pylori, may cause chronic active gastritis. Like C. pylori, the number of organisms can probably be suppressed but complete eradication will probably be difficult. Was case 2 endoscoped and assessed symptomatically at a later date, one of the organisms may well have been detectable. Dr Logan and his colleagues may be right that "Gastrospirillum hominis" causes non-ulcer dyspepsia, but larger studies are needed, and I think it is still premature to draw conclusions from single patient histories.

Lack of significant effect of therapeutic propranolol on measurable platelet function in healthy subjects

Pamphilon and colleagues have shown that propranolol, a non-selective β blocker, does not significantly inhibit platelet function when therapeutic doses are administered to healthy subjects. They suggest that a different response might be obtained in patients with cardiovascular disease and hyperactive platelets. Some additional comments may be of further interest:

The authors discuss the possibility that β blockers exert their action in situations where circulating catecholamine concentrations are very high. We assessed the effect of acute hypoglycaemia (during insulin stress tests) on various haematological variables in healthy subjects who had been given either placebo, nadolol, or propranolol, orally, for 10 days. These non-selective β blockers significantly inhibited some cholinergic-mediated effects (hypokalaemia; a rise in factor VIII), but only propranolol had a marginal inhibitory effect on platelet aggregation.

In another study we found that platelet aggregation induced by adrenaline was significantly decreased in samples obtained from patients with a diagnosis of acute myocardial infarction or ischaemic heart disease who were taking β blockers when compared with a similar group of patients not taking such medication. Beta blockade may, indeed, be associated with platelet antiaggregatory effects but that these may only be elicited in completely healthy subjects. The pronounced platelet hyperaggregability which may occur in ischaemic heart disease.

There are also important methodological considerations in assessing the effect of drugs on platelet function. For example, whole blood platelet aggregometry (impedance or "free" cell count techniques) allows the effects of drugs on platelet, red or white cell interactions to be measured. This has occasionally resulted in a better definition, even at lower doses, of the effects of several drugs, such as nifedipine, dipryramidole, heparin and ethanol, on platelet aggregation. Mean platelet volume, measured by very sensitive techniques (using a Coulter C256 channeler), may also be another very sensitive method to assess the effect of a variety of agents on platelets.

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Dr Pamphilon et al comment: The comments of Barradas and Mikhailidis are of interest and point to the relevant mechanism whereby β blockers may exert a beneficial effect in patients with myocardial infarction and ischaemic heart disease—that is, modulation of platelet hyperaggregability in susceptible subjects. The observation that propranolol but not metoprolol enhances platelet aggregation is new. It is likely that platelet effects of high concentrations of circulating catecholamines is of central importance. We did not observe significant changes in white blood cell volume in either group of subjects using the Coulter S Plus 4 rather than the Coulter C256 channeler.


Leukaemic phase of mantle zone (intermediate) lymphoma: its characterisation in 11 cases

In his parody of lymphoma classifications a distinguished editor of the Journal of Clinical Pathology reflected the confusion and cynicism of the average pathologist at the perceived hair-splitting of the lymphomaniacs in their attempts to categorise non-Hodgkin's lymphomas. The confusion over the classification of low grade non-Hodgkin's lymphoma is well illustrated in the report on the leukaemic phase of mantle zone (intermediate) lymphoma by Pombo de Oliveira et al.1 The category of intermediate cell lymphoma was first proposed by Berard et al.2 It was noted that in some instances it contained some lymphocytes resembling those of well differentiated lymphocytic tumours and some atypical cells more closely resembling the poorly differentiated lymphocytic lymphomas of nodular or follicular lymphomas.

It is now widely accepted that lymphocytic lymphoma of intermediate differentiation (INT) and mantle zone lymphoma (MZL) are the same tumour, perhaps at different stages of evolution, and Jaffe et al have suggested that MZL should be the preferred term.3

The category of centrocycytic lymphoma was introduced into the Kiel classification to describe a diffuse lymphoma of small, slightly irregular lymphoid cells that were originally thought to be of follicle centre derivation (hence the name centrocye).4 Subsequent studies have shown that centrocycytic lymphoma is a distinct entity, clinically, morphologically, and phenotypically distinct from follicle centre cell lymphoma.5 It is unfortunate and confusing that the term centrocycytic lymphoma6 is still applied to this tumour even as it has been shown not to be of centrocye origin. Most authors have suggested that INT/MZL is the same entity as centrocycytic lymphoma. In a review of INT/MZL, Jaffe et al concluded that this tumour, "clinically, morphologically, and immunophenotypically appears virtually identical to centrocycytic lymphoma of the Kiel classification."7 Pombo de Oliveira et al suggested slightly from that position and conclude that, "centrocycytic lymphoma and INT are clearly closely related morphologically and phenotypically but may not be entirely inter-changeable pathological entities."8 The authors further state that, "perhaps the application of molecular, genetic, or cytogenetic markers may allow such cases to be appropriately classified in future". In fact, cytogenetic studies suggest considerable overlap between INT and lymphocytic lymphoma.9

It is my opinion that the recognition of INT based on the finding of a mixture of cells with round and cleaved nuclei is flawed. It has been recognised for years that quite apart from biological variability, fixation and processing artefacts can induce considerable variation within a single neoplasm. Lymphocytic lymphomas and centrocycytic lymphomas have been cell lines and have been studied histologically. It can, however, be difficult to separate these neoplasms on the morphology of the lymphoid cells alone, particularly in suboptimally fixed tissues. There are, however, many other features that assist in the differentiation of these neoplasms, perhaps the most reliable being the identification of paraimmunoblasts which are always present in variable numbers in lymphocytic lymphomas and never found in centrocycytic lymphomas. On the basis of this criterion, figs 7 and 8 of the paper by Pombo de Oliveira et al show a centrocycytic lymphoma and figs 10 and 11 a lymphocytic lymphoma. Clearly, the uses of INT will not be resolved until a more reliable means of identification, other than variability of nuclear shape, is used to select cases for study.

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Lupus cofactor phenomenon

I read with interest the recent paper by Mathey et al about a case of familial anti-phospholipid syndrome. The authors stated that the lupus anticoagulant could not be confirmed in the father, although the APTT test 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 phenomenon.

Although the exact nature of this cofactor is unknown, it cannot exert its effects unless the lupus anticoagulant is present. 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 normal does not conflict with this conclusion as a recent study has shown that the DRVVT will not detect all lupus anticoagulants. 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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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 DRVVT as a confirmatory test with a platelet neutralisation procedure, using fresh, thawed, 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. Most recent comparisons of screening and confirmatory tests have found that the DRVVT 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 DRVVT 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 criteria classifications would allow him to be formally antiphospholipid syndrome patient.