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Letters to the Editor

Diabetes Mellitus: A New Look at Diagnostic Criteria

Sir,

Dr. Watkins' rebuttal [1] of the proposed new diagnostic criteria for diabetes (editorial 5 May 79) will no doubt arouse a sympathetic cheer from the back benches. Apart from the inherent antagonism amongst the medical profession to accept change, the initial reaction to what at first sight appears to be a more complicated definition might be to retort that this is a typical example of scientists playing around with epidemiology data which is irrelevant to the management of patients attending a typical diabetic clinic. The issues involved however are worthy of a less superficial appraisal.

Physicians with a watchful eye on the scene will be fully aware of the growing evidence that 'diabetes mellitus' is not a *single* disease but represents a heterogeneous group of disorders with different underlying aetiologies. It follows that different management policies need to be considered both in relation to the *type* of glucose intolerance and the particular individual concerned. Therefore, to simply label subjects as 'diabetic' or 'non-diabetic' based on a single rigid set of criteria ignores the whole question of heterogeneity and the implications which emanate from this concept. It is long overdue that we updated our ideas and adopted an internationally accepted policy. The case put in your editorial has provided an important initiative.

Leaving aside the problems of reproducibility of the oral glucose test and the gradual deterioration of glucose handling with advancing age, the guide lines for realistic diagnostic criteria can best be obtained from carefully analysed prospective population studies. Extensive experience in the U. K. has shown that blood glucose concentrations in response to an oral glucose challenge exhibit a unimodal distribution, raw values showing a slight positive skew. The question which arises is where does normality end and pathological glycaemia begin? Microvascular disease is the specific complication of diabetes with increasing evidence that blood glucose control is probably the major aetiological factor [2]. The summary of the data presented in your editorial clearly indicates that the risk of developing this problem is almost exclusively confined to subjects with a 2 hr. blood glucose exceeding 11.0 mM/L. On the other hand, macrovascular disease is enhanced in all types of diabetes, including those with lesser degress of glucose intolerance. Almost certainly many factors contribute to the overall susceptibility to this problem which is essentially a disease of 'Western' society (the absence of significant macrovascular complications in the diabetic Pimas emphasizes this point). It could be argued that these previously defined lesser degrees of glucose intolerance simply reflect the complex processes involved in the pathogenesis of large vessel disease and which does not necessarily indicate a state of 'diabetes mellitus'. In support of this argument is the extremely low 'worsening to diabetes' observed in the 'borderline' groups in both the Bedford and Whitehall studies, and which was uninfluenced by anti-diabetic therapy [3]. In addition, many subjects in this group showed a spontaneous improvement of glucose handling.

It is also important to emphasize that these arguments concerning diagnostic criteria in relation to long term morbidity should not be confused with the harmful effects of equivalent degrees of glycaemia in pregnancy. This is a totally different ball game in which the rigorous maintenance of physiological levels of blood glucose to prevent foetal loss is now well validated.

In conclusion, separate criteria must be considered for the many different problems which confront the diabetologist. Drs. Keen et al should be congratulated for attempting to sort out some of the difficult aspects to this question. The original criteria of the BDA [4] were essentially derived by consensus without any supporting data. The proposed changes have their origin based on logic and fact.

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References

1. Watkins, P. J.: Diabetes mellitus: A new look at diagnostic criteria (Letter to the Editor). Diabetologia 17, 127–128 (1979)
2. Tchobroutsky, G.: Relation of diabetic control to development of microvascular complications. Diabetologia **15**, 143–152 (1978)
3. Jarrett, P. J., Keen, H., Fuller, J. H., McCartney, M.: Worsening to diabetes in men with impaired glucose tolerance ("borderline diabetes"). Diabetologia **16**, 25–30 (1979)
4. FitzGerald, M. G., Keen, H.: Diagnostic classification of diabetes. Br. Med. J. **1964 I**, 1568

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Catecholamines and Diabetes Mellitus

Dear Sir,

The recent survey of Dr. Christensen (1979) on catcholamines and diabetes mellitus covers most of the present knowledge in this field of research. It appears necessary, however, to stress the potential importance of one particular aspect of catecholamine action which has been neglected by the author.

Only recently has it been recognized that chronic elevated or decreased levels of hormones tend to be associated with changes of hormone responsiveness of target tissues. These changes include hormone refractoriness or changes in the qualitative pattern of effects of a number of hormones, including catecholamines [4]. In vitro experiments with human adipose tissue showed that the lipolytic effects of the naturally occurring catecholamines are impaired in untreated juvenile diabetics [1, 2]. This impairment was due to an altered balance of α- and β-adrenergic responsiveness with increased with increased receptivity for both components of catecholamine action. The conclusion of Dr. Christensen that elevated catecholamine levels in untreated insulin-deficient diabetics serve to compensate for volume depletion at the expense of an aggravated metabolic disturbance, is therefore, an overextrapolation. At least in adipose tissue, metabolic disturbance by elevated catecholamine levels is likely to be prevented via an adaptive change of hormone sensitivity at the level of the target tissue.

It is of special interest to clarify the mechanism of this type of adaptive change or hormone responsiveness. This involves questions concerning the modulation of the response to drugs by disease and is pertinent to the actual discussion about the use of β-blocking agents in diabetics. This phenomenon, for instance, may contribute to the fact that carbohydrate tolerance can improve and insulin secretion can increase when mild diabetics are changed from a non-selective β-blocking drug to metroprolol, where as longterm treatment with either propranolol or metroprolol failed to change carbohydrate tolerance in non-diabetic subjects [5]. In addition, the increased responsiveness towards β_2-selective agonists lacking the inhibitory alpha-adrenergic component of action, which was observed by Fredholm et al. [3] in diabetic women, is perhaps due to this type of adaptive change of hormone responsiveness at the level or target tissues.

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References

1. Arner, P., Östman, J.: Abnormalities in the adrenergic control and the rate of lipolysis in isolated human subcutaneous adipose tissue in diabetes mellitus. Diabetologia **12**, 593–599 (1976)
2. Arner, P., Engfeldt, P., Östman, J.: Relationship between lipolysis, cyclic AMP, and fat-cell size in human adipose tissue during fasting and in diabetes mellitus. Metabolism **28**, 198–209 (1979)
3. Fredholm, B. B., Lunell, N. O., Persson, B., Wager, J.: Actions of salbutamol in late pregnancy: Plasma cyclic AMP, insulin and C-peptide, carbohydrate and lipid metabolites in diabetic and non-diabetic women. Diabetologia **14**, 235–242 (1978)
4. Tell, G. P., Haour, F., Saez, J. M.: Hormonal regulation of membrane receptors and cell responsiveness: A review. Metabolism **27**, 1566–1592 (1978)
5. Waal-Manning, H. J.: Metabolic effects of β-adrenoceptor blockers. Drugs **11** (Suppl.), 121–126 (1978)

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