

CORRESPONDENCE

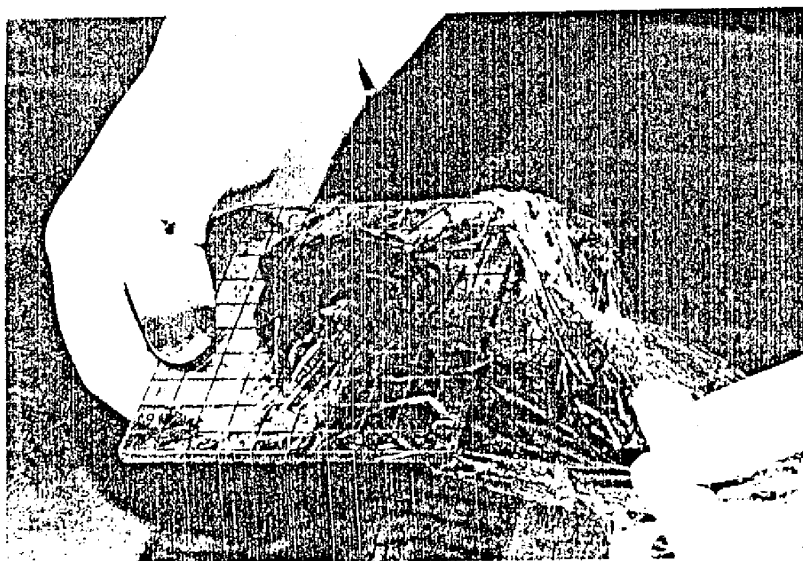
Modification of the alcian blue method for marking breast biopsy specimens

We totally agree with Drs Birch, Jeffrey, and Andrews on the utility of alcian blue as a method of marking breast biopsy specimens and wish to describe a local modification. This entails placing the dipped specimen on a locally produced grid to allow the appropriate sectors for block selection to be chosen and sampled after specimen mammography. This grid is similar to the previously described grid.² Covering the grid with kitchen plastic wrap prevents the specimen from moving on the grid before block selection and allows macroscopic description of margins selected to be compared with the radiographic

margins: this avoids some of the problems encountered when a grid is not used. We consider that this simple method allows inexperienced staff to carry out handling without compromising the safety of patients.

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- 1 Birch PJ, Jeffreys MJ, Andrews MJ. Alcian blue: reliable rapid method for marking resection margins. *J Clin Pathol* 1990;43:608.
- 2 Champ CS, Mason CH, Coghill SB, Robinson M. A perspex grid for localization of non palpable mammographic lesions in breast biopsies. *Histopathology* 1989;14:311-5.



Breast resection marked with alcian blue, placed on localisation grid, and covered with plastic wrap

Hepatitis C virus and transfusion transmitted liver disease

In his comprehensive review on hepatitis C virus and transfusion transmitted liver disease, Underwood states that, "exclusion, by antibody testing, of HCV positive blood donors should reduce very substantially the risk of transmitting this virus to transfusion recipients." He fails, however, to address some very important points:

1 Several of the current procedures for inactivation of viruses in fractionated blood have been shown to prevent non-A, non-B hepatitis (NANBH) transmission to recipients.^{1,2} Confidence in inactivation methods is so high that the Food and Drugs Administration does not require plasma destined for fractionation to be tested for anti-HCV (AABB News Briefs, March 1990, Vol 3, No 3).

2 The incidence of post-transfusion NANBH is significantly lower in the United Kingdom compared with the USA. Furthermore, since the introduction of methods of

self-exclusion for subjects at risk of transmitting HIV, the incidence of post-transfusion NANBH has decreased considerably in all countries. For example, in the USA the incidence has decreased from about 10% or more to less than 1%. The proportion of NANBH attributable to transfusion has decreased by 69% since 1985.¹

3 Several workers have shown that a proportion of donors who test positive for anti-HCV do not transmit NANBH.⁴ Hence it is important that supplementary tests to discriminate between infectious and non-infectious anti-HCV positive donors are available before mandatory screening of blood donors is introduced.

4 Two commercial companies have developed screening tests for anti-HCV. These tests are expensive, however; the current price is more than £2 per test when reagents are purchased in bulk. In addition, the currently available supplementary recombinant immunoblot assay is extremely expensive at more than £20 per test. With two million donations collected annually in the

United Kingdom, the reagent cost of screening all donations would be over £4m. Since 0.3-0.6% of donations are anti-HCV positive, an additional £200 000 would be required for supplementary tests. If confirmation by the polymerase chain reaction was also required the cost would rise substantially and the strain on laboratory services would be enormous.

5 Counselling anti-HCV positive donors will be an expensive and time consuming procedure. What will we tell our donors? That they test positive for an assay whose clinical importance we do not know?

