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Letters to the Editor

Diagnostic Criteria

Dear Sir,

Massari et al. [1] are correct in several of their criticisms of the diagnostic critieria suggested by the National Diabetes Data Group [2] and the WHO [3], but it is fair to add that both groups of experts were attempting, whether consciously or not, to increase the *specificity* of the diagnostic criteria. This led in the case of the National Diabetes Data Group to the requirement for two blood glucose levels in excess of the cut-off points in two glucose tolerance tests. Thus a single failure to reach the cut-off – even by 0.1 mmol/l – puts the individual into the rag-bag of the non-diagnostic category. This example also illustrates the unreality of the authors' suggestion [1] of 'a flow diagram with the recognition of all the possible blood glucose combinations'. These approach the infinite if second, third and more tests are introduced in an attempt to classify an individual. While the blood glucose level remains the major item underlying the diagnostic decision, some discretion must be left to the clinician in deciding, just as clinicians must take individual decisions upon the level of blood pressure which it is justified to treat. For the epidemiologist, the 2-h blood glucose level is adequate, if not perfect, as a measure. It has the advantage over intermediate values in being much less subject to arterio-venous differences [4]. Furthermore, most of the epidemiological evidence, whether from cross-sectional or prospective studies, underpinning any minimum diagnostic criteria is based upon 2-h blood glucose values.

In the present state of knowledge, I believe that for both clinical and epidemiological purposes the use of fasting and/or 2-h blood glucose levels, as recommended by the WHO Expert Committee (though without their rounding of SI values) is the most practical procedure. However, for solely epidemiological purposes, as Taylor and Zimmet have demonstrated [5], the 2-h value is preferable. I would add a personal plea for the reporting of percentile values in epidemiological studies so that distributions can be compared between populations and for the use of capillary blood to avoid at least one source of variation, the arterio-venous difference, which is inconstant even within individuals [6].

Yours sincerely,
R. J. Jarrett

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Dear Sir,

Massari et al. have managed to write a thoughtful, but peculiarly irritating article in your pages entitled the Imprecision of New Criteria for the Oral Glucose Tolerance Test [Diabetologia (1983) 24: 100–106]. The title alone causes concern, in that it implies that the old criteria were (a) precise (and by implication right), and (b) that all the new criteria are therefore wrong and unhelpful. Several comments can be made about this. First, there was poor agreement between the different old criteria with the proportion of diabetics in their 543 subjects varying from 11 to 43% depending on the criteria used – hardly precise (see their Table 3). Second, they ignore the fact that the old criteria, although they may have been diagnosing something, in many cases it was certainly not diabetes.

Efforts were made 4 years ago by two major groups to produce more rational meaningful criteria, based on existing data, both epidemiological and clinical, which could be applied on a world-wide basis and would enable comparisons to be drawn up between different studies. (There was even a faint hope that the new criteria might prove clinically useful.) The National Diabetes Data Group deliberated for many months and produced a series of criteria and recommendations [1]. Unfortunately, their criteria were rather like the old adage that "a camel is a horse designed by a Committee" and they certainly produced a camel. It is presumably these criteria which Massari et al. refer to as "imprecise". However, the United States does not represent the world, and the World Health Organization also came up with recommendations [2]. These, although not ideal, are not imprecise, and it is worth pointing out to Massari et al: (1) that WHO represents many nations, not just one voluble North American State; (2) the recommendations are not yet precise enough, but are at least a considerable improvement on the previous inaccurate, meaningless and confusing individualistic criteria that abounded; (3) the situation is a constantly evolving one and criteria will, and should, undoubtedly be changed again; (4) the inclusion of the impaired glucose tolerance group is a recognition of the inherent variability and imprecision of the oral glucose tolerance test itself. Thus, when the authors refer to imprecision, they are criticising, presumably, not WHO but National Diabetes Da-

ta Group, which theoretically at least, should have a much smaller impact worldwide.

What is the purpose of the oral glucose tolerance test? Clinically it is a minor diagnostic tool (except in pregnancy). In my own clinic last year, we performed less than ten glucose tolerance tests for diagnostic purposes. The main purpose of the oral glucose tolerance test is the identification of at-risk groups in population surveys. One major group contains those individuals at risk of developing macrovascular disease, and the recent survey by Fuller et al. [3] would suggest that the impaired glucose tolerance criteria fulfil this need, although 'normality' may have been set too high rather than too low, as suggested by Massari et al. The second group are those at risk of developing diabetic microangiopathy and neuropathy. Only time, and prospective studies, will tell whether the new criteria for diabetes accurately identify these individuals. Certainly based on information available today the new criteria are a considerable improvement on the old.

Finally, Massari et al. criticise the rounding up of numbers in the WHO criteria – most of us would agree with their criticism, not because one set of values is wrong and one is right, but more because it detracts from efforts to obtain uniformity of approach.

In summary, Massari et al. have emphasized the differences between the old and the two new sets of criteria. Sadly they have unwarrantedly included the new WHO criteria in their accusations of imprecision when this criticism can only really be levelled at the National Diabetes Data Group criteria, where 33% of subjects were unclassifiable. I would suggest that all future studies be based on the new WHO criteria and that studies to test the predictive accuracy of these new criteria should be set in train now.

Yours sincerely,
K. G. M. M. Alberti

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HLA-DR Antigens and Diabetic Nephropathy

Dear Sir,

In a recent preliminary communication, Christy et al. claimed an association between the HLA-DR3/DR4 phenotype and diabetic nephropathy in patients with Type 1 (insulin-dependent) diabetes [1]. In their series of 26 patients with Type 1 diabetes and nephropathy, the phenotype DR3/DR4 was significantly less common than in a matched group of patients with Type 1 diabetes without nephropathy.

A former study at our clinic [2] showed no evidence for association between HLA-B locus antigens and Type 1 diabetic patients with nephropathy, although associations of HLA-B15 [3] and DR4 [4, 5] with diabetic proliferative retinopathy were suggested.

We have studied HLA-DR antigen frequencies in 61 Type 1 diabetic patients with nephropathy and in 61 Type 1 diabetic patients free of renal disease (no proteinuria) matched as closely as possible for duration of disease and age at onset (mean age at onset: 10.9 versus 10.8 years; mean duration of disease: 24.97 versus 25.11 years, respectively).

Table 1. HLA-DR antigen frequencies in Type 1 diabetic patients with and without nephropathy

HLA-DR	Type 1 diabetic patients			
	With nephropathy ($n=61$)	(%)	Without nephropathy ($n=61$)	(%)
3,*	15	24.59	11	18.03
4,*	21	34.43	24	39.34
3, 4	22	36.06	22	36.04
,	3	4.92	4	6.56

* HLA antigen other than DR3 or DR4

Out of the 61 diabetic patients with nephropathy, 35 have received a renal allograft. Table 1 shows that we do not confirm the suggested association between DR3/DR4 and nephropathy, even though the number of patients in our study was larger than in the Danish study.

We conclude that there is no evidence for an association between HLA and diabetic nephropathy.

Yours sincerely,
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Free Inositol, Sorbitol and Fructose Levels in Sciatic Nerve

Dear Sir,

In a recent paper by Mayhew et al. [1], free inositol, sorbitol and fructose levels in sciatic nerve, obtained post-mortem from diabetic and control subjects, were compared with data we obtained on sural nerve biopsy [2]. Mayhew et al. found inositol levels to be lower in diabetic patients ($n=23$) than in control subjects ($n=15$; $p=0.016$). This is the expected direction of change based on studies in experimental