Dr Poller comments:

Dr Easton makes two relevant comments regarding North American and United Kingdom quality control results in prothrombin time testing. The first is his surprise at the better precision of manual *versus* automated results in the United Kingdom surveys. The long established proficiency in the manual technique in the United Kingdom is well recognised and may relate to the centralisation of coagulation procedures in the United Kingdom in district general hospitals and other large laboratories.

The second point concerns the relative precision (CV) in prothrombin time testing obtained in recent United Kingdom and College of American Pathologists' (CAP) surveys. The CV is influenced by the difference in sensitivity of reagents used in the United Kingdom compared with those in North America. The former, with ISI values close to 1·0, give considerably longer prothrombin times on Coumarin treatment and hence higher CV. For meaningful comparison of precision, however, the results must be expressed on a uniform scale using INR. We have shown that the CV of the INR approximates to the CV of the PT ratio × ISI. For example, with a thromboplastin with an ISI of 2·0 (most North American reagents have even higher ISI values), a CV of 4% for a prothrombin time expressed in seconds, quoted for the North American surveys by Dr Easton, increases to 8% when expressed as INR. In contrast, as most hospitals in the United Kingdom use a thromboplastin with an ISI of 1·1 the effect is relatively insignificant. Thus when results are reported as INR precision with this thromboplastin is at least as good as with American reagents.

Responsive thromboplastins with an ISI close to 1·0 have been shown to give greater safety in anticoagulant dosage.[3] They also provide at least equal precision in testing to high ISI reagents using the INR system, irrespective of whether a manual or automated technique is used.

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Morphometric analysis of suprabasal cells in oral white lesions

Shabana *et al* compare what they describe as *two* morphometric indices of cell shape.[1] They define the "first" of these the form factor (PE) given by:

$$PE = 4 \times \frac{22}{7} \times \frac{\text{cell area}}{\text{cell perimeter}^2}$$

The "second" of these, the contour index (CI), is given by:

$$CI = \frac{\text{cell perimeter}}{\sqrt{\text{cell area}}}$$

Both of these are indices of departure of any outline from a perfect circle[2] that are in widespread use to describe shape.[3] Although superficially, the two formulae seem to be different—PE for a circle being 1 while CI for the same shape is 3·54 ($=2/\sqrt{\pi}$)—it is clear that both indices are a ratio of perimeter[2] to area with some constants included in the former case.

Indeed, if we substitute the second formula into the first we get:

$$PE = (4 \times \frac{22}{7})/CI^2$$

These indices are therefore not separate but a fixed mathematical function of each other, both describing the same features of shape in the same way. It is not surprising that the authors state, "the contour index seemed to have a similar pattern to the factor PE."

In defining the indices separately and devoting a section of the discussion to comparison between them, the authors create a misleading impression that they are measuring different attributes. A range of morphometric shape descriptors has been advocated as having genuine differences in properties,[4] some of which are better detectors of departure from circularity than the relatively insensitive[2] form factor.

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3 Crocker J. Morphometric and related quantitative techniques in the study of lymphoid neoplasms. A review. *J Clin Pathol* 1984;**143**:69–80.

4 Gschwind R, Umbricht CB, Torhorst J, Obergolzer M. Evaluation of shape descriptors for the morphometric analysis of cell nuclei. *Path Res Pract* 1986;**181**:213–22.

Dr Shabana comments:

I would like to advise that our work started in 1982 when the two described factors were available. Whereas form PE was a "built-in" parameter in program Videoplan of the IBAS-1, CI was described in the literature. The practical experiment using the two factors showed differences in reproducibility, PE being more reproducible than CI. This could be explained by the differences in reproducibility in measuring the perimeter which would change the results of these factors to a greater extent than similar changes in area. The results then reflect the accuracy of the system, including the operator.

ISI value of thromboplastin

Taberner *et al* argued that the ISI value of a thromboplastin strongly influences the interlaboratory variability of the INR obtained with it.[1] A few comments on this are appropriate. The authors derived the equation CV(INR) = CV(PR) * ISI in which CV(PR) is the interlaboratory variation of the measured prothrombin time ratio. In this equation the variation of the ISI and the biological variation among individual anticoagulated patients are not accounted for. The purpose of external quality assessment is to determine the deviation of an individual laboratory's test result from the true value.

