metabolic acidosis caused by insulin deficiency]) and to prevent or delay chronic macrovascular and microvascular complications. Regular screening for nephropathy, hypertension, dyslipidemia, neuropathy, and retinopathy is important in patients with DM1. Although life expectancy has improved, a good prognosis depends on treatment adherence to avoid complications associated with DM1.

Facts and Figures
Approximately 422 million people live with diabetes mellitus (DM) worldwide. DM1 affects ~ 1 million people in the United States and accounts for 5–10% of all cases of diabetes. Although it can occur at any age, about half of patients who are newly diagnosed with DM1 are younger than 20 years of age. DM1 is the most common metabolic disease in children, affecting 1 in 400–600 children and adolescents; ~ 15,600 young adults are diagnosed with DM1 each year in the U.S. The incidence in the U.S. is highest among whites and lowest among blacks. Over the past decade, the incidence of DM1 in younger children (< 5 years of age) has increased. DM1 affects males more often than females; the male-to-female ratio is > 1.5:1 in populations of European descent. Cardiovascular disease is responsible for 65–75% of deaths in patients with DM1 compared with 35% of deaths in persons without diabetes. The incidence of end-stage renal disease is 2.2% at 20 years after
diagnosis of DM1, and 7.8% after 30 years. Each 1% increase in glycosylated hemoglobin (HbA1C; i.e., a measure of long-term glycemic control) is associated with a 19% increase in risk of myocardial infarction.

Risk Factors
Certain human leukocyte antigen (HLA) haplotypes (HLA DR3-DQ2, HLA DR4-DQ8) have been associated with increased risk of DM1. The risk of developing DM1 increases if there is a first-degree relative with a history of DM (3% if the relative is the mother, 5% if it is the father, 8% if it is a sibling). Risk rises as geographic latitude increases. Viral infections, including mumps, congenital rubella, and coxsackievirus, appear to trigger an autoimmune response that results in the destruction of pancreatic β-cells. Having been breastfed appears to be protective against DM1, and consuming a diet high in dairy products may increase risk. Other factors that have been proposed as potential triggers for autoimmunity in DM1 include early exposure to cereal or solid foods. Lack of vitamin D supplementation, high birth weight, childhood obesity, accelerated growth, and older maternal age may also be risk factors. The prevalence of DM1 is increased in patients with other autoimmune diseases, including Graves’ disease, Hashimoto thyroiditis, and Addison disease. Patients with DM1 have a 10-fold higher risk of developing cardiovascular complications. Patients with DM1 have an increased risk of fractures due to bone fragility and decreased bone mineral density.

Signs and Symptoms/Clinical Presentation
The clinical presentation of DM1 includes the sudden development of polydipsia (i.e., increased thirst), polyuria (i.e., increased urination), unexplained weight loss, dehydration, and fatigue. Other signs and symptoms include sudden vision changes, polyphagia (i.e., increased appetite), tingling or numbness in the hands or feet, dry skin, recurrent infection, and slow wound healing. If DKA is present, signs and symptoms may include abdominal pain, nausea, vomiting, hyperventilation, fruity breath odor, and altered level of consciousness.

Assessment
› Patient History
   • Ask about history of DM1 in first-degree relatives and patient history of viral infection (e.g., mumps, congenital rubella, coxsackievirus)
› Physical Findings of Particular Interest
   • Abnormally high blood glucose levels and identification of DM1-related manifestations during medical history and physical examination are diagnostic of DM1
› Laboratory Tests That May Be Ordered
   • Plasma glucose concentration will be ≥ 200 mg/dL (non-fasting) or ≥ 126 mg/dL (fasting)
   • HbA1C will be increased (e.g., > 7%)
   • UA may show abnormal levels of acetone or glucose
   • Tests that are performed to differentiate DM1 from diabetes mellitus, type 2 (DM2) include assessment for islet cell autoantibodies and evaluation of C-peptide levels
     – Islet cell autoantibodies to insulin, zinc transporters-8, and glutamic acid decarboxylase, can be present in early-stage DM1 but not in DM2
     – C-peptide levels are decreased in DM1 and are normal or elevated in DM2

