PREDIABETES

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Prediabetes (intermediate hyperglycemia) is a high-risk state for diabetes that is defined by glycemic variables higher than normal, but lower than diabetes thresholds. As defined by the American Diabetes Association (ADA), prediabetes encompasses a fasting plasma glucose of at least 100 mg/dl but less than 126 mg/dl (impaired fasting glucose, IFG), and an abnormal 2-h response to a 75-g oral glucose tolerance test of at least 140 mg/dl and less than 200 mg/dl (impaired glucose tolerance, IGT). The World Health Organization defines IGT similarly as the ADA, but IFG is defined at a fasting glucose of at least 110 mg/dl. Furthermore, the ADA recommends that a glycated hemoglobin A_{1c} (HbA_{1c}) between 5.7% and 6.4 % as another measure for diagnosing prediabetes.

Prevalence of prediabetes is increasing worldwide and experts have projected that more than 470 million people will have prediabetes by 2030. The prevalence varies in different ethnic groups and both disorders are more common in people older than 40 years. Additionally, IFG is more prevalent in men than in women. Prediabetes is associated with the simultaneous presence of insulin resistance and β-cell dysfunction–abnormalities that start before glucose changes are detectable. IFG and IGT differ in their pathophysiologic mechanisms. While subjects with IGT have marked muscle insulin resistance with only mild hepatic insulin resistance, subjects with IFG have severe hepatic insulin resistance with normal or near-normal muscle insulin sensitivity. Both IFG and IGT are characterized by a reduction in early-phase insulin secretion, while subjects with IGT also have impaired late-phase insulin secretion. Although genetic influences affect β-cell function, becoming overweight is the main acquired challenge to insulin action.

Around 5–10% of people per year with prediabetes will progress to diabetes, with the same proportion converting back to normoglycemia. According to an ADA expert panel, up to 70% of individuals with prediabetes will eventually develop diabetes. In addition to glycemic values, multifactorial risk scores using non-invasive measures and blood-based metabolic traits such as age, sex, body mass index, blood pressure, diabetes family history, and lifestyle information, could optimize estimation of diabetes risk. People with prediabetes can have concomitant damage to end organs such as eyes, kidneys, blood vessels, and heart, which is traditionally thought to be a complication of diabetes. Prediabetes has been linked to increased risk of early forms

of nephropathy and chronic kidney disease, diabetic retinopathy and diabetic neuropathy, in particular autonomic neuropathy. During the pre-diabetic state, the risk of a cardiovascular event is modestly increased. There is an excess prevalence of coronary disease in people with fasting or postload hyperglycaemia lower than the diabetic threshold. The dose–response effect of postload glucose for vascular mortality might be stronger than the effect of fasting hyperglycaemia.

Prediabetes should be treated to prevent progression to diabetes, mitigate some of the potential results of progression to diabetes, and prevent the potential effects prediabetes itself. For prediabetic individuals, lifestyle modification is the cornerstone of diabetes prevention, with evidence of a 40-70% relative-risk reduction. The primary aim of lifestyle interventions is to prevent or delay development of type 2 diabetes and its complications by targeting obesity and physical inactivity. Successful lifestyle interventions improve insulin sensitivity and β-cell function. Evidence of potential benefits from pharmacotherapy is accumulating. In people with IGT, metformin, acarbose, rosiglitazone, pioglitazone, and orlistat have been shown to lower the risk of type 2 diabetes. In addition, glucagon-like peptide-1 analogues exenatide and liraglutide both were associated with increased reversion from prediabetes to normoglycemia. In view of long-standing safety information, metformin could be used in people who are unable to comply with lifestyle advice. For other potential drugs, further long-term studies are needed on safety and vascular outcomes before lifelong treatment can be recommended.