

# PostScript

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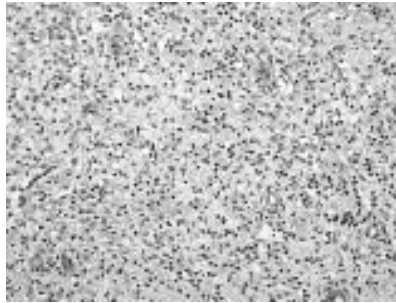
### A rare presentation of a rare disease

A 29 year old woman presented to the gynaecology services with a history of cervical smear cytology and punch biopsy showing human papillomavirus related changes, associated with moderate dyskaryosis. She had undergone laser loop excision biopsy of the transformation zone (LLETZ) two years before for previous abnormal smears. This showed moderate dysplasia in the ectocervical epithelium, but was otherwise unremarkable. A second laser loop biopsy was performed. This was received in the histopathology department in two pieces, 1.5 and 1.2 cm in greatest dimension, respectively. On microscopic examination, focal mild squamous dysplasia was identified in each piece. However, in addition to this numerous eosinophils were seen in the cervical stroma. On close inspection, these were admixed with histiocytic cells, the nuclei of which displayed a degree of atypia, with a convoluted shape (see figs 1 and 2 for low and high power views, respectively). Immunohistochemistry revealed these cells to be positive both for S100 protein (fig 2) and CD1a (fig 3). A diagnosis of Langerhans cell histiocytosis (LCH) was made.

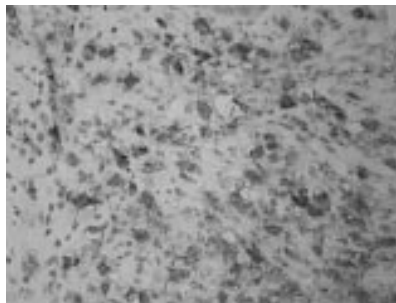
Following this diagnosis, the previous cervical smears were reviewed, but apart from the dyskaryotic squamous cells reported previously, no other abnormal cells were identified.



**Figure 1** Low power view showing S100 protein positive histiocytoid cells in cervical stroma.



**Figure 2** High power view of S100 protein positive histiocytoid cells in cervical stroma.



**Figure 3** High power view of CD1a immunohistochemical stain showing positivity in the histiocytoid cells.

This is not surprising because the Langerhans cells were confined to the cervical stroma, and the overlying epithelium was not ulcerated, and hence it is difficult to see how a cervical smear could sample the tissue affected by LCH.

A review of the world literature by Axiotis and colleagues<sup>1</sup> has revealed only 38 previous cases of LCH, to which four more were added in their report. Cases appeared to fall into four groups, namely: (1) those limited to the genital tract, or (2) associated with genital LCH with subsequent multiorgan involvement, (3) associated with oral or cutaneous LCH with subsequent genital involvement, or (4) associated with diabetes insipidus with subsequent genital and multiorgan LCH.

Most of the references in the literature to genital LCH are related to vulval lesions, such as the case report by Schwartz *et al.*,<sup>2</sup> with only rare references to cervical involvement, such as the case reported by Issa *et al.*<sup>3</sup>

No case has been found in the literature in which the diagnosis of cervical LCH was made as an incidental finding in a LLETZ biopsy, as in our present case.

In summary, our present case is of interest in that it draws attention to a disease with potential systemic importance, which is not only rare in itself, but only very rarely presents with a cervical lesion.

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### Sputum cytology: an unsatisfactory test?

