

Letters

clularity or cellularity of the neoplasms and PR values has been found. We are continuing our studies on a larger group of neoplasms to investigate the influence of histological subtype (WHO) on PR values.

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Identifying "high risk" laboratory specimen's

Dr Whale questions the value of "high risk" labelling in her letter.¹ It is inevitable that specimens containing hepatitis B or HTLV-III viruses, or both, will be submitted to laboratories without the sender or recipient of the specimen being aware of the hazard. This fact has continually (and correctly) been used as an argument that laboratory practice should always be of a standard that should prevent laboratory infection. The argument that "high risk" labelling should therefore be abandoned overlooks another aspect of such identification of specimens that is related to laboratory accidents. These may fall into two groups: where the worker is at risk of infection by gross splashing or needle stick

injury; where the specimen is damaged in transit, and a decision has to be taken regarding its retrieval or disposal. In the first instance if the specimen is known to be hepatitis B positive immune globulin can be used as a prophylactic where appropriate. With regards to an HTLV-III infected specimen, an acute serum can be taken from the worker who is then followed up to see the outcome of the accident and who can be reassured or counselled as appropriate. In the second situation it can be argued that it is much safer, under carefully controlled laboratory conditions, for a senior member of the laboratory staff to salvage damaged specimens than it is for somebody to go and venepuncture the patient. Of course, we are still in the same situation when it comes to the unrecognised specimen, but to abandon the labelling of specimens where there is a known risk would certainly be unhelpful in the case of accident.

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Reference

- Whale K. Is it time to rethink "high risk" labelling? *J Clin Pathol* 1986;39:114.

Dr Whale replies as follows:

I appreciate Dr Fallon's concern regarding unlabelled specimens in the two situations cited.

In the first I would propose that we extend the same service to our laboratory staff that most of us, in our role of control of infection officer, offer to other health care personnel—that is, inquiry regarding risk factors in the individual patient, if known, coupled with testing of a specimen of blood for hepatitis B antigen, followed by appropriate action, or, if HTLV-III infection is a possibility, counselling and reassurance, with collection of blood at intervals, with the informed agreement of the member of staff concerned, and, if necessary, regular follow up in the occupational health or other appropriate department.

With regard to the salvage of damaged specimens, clearly, action would depend on the nature of the specimen and on the expertise of the venepuncturist, but the risk from venepuncture seems to be minimal, and I venture to suggest that laboratory staff would far rather not have to deal with a leaking blood specimen, whatever the source, if another specimen could be

obtained without causing too much distress to the patient.

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Necrotising lymphadenitis without granulocytic infiltration (Kikuchi's disease)

I read with interest the article by Ali and Horton describing four cases of Kikuchi's disease in the United Kingdom¹; I was astonished, however, by the authors' failure to cite and discuss our report of 30 cases in 1983.² With the exception of one patient admitted to Stanford University Hospital, these cases had been submitted to me in consultation and included 21 residents of the United States. We emphasised the remarkable predilection of this disorder for the cervical lymph nodes of young women and confirmed the paucity of granulocytes and plasma cells in affected lymph nodes. Similar observations had previously been made by Kikuchi³ and others^{4,5} in Japan and subsequently by Pileri *et al*⁶ in West Germany.

Prior to this report Dr Haruki Wakasa and I had presented the results of clinicopathological studies on 140 Japanese and 30 American cases, respectively, as part of the proceedings of the United States and Japan seminar on lymphoproliferative diseases, held in Seattle, Washington, in 1982.⁷

Since the publication of these reports I have received many more cases in consultation, and these now total 77. Of these, 62 are women and 15 men (a ratio of 4:1). The mean age of these patients is 29 years (range 11-75).

In none of these patients did we identify any evidence of an evolution to a malignant disorder. In most cases lymphadenopathy resolved spontaneously. Two patients (both young women) developed recurrent lymphadenopathy, biopsy specimens of which showed the characteristic morphological features of Kikuchi's disease.

We used the Leder method for showing esterase activity⁸ (the naphthol-ASD-chloroacetate method, which identifies only mast cells and myeloid cells in paraffin embedded material), in an effort to evaluate the paucity of granulocytes in Kikuchi's disease. To my surprise some of the karyorrhectic debris stained positively, suggesting the phenomenon of leucocytoclasia. This may support the concept that Kikuchi's dis-

ease represents a hyperimmune reaction to an unknown aetiological agent such as a virus.

Our use of the "unqualified term necrotizing lymphadenitis" was criticised by Dr JM Woodruff of the Memorial Sloan-Kettering Cancer Center in a letter to the editor of the *American Journal of Surgical Pathology*.⁹ In response to this,¹⁰ I proposed the eponym "Kikuchi's disease," and I am pleased to note the positive reaction to this suggestion.

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¹ Ali MH, Horton LWL. Necrotising lymphadenitis without granulocytic infiltration (Kikuchi's disease). *J Clin Pathol* 1985; **38**:1252-7.

² Turner RR, Martin J, Dorfman RF. Necrotising lymphadenitis. A study of 30 cases. *Am J Surg Pathol* 1983; **7**:115-23.

