

this unfairly penalises the next generation of potential ophthalmologists. Until a true unified training grade is established the number of career senior house officers in ophthalmology must be brought into line with the predicted number of specialist registrars. Only this will prevent capable juniors wasting immense effort and several crucial years.

Maintaining the current service commitment after such rationalisation requires a rethinking of the working practice of senior house officers, with skill mix and the employment of paramedical staff to reduce the non-medical workload and amalgamation of inpatient units where appropriate. An expansion in the number of visiting senior house officers and general practice trainees (with clearly defined objectives and appraisal) seems timely.

We have no wish to discourage potential ophthalmologists from a rewarding choice of career, but competition at the most junior level is fierce and some will be disappointed after several years of highly specialised training and examination. The Ophthalmic Trainees' Group is preparing a career information pamphlet, available on request to all those intending to become ophthalmologists.

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1 Hopkinson B. Word of warning to junior ophthalmologists. *BMJ* 1995;310:62. (7 January.)

More urologists are needed

EDITOR,—The classified advertisements supplement of 14 January contains advertisements for seven consultant posts in urology. Throughout Britain about 40 specialist urology posts are unfilled. This year 10 accredited trainees will become eligible to apply for consultant posts. The new deal for junior doctors demands a substantial increase in the number of consultants. In my segment of south east London (Greenwich, Bexley, and Bromley) 3.5 consultant urologists struggle to serve 750 000 people. When we recently advertised for a new consultant none of the applicants was accredited. Even if the number of training posts was doubled tomorrow those in them would take five years to be ready to practise.

Who then is to provide the service to the increasing number of patients with urological problems? At present only two courses of action exist: the creation of a substantial number of staff grade posts to fill the urgent shortfall in services and a recruitment drive on the Continent, led and financed by the government, for suitably trained people. The need is acute; action is necessary now.

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Assessing blood glucose control in diabetes mellitus

Use precise analytical methods

EDITOR,—In their study of the use of glycated haemoglobin concentrations to indicate glycaemic control Eric S Kilpatrick and colleagues used targets, related to the methods used, which were based on multiples of the SD of a reference range derived from non-diabetic subjects.¹ They found considerable differences in the classification of diabetic patients, which depended on the method, despite the methods giving similar absolute values for haemoglobin A_{1c} (HbA_{1c}).² This, however, does

not necessarily show different measurements of glycated haemoglobin to be inherently non-comparable indicators of glycaemic control. The electrophoretic method used is much more imprecise than the high performance liquid chromatography with which it was compared.² This is relevant because the estimate of a population reference range has components of both analytical and biological variation and will be broader for a method with high variability. Therefore, a given HbA_{1c} measurement will be fewer multiples of the SD from the non-diabetic reference mean when the imprecise method is used. Indeed, the authors have shown exactly this point, with the results of electrophoresis indicating apparently better glycaemic control.

This effect can be minimised by using multiples of the biological SD to define target concentrations. This can be illustrated by using the authors' quoted reference ranges and estimates of the analytical variation for the two methods of measuring HbA_{1c}.² If coefficients of variation for the analytical component are assumed to be 2.0% for high performance liquid chromatography and 8.3% for the electrophoretic method, the biological coefficients can be estimated as 7.54% and 8.53% respectively.³ These are similar, and if a mean of 8.0% is taken the biological SDs at the midpoint of the reference interval are 0.45% for high performance liquid chromatography and 0.50% for electrophoresis. If these are used to set clinical targets an HbA_{1c} concentration of 12.3% is 13.7 biological SD above the mean for high performance liquid chromatography and 12.0 biological SD above the mean for electrophoresis, compared with 14.0 total SD for high performance liquid chromatography but only 8.0 for electrophoresis. Therefore, targets derived from biological variation would have given a much better consensus in the classification of patients by the two methods. In practice the total SD is close to the biological SD when the analytical variation is small, as is the case with high performance liquid chromatography.^{3,4}

It is important that precise analytical methods are adopted and that bias between methods is minimised. Until this is more universally achieved, however, we suggest that target concentrations should always be defined on the basis of biological variation when the analytical imprecision is large.