After the correspondence of Burton and colleagues<sup>1</sup> and the Royal College of Pathologists' working group guidelines<sup>2</sup> on the use of sputum cytology as a diagnostic test, we reviewed sputum figures for our department for the period 1998–2001. The results are shown in table 1. These figures confirm that a high proportion of samples are unsatisfactory (30%), although our diagnostic rate (8%) for malignancy was higher than that of Burton *et al.*,<sup>1</sup> who identified only a solitary carcinoma. In addition, although most of the unsatisfactory specimens were submitted by non-respiratory physicians, it was this group that yielded the high pick up rate of malignancy (73%). We consider from these results that sputum cytology still has a place in the investigation of patients with suspected lung malignancy who are unsuitable for bronchoscopy. We agree however that careful selection of patients and correct collection of adequate lower tract material are essential. Although sputum sampling is thought of as a relatively quick, easy, and cheap investigation, it is labour intensive for pathology laboratory and medical staff to prepare and examine. In this present climate of pathology staff shortage, we agree that the use of this test should be restricted.

**Table 1** Sputum data for our department for the period 1998 to 2001

Diagnosis	Number	Clinical source
Benign	394 (51%)	
Cytological atypia	82 (11%)	
Malignant	58 (8%)	Respiratory physicians, 27%
		Non-respiratory physicians, 73%
Unsatisfactory	238 (30%)	Respiratory physicians, 10%
		Non-respiratory physicians, 90%
Total	772 (100%)	

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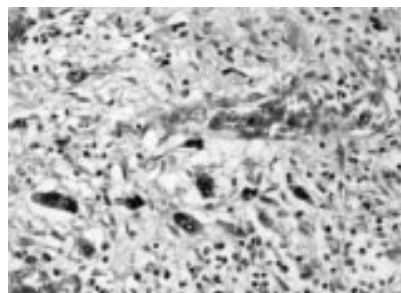
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## Glottis oedema and interstitial pulmonary disease as a result of extramedullary haemopoiesis in polycythaemia vera rubra causing asphyctic death

Polycythaemia vera rubra (PV) is a clonal disorder of the pluripotent haemopoietic progenitor cell, with overproduction of phenotypically normal erythrocytes, granulocytes, and platelets in the absence of recognisable stimuli.<sup>1</sup> PV usually becomes clinically apparent as a result of splenomegaly, hyperuricaemia, or aquagenic pruritus, in addition to the most important complications and leading causes of death—symptoms related to the raised blood cell mass and increased blood viscosity, such as hypertension, erythromelalgia, vertigo, visual disturbances, myocardial, mesenteric and cerebral infarctions, hepatic vein thrombosis, pulmonary thromboembolism, and heart failure.<sup>1,2</sup> Ten per cent of patients with PV die of an acute leukaemic transformation and about 2% develop severe myelofibrosis, with extramedullary haemopoiesis in the liver and spleen.<sup>2</sup> An aggressive systemic spread is a rare complication of PV. Asphyxia caused by infiltration of the respiratory organs by PV has not been reported, although both extramedullary haemopoiesis in the subglottis and in the pulmonary interstitium have been observed.<sup>3,4</sup>

We report a 58 years old male patient suffering from PV and supportively treated by phlebotomies. His disease was stable and he had moderate splenomegaly, hyperuricaemia, and polycythaemia, with greatly decreased concentrations of erythropoietin. Trephine bone marrow biopsies showed erythroid hyperplasia, clustered polymorphous megakaryocytes, depleted iron stores, and minimal argyrophilic myelofibrosis.<sup>5</sup> After an indolent disease course for 12 years, unexpectedly the patient became dyspnoic, with head and neck oedema and threatening asphyxia, without preceding medical manipulations or medication. Despite intubation, aggressive diuresis,



**Figure 1** Extramedullary haemopoietic infiltration of the laryngeal submucosa consisting of megakaryocytes, myelopoietic cells, and erythropoietic cells. Original magnification,  $\times 400$ .

