Insulin resistance: beyond glucose uptake

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Insulin resistance is an inherent feature of the pathogenesis of altered glucose metabolism in the common insulin resistant form of type 2 diabetes. Recently, the possibility that defects in non-glycemic effects of insulin might provide mechanistic links between type 2 diabetes and vascular disease has received increasing attention. These actions include insulin action on lipoprotein metabolism, autonomic nervous system activity, platelet function and possibly (based on animal data) direct antiatherogenic vascular actions of insulin, especially stimulation of nitric oxide (NO) synthesis in endothelial cells. Normal effects of insulin are antiatherogenic: inhibition of glucose and VLDL synthesis in the liver, antilipolysis in adipose tissue, stimulation of glucose utilization, inhibition of platelet aggregation and adhesion to collagen, stimulation of NO production in endothelial cells. Defects in these multiple insulin actions can be considered atherogenic, as they result in hyperglycemia, diabetic dyslipidemia (high triglycerides, low HDL, small LDL size, defects in autonomic control of e.g. heart rate variability, hyperaggregating platelets and endothelial dysfunction. Reversal of insulin resistance by insulin sensitizing therapies results in an improved cardiovascular risk profile.

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