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- 1 Kilpatrick ES, Rumley AG, Dominiczak MH, Small M. Glycated haemoglobin values: problems in assessing blood glucose control in diabetes mellitus. *BMJ* 1994;309:983-6. (15 October.)
- 2 Standing SJ, Taylor RP. Glycated haemoglobin: an assessment of high capacity liquid chromatographic and immunoassay methods. *Ann Clin Biochem* 1992;29:494-505.
- 3 Cotlove E, Harris EK, Williams GZ. Biological and analytic components of variation in long-term studies of serum constituents in normal subjects. III. Physiological and medical implications. *Clin Chem* 1970;16:1028-32.
- 4 Lytken Larsen M, Fraser CG, Hyltoft Petersen P. A comparison of analytical goals for haemoglobin A_{1c} assays derived using different strategies. *Ann Clin Biochem* 1991;28:272-8.

Variant haemoglobin may affect measurements

EDITOR,—We agree that Eric S Kilpatrick and colleagues' study suggests the need for greater standardisation of methods used for estimating glycated haemoglobin concentrations.¹ The estimation of glycated haemoglobin in patients with variant haemoglobins also urgently needs standardisation. An external quality assessment of the measurement of glycated haemoglobin in such patients by laboratories in the North West Thames region showed alarming discrepancies in the results obtained (C E Andrew and P Harrison,

national meeting of Association of Clinical Biochemists, 1991). For some samples the variability was so large as to alter completely the interpretation from one of very poor diabetic control to one of overcontrol likely to lead to hypoglycaemic episodes. An additional worrying finding was the varying methods used to calculate results, which partly accounted for the discrepancies. While some of the laboratories that used electrophoresis or ion exchange methods expressed haemoglobin A₁ and haemoglobin A_{1c} as a percentage of total haemoglobin—that is, haemoglobin A plus variant—others expressed their results as a percentage of the non-glycated fraction, haemoglobin A₀, or of haemoglobin A₀ plus haemoglobin A. In these circumstances comparison of results obtained with different methods from any one sample becomes meaningless.

To add to these difficulties, most ion exchange and electrophoretic methods have the problem of coelution of haemoglobin F (HbF) with glycated haemoglobin, which leads to overestimation of the latter.² Small increases in HbF are not uncommon in diabetic patients and are often unrecognised.³ Hence methods that cannot resolve HbF from glycated haemoglobin adequately are unsuitable for estimating glycated haemoglobin and should be abandoned as soon as possible.

Until we have greater standardisation and guidelines about estimating glycated haemoglobin concentrations in diabetic patients with variant haemoglobins, all patients with newly diagnosed diabetes should undergo a haemoglobinopathy screen. This should include measurement of HbF at the time of initial presentation to enable correct interpretation of results.

All laboratories should be willing to provide information about the method used to measure glycated haemoglobin, the mode of calculations of results, and interference from variant haemoglobins including HbF. Clinicians would also be well advised to ascertain necessary information about the methods used from their laboratory colleagues.

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- 1 Kilpatrick ES, Rumley AG, Dominiczak MH, Small M. Glycated haemoglobin values: problems in assessing blood glucose control in diabetes mellitus. *BMJ* 1994;309:983-6. (15 October.)
- 2 Yatscoff RW, Tevaarwerk JM, Clarson CL, Warnock LM. Interference of foetal haemoglobin with the measurement of glycosylated haemoglobin. *Clin Chem* 1983;29:543-5.
- 3 Kilpatrick ES, Rumley AG, Small M, Dominiczak MH. Increased foetal haemoglobin in insulin-treated diabetes mellitus contributes to the imprecision of glycohaemoglobin measurement. *Clin Chem* 1993;39:833-5.

Like should be compared with like

EDITOR,—Eric S Kilpatrick and colleagues conclude that measurement of haemoglobin A_{1c} (HbA_{1c}) concentration is to be preferred to measurement of haemoglobin A₁ (HbA₁) concentration on the grounds that the former classified a higher proportion of diabetic patients as having poorly controlled disease.¹ But the basis of this classification—poor control being equated with a glycated haemoglobin concentration > 5 SD from the reference population mean—is flawed because the coefficient of variation of the reference population mean is not the same for the methods of measurement compared. Inevitably, if (as is the case) the SD is much smaller for HbA_{1c} than for HbA₁ measured by electrophoresis but the means differ proportionately much less, any criterion of poor control based on the same number of SDs above the mean will classify a higher proportion of the HbA_{1c} values as indicating poor control than will be the case for HbA₁ values measured by electrophoresis. In numerical terms a limit of 5 SD for HbA_{1c} (mean 4.02% (SD 0.28%)) is 5.44%, representing a 35.3% increment; whereas a limit of