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LETTERS

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Comment on: Godsland IF, Jeffs JAR, Johnston DG (2004) Loss of beta cell function as fasting glucose increases in the non-diabetic range. Diabetologia 47:1157–1166

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To the Editor For more than two decades I have awaited data such as those published by Godsland and co-workers [1] in the July issue of your journal. Although they focused primarily on the identification of the early disturbances that occur in the natural history of type 2 diabetes (the progressive loss of the first, and then of the second phase of insulin response), it seems of great importance to me that these changes occur at blood glucose levels between 5.0 and 5.4 mmol/l. This is well within the range considered as normal, even after the latest modifications of the higher limits of the definition for IFG proposed by the American Diabetes Association in 2003 [2], i.e. from 6.1 to 5.5 mmol/l. The rationale behind this decision was the increased risk of progression to clinical overt diabetes and cardiovascular events of individuals with fasting plasma glucose levels between 5.5 and 6.1 mmol/l, as compared with subjects with levels below 5.5 mmol/l. To these two arguments, I would add another, which is of physiological significance. Continuous glucose monitoring in non-diabetic individuals [3] provided evidence that, for an apparently healthy person, normal glycaemia could be considered the blood glucose value, which, when exceeded, is followed by a beta cell response aiming to bring blood glucose back to basal levels. From this viewpoint, normal values may in some cases fall well below 5.5 mmol/l and even below 5 mmol/l.

The data of Godsland et al. [1] provide convincing evidence in support of the ADA initiative and offer both evidence and logic for lowering the upper normal limits for fasting plasma glucose, which Schriger and Lorber [4] question aggressively in their paper on the Expert Committee's proposal. The anxiety of these two researchers derives from the calculation that, due to the changes proposed by the Expert Committee, the number of patients with impaired fasting glucose in the USA will rise from 10 to 35 million, thus affecting 22.5% of the adult population. The mathematical and economic justifications of this critique overlook a reality that physicians face daily. This is that every day patients with no prior history of diabetes are referred to us in the acute phase of myocardial infarction or stroke, and in more than 80% of cases have raised blood glucose levels. Later follow-up investigations after the acute episode often establish that these patients do indeed have diabetes. It is therefore quite evident that diabetes in these patients began silently some years earlier, with fasting plasma glucose values between 5.5 and 6.1 mmol/l, values which were ignored at the time, but in the end led to the actual acute myocardial infarction or stroke. As an old Chinese saying has it, "to wait for the disease to appear in order to treat it is like waiting for the onset of thirst before beginning to sink a well". For this reason, I agree with the point of view of the ADA Expert Committee [2], rather than the option of Schriger and Lorber [4]. All prevention studies of type 2 diabetes, mostly using lifestyle interventions, have targeted either non-hyperglycaemic populations or individuals with IFG/IGT and reduced by up to 1/3 the progression to clinical diabetes. The results communicated in the past 2 years are highly encouraging [5, 6] and demonstrate the importance of therapeutic intervention in the early stages of metabolic impairment.

Returning to the work of Godsland and co-workers [1], I believe that it may serve not only to challenge the definition of normal glycaemic values, but also to support the reassessment of the concept of prediabetes, i.e. that there is a non-hyperglycaemic stage of diabetes—just as diabetologists such as Rolf Luft and Stefan Fajans suggested almost 50 years ago. For this reason, the reintroduction of the notion of "prediabetes" in the latest version (1998) of the World Health Organization classification of diabetes (after it had disappeared from the WHO classification of 1985) is justified. Unfortunately,

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the definition of prediabetes in the latest version has been modified from the initial concept. It thus no longer includes the normoglycaemic stages of diabetes, but only IFG and IGT, both of which are prediabetic, but nevertheless hyperglycaemic states. I suggest that the next version of the classification should include hyperglycaemic states such as IFG and IGT in the definition of diabetes mellitus and that the designation "prediabetes" should be retained only for the non-hyperglycaemic prediabetic states.

Reference

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