Transcript Details
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The Progressive Nature of T2D: Beta-Cell Dysfunction & Apoptosis

Announcer:
Welcome to ReachMD. This medical industry feature, titled “The Progressive Nature of T2D: Beta-Cell Dysfunction & Apoptosis” was created and sponsored by Novo Nordisk. This program is intended for healthcare professionals.

Dr. DeFronzo:
Hello, I’m Dr Ralph DeFronzo and I am Professor of Medicine and Chief of the Diabetes Division at The University of Texas Health Science Center in San Antonio, Texas. I also serve as the Deputy Director of the Texas Diabetes Institute.

This video will review “The Progressive Nature of Type 2 Diabetes: Beta-Cell Dysfunction & Apoptosis”. Type 2 diabetes is a progressive disease characterized by persistent hyperglycemia, insulin resistance, and progressive beta-cell failure.

Multiple genetic and environmental factors have been identified as drivers that predispose patients to develop type 2 diabetes. Key environmental factors include obesity as well as lifestyle behaviors such as sedentary lifestyle and a high-fat and/or high-caloric-intake diet. Beta-cell dysfunction reflects impaired secretion of insulin relative to the severity of insulin resistance in insulin target tissues. This imbalance between insulin secretion and insulin resistance results in impaired glucose tolerance (which is also referred to as prediabetes) and often progresses to type 2 diabetes. Insulin resistance is established early in the natural history of type 2 diabetes, but as long as the beta-cell secretes sufficient amounts of insulin to offset the defect in insulin action, glucose tolerance remains normal. However, with time, the beta-cells’ secretion of insulin begins to decline, leading to the development of prediabetes and, potentially, overt type 2 diabetes. Further decline in insulin secretion results in a progressive deterioration of glycemic control reflected by a rise in postprandial glycemia, followed by a rise in fasting glycemia.

These chronic changes lead to a rise in the hemoglobin A1C. The rise in hemoglobin A1C, thus, provides a clue that the beta-cells are failing. The decline in beta-cell function occurs early in the natural history of type 2 diabetes. So how do we measure beta-cell function? The gold standard for measuring beta-cell function is the increment in plasma insulin concentration divided by the increment in plasma glucose concentration during the oral glucose tolerance test, all factored by the severity of insulin resistance, as measured by the euglycemic insulin clamp technique. Obviously, this gold standard measure of beta-cell function is not readily available to the practicing physician.

The American Diabetes Association defines normal glucose tolerance as a 2-hour plasma glucose concentration during the OGTT less than 140 mg per deciliter. The diagnosis of diabetes is made if the 2-hour plasma glucose concentration reaches or exceeds 200 mg per deciliter. Individuals with prediabetes or impaired glucose tolerance have a 2-hour plasma glucose concentration between 140 to 199 mg per deciliter. In the upper tertile of impaired glucose tolerance or (“prediabetes,” i.e., a 2-hour plasma glucose concentration during an OGTT equal to 180 to 199 mg/dL), approximately 80% of beta-cell function has been lost. Thus, at the time of diagnosis of type 2 diabetes (a 2-hour plasma glucose concentration of 200 mg/dL or greater), severe beta-cell dysfunction is present.

Not surprisingly, even further small decrements in insulin secretion in the presence of severe insulin resistance lead to marked increases in the plasma glucose concentration. Hyperglycemia and other metabolic disturbances associated with the diabetic state can lead to progressive loss of beta-cell mass that results from both beta-cell apoptosis and failure of beta-cells to proliferate due to the effects of glucolipotoxicity, oxidative stress, and activation of inflammatory pathways.

Although severe beta-cell dysfunction is present early in the natural history of type 2 diabetes, i.e., prediabetes, beta-cell mass is only modestly reduced. However, with progressively deteriorating glycemic control, there is progressive loss of beta-cell mass. Although not directly correlated with the reduction in beta-cell mass, there is an even greater relative decrease in beta-cell function, which amounts to

approximately 80% by the time of initial diagnosis of type 2 diabetes. To summarize, increasing beta-cell dysfunction is an important feature of the progression from prediabetes to type 2 diabetes. Beta-cell dysfunction continues to progress after the diagnosis of overt diabetes. Together, loss of beta-cell mass and function results in even greater insulin deficiency. In clinical practice, the rising A1C laboratory value is a barometer of beta-cell failure.

Ongoing studies are exploring how to predict, delay, and/or reverse the decline in beta-cell function and loss of beta-cell mass. And while it may be difficult to predict the impact of exploratory research, understanding the progression of type 2 diabetes may be a path forward to improving long-term outcomes for patients with this disease.

Announcer:
The preceding program was created and sponsored by Novo Nordisk. If you have missed any part of this discussion or to view the on-screen visuals, visit ReachMD.com/t2dprogression. This is ReachMD. Be Part of the Knowledge.