Tests for diagnosing diabetes mellitus

Glucose tolerance test is most sensitive

EDITOR,—David R McCance and colleagues state that the two hour plasma glucose, glycated haemoglobin, and fasting plasma glucose concentrations are equivalent predictors of the development of retinopathy and nephropathy.¹ They therefore consider all three glycaemic variables to be equivalent for diagnosing diabetes. This conclusion should be viewed with caution.

With regard to the sensitivity and specificity of glycaemic variables used, their roles in predicting microangiopathy and diagnosing diabetes need to be clearly distinguished. On the basis of data presented in tables I and II in the authors' paper (table), the oral glucose tolerance test has the highest sensitivity in diagnosing diabetes.

Number (percentage) of patients with values above cut off points in McCance and colleagues' study

	Two hour plasma glucose	Fasting plasma glucose	Glycated haemoglobin
Prevalence (from table I)			
Retinopathy	210 (22.0)	135 (14.1)	135 (14.1)
Nephropathy	211 (22.1)	134 (14.0)	134 (14.0)
Five year incidence (from table II)			
Retinopathy	158 (17.0)	105 (11.3)	85 (9.16)
Nephropathy	173 (18.4)	117 (12.4)	97 (10.3)

It would be important to know whether all three glycaemic variables in an individual subject had identical centile positions in the distributions of the variables used. This requirement will be fulfilled if there is a positive linear correlation between the two hour glucose and glycated haemoglobin concentrations in an individual. No evidence can be found about this in McCance and colleagues' paper. This correlation is more likely in patients with poor metabolic control than in those with strict control. If the centile positions of the three glycaemic variables for an individual subject differ this means that the prediction of microangiopathy varies as a function of the glycaemic variables used.

The Diabetes Control and Complications Trial Research Group has documented that better glycaemic control can delay the onset and slow the progression of microangiopathy in patients with insulin dependent diabetes mellitus.² Better control implies early diagnosis and treatment of diabetes. Since the oral glucose tolerance test has

the highest sensitivity in detecting patients with impaired glucose homeostasis it will continue to be the preferred method for diagnosing diabetes.

KORNEL SIMON
Consultant physician

Department of Medicine,
St George's Hospital,
Székesfehérvár-8000.
Hungary

- 1 McCance DR, Hanson RL, Charles MA, Jacobsson LTH, Pettitt DJ, Bennett PH, *et al.* Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. *BMJ* 1994;308:1323-8. (21 May.)
- 2 Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-86.

Interpreting fasting glucose concentration is tricky

EDITOR,—David R McCance and colleagues conclude that measurement of glycated haemoglobin concentrations and measurement of fasting plasma glucose concentrations are acceptable alternatives to a formal glucose tolerance test in the diagnosis of diabetes.¹ This surprises me for two reasons: firstly, my clinical experience indicates that interpretation of fasting glucose concentrations requires considerable care for diagnosis, and, secondly, an earlier study in which two of the authors of this paper participated found that more than half of patients newly diagnosed as having diabetes had "normal" fasting glucose concentrations.² Perhaps the authors can offer an explanation for this discrepancy.

ALAN J SINCLAIR
Senior lecturer

University Department of Geriatric Medicine,
University of Wales College of Medicine,
Cardiff Royal Infirmary,
Cardiff CF2 1SZ

- 1 McCance DR, Hanson RL, Charles M-A, Jacobsson LTH, Pettitt DJ, Bennett PH, *et al.* Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. *BMJ* 1994;308:1323-8. (21 May.)
- 2 Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in US population aged 20-74 years. *Diabetes* 1987;36:523-34.

Extrapolation of findings is incorrect

EDITOR,—David R McCance and colleagues may have included some statistical malapropisms in their paper.¹ Their clearly stated objective was to compare the ability of three tests to predict microvascular complications of non-insulin dependent diabetes mellitus. If you persevere through their detailed analyses and frequency distributions it seems that they achieved their stated objective.

In suggesting that measurement of the haemoglobin A_{1c} concentration may be an acceptable method for diagnosing diabetes mellitus they are guilty of false extrapolation of data from an atypical population, as well as being at odds with the World Health Organisation's guidelines² and expert British opinion.³ In their results, if, in predicting the incidence of retinopathy, the haemoglobin A_{1c} concentration has a sensitivity of 65.6% and a specificity of 87.6% in Pima Indians then the predictive value of a positive result is 83%. In

England, if the point prevalence of diabetes mellitus is estimated to be 2%, the predictive value of a positive result is only 9%. Mant and Fowler have suggested that the predictive value is the most important characteristic of a test for clinicians.⁴

The first five clinical implications listed by the authors are certainly true. It may be flawed and potentially misleading, however, to suggest that measurement of the haemoglobin A_{1c} concentration might have a diagnostic role in routine practice in Britain and the United States.

DAMIAN MCHUGH
General practitioner

Market Street Surgery,
Heywood,
Lancashire OL10 4LY

- 1 McCance DR, Hanson RL, Charles M-A, Jacobsson LTH, Pettitt DJ, Bennett PH, *et al.* Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. *BMJ* 1994;308:1323-8. (21 May.)
- 2 World Health Organisation Study Group. Diabetes mellitus. *WHO Tech Rep Ser* 1985; No 727.
- 3 Turner R. Non-insulin dependent diabetes mellitus. *Medicine International* 1993;21:257.
- 4 Mant D, Fowler G. Mass screening: theory and ethics. *BMJ* 1990;300:916-8.

Measuring glycated haemoglobin concentration is acceptable

EDITOR,—David R McCance and colleagues compared tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes in Pima Indians.¹ Our findings in a recent study in 65 adult patients referred by their physicians for diagnosis were similar to theirs.

Each patient underwent a two hour oral tolerance test with a 75 g glucose challenge; the glycated haemoglobin concentration was measured simultaneously with an immunochemical method (DCA 2000 analyser, Ames) that has a high correlation with high performance liquid chromatography.² We also calculated the area under the curve as we had previously found that this correlates well with the results of the oral glucose tolerance test (unpublished data). Patients were classified according to the criteria of the National Diabetes Data Group into three categories: normal, intolerant, and diabetic.³ The table summarises the results.

We found a good correlation between the glycated haemoglobin concentration and the fasting plasma glucose concentration, the two hour plasma glucose concentration, and the area under the curve ($r=0.82$, 0.88 , and 0.85 respectively). With a cut off value for the glycated haemoglobin concentration of 5.3% this variable discriminated between normal results and abnormal results of the oral glucose tolerance test (that is, those in

Glycated haemoglobin concentration and area under glucose concentration curve in patients classified according to criteria of National Diabetes Data Group

	Group		
	Normal (n=42)	Intolerant (n=6)	Diabetic (n=17)
Glycated haemoglobin (%)			
Mean (SD)	5.15 (0.36)	5.65 (0.38)	6.39 (1.15)
Range	4.4-5.9	5.2-6.2	5.5-10.4
Area under curve (mmol/l/2 h)			
Mean (SD)	827.7 (173.6)	1284.1 (123.9)	1596.0 (374.5)
Range	521.1-1195.8	1111.5-1451.7	1133.4-2583.6

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