Pathophysiology Type 2 DM is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production, abnormal fat metabolism, and systemic low-grade inflammation. Obesity, particularly visceral or central (as evidenced by the hip-waist ratio), is very common in type 2 DM (≥80% of patients are obese). In the early stages of the disorder, glucose tolerance remains near-normal, despite insulin resistance, because the pancreatic beta cells compensate by increasing insulin output **(Fig. 403-7)**. A number of pathophysiologic mechanisms contribute to type 2 DM and their relative importance varies from individual to individual. As insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to sustain the hyperinsulinemic state, manifesting as IGT, defined as elevations in postprandial glucose. A decline in insulin secretion and/or increased glucagon secretion causes an increase in hepatic glucose production leading to fasting hyperglycemia. Ultimately, frank beta cell failure ensues as a combination of these mechanisms leading to the manifestation of type 2 diabetes.

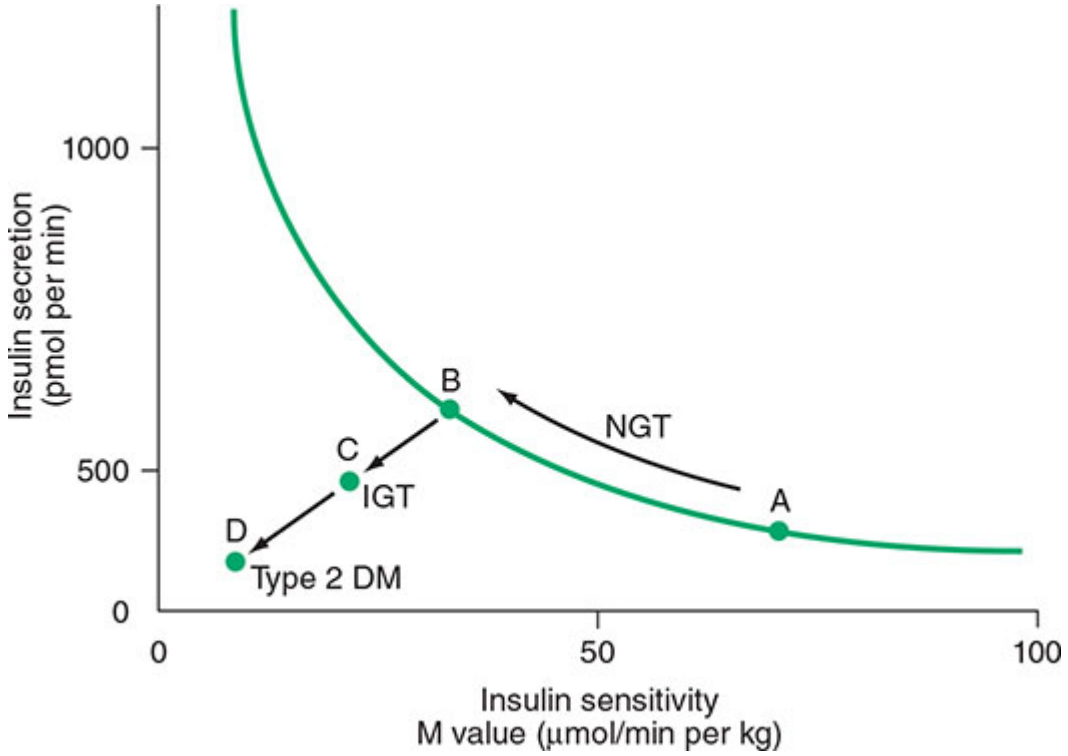

FIGURE 403-7 Metabolic changes during the development of type 2 diabetes mellitus (DM). Insulin secretion and insulin sensitivity are related, and as an