Insulin Resistance and the Many Faces of the Metabolic Syndrome

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Insulin-mediated glucose disposal varies by more than 600% in an apparently healthy population, with approximately 50% of the variability in insulin action resulting from differences in degree of adiposity (25 %) and physical fitness (25 %). The remaining 50% is familial, likely to be of genetic origin, with powerful ethnic differences. Type 2 diabetes develops when insulin resistant individuals cannot secrete the increased amounts of insulin needed to overcome the insulin resistance. However, the majority of insulin resistant individuals are able to maintain the degree of hyperinsulinemia required to prevent manifest decompensation of glucose homeostasis. Although compensatory hyperinsulinemia prevents the development of frank hyperglycemia in insulin resistant persons, insulin resistant/hyperinsulinemic individuals are at greatly increased risk of being somewhat glucose intolerant, with a dyslipidemia characterized by a high plasma triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) concentration, and an increase in blood pressure. These changes increase cardiovascular disease (CVD) risk, and because the importance as CVD risk factors of insulin resistance/compensatory hyperinsulinemia and its associated cluster of abnormalities was not widely appreciated at the time, the term Syndrome X was introduced in 1988 to focus attention on these relationships.

An enormous amount of new information relevant to the role of insulin resistance in human disease had appeared since the introduction of the concept of Syndrome X, and two different approaches to thinking about the clinical implications of insulin resistance and its consequences have evolved. One view emphasizes that the abnormalities related to insulin resistance have broadened considerably, and the adverse clinical outcomes extend beyond type 2 diabetes and CVD. For example, in addition to type 2 diabetes and CVD, insulin resistant individuals are at increased risk to develop essential hypertension, polycystic ovary syndrome, nonalcoholic fatty liver disease, congestive heart failure, sleep disordered breathing, cognitive dysfunction, and certain forms of cancer. In addition, insulin resistance and its consequences have been shown to complicate protease inhibitor treatment of HIV/AIDS, as well as the use of atypical antipsychotic drugs in patients with schizophrenia.

Alternatively, attention has focused on the CVD risk associated with insulin resistance and its consequences, leading to three different definitions of a diagnostic entity entitled the metabolic syndrome (MetS): WHO (1998), ATP III (2001), and the IDF (2005). The three versions of the MetS: 1) all feature components similar to those that comprised Syndrome X; 2) share the goal of establishing a new diagnostic category with which to identify individuals at

increased CVD risk; but 3), differ profoundly in the philosophical basis underlying their approach to separating those who merit (or do not merit) a diagnosis of the MetS. The goals of this presentation are to: 1) review the similarities and differences between the WHO, ATP III, and IDF definitions of the MetS; 2) question the clinical and/or pedagogical utility of making a diagnosis of the “metabolic syndrome”; and 3) present evidence that insulin resistance is the central feature that accounts for all of the component parts of each version of the MetS.

Citations

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