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? If so, 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.¹ They suggest that a different response might be obtained in patients with cardiovascular disease and hyperactive platelets. Some additional comments may be of 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 metabolic and haemostatic variables in healthy subjects who had been given either placebo, nadolol, or propranolol, orally, for 10 days.² These non-selective β blockers significantly inhibited some catecholamine-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.³ Beta blockade may, indeed, be associated with platelet antiaggregatory effects but that these may only be elicited in conditions associated with pronounced platelet hyperaggregability such as myocardial infarction and ischaemic heart disease.³

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, dipyridamole, heparin and ethanol, on platelet aggregation.⁴ Mean platelet volume, measured by very sensitive techniques (using a Coulter C256 channelyser), may also be another very sensitive method to assess the effect of a variety of agents on platelets.⁵

M A BARRADAS
D P MIKHAILIDIS

Department of Chemical Pathology and Human Metabolism, Royal Free Hospital and School of Medicine, Pond Street, London NW3 2QG

1 Pamphilon DH, Boon RJ, Prentice AG, Rozkovec A. Lack of significant effect of therapeutic propranolol on measurable platelet function in healthy subjects. *J Clin Pathol* 1989;42:793-6.

2 Mikhailidis DP, Barradas MA, Hutton RA, Jeremy JY, Sabur M, Dandona P. The effect of non-specific β -blockade on metabolic and haemostatic variables during hypoglycaemia. *Diabetes Res* 1985;2:127-34.

3 Mikhailidis DP, Barradas MA, Mier A, et al. Platelet function in patients admitted with a diagnosis of myocardial infarction. *Angiology* 1987;38:36-45.

4 de Almeida PJ, Pires JGP, Marquezini AJ, Barradas MA, Mikhailidis DP. Platelets, vessels and coagulation: an overview of basic mechanisms with special reference to drug action. *J Drug Develop* 1990 (in press).

5 Whitworth NH, Barradas MA, Mikhailidis DP, Dandona P. An investigation into the effects of bacterial lipopolysaccharide on human platelets. *Eur J Haematol* 1989;43:112-9.

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.¹ The observation that propranolol but not metoprolol enhances platelet aggregatory responses to adrenaline remains unexplained.² Thus it seems likely that blockade of the effects of high concentrations of circulating catecholamines is of central importance. We did not observe significant changes in the mean platelet volume in either group of subjects using the Coulter S Plus 4 rather than the Coulter C256 channelyser.

1 Mikhailidis DP, Barradas MA, Mier A, et al. Platelet function in patients admitted with a diagnosis of myocardial infarction. *Angiology* 1987;38:36-45.

2 Winther Hansen K, Klysner R, Geisler R, Bjerra Knudsen J, Glazer S, Gormsen J. Platelet aggregation and beta-blockers. *Lancet* 1982; i:224-5.

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.¹ The confusion over the classification of low grade non-Hodgkin's lymphomas is well illustrated by the report on the leukaemic phase of mantle zone (intermediate) lymphoma by Pombo de Oliveira et al.² The category of intermediate cell lymphoma was first proposed by Berard et al.^{3,4} It was noted that, "these tumours contain some lymphocytes resembling those of well differentiated lymphocytic tumours and some atypical cells more closely resembling the poorly differentiated lymphocytes of nodular or follicular lymphoma".⁵ It is now widely accepted that lymphocytic non-Hodgkin's lymphoma of intermediate differentiation (INT) and mantle zone lymphoma (MZL) are the same tumour, perhaps at different stages of evolution,⁶ and Jaffe et al have proposed that MZL should be the preferred term.⁵

The category of centrocytic 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 centrocyte).⁷ Subsequent studies have shown that centrocytic lymphoma is a distinct entity, clinically, morphologically, and phenotypically distinct from follicle centre cell lymphoma.^{8,9} It is unfortunate and confusing that the term "centrocytic lymphoma" is still applied to this tumour even after it has been shown not to be of centrocyte origin.

Many authors have suggested that INT/MZL is the same entity as centrocytic lymphoma.

In a review of INT/MZL, Jaffe et al concluded that this tumour, "clinically, morphologically, and immunophenotypically appears virtually identical to centrocytic lymphoma of the Kiel classification".³ Pombo de Oliveira et al seem to have retreated slightly from that position and conclude that, "centrocytic lymphoma and INT are clearly closely related morphologically and phenotypically but may not be entirely interchangeable pathological entities".² 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 a close relation between INT and lymphocytic lymphoma.¹⁰

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 centrocytic lymphomas have been well described and defined 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 two neoplasms, perhaps the most reliable being the identification of paraimmunoblasts which are always present in variable numbers in lymphocytic lymphomas and never found in centrocytic lymphomas. On the basis of this criterion, figs 7 and 8 of the paper by Pombo de Oliveira et al² show a centrocytic lymphoma and figs 10 and 11 a lymphocytic lymphoma. Clearly, the status 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.

D H WRIGHT

University Department of Pathology, Southampton General Hospital, Southampton SO9 4XY

1 Kay HEM. Classification of non-Hodgkin's lymphomas. *Lancet* 1974;i:586.

2 Pombo de Oliveira MS, Jaffe ES, Catovsky D. Leukaemic phase of mantle zone (intermediate) lymphoma: Its characterisation in 11 cases. *J Clin Pathol* 1989;42:962-72.

3 Braylan RC, Jaffe ES, Berard CW. Malignant Lymphomas: current classification and new observations. In: Sommers SC, ed. *Pathology annual*. Volume 10. New York: Appleton-Century-Crofts, 1975:213-70.

4 Berard CW, Jaffe ES, Braylan RC, Mann RB, Namba K. Immunologic aspects and pathology of the malignant lymphomas. *Cancer* 1978;42:911-21.

5 Jaffe ES, Bookman MA, Longo DL. Lymphocytic lymphoma of intermediate differentiation-mantle zone lymphoma: A distinct subtype of B-cell lymphoma. *Hum Pathol* 1987;18:877-80.

6 Weisenburger DD, Kim H, Rappaport H. Mantle zone lymphoma: A follicular variant of intermediate lymphocytic lymphoma. *Cancer* 1982;49:1429-38.

7 Tolksdorf G, Stein H, Lennert K. Morphological and immunological definition of a malignant lymphoma derived from germinal centre cells with cleaved nuclei (centrocytes). *Br J Cancer* 1980;41:168-82.

8 Swerdlow SH, Habeshaw JA, Murray LJ, Dhaliwal HS, Lister TA, Stansfeld AG. Centrocytic lymphoma: A distinct clinicopathologic and immunologic entity. A multi-parameter study of cases at diagnosis and relapse. *Am J Pathol* 1983;113:181-97.

9 Harris NL, Nadler LM, Blank AK. Immunohistologic characterisation of two malignant lymphomas of germinal center type (centroblastic/centrocytic and centrocytic) with monoclonal antibodies. Follicular and diffuse lymphoma of small cleaved type are related but distinct entities. *Am J Pathol* 1984;11:262-72.