Cross-linked fibrin degradation products as a predictor of pulmonary embolism

A simple blood test that could exclude pulmonary thromboembolism would have obvious appeal. Not only would it reduce the number of ventilation and perfusion scans performed, but more importantly it would reduce inappropriate anticoagulation.

Monoclonal antibodies to a neoantigen produced by proteolysis of cross-linked fibrin have been produced. Both an enzyme linked immunosorbent assay and a latex agglutination test are now commercially available and have the potential for detecting intravascular thrombosis. Raised concentrations of cross-linked fibrin degradation products (XDP) are found in intravascular coagulation which accompanies a wide range of conditions. They are not specific for venous thromboembolism, but a normal concentration might be expected to exclude venous thromboembolic disease.

All inpatients with a suspected diagnosis of pulmonary thromboembolism referred for ventilation perfusion lung scans over a one year period were studied. Ventilation images were obtained using 40 MBq of a 5 μm aerosol preparation of technetium-99m labelled DTPA (diethylene triamine penta-acetic acid) while perfusion images were acquired about four hours later after injection of 75 MBq of technetium-99m labelled macroaggregates of human serum albumin. Cross-linked fibrin degradation products were measured using the Dimertest latex agglutination kit (Porton Products Ltd). Results were classified negative if less than 250 μg/l or positive if more than 250 μg/l.

Of the 115 patients referred, six had either no ventilation scan or XDP measurement. Results of the remaining 109 patients are shown in the table. The negative predictive value of the test was 84% and the positive predictive value 51%. The sensitivity was 70% and the specificity 71%. There was no clear relation between the titre of XDP and the lung scan result, and analysis of the case histories of the patients with positive scans showed that there was no relation between a negative XDP test and heparin treatment before scanning nor with the length of clinical history. Of the 10 patients with positive scans and negative XDP results, eight had scans classified as high probability of pulmonary embolism (two or more mismatching defects).

A large number of substances may be measured in blood to follow coagulation, fibrinolysis, and platelet activation, but no test has yet been found that has the sensitivity and specificity for venous thrombosis and a methodology suitable for routine and emergency situations. The development of a simple latex agglutination test seemed to offer the possibility of at least excluding venous thrombosis.

As with other studies involving smaller numbers of patients, however,[1-5] the results of this study were disappointing. Raised XDP concentrations have not been shown to be present in all patients with venous thrombosis. The explanation for this is unclear. In this study the timing of the investigation in relation to the thrombosis, the decision to start heparin treatment before testing, and other drugs did not seem to influence the results. Patients with scans with only a medium probability of pulmonary embolism were no more likely to have a negative XDP test than those with a high probability. A possible explanation may be found in individual differences in the fibrinolytic capacity of the pulmonary circulation. Alternatively, the explanation may be that the latex test cannot detect slightly increased concentrations. This may account for the higher negative predictive values obtained with the enzyme immunoassay. It may be possible to improve the latex test in this respect.

In conclusion it is considered unsafe to use the latex test for XDP on its own to exclude pulmonary embolism. The high negative predictive value of 84%, however, could prove useful in particular situations and might influence management of patients while a lung scan is awaited.

Association between lung scan and XDP test result

	XDP		
Number of patients	*Positive*	*Negative*	*Total*
Lung scan result			
Positive	23	10	33
Negative	22	54	76
Total	45	64	109

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4 Goldhaber SZ, Vaughn DE, Tumeh SS, Loscalzo J. Utility of cross-linked fibrin degradation products in the diagnosis of pulmonary embolism. *Am Heart J* 1988;**116**:505–8.
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BOOK REVIEWS

ABC of Transfusion. Ed M Contreras. (Pp 66; UK £10.95; Abroad £13.00.) British Medical Journal. 1990. ISBN 0-7279-0288-1.

This paperback is a compendium of 16 articles which appeared recently in the *British Medical Journal* and dealt with transfusion medicine. Taken together they form a useful and digestible primer. With 21 authors in 16 chapters on only 62 pages of heavily illustrated text there are variations in chapter quality and some repetition of illustrations and subject matter, occasionally within chapters. Laudable attempts to make the separate articles attractive to the general reader in the journal with plentiful illustrations work less well in the book format. For example, a colour illustration of a theatre scene with the legend "A number of operations do not require blood to be crossmatched" and a colour illustration of six empty cryoprecipitate bags might be deemed superfluous. I would wish, though, that this brief overview of the subject of blood procurement and transfusion practice might be read by all house staff and reread by aspiring surgeons and anaesthetists but it may not be so. It will be useful too to transfusion laboratory staff in training in regional centres and hospitals.

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Atlas of Serous Fluid Cytopathology. Current Histopathology Vol 14. AI Spriggs, MM Boddington. (Pp 144; £75.) Kluwer Academic Publishers Group. 1990. ISBN 0-7462-0091-9.

As one would expect from these authors the microphotographs are outstanding and the publishers have done them proud. In some of the previous editions of this series the reproduction has been too small and too blurred, but in this edition the photomicrographs are produced at four or five to the page and the cytology of the cytoplasm and the nucleus, together with reproduction of the colour, is crisp and clear.

It was thanks to their previous book, first published in 1957 by another publisher, *Cytology of Effusions and Cerebrospinal Fluid* (now out of print), that I was persuaded to use May Grünwald-Giemsa stain on fluids, and for this I am very grateful. It has taken them a long time to update the original book but I think that the delay has been very worthwhile as the present book is yards ahead of its nearest competitor.

The only negative words I have to say about this atlas is that it costs too much. I know that colour printing is expensive but the price of £75 puts it out of the range of individual purchasers and this is a shame. I suggest that if the publishers halved the price they would sell more than twice the number of copies. Being that as it may, no cytopathology department should be without this atlas.

DH MELCHER

Lymphoproliferative Diseases. Immunology and Medicine. Vol 15. Ed DB Jones, DH Wright. (Pp 216; £45; $85.) Kluwer Academic Publishers Group. 1990. ISBN 0-85200-965-8.

The number and variety of books on lymphoproliferative disorders which have appeared in the past decade testify to the current interest in this area and reflect the remarkable progress in our understanding of the immune system resulting from the monoclonal antibody "revolution" and the introduction of DNA analysis.

This latest volume is number 15 in the Immunology and Medicine series and is edited by two experts in this field, each of whom has contributed a chapter. Of the 18 contributors, all but two are from the United Kingdom, and understandably the bulk of the text reflects the British viewpoint. In addition to chapters of practical value in the diagnosis of leukaemia and lymphomas, other topics discussed include cell mediated immunity in lymphomas, analysis of immunoglobulin changes in lymphoproliferative diseases, and the origin of the Reed-Sternberg cell.

The book is well produced and can be recommended as a useful review of the current position in this rapidly advancing subject.

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