10 Weisenburger DD, Sanger WG, Armitage JO, Purtillo DT. Intermediate lymphocytic lymphoma: Immunophenotypic and cytogenetic findings. *Blood* 1987;**69**:1617–21.

Drs Jaffe and Catovsky comment:

Professor Wright is critical of our report on the leukaemic phase of intermediate mantle zone (INT/MZL) lymphoma. The main object of our paper was to describe the peripheral blood features of this lymphoma in its leukaemic phase and to draw a distinction from chronic lymphocytic leukaemia; not to discuss the relation of INT/MZL and centrocytic lymphoma. We are confident that his comments and this letter will clarify any remaining confusion.

We have not departed from the view proposed by Jaffe *et al* that INT/MZL is essentially the same entity as centrocytic lymphoma.[1] As the article by Jaffe *et al* was an editorial comment and opinion piece, however, we felt that some caution was warranted regarding this conclusion. While the term INT/MZL as we use it would encompass all lesions recognised as centrocytic lympoma, we are not sure that the converse would apply for those pathologists who use the category "centrocytic"—that is, some cases which we would diagnose as INT/MZL others might not feel compatible with the diagnosis of centrocytic as they use it. Thus we did not wish to conclude that these lesions are "entirely interchangeable pathologic entities".

We agree with Professor Wright that varying degrees of nuclear irregularity may be difficult to detect in routinely processed paraffin wax sections, particularly if they are processed in different laboratories with different fixatives and sectioning techniques. We would also agree that the lymph node shown in figs 9–11 would not be classified as INT, and that the overall features are more compatible with the diagnosis of SLL/CLL. These cases (12–16) were classified by us as small lymphocytic with cleaved cells, rather than INT (see table 3). As we noted in our description, the presence of pseudofollicular growth centres and paraimmunoblasts ("larger lymphoid cells with prominent central, often eosinophilic, nucleoli") were the principal criterion in this distinction. Thus we would agree with Professor Wright that figs 7 and 8 show a centrocytic lymphoma and figs 10 and 11 a small lymphocytic lymphoma. When relying solely on the peripheral blood film, however, it may be difficult to distinguish INT from small lymphocytic lymphoma as the paraimmunoblasts do not usually circulate in large numbers. Cases 12–16 were included in the study because in the peripheral blood film they were indistinguishable from INT and would have been classified in the lymph nodes as INT using the criteria of Weisenburger (personal communication).[2]

We stated that the application of molecular genetic or cytogenetic markers might allow such cases to be appropriately classified in the future. We still believe this statement to be correct. While the paper by Weisenburger *et al* does suggest a close relation between INT and lymphocytic lymphoma,[2] we believe those authors reached that conclusion because they included within INT cases similar to those illustrated in figs 9–11. Thus while Professor Wright and we both recognise that cases 12–16 are not appropriately included within INT/MZL, this opinion may not be universally held. In fact, we would conclude that the study by Weisenburger supports the conclusion that we reached—namely that cases 12–16 are more appropriately included within small lymphocytic lymphoma/CLL and not INT/MZL. Hopefully, further studies will help bear out this conclusion, providing support for the distinction between INT (cases 1–11) and small lymphocytic lymphoma with cleaved cells (cases 12–16).

1 Jaffe ES, Bookman MA, Longo DL. Lymphocytic lymphoma of intermediate differentiation-mantle zone lymphoma: A distinct sub-type B-cell lymphoma. *Hum Pathol* 1987;**18**:877–80.
2 Weisenburger DD, Sanger WG, Armitage JO, Purtillo DT. Intermediate lymphocytic lymphoma: Immunophenotypic and cytogenetic findings. *Blood* 1987;**69**:1617–21.

Lupus cofactor phenomenon

I read with interest the recent paper by Mathey *et al* about a case of familial antiphospholipid syndrome.[1] The authors stated that the lupus anticoagulant could not be confirmed in the father, although the APTT did not correct with normal plasma. The results showed that the addition of normal plasma further prolonged the APTT by five seconds, making it seven seconds prolonged. This is an example of the lupus cofactor phenomenen.

Although the exact nature of this cofactor is unknown, it cannot exert its effects unless the lupus anticoagulant is present.[2] This is indirect confirmation that the lupus anticoagulant is present in this patient. The fact that the dilute Russell's viper venom time (DRVVT) was equivocal does not change this conclusion as a recent study has shown that the DRVVT will not detect all lupus anticoagulants.[2] Perhaps a further confirmatory test would have been useful for this patient—a tissue thromboplastin inhibition test or platelet neutralisation procedure.

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1 Mathey F, Walshe K, Machie IJ, Machin SJ. Famialial occurrence of the antiphospholipid syndrome. *J Clin Pathol* 1989;**42**:495–7.
2 Samuel CLL, Oldmeadow MJ, Howard MA, Firkins BG. Comparisons of laboratory tests used for identification of the lupus anticoagulant. *Am J Haematol* 1989;**30**:213–20.

Dr Mackie et al comment:

We stated that the APTT was performed as a screening test, using control plasma, patient plasma, and a 50/50 mixture, and that the presence of a lupus anticoagulant was confirmed by a more specific technique. The APTT alone is generally not suitable for determining the presence or absence of lupus anticoagulant because even if a sensitive reagent is used, it is not specific, and may be influenced by factor deficiency, increased concentrations of coagulation factors, as well as by various inhibitors, including: antiphospholipids, antibodies against coagulation factors, and heparin.

We used the DRVT as a confirmatory test with a platelet neutralisation procedure, using freeze-thaw, lysed, washed normal platelets. Tissue thromboplastin inhibition tests are less sensitive and give false negative results in many patients, especially those with IgM lupus anticoagulant.[2] Most recent comparisons of lupus anticoagulant tests have found that the DRVT and kaolin clotting times are the most sensitive and reliable, although no single test has a 100% detection rate. Unfortunately, it is not always possible to perform more than one of these tests.

In the family described the APTT did not correct in the father, but APTT tests are notoriously erroneous, and this result did not fulfill our criteria for the presence of lupus anticoagulant.

As the father was asymptomatic, there was no justification for further studies at this stage, and the question of whether he had a lupus anticoagulant remains academic. On the basis of an abnormal, though equivocal DRVT result, and positive anticardiolipin antibodies, with his family history it is very likely that future samples would give unequivocally positive lupus anticoagulant tests, and development of suitable clinical criteria would classify him as a true antiphospholipid syndrome patient.

1 Thiagarajan P, Pengo T, Shapiro SS. The use of the dilute Russell viper venom time for the diagnosis of lupus anticoagulant. *Blood* 1986; **68**:869–74.

NOTICES