## The Diabetes Syndrome – A Collection of Conditions with Common, Interrelated Pathophysiologic Mechanisms

The four basic pathophysiologic mechanisms which damage the  $\beta$ -cell within diabetes (ie, genetic and epigenetic changes, inflammation, an abnormal environment, and insulin resistance [IR]) also contribute to cell and tissue damage and elevate the risk of developing all typical diabetes-related complications. Genetic susceptibility to damage from abnormal external and internal environmental factors has been described including inflammation and IR. All these mechanisms can promote epigenetic changes, and in total, these pathophysiologic mechanisms interact and react with each other to cause damage to cells and tissues ultimately leading to disease. Importantly, these pathophysiologic mechanisms also serve to link other common conditions including cancer, dementia, psoriasis, atherosclerotic cardiovascular disease (ASCVD), nonalcoholic fatty liver disease (NAFLD), and nonalcoholic steatohepatitis (NASH). The "Diabetes Syndrome", an overarching group of interrelated conditions linked by these overlapping mechanisms, can be viewed as a conceptual framework that can facilitate understanding of the inter-relationships of superficially disparate conditions. Recognizing the association of the conditions within the Diabetes Syndrome due to common pathophysiologies has the potential to provide both benefit to the patient (eg, prevention, early detection, precision medicine) and to the advancement of medicine (eg, driving education, research, and dynamic decision-based medical practice).

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