In these times of financial constraints, with ward closures and long waiting lists, should we not evaluate the problem pertaining to this country before making decisions based on data from others where the incidence of post-transfusion NANBH might be much higher? The economic impact of screening would be enormous. In the North West Thames Region testing for anti-HCV, performing supplementary tests, counselling and replacing donors found positive would cost in the order of £700 000 a year.

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- 1 Skidmore SJ, Pasi KJ, Mawson SJ, Williams MD, Hill FGH. Serological evidence that dry heating of clotting factor concentrates prevents transmission of non-A, non-B hepatitis. *J Med Virol* 1990;30:50-2.
- 2 Study Group of UK Haemophilia Centre Directors on Surveillance of Virus Transmission by Concentrates. Effect of dry heating of coagulation factor concentrates at 80°C for 72 hours on transmission of non-A, non-B hepatitis. *Lancet* 1988;ii:814-16.
- 3 Alter MJ. Disease transmissions: The relationship of blood transfusion to other modes of transmission. In: Fairchild VD, Holland NR, Lyons AR, eds. *Antologous blood transfusions. Principles, policies and practices*. Alexandria, Virginia: American Blood Commission, 1989:4-6.
- 4 Van der Poel CL. Infectivity of blood seropositive for hepatitis C virus antibodies. *Lancet* 1990;335:558-60.

Professor JCE Underwood comments:

These comments and others have been made elsewhere by Drs Contreras and Barbara¹ and have been responded to.² In my opinion the morbid consequences of HCV infection and the cost of management are sufficiently great to justify measures to reduce as much as possible the risk of transmitting this virus by the administration of blood and blood products. These measures should include not only the procedures for virus inactivation cited by Contreras *et al*, but also the screening of donors, currently by antibody testing, advocated as a necessary step in "good manufacturing practice" of plasma fractions.^{3,4}

Although HCV antibody positive donations are relatively rare in the United Kingdom, they may, nevertheless be responsible for a high proportion of the residual cases of post-transfusion hepatitis. A substantial reduction in the risk of this iatrogenic event is, therefore, anticipated to follow the introduction of screening. The safest clotting factor concentrates are likely to be achieved through a prudent combination of donor selection and viral inactivation.²

- 1 Barbara JAJ, Contreras M. Prevention of hepatitis C virus infection in haemophiliacs. *Lancet* 1990;336:62-3.

- 2 Preston FL, Makris M, Friger DR, Underwood JCE. Prevention of hepatitis C virus infection in haemophiliacs. *Lancet* 1990;336:63.
- 3 Habib H, Garreta M. Screening for hepatitis C antibody in plasma for fractionation. *Lancet* 1990;335:855-6.
- 4 Cash J. Screening for hepatitis C virus antibody in plasma for fractionation. *Lancet* 1990;335:1216.

Platelet aggregation in Raynaud's phenomenon

Biondi and Marasini recently reported that patients with Raynaud's phenomenon showed increased platelet aggregation induced by serotonin and adenosine diphosphate (low doses), and normal platelet aggregation induced by adrenalin.¹

We also investigated adrenaline (5 µg/ml) induced platelet aggregation in 20 healthy volunteers, 27 patients with primary Raynaud's phenomenon, and 25 patients with obliterative atherosclerosis. We registered the time to the start of aggregation rather than its intensity. The mean (SD) figures were 34.2 (5.57) seconds in Raynaud's phenomenon and 37.8 (5.54) seconds in obliterative atherosclerosis. The time registered to the start of aggregation was significantly shorter in Raynaud's phenomenon compared with that in normal adults (46.3 (4.37) seconds ($p = 0.01$)) and even with that in atherosclerotic patients ($p = 0.05$).

It is interesting to note that both the time to the start of aggregation and its intensity are abnormal in patients with Raynaud's phenomenon. The observation of both variables may be useful in such patients.

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- 1 Biondi L, Marasini B. Abnormal platelet aggregation in patients with Raynaud's phenomenon. *J Clin Pathol* 1989;42:716-8.

Immature lymphocytes in transient erythroblastopenia of childhood

The report by Foot *et al* on bone marrow lymphocytes in transient erythroblastopenia of childhood (TEC)¹ is important because it redirects our attention to the patterns of immature lymphocytes which may be found in children's bone marrow. Such cells were once called haematogones. A recent study by Longacre *et al* described detailed studies of these cells in 12 children with a variety of malignant and non-malignant disorders, among which were three cases of red cell aplasia.² They showed a complex pattern of phenotypic and morphological appearances of these lymphoid cells. These observations highlight what should now be axiomatic for haematologists: cell marker studies should not be used to make a diagnosis of leukaemia, but, once such a diagnosis has been made by the usual methods, may give an indication of what sort of leukaemia it is.

