



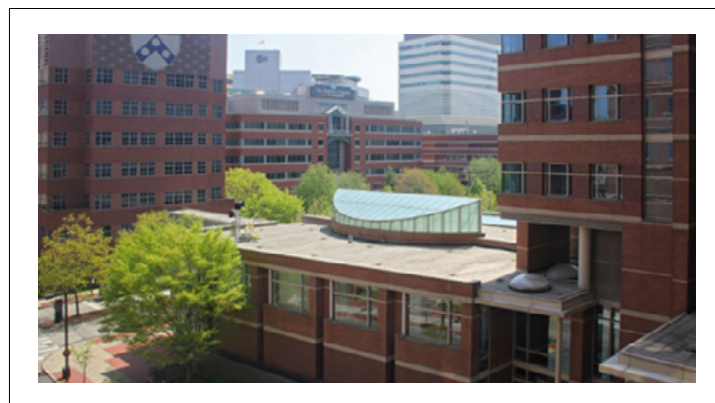
The syndrome of diabetes- A unified pathophysiologic approach to its omplications and conditions with overlapping pathophysiologic mechanisms in the context of the beta-cell classification of diabetes: Implications for precision medicine

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Abstract

The author have previously presented a proposal for a new, beta-cell centric classification of diabetes based on a consilience of genetic, metabolic, and clinical research that have accrued since the current classification was instituted. It recognizes that the beta-cell is the core defect in all patients with diabetes. Differences in the genetics (and epigenetics), insulin resistance, environment and inflammation/immune characteristics resulting in the damage to the beta-cell in each individual will determine the phenotypic presentation of hyperglycaemia and allow for a patient-centric, precision-medicine therapeutic approach, part of which we labelled 'the Egregious Eleven'. The same pathophysiologic mechanisms that account for damage to the beta-cells govern the susceptibility of the cells involved in the complications and other conditions 'tied to' diabetes to damage by the abnormal metabolic environment that typifies beta-cell dysfunction and fuel excess were recognised now. This abnormal metabolic environment is typified by oxidative stress which alters metabolic pathways (a la Brownlee's Hypothesis model), alterations in gene expression, epigenetics, and inflammation. This unifying pathophysiological approach to diabetes, its complications and conditions with overlapping pathophysiologic mechanisms in the context of the beta-cell classification of diabetes e.g., The diabetes syndrome allows us to understand the varied risk of developing complications of diabetes, including ASCVD, malignancies, dementia, NASH, psoriasis with similar levels of glycaemic control, how non-glycaemic effects of some medications for diabetes result in marked complication risk modification and the value treating comorbidities of diabetes in modifying complication risk. Principles outlined in using 'the Egregious Eleven' model use agents that preserve beta-cell function, treat with least number of agents that treat most number of mechanisms of hyperglycaemia can be extended to use those agents, in combination, that also engender weight loss, and decrease CV outcomes. This approach allows for a more accurate assessment of each patient's disease and effecting true precision medicine.



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