

# PostScript

## LETTERS TO JCP

### Small cell melanoma

The recent correspondence<sup>1-2</sup> following the paper on small cell melanoma<sup>3</sup> indicates that experts cannot agree on this entity. It may well be the next Spitz's naevus, and will it be OK with Blessing *et al* if it is the equivalent of an activated junctional naevus, a metastasising Spitz's naevus, or one of the many other diagnostic (non) entities that clutter the field of melanocytic pathology. And if it does turn out to be benign, what of the overtreatment, morbidity, and life insurance problems that have been created? A diagnostic category avoided by most experts is "don't know". If the lesion is absent from the margins it is probably completely and adequately excised and no further treatment has been proved to be beneficial. In such cases the referring clinician may seek a second opinion that will provide the "answer", but a more pragmatic and honest approach is it "definitely either benign or malignant".

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### Unnecessary repeat requesting of tests in a university teaching hospital immunology laboratory: an audit

Unnecessary repeat requesting of tests can make up a large proportion of a laboratory's workload. It is often difficult to know whether a repeated request is unnecessary because re-testing may be helpful for many chemistry or haematology tests. This audit set out to establish the size of this problem in an immunology laboratory. This setting is informative because most immunology tests are slow to change and

repeat testing within a short time serves no useful clinical purpose. We also tried to identify the circumstances under which these repeat requests were made because this information might suggest what action could be taken to reduce the rate of such requests. We selected three tests commonly requested from the immunology laboratory, the results of which are unlikely to change greatly over short time periods. We analysed the requesting patterns for autoimmune screens (which test for antibodies against nuclei, mitochondria, gastric parietal cells, smooth muscle, and reticulin on a rodent tissue composite block and thyroid antibodies on primate thyroid sections), rheumatoid factor screens, and immunoglobulin values over a 12 month period, identifying tests that were repeated within three months of a previous request. This was achieved by interrogating the CILMS laboratory computer system using a MUMPS enquiry protocol. A total of 25 067 requests were made for these three tests over the year (table 1). Repeat requests within three months of a previous request represented 7.3% of the total workload for these tests. For individual tests the corresponding proportions were: autoimmune screens, 4.5%; rheumatoid factor screens, 4.1%; and immunoglobulin values, 18.7%. The total cost of the tests was estimated at just over £13 000. It is very rare for repeat requests to be indicated for these tests within two to four weeks, so shorter time periods were also analysed. Tests repeated within the two week time period accounted for 2.3% of the total workload for the year. Similarly, repeat autoantibody tests are not indicated within a four week period. Re-requesting of autoimmune screens and rheumatoid factors within a four week period accounted for 2.5% of the total workload for these tests during the year analysed. If this figure is applied across the laboratory's autoantibody repertoire, the cost of such unnecessary tests amounts to nearly £7500. Therefore, it is clear that unnecessary repeat testing is both time consuming and expensive. Possible reasons for repeat testing were sought within the data collected. Tests performed in general practice and then repeated on referral to hospital accounted for only 10.6% of all the tests repeated within three months. Similarly, a change of consultant or location within the hospital only contributed 13%. However, 76.4% of all repeated tests were performed by the same consultant team in the same location. This effect was even greater in the short term, where 82.2% of all tests repeated within a two week period were requested by the same team. Clearly, hospital consultants and their teams should be the target of any intervention to change this requesting behaviour. Feedback of individual test use data to

consultants has been shown to reduce overall request frequency for haematology and clinical chemistry tests.<sup>1,2</sup> Whether this results in an improvement in clinical care has been contested,<sup>3</sup> but with the tests we have analysed there is no doubt that frequent repeats are unnecessary. Test reduplication may also occur simply because the requesting clinician is not aware that the test has already been performed. Where no result is immediately available a new test is ordered rather than checking whether a result is pending. Such behaviour might be modified by an interactive electronic requesting system that gives details of tests already ordered, and may also block the re-requesting of selected tests within a specified time frame. As a result of this audit, this capacity is now a required output specification for our planned new laboratory computer system.

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### Detection of HHV-8 in reactive lymphoid tissue of patients from São Paulo state, Brazil

Recent studies have assessed the seroprevalence of human herpesvirus 8 (HHV-8) in patients infected with human immunodeficiency virus 1 (HIV-1) and healthy blood donors in Brazil.<sup>1-3</sup> We decided to assess the prevalence of HHV-8 infection by another strategy, based upon the polymerase chain reaction (PCR) and immunodetection of HHV-8 positive cells in a series of tissue samples from patients living in the São Paulo state in Brazil. For that purpose, we used three different primers corresponding to three different regions of the viral genome, using a PCR protocol described previously.<sup>4</sup> In parallel, we used primer sets specific to the open reading frame K1 (ORF-K1) sequence to classify the viral strains.<sup>3</sup> Lastly, we applied immunohistochemistry with an anti-latent nuclear antigen 1 (LNA-1) (LN53; ABI, Columbia, Maryland,

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**Table 1** Requests for three common immunological tests over a 12 month period

	Weeks between requests					
	Same day	<1	>1-2	>2-4	>4-8	>8-12
AIS	29	176	65	89	110	110
Igs	25	141	76	202	394	164
RF	35	88	32	57	74	57

1835 repeat requests related to time since previous sample.  
AIS, autoimmune screen; Igs, immunoglobulins; RF, rheumatoid factor.