³ Kikuchi M. Lymphadenitis showing focal reticulin cell hyperplasia with nuclear debris and phagocytes: a clinicopathological study. (in Japanese). *Acta Haematol (Japan)* 1972; **35**: 379-80.

⁴ Kikuchi M, Yoshizumi T, Nakamura H. Necrotizing lymphadenitis: possible acute toxoplasmic infection. *Virchows Arch (Pathol Anat)* 1977; **376**:247-53.

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⁶ Pileri S, Kikuchi M, Helbron D, Lennert K. Histiocytic necrotizing lymphadenitis without granulocytic infiltration. *Virchows Arch (Pathol Anat)* 1982; **395**:257-71.

⁷ Kadin ME, Berard CW, Nanba K, Wakasa H. Lymphoproliferative diseases in Japan and in western countries: proceedings of the United States-Japan seminar, September 6 and 7, 1982 in Seattle, Washington. *Prospectives in pathology. Hum Pathol* 1982; **14**:745-72.

⁸ Leder LD. The selective enzymocytochemical demonstration of neutrophil myeloid cells and tissue mass cells in paraffin sections. *Klin Wochenschr* 1964; **42**:553.

⁹ Woodruff JM. Necrotizing lymphadenitis. *Am J Surg Pathol* 1984; **8**:79.

¹⁰ Dorfman RF, Turner RR. Necrotizing lymphadenitis. *Am J Surg Pathol* 1984; **8**:79.

Drs Ali and Horton reply as follows:

Clearly, our literature search was not as thorough as we had thought, and we stand admonished!

We stained our material using the naphthol-ASD-chloroacetate method, but were unable to identify any convincingly positive cells or debris. Feller *et al*¹ also used this technique but do not mention any positive findings.

The exact nature of the cells around the necrotic foci must remain in doubt. Professor Dorfman's study² suggested in the one case examined that the cells staining positively with T cell markers around the necrotic foci were cytotoxic/suppressor T cells, yet Feller *et al*¹ reported these cells to be of the helper/inducer type. Further, there are clearly some T cells that share differentiation antigens with histiocytes,³ and we found apparent transitional forms between immunoblasts and histiocytes ultrastructurally.⁴

The advantage of the eponymous term "Kikuchi's disease" is that it cannot be reduced to an acronym which would probably be the fate of necrotising lymphadenitis without granulocytic infiltration (NLGI).

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³ Ali MH, Horton LWL. Necrotising lymphadenitis without granulocytic infiltration (Kikuchi's disease). *J Clin Pathol* 1985; **38**: 1252-7.

⁴ Kadin ME. T Gamma cells, a missing link between malignant histiocytosis and T cell leukemia—lymphoma. *Hum Pathol* 1981; **12**:771-2.

Classification of haemolytic uraemic syndrome

An increasing number of micro-organisms have been implicated in the pathogenesis of the haemolytic uraemic syndrome.¹ This syndrome is characterised by microangiopathic haemolytic anaemia, thrombocytopenia, and renal failure; and seems to be a disorder of platelet and endothelial cell interaction.

In several cases verotoxin, an exotoxin cytopathic for monkey kidney cells (Vero), and neuraminidase, an enzyme chemically similar to verotoxin, have been identified. Of the stool isolates reported in haemolytic uraemic syndrome, various serotypes of *Escherichia coli*,² *Shigella dysenteriae serotype 1* (Shiga toxin),³ and *Campylobacter fetus jejuni*⁴ produce verotoxin and cause bloody diarrhoea, a typical prodromal symptom. So far, six cases of childhood haemolytic uraemic syndrome associated with *Streptococcus pneumoniae*, a neuraminidase producer, have been described.⁵ Case reports of different bacterial and viral isolates in haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura (an analogous adult syndrome) continue to flourish. There is often no attempt to identify the production of these important toxins, however, which may signify a common aetiology for the different micro-organisms implicated in the pathogenesis of haemolytic uraemic syndrome.

Incubation of sterile culture filtrates of verotoxin producing *E coli* with normal plasma will result in potent platelet aggregating activity.⁶ This is dependent on the platelet membrane glycoproteins IIB and IIIA. The premature release of unusually large factor VIII multimers, seen in haemolytic uraemic syndrome plasma,⁷ may also be an important mode of pathogenesis and result from damage to vascular endothelium by verotoxin. Neuraminidase, produced by a wide variety of micro-organisms, may have several pathogenic mechanisms. Direct platelet aggregating activity; deasialation of factor VIII to produce platelet aggregation; and exposure of the Thomsen cryptantigen of platelets, red cells, and vascular endothelium have all been postulated.

Further work is necessary to define the mode of action of verotoxin and neuraminidase in producing this disorder of platelet and endothelial cell interaction. The pathogenic role of these exotoxins, however, is becoming increasingly obvious. Early detection of free faecal verotoxin and the identification of neuraminidase and verotoxin producing micro-organisms are essential steps in the diagnosis and management of haemolytic uraemic syndrome. Classifying haemolytic uraemic syndrome into verotoxin, neuraminidase, and non-exotoxin cases could provide valuable clinical information about this heterogeneous condition. The increased morbidity recently observed in childhood haemolytic uraemic syndrome⁸ and the difference in prognosis of epidemic and sporadic cases may be due