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Diagnosing diabetes and prediabetes seems to be trivial but is often delayed

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Diagnosis of diabetes is based on parameters of abnormal blood glucose regulation. Blood glucose is one of the most frequently measured analyte in clinical medicine.

Making the diagnosis seems to be simple. The clinical presentation of a patient with symptomatic severe hyperglycaemia (>11 mmol/l) or with type 1 diabetes usually does not pose diagnostic problems nor requires an extensive discussion on diagnostic cut-off levels. However, the more insidious onset of type 2 diabetes with slowly increasing glucose levels over months and years without symptoms necessitates the definition of glycaemic thresholds. This is to identify persons with established diabetes needing treatment as well as those at high risk of developing in the future type 2 diabetes (called "prediabetes"), with the purpose of targeted prevention. The diagnostic cut-off levels of fasting plasma glucose levels and, more recently, of glycated haemoglobin (HbA1c) have been published by the American Diabetes Association [1] (table 1).

Both fasting plasma glucose and HbA1c can be used for diagnosis. Since plasma glucose concentrations reflect the acute state of glycaemia and HbA1c the degree of chronic hyperglycaemia it is not surprising that the results of the two methods are not always in complete agreement, as was the case in the paper by Escobar et al. in this journal [3].

There are several pitfalls in measuring blood glucose concentrations which may lead to errors, including unjustified anxiety (in the case of falsely increased blood glucose levels) or to missed or delayed diagnosis (in case of false "normal" levels).

First, many physicians use hand-held glucometers with test strips (e.g. AccuChek®, Ascensia®, etc) for the diagnosis of diabetes. They yield results in seconds and the analysis is relatively cheap. However, the fact that these devices are not meant for diagnosing diabetes because their (accepted) accuracy limits are ± 10–15% is often ignored. Similarly, even larger devices using dry chemistry such as Reflotron® or Dri-Chem® demonstrate a coefficient of variation of approximately 10% and are therefore unsatisfactory in cases of borderline abnormal blood glucose levels [4].

Second, glucose in tubes is rapidly broken down by erythrocytes as a result of glycolysis. This means that glucose concentrations in whole blood decrease by 5–7% per hour if the tubes do not contain an inhibitor of glycolysis (fluoride) or if the tubes are not rapidly centrifuged.

Therefore, for diagnostic purposes fasting plasma glucose should be measured after an 8–10 hour overnight fast in venous blood using wet chemistry with a small coefficient of variation (CV). This methodology was used in the study by Escobar et al. (CV <3%, [3]).

HbA1c is the most convenient and useful method to diagnose diabetes in screening examinations. The lack of need to repeat the analysis, the convenience of feasibility independent of food intake and the higher degree of reproducibility outweigh its higher cost than measurement of fasting plasma glucose [5].

Diagnosis of type 2 diabetes is often delayed, the reported delay being 4–7 years [6]. Escobar et al. [3] found in their study in elderly Swiss subjects that 8.4% did not know or

Table 1: Diagnosis of type 2 diabetes and prediabetes in nonpregnant adults, adapted from [2].

		Fasting plasma glucose* (mmol/l)*	HbA1c
Diagnostic cut points	Diabetes	≥7 mmol/l	≥6.5%
	Prediabetes	5.6–6.9 mmol/l (ADA) 6.1–6.9 mmol/l (WHO)	5.7–6.4%
Evaluation of methods	Advantages	Easy, inexpensive measurement	Convenient, best measure of chronic glycaemia, more closely associated with risk of complications, and less biological variability than glucose-based tests. A single measurement is usually sufficient for diagnosis.
	Disadvantages	Relatively insensitive, fluctuates, is affected by stress, requires an overnight fast, and requires a fluoride-containing tube. Measurement should be repeated for confirmation.	More expensive than fasting glucose, and cannot be performed in the setting of alterations of red blood cell turnover and with some haemoglobinopathies.

ADA = American Diabetic Association; HbA1c = glycated haemoglobin; WHO = World Health Association

* The oral glucose tolerance test is inconvenient, time consuming and expensive, and is therefore rarely performed in clinical routine outside pregnancy.

were not told that they had diabetes. The delay is often due to "clinical inertia" and not only to lack of screening [6].

It is my personal experience that many patients are told that their blood sugar is somewhat "high" and that they should pay some attention to it. However, the diagnosis of "diabetes" is not communicated – maybe also in part owing to the uncertainty in interpretation of the results of glycaemia, and possibly owing to fear of the multifaceted therapeutic sequelae.

The impact of early diagnosis of diabetes is enormous – not only on well-being and premature mortality but also on healthcare costs.

Prediabetes has been defined as a specific term to describe a state of increased risk of developing diabetes and cardiovascular disease [7]. As glycaemia demonstrates a continuum within a population the definition of cut-off levels for categories is always somewhat arbitrary, and the definition of prediabetes (called impaired fasting glucose) by a World Health Organization panel is somewhat different [8].

Several large trials in subjects with prediabetes demonstrated that preventive measures aiming, for example, at changes of lifestyle diminished the rate of progression to manifest diabetes [1].

The prevalence of prediabetes was surprisingly high (64.5%) in elderly and very old subjects in the study by Escobar et al. [3]; however, a similar prevalence (54.4%) was found in the NHANES cohort (2011–2012) in subjects aged >65 years using the same diagnostic criteria [9].

The finding of a high prevalence of undiagnosed diabetes in a population of "healthy" elderly Swiss people [3] emphasises the need to screen correctly subjects with increased risk for diabetes. This means that elderly people or subjects with a body mass index above 25 kg/m^2 aged above 45 years, or persons with other risk factors for diabetes should be regularly screened, e.g., every 3 years [1]. If diabetes is diagnosed this should be communicated to the patient without delay, and the resulting consequences regarding counselling and treatment should be drawn.

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