USA) antibody on routinely processed paraffin wax embedded sections of lymphoid tissues.<sup>4</sup>

The patients (n = 82) were selected randomly at the department of pathology of the State University of Campinas (UNICAMP), São Paulo, Brazil. The samples comprised reactive lymph nodes removed from adult patients (HIV negative), treated for cancer of the gastrointestinal tract, male and female urogenital tract, and head and neck. Ages ranged from 22 to 87 years. DNA was found to be intact in only 25 patients. Three of these 25 patients had HHV-8 DNA sequences in the lymph nodes, as assessed using three different sets of primers—ORF-26, ORF-72, and ORF-75—after one round of PCR, as described previously.<sup>4</sup> In addition, according to the description of subtypes by Zong *et al.*,<sup>5</sup> the analysis of the ORF-K1 sequences showed that in one patient HHV-8 belonged to group A (subtype A) and in the other two the virus belonged to group B (subtype B). Unexpectedly, immunohistochemistry was negative in all 82 patients, including the three PCR positive ones. Overall, our results, although based on a small series, are in keeping with those published by Caterino de Araujo *et al.*<sup>1</sup> A recent interesting serological study performed in 781 Brazilian Amerindians from different tribes revealed a high prevalence of HHV-8 in this population.<sup>3</sup> In that study,<sup>3</sup> the viral strains were of different subtypes, but the authors described a new variant (subtype E), which is hyperendemic in Brazilian Amerindians. Therefore, as suggested by our study and that of Caterino de Araujo,<sup>1</sup> HHV-8 subtype B seems to prevail in the São Paulo state. We were surprised by the lack of LNA-1 positive cells in tissue sections from the three PCR positive patients. This could result from the scarcity of HHV-8 infected cells or a restricted expression of latent genes, such as LNA-1, in reservoir cells. This phenomenon has been seen in Epstein-Barr virus (EBV) positive bystander lymphoid cells with the lack of expression of most latent genes (EBV encoded nuclear antigen 2 negative, latent membrane protein 1 negative).

We cannot completely exclude technical problems related to antigen alteration by tissue processing, but samples from patients with Kaposi's sarcoma from the same institution, processed with the same protocol, were strongly positive for LNA-1. HHV-8 serology was not available for these patients, but our results imply that the real incidence of HHV-8 infection is underestimated. However, the correlation of PCR detection with serology should be undertaken in a larger series of patients to determine the seroprevalence of the virus, at least in São Paulo state. In the report by Biggar *et al.* there was a discrepancy between the serology results and PCR on mononuclear cells from peripheral blood of seropositive patients.<sup>3</sup> This last technique appears to be less sensitive in detecting HHV-8 positive patients but remains mandatory to perform a strain subclassification.

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## CALENDAR OF EVENTS

Full details of events to be included should be sent to Maggie Butler, Technical Editor JCP, The Cedars, 36 Queen Street, Castle Hedingham, Essex CO9 3HA, UK; email: [maggiebutler@pilotree.prestel.co.uk](mailto:maggiebutler@pilotree.prestel.co.uk)

### Urological Surgical Pathology for the Practising Pathologist

18–21 January 2002, Doubletree La Posada Resort, Scottsdale, Arizona, USA

Further details: Department of Continuing Education, Harvard Medical School, PO Box 825, Boston, MA02117-0825, USA. (Tel +1 617 384 8600; Fax +1 617 384 8686; email [hms-cme@hms.harvard.edu](mailto:hms-cme@hms.harvard.edu))

### British Association of Ophthalmic Pathology

21–22 March 2002, Dunchurch Conference Centre, Dunchurch, Rugby, UK

Further details: Dr D Snead, Pathology Department, University Hospitals Coventry and Warwickshire, Coventry CV2 2DX, UK. (Tel +44 02476 538855; Fax +44 02476 538715; email [david.snead@wh-tr.wmids.nhs.uk](mailto:david.snead@wh-tr.wmids.nhs.uk))

### Surgical Pathology for the Practising Pathologist: Selected Topics

22–25 March 2002, Sanibel Harbour Resort and Spa, Fort Myers, Florida, USA

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