Multicentre calibration studies have shown that there is variability of the ISI.[2] If the variation of the ISI is also taken into account, the total variation of the INR may be obtained as:

$$CV(INR) = \sqrt{(CV(PR) \bullet ISI)^2 + (1n(INR) \bullet CV(ISI))^2}$$

It should be noted that if the total variation of the INR of an individual patient's sample is to be assessed, the biological variation of the INR among patients should be included as well.[2]

My second comment relates to the observed difference of CV(INR) between two different groups of laboratories using different (rabbit) thromboplastin reagents. A CV of 13% was obtained for the laboratories using a reagent with an ISI of 1·4, and a CV of 9% was obtained for the other group using a reagent with an ISI of 1·1. Although

the interlaboratory variation includes both random variation and systematic differences, the latter is by far the predominating factor.[3,4] The origin of the systematic differences is to be found in the test procedures used by the individual laboratories. The test procedures include the techniques for determination of the clotting end point. It has been shown that coagulometers influence the PT ratio and hence the ISI. The ISI recommended by the manufacturer may not apply to all instruments used by the NEQAS participants. Although laboratories used the same thromboplastin, they used different techniques for determining the PT ratio (PR). Consequently, the CV(PR) is not only determined by the reagent, but also by the techniques and the individual laboratories using them. In conclusion, the difference in CV(INR) obtained by Taberner and colleagues should not be attributed to the different reagents alone, but may also be explained in part by different test procedures.

In my opinion, a fair comparison of thromboplastin reagents can be performed only if the reagents are tested by the same laboratories using the same procedures.

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4 Van Dijk-Wierda CA, Van den Besselaar AMHP, Loeliger EA. Quality control of prothrombin time determinations in The Netherlands. *Scand J Haematol* 1980;**25** (suppl 37):153–5.

Dr Taberner comments:

Dr van den Besselaar states that the formula: CV(INR) = CV(PR) × ISI did not take into account the CV(ISI). We agree, but the report showed that using the cumulative data from the UK NEQAS exercises, the simple formula successfully predicted the difference between the CV(PR) and CV(INR). There is therefore no need to take into account the additional component of the CV(ISI). The biological variation between individual anticoagulated patients' results is, however, largely reflected in the PR. The view that systematic differences influence the PT ratio is supported and elaborated in the final paragraph of the paper as follows:

"Overall precision in PT testing with a reagent is affected by factors other than the ISI. For instance, the stability of the reagent, interbatch variation, and methods of end point detection may have a direct influence."

Nevertheless, the differences between the CV(PR) and CV(INR) seem to be largely explained by the ISI. Therefore, on the present evidence, the ISI must be regarded as an important influence on the precision of the INR. As shown in our accompanying paper, automation may affect the slope of the regression line and hence the ISI.[1] The differences introduced by coagulometers are small in comparison with the effect of the wide range of ISI values for thromboplastins in current use.

Finally, it was not our objective to assess thromboplastin reagents but to elucidate the basic principle of the importance of a low ISI thromboplastin for the precision of the INR. An important factor in the latter, as Dr van den Besselaar suggests, is the precision of the PR on which the INR is based.

Reference

1 Poller L, Thomson JM, Taberner DA. Effect of automation on prothrombin time test in NEQAS surveys. *J Clin Pathol* 1989;**42**: 97–100.

Book reviews

Molecular Basis of Inherited Disease. In Focus. KE Davies, AP Read. (Pp 87; softbound £5.95.) IRL Press. 1988. ISBN 1 85221 073 7.

My suspicions deepen that students of today are brighter than those of two decades or more ago. This slim handbook confidently zips along at a pace which current undergraduates may find a simple jog but which surreptitious mature "students" who are looking for a simple text to help them finally understand all this molecular genetics business will find exhausting. If you do not know what an open reading frame observed during DNA sequencing studies is all about you will trip up on line 8 of page 1. Picking yourself up, there are several stumbles ahead unless the field is at least partly familiar. The PCR technique is described in a diagram; hardly enough unless you understand it already, and in some of the diagrams the contrasting light pink colour of the two-tone scheme is barely visible. To be fair, the jacket indicates that the book is designed to complement course work. As a way of consolidating what someone has already explained in class or extending and updating a simpler introductory review it would be excellent.

JS LILLEYMAN

Making Monoclonals. DG Newell, BW McBride, SA Clark. (Pp 93; paperback £10 (inc postage.)) PHLS Supplies, 61 Colindale Avenue, London NW9 5DF. 1988. ISBN 0-901144-23-1.

This book sets out to provide a detailed guide to the production of monoclonal antibodies. It will appeal to the laboratory worker with little experience in this area. For such an individual, the text could prove to be indispensable as it covers many of the pitfalls that might be encountered in antibody production. Whilst there is obviously no substitute for being taught a laboratory technique "at the bench", books such as this can go a long way to guiding an inexperienced person into the field.

Every aspect of antibody production is covered and the authors are to be complemented on their thorough approach to the subject. The text is well written and the layout of the book makes it easy to obtain information relating to different aspects of antibody production. A very good buy for those wishing to set up a hybridoma facility who do not have access to groups that can supply the practical experience detailed in the book.

JT KEMSHEAD

The Kidney in Plasma Cell Dyscrasias. Eds. L Minetti, G D'Amico, C Ponticelli. (Pp 304; £60·95.) Kluwer Academic Publishers Group. 1988. ISBN 0 89838 385 4.

This book consists of a collection of short and concise papers prepared by many of the leading workers in myeloma, amyloid, and