Foot *et al* also wonder why bone marrow lymphocytosis should occur in TEC. Among a range of possibilities is the fact that normal children of this age may have up to, or more

than, 40% lymphocytes in their marrow. Removal of the erythroblast population, say 20%, could result in the lymphocytes reaching 50% of the total nucleated cell population without any apparent reduction in the cellularity of the sample, and without an absolute increase in the number of lymphocytes. "Lymphocytosis" in the bone marrow is of course relative. Nevertheless, the increased proportion of early lymphoid cells in the mononuclear cell population obtained by density separation does suggest that it may be "a consequence of an outpouring of immature lymphocytes," unless a corresponding decrease in the absolute number of mature lymphocytes has occurred. Perhaps all three of these processes contribute to the increased proportion of immature lymphoid cells in the bone marrow of those with TEC.

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- 1 Foot ABM, Potter MN, Ropner JB, Wallington TB, Oakhill A. Transient erythroblastopenia of childhood with CD10, TdT, and cytoplasmic α lymphocyte positivity in bone marrow. *J Clin Pathol* 1990;43:857-9.
- 2 Longacre TA, Foucar K, Crago S, *et al*. Haematogones: a multiparameter analysis of bone marrow precursor cells. *Blood* 1989; 73:543-52.

Immunoalkaline phosphatase technique in renal pathology

It was a pleasure to read the article by Jackson *et al* regarding the immunoalkaline phosphatase technique on formalin fixed renal biopsy specimens. We are writing merely to comment on two problems outlined by the authors in their article.

The problem of weak or negative staining encountered in cases of anti-glomerular basement membrane disease (anti-GBM) may result from the fixative used; buffered formalin has a stronger effect on the antigenicity than acid formalin and also requires a greater digestion time to unmask the epitopes. By using formol saline, we have much shorter digestion times in trypsin and the staining of complement is usually stronger. We find C3 of more diagnostic value than IgG in cases of anti-GBM disease probably because of the lower background staining.

The other problem of spurious staining of plasma in capillary loops can be reduced or even stopped by washing the specimen in physiological saline for around one hour before fixation.

We use immunoperoxidase routinely on renal biopsy specimens as well as immuno-fluorescence performed in another department. Having read the article by Jackson *et al* we will be assessing the immunoalkaline phosphatase technique.

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- 1 Jackson R, Holme ER, Phimister GM, Kennedy A, McLay ALC. Immunoalkaline phosphatase technique applied to paraffin wax embedded tissues in diagnostic renal pathology. *J Clin Pathol* 1990;43:665-70.

BOOK REVIEWS

Diagnostic Seminars in Pathology. Vol 1. Ed E Grundmann. (Pp 318; 45 tables; soft cover DM 89.). Gustav Fischer. 1990. ISBN 3-437-11336-4.

This new series "summarises articles previously published in pathology - research and practice". Volume 1 contains nine articles on neuroendocrine tumours, and single articles on prostatic carcinoma, cytological diagnosis of lung cancer, myositis, viral encephalitis, storage disorders, electron microscopy of large cell undifferentiated and giant cell tumours, Niemann-Pick diseases, chronic renal failure, and the use of lectins in histopathology. With such diverse subject matter this book may not immediately appeal to pathologists as "an up to date reference source", but I must confess to finding several of the articles most informative and helpful. The chapter on neuroendocrine tumours of the gastrointestinal tract is a gem; if you are not quite clear about enterochromaffin like (ECL) hyperplasias and neoplasms of the stomach in relation to various syndromes, this chapter will sort things out. It concludes with a most useful and erudite discussion of the terminology of gut neuroendocrine tumours and the use of the term "carcinoid". The chapter on pheochromocytomas and paragangliomas begins with very clear definitions of these tumours. The chapter on thymic neuroendocrine neoplasms is especially useful in its discussion of the differential diagnosis of such tumours. This is certainly a book that candidates for final MRCPATH would be well advised to dip into.

DA LEVISON

Macro Techniques in Diagnostic Histopathology. DG Lowe, IM Jeffrey. (Pp 144; £40.) Wolfe. 1990. ISBN 0 7234 0945 5.

Many histopathologists learn to deal with specimens in an apprenticeship of varying length, collecting tips haphazardly from older colleagues whose skill was similarly acquired. Even in maturity our reports may not always make it clear to clinicians or reviewing pathologists precisely what we found.

Following the advice of this attractive, highly practical guide to specimen examination, description and block selection, should result in consistent high quality macroscopical reports and proper blocks.

Fourteen short chapters on different systems are written in an easy, carefully edited style with excellent closely matched photographs, tables, and diagrams. The 100 specimens illustrated well represent the daily work of the average histopathology laboratory. Procedures suggested are consistent and reasonable, although some might balk at the number of blocks advocated. Clarification of why certain blocks are taken might have been desirable. None the less I wish I had this volume when I started.

AM MACKAY

Progress in Reproductive and Urinary Tract Pathology. Vol 1. Ed I Damjanov, AH Cohen, SE Mills, RH Young. (Pp 217; 49.) John Wiley. 1990. ISBN 0 938607 13 8.

The editors have embarked on a new series of books containing "review articles... written