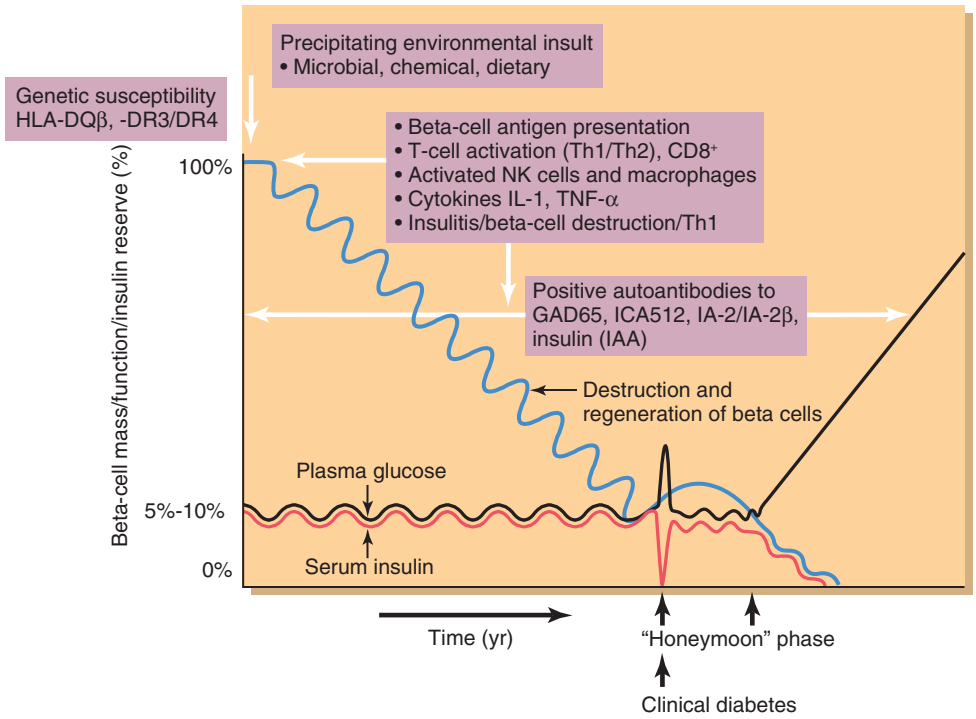

FIGURE 66-1 Natural history of type 1 diabetes mellitus. The honeymoon period with temporary improvement in beta-cell function occurs with the initiation of insulin therapy at the time of clinical diagnosis. GAD, Glutamic acid decarboxylase; HLA, human leukocyte antigen; IA-2, IA-2β, tyrosine phosphatases; ICA, islet cell antibody; ICA512, islet cell autoantigen 512 (fragment of IA-2); IL-1, interleukin-1; NK, natural killer; Th1, subset of CD4+ helper T cells responsible for cell-mediated immunity; Th2, subset of CD4+ helper T cells responsible for humoral immunity; TNF-α , tumor necrosis factor-α.

hypovolemia and increased serum osmolality). The polyuria may be evident as bed wetting or daytime incontinence in children and as nocturia in adults. There typically also is weight loss, and patients often describe low energy and lethargy. Approximately 25% of patients with T1DM have progressed to DKA by the time of clinical presentation.

Treatment

The management of T1DM involves immediate treatment at the outset to correct hyperglycemia, fluid deficits, and DKA, if present, plus attention to possible precipitating or complicating factors such as infection. The initial treatment of T1DM should be coupled with education of patients and their family members (appropriate to the patient's age) concerning the needed skills to manage insulin administration, blood glucose testing, nutrition, and exercise. This often is best accomplished by a team involving the physician, educators (typically specially trained nurses or pharmacists), and a dietician. Medical advice, patient education, and psychological support should be provided on an ongoing, long-term, individualized basis. The primary goal of glucose management is to minimize the degree of hyperglycemia, and its attendant risks of long-term complications of diabetes, while avoiding the acute and chronic risks of hypoglycemia. Medical care also should include attention to control of lipid levels, blood pressure, and other factors that affect the risks of long-term diabetes complications. Routine assessments of foot care, peripheral nerve function, retinal status, and renal function should be used to detect incipient diabetes complications and enable early treatment interventions. Other sources should be consulted for information on specific issues related to T1DM management in children and adolescents.

Blood Glucose Control

Patients with T1DM have an absolute requirement for exogenous insulin. The Diabetes Control and Complications Trial (DCCT) and other studies have established that improved glycemic control in patients with T1DM decreases long-term microvascular complications (retinopathy, nephropathy, and neuropathy). A follow-up study of the same patients (the Epidemiology of Diabetes Interventions and Complications [EDIC] study) further demonstrated lower cardiovascular morbidity and mortality with intensive insulin management. Based on these and other studies, the most generally accepted target goal for HbA_{1c} in T1DM is 7.0%. For patients who have difficulty sensing hypoglycemia or who have other factors complicating blood glucose management (e.g., renal failure), it is appropriate to set an individualized HbA_{1c} goal of 8.0% or even higher.

Many preparations of insulin are available. They differ in rapidity of onset, degree of peaking of blood levels, and duration of action after subcutaneous injection (Table 66-5). The different kinetics of recombinant human insulin preparations derive from their specific complexing with proteins and zinc. Additionally, multiple analogues of human insulin are available that have rapid or slow kinetics as a consequence of altered solubility at subcutaneous injection sites. Most insulin preparations are provided at a concentration of 100 U/mL (U-100). Self-monitoring of blood glucose (SMBG) by patients using glucose meters is critical to the implementation of an effective insulin regimen. Ideally,