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Letters to the Editor

Risk of nephropathy in diabetes mellitus: problems of methodology and terminology

Dear Sirs,

Three studies have shown that in Type 1 (insulin-dependent) diabetic subjects a raised albumin excretion rate (AER) is a good predictor of the development of Albustix-positive proteinuria and/or of renal failure [1–4]. Two other studies have demonstrated that a raised AER or albumin concentration predicts morbidity/mortality in Type 2 (non-insulin-dependent) diabetic patients [5, 6]. However, of the three groups involved in these studies, each has used different conditions for estimating the AER and different terminology. The levels of AER found to predict clinical proteinuria in Type 1 diabetic subjects differ amongst the groups, with the Steno Memorial Hospital group reporting a value in excess of 70 μg/min, the Aarhus group a value in excess of 15 μg/min and ourselves a value in excess of 30 μg/min. These differences may be partly due to different lengths of follow-up (6 years for the Steno group, 10 years on average for the Aarhus group and 14 years in our study), but other factors may also be involved, and it seems to us that the present time is opportune to attempt some standardisation of methods and terminology and offer the following suggestions.

In Type 1 diabetic patients we used timed overnight collections of urine while the Steno Memorial Hospital group used 24-h collections. The conditions in the Aarhus investigations were not clearly outlined in the study quoted but were, we believe, usually a forced diuresis. In Type 2 diabetic patients, we again used overnight collections for AER estimation, while the Aarhus workers measured albumin concentration in 'morning urine samples'. All the Type 1 diabetic patients reported from Aarhus were male and it may be that the conditions required are less convenient for female patients. Overnight and 24-h collections are applicable to both sexes, though the latter procedure is less convenient for women. Furthermore, 24-h urine collections are, at least in theory, more prone to variability in AER induced by physical exercise, changes in arterial pressure and possibly diet. Admittedly, comparisons between overnight and 24-h collections in terms of variability have yet to be reported, but even if there is no significant difference, we would prefer overnight collections because of their convenience. It may be that an even simpler collection will become feasible for screening purposes, for Gatling et al. [7] have demonstrated that albumin concentration in excess of 20 μg/ml in an overnight collection (and thus presumably in an early morning sample) is a good predictor of an AER > 30 μg/min. The albumin/creatinine ratio in an early morning specimen offers another potential screening test [8]. Thus, although it is premature to recommend a definitive screening test, we propose that interested investigators, perhaps as a cooperative enterprise, compare these surrogate measures with definitive measurements of AER as well as investigating the variability of AER in overnight collections.

With regard to terminology, we have used the term 'microalbuminuria'; the Aarhus workers have used this and have also introduced the term 'incipient nephropathy'; which has been adopted by the Steno Memorial Hospital Group. The latter term suggests a disease state and implies certain progression to overt proteinuria and renal failure. Although this may be so for many Type 1 diabetic patients with elevated AER, it does not apply to all and it is less appropriate to patients with Type 2 diabetes at the present level of knowledge. Our information concerning the progression from an elevated AER to clinically significant renal disease is limited and we feel that it would be better to use a more neutral, descriptive terminology at least for the present. The simplest and probably the best solution is to characterise an individual patient by the AER (under defined conditions of measurement) just as one does for blood pressure, serum cholesterol or any other putative 'risk factor'. Thus we avoid the semantic confusions already existing with terms such as 'hypertension', 'hypercholesterolaemia', 'obesity', etc., which are more literary than scientific. For analytical and investigative purposes, patients can be considered in AER groups or even put into 'at risk' categories. However, we do not yet know enough about the conditions of measurement of AER or the effects of other variables, e.g. blood pressure level, to be categorical about estimates of risk based upon AER measurements alone.

Yours sincerely,

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