Occasional articles

Leader

United Kingdom external quality assessment in blood coagulation: the first 21 years

The external quality assessment scheme in blood coagulation has been organised from the United Kingdom Reference Laboratory for Anticoagulant Reagents and Control in Manchester since 1967. Participation has remained voluntary, but it is thought that in recent years all the hospitals performing coagulation studies have taken part. Confidentiality of the results has been maintained throughout with identification only possible to the organiser.

There have been many changes in the type of tests used and the standard of performance of these procedures over the years. Part at least of these advances may have been due to the educational role and continuous self-assessment resulting from the series of exercises undertaken at three monthly intervals by over 400 centres. Originally, there were more than 30 different techniques used for the estimation of fibrinogen. Some of the procedures undertaken were inaccurate or at best semiquantitative.¹ The less satisfactory techniques were gradually replaced by more reliable quantitative procedures. Nearly all participants now used the Clauss method or some other quantitative test. For most of the tests, plasmas with naturally occurring coagulation defects have been preferred. The limiting factor has been the volume of plasma available from the patient donors.

For the prothrombin time (PT), serial NEQAS surveys indicated progressive improvement in performance which continued until early 1986.²⁻⁵ Pronounced deterioration followed the enforced withdrawal of human brain Manchester Comparative Reagent (MCR) in early 1986 and the introduction of rabbit brain thromboplastins with a higher international sensitivity index (ISI) (between 1.1 and 1.6). NEQAS participants who changed to the rabbit reagent with an ISI of 1.1, however, showed no loss of precision.⁵ A possible explanation for the inferior precision with reagents with higher ISI is that the coefficient of variation of the international normalised ratio (INR) depends on the magnitude of the ISI.⁶

There has been a progressive change to using

automated or semiautomated instruments for the performance of the PT. The effects of automated procedures on the PT was first reviewed in 1978.⁷ By early 1988 nearly 50% of British hospitals had automated their PT. The manual technique has always been regarded as the reference method in the United Kingdom and the yardstick of performance. Surprisingly, the surveys indicated that coagulometers give less precise PT results overall than the manual technique, and furthermore, have had an effect on the

Accuracy (percentage deviation from manual INR) and precision (CV% of INR) with coagulometers in NEQAS surveys.

INR (figure).⁸ Furthermore, the within instrument differences in INR results are similar to those produced by different types of coagulometers. Overall, coagulometers have been shown to underestimate the INR, although there were exceptions, particularly at high INR values. The NEQAS surveys have provided a method of assessing the reliability of coagulometers by the precision of the INR and its deviation from the manual result. The evidence is reviewed on pages 92–96 of this issue.

Classification of performance in the PT has proved possible. Results which deviated from the overall mean British ratio or INR by more than 15% were classified as being of poor performance. Since early 1986, with the introduction of rabbit thromboplastins, INRs have been analysed against the reagent mean where there were more than 20 users or against the overall manual mean with reagents used in small numbers. Deviation of more than 15% was redesignated as an unsatisfactory performance. Hazardous performance was a corresponding 30% deviation. Persistent poor performance (PPP) is where participants obtain two consecutive unsatisfactory performances or three unsatisfactory performances in five consecutive surveys. The number of PPPs escalated after the change to rabbit brain reagents but the proportion of those participants who used the rabbit reagent with an ISI of 1.1 was similar to previous results with human MCR.⁶ The importance of a low ISI thromboplastin for precision of the INR is described in this month's issue. Many of the problems of unsatisfactory performance in the PT have been resolved as a result of supplementary exercises in the scheme. The need for professional or committee intervention has therefore been minimal over the years.

In the activated partial thromboplastin time (APTT) the spectrum of phospholipid reagents has changed over the years. Some APTT systems, less reliable in factor VIII screening, have largely been replaced as a result of the ongoing programme. Poor performance has been defined as the misclassification of factor VIII deficiency of 0.3 IU/ml or less as normal, and may have been the motivation for less satisfactory APTT reagents being discarded. For heparin control the APTT has displaced less satisfactory techniques such as the thrombin time and calcium thrombin time methods. APTT heparin studies in NEQAS surveys have shown that only in vivo heparinised samples from treated patients give a true assessment of the responses of the various APTT systems. In vitro heparinised samples misrepresent the in vivo responses of these reagents.

The number of participants who perform factor VIII assays has progressively increased to nearly 200 in current surveys. Hazardous performance had been

defined as classifying a plasma containing 0.25 IU/dl factor VIII or less as normal. A new and original system of grading performance based on an idealised standard deviation was introduced in 1984.⁹ This was derived from the best results achieved previously in NEQAS factor VIII assays. A grading system from A to E was adopted and has resulted in increasing numbers of participants achieving the highest grade. After two years it proved possible to reassess the idealised SD in the light of better performance and there was subsequent further improvement in the numbers achieving grade A.

Measurements of fibrin degradation products on plasma from patients with disseminated intravascular coagulation have been introduced from time to time. Specific clotting factor assays, antiprotease estimations (particularly antithrombin III), etc, which are less commonly performed, have also been included at less regular intervals in the surveys.

Circulating inhibitors, which have been a regular feature of the programme have comprised factor VIII inhibitors and various lupus-like anticoagulants.

The clinical importance of results has been an important aspect of the scheme. For example, in the APTT poor performance has been based on incorrect clinical interpretation of an important abnormality. This approach seems to have been welcomed. Similarly, assessment of dosage in samples from patients receiving oral anticoagulants or heparin has been a regular feature. Significant variation in dosage schedules, arising from differences in laboratory reagents, has been revealed.

Some procedures which cannot be assessed by external monitoring have been the subject of a series of questionnaire enquiries. The bleeding time,¹⁰ platelet function tests, and fibrinolytic tests have been reviewed on this basis and have been the subject of subsequent reports. The therapeutic ranges established in oral anticoagulant control, contained in the BCSH Guidelines,¹¹ were largely based in the data derived from a NEQAS questionnaire survey on current practice conducted in 1984.

The success of the surveys has led to the recognition by the WHO of the United Kingdom Reference Laboratory for Anticoagulant Reagents and Control in Manchester as its Collaborating Centre for Quality Control in Blood Coagulation, responsible for the ongoing international programme undertaken under the auspices of the International Committee for Standardization in Haematology.

After 21 years the organisation of the United Kingdom national scheme is, however, now being transferred from Manchester to London where it is to be under the direction of Dr Peter Kernoff of the Royal Free Hospital. It is hoped that the enthusiasm

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and goodwill of the NEQAS participants, which have been the basis for the success of the scheme to date, will be transferred to the new organiser and that progress will continue unabated in the years to come.

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