Insulin deficiency and insulin resistance interaction in diabetes: estimation of their relative contribution by feedback analysis from basal plasma insulin and glucose concentrations.

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The liver and beta cells function in a negative feedback loop, which appears to have a predominant role in regulating both the basal plasma glucose and insulin concentrations. The degree of basal hyperglycemia in diabetes probably provides a bioassay of both the effect of a reduction in insulin secretory capacity and the degree of insulin resistance. A mathematic model of the interaction of insulin deficiency and insulin resistance has been constructed, based on the known response characteristics of the beta cells to glucose, and of plasma glucose and insulin control of hepatic and peripherpal glucose flux. The degree to which beta cell deficiency increases basal plasma glucose reflects the hyperbolic shape of the normal insulin secretory response to different glucose concentrations. The height of basal plasma insulin is a function of the degree of insulin resistance. From the basal plasma insulin and glucose concentrations, the model provides an estimate of the degree to which both beta cell deficiency and insulin resistance contribute to diabetes. The predictions arising from the model are in accord with experimental data in man and in animals. In normal-weight diabetics who do not have increased insulin resistance, the model predicts that more than 85% of beta cell function has to be lost for the basal plasma glucose to rise to 6 mmol/liter, but a further 5%--10% loss increases the basal plasma glucose to over 10 mmol/liter. In a third of a consecutive series of 65 newly presenting, uncomplicated diabetics, both normal weight and obese, the analysis from the model suggested that insulin resistance, rather than beta cell deficit, was the predominant feature.