Treatment Goals
› Stabilize Diabetic Manifestations and Reduce Risk for Acute Complications
   • Monitor vital signs, assess all physiologic systems, and review results of laboratory tests; confirm that the treating clinician is aware of patient status and administer prescribed treatment
   • Treat hypoglycemia (i.e., low blood glucose levels) with rapid acting glucose, and hyperglycemia (i.e., high blood glucose levels) with insulin and/or insulin analogues, as ordered. Glucagon can be prescribed for severe patients at high risk of hypoglycemia
   • Monitor and provide prescribed treatment for DKA by correcting dehydration, inadequate nutrition, electrolyte loss, and acidosis as ordered to prevent coma and death
   • Follow facility protocols for perioperative care of the patient with DM1 if patient becomes a candidate for surgery (e.g., amputation or surgery that is unrelated to DM1); reinforce pre- and postsurgical education and verify completion of facility informed consent documents
› Educate and Promote Adherence to the Prescribed Treatment Regimen
• Assess patient/family anxiety level, coping ability, and for knowledge deficits regarding DM1; provide emotional support, educate, and encourage discussion regarding
  – self-administration of insulin and self-monitoring of blood glucose (usually 2–4 times/day) to adjust the prescribed insulin treatment regimen for optimal control, especially during illness or other periods of stress
  – self-monitoring of urine ketones if ordered by the treating clinician
  – important foot, eye, oral, and skin care, and risks and benefits of treatment
  – potential complications and strategies for reducing the risk of complications
  – the importance of lifestyle changes related to diet, exercise, weight control and stress management
• Request referral, if appropriate, to a
  – nutritionist specializing in diet planning and education for diabetics
  – social worker, case manager, and/or other social services provider

Food for Thought
› DM1 education should be initiated as soon as possible after diagnosis. Teaching a patient to self-inject insulin is often the most effective first step in DM1 education because self-injection causes the greatest fear among patients. When self-injection is mastered, patients report reduced anxiety and increased comprehension in other areas and skills
› Clinicians should be knowledgeable about factors that contribute to hyper-and hypoglycemia in patients who are undergoing treatment that is unrelated to DM1 (e.g., for a non-diabetic physiologic disease process; involving changes in medication). In patients who have poor glucose control, it is important to identify the reason for poor control (e.g., non-adherence, knowledge deficits, and self-care deficits)
› Although exercise is considered important in the management of DM1—having previously been shown to improve aerobic fitness, reduce cardiovascular risk, reduce bodyweight and body fat, and improve glycemic control by enhancing insulin sensitivity—it can result in episodes of hypoglycemia; continuous glucose monitoring systems can effectively reduce the risk of severe hypoglycemia
› Screening for autoimmune diseases (e.g., thyroid dysfunction, celiac disease, vitamin B12 deficiency), which occur at an increased frequency in those with DM1, may be appropriate in response to individualized patient manifestations (Pociot et al., 2016)
› Diabetic neuropathy frequently results in recurrent trauma on the small bones of the feet, which can lead to bone abnormalities. Carpal tunnel syndrome and Dupuytren’s contracture are also frequent in patients with diabetes mellitus (Hough et al, 2016)
› Alternative methods of insulin administration including inhaled insulin or polymeric nanoparticles and micelles that act as nanocarriers for oral delivery of insulin, are being researched (Sharma et al., 2015)
› Researchers conducting a meta-analysis report that patients with diabetes have higher blood levels of copper than non-diabetic patients (Qiu et al, 2017)
› Researchers in Germany and Austria report improved glycemic control in 660 youth with type 1 diabetes who used a tubeless insulin pump delivery system compared to 1869 youth with type 1 diabetes who utilized multiple daily insulin injections (Danne et al, 2018)

Red Flags
› Drugs and other substances that can cause hyperglycemia include hormones (e.g., glucocorticoids, growth hormone, estrogen, progesterone), thiazide diuretics, beta-blockers, calcium channel blockers, epinephrine-like drugs (e.g., decongestants, diet pills), NSAIDs, nicotine, caffeine, and fish oil
› Hypoglycemia (plasma glucose level < 70 mg/dL) is a life-threatening complication that can occur following an intensive treatment regimen and result in seizures or coma; careful screening, patient and family education, and comprehensive assessment of anticipated patient adherence should precede initiation of an intensive treatment regimen
› Diabulimia, the omission or reduction of insulin use as a weight loss/control strategy, is associated with increased risk for dehydration, muscle tissue breakdown, and fatigue in the short term and kidney failure, blindness, vascular disease, and death in the long term
› DM1 appears to be associated with increased risk of non-Hodgkin lymphoma, leukemia, pancreatic cancer, and colorectal cancer
What Do I Need to Tell the Patient/Patient’s Family?

› Treatment for DM1 involves continued medical surveillance and modification of the therapeutic treatment plan as appropriate to individual patient needs
› Lifelong education and communication with patients regarding physical/emotional status, lifestyle changes, and advances in treatment options are important
› It may be possible for asymptomatic family members of patients with DM1 to be screened for DM risk via participation in a research study

References