and the application of corticosteroids he died of a treatment resistant asphyxia with respiratory acidosis. Laboratory examination revealed polyglobulia with 0.5% blasts in addition to 4% myeloid precursor cells at that time. Nasopharyngeal, laryngeal, and oral mucosae appeared to be extensively swollen at necropsy. Both subendocardial petechiae in the left outflow tract and cerebral oedema were observed. The spleen was moderately enlarged (16 cm). Microscopic examination of the laryngeal, pharyngeal, and oral mucosae revealed dense predominantly perivascular, factor VIII, glycophorin C, and myeloperoxidase positive haemopoietic cell infiltrates—extramedullary haemopoiesis (fig 1). Haemopoietic cells also infiltrated the neck lymph nodes, the spleen, and the liver, in addition to the pulmonary interstitium, even the alveolar septa. Postmortem bone marrow examination revealed a 95% cellularity with moderate fibrosis and 1% CD34 positive blasts. Asphyxia caused by treatment resistant respiratory insufficiency on the background of laryngeal and interstitial pulmonary infiltration by PV was determined as the cause of death. Both factors impaired external and internal respiration, perturbing ventilation and gas diffusion.<sup>6</sup> Concerning adequate treatment in such circumstances, a good response to local radiotherapy has been described in one less dramatic case.<sup>3</sup>

Clinicians should be aware that PV can progress to an uncontrollable generalised disease and infiltrate the respiratory organs.

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## CD10 is useful in demonstrating endometrial stroma at ectopic sites and in confirming a diagnosis of endometriosis

We read with interest the article by Sumathi and McCluggage entitled “CD10 is useful in demonstrating endometrial stroma at ectopic sites and in confirming a diagnosis of endometriosis” in a recent issue of this journal.<sup>1</sup> Coincidentally, we did the same kind of study regarding CD10 for our intradepartmental research work. Regarding cases of endometriosis of the ovary, we also included cases that were “suggestive of endometriosis”, which is described in *Ackerman's surgical pathology*.<sup>2</sup> It reads: “Not frequently, the repeated hemorrhages have totally destroyed the endometrial

tissue, the cyst being lined by several layers of hemosiderin-laden macrophages. Under these circumstances, the most the pathologist can do is to report the case as a hemorrhagic cyst and comment that the changes are ‘consistent’ with those of endometriosis.” The term “presumptive endometriosis” is also used in *Blaustein's pathology of female genital tract*.<sup>3</sup> Our cases that were suggestive of endometriosis showed positive cytoplasmic staining of CD10 in their stromal component, and were in agreement with the description in *Ackerman's surgical pathology*. Thus, by using CD10 immunostaining, we can make a definite diagnosis of ovarian endometrial cyst even if there is no obvious component of endometrial epithelium. We also had an interesting case of diaphragmatic endometriosis in a patient with catamenial pneumothorax,<sup>4</sup> in addition to a very rare case of intraluminal endometriosis of the fallopian tube occluding the tubal lumen.<sup>5</sup> In these cases, CD10 was also useful to confirm the diagnosis because glandular components were noted within the muscle of the diaphragm and in the muscle layer of the fallopian tube, mimicking invasive adenocarcinoma with lymphoid stroma. Sumathi and McCluggage described three cases that were negative for CD10 in their study. I wonder if they found cilia in those glands in these cases, and if they changed their diagnosis of endometriosis because of the negativity of CD10. Some cases of endometrial polyp are clinically misdiagnosed as “cervical polyp” and these cases can correctly be diagnosed by using CD10 immunostaining. CD10 was useful in our study for the confirmation of such cases. In addition, we incidentally found that some endocervical looking glands situated within the lamina propria of the uterine cervix were surrounded by CD10 positive stromal cells, which could be indicative of superficial endometriosis of the uterine cervix. However, the diagnosis can be missed by haematoxylin and eosin staining alone because the stromal component is too sparse or loose for the endometrial stroma.<sup>3</sup> Finally, we would like to add some more information regarding CD10 in the field of gynaecological pathology. It is of note that mesonephric remnants and tumours are positive for CD10.<sup>6</sup> Because there have been no good markers to identify mesonephric remnants and mesonephric derived tumours, the use of CD10 can be valuable in such instances.

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## BOOK REVIEWS

### Essentials of Anatomic Pathology

Cheng L, Bostwick DG, eds. (\$175.00.) Humana Press, 2002. ISBN 1 58829 118 9.

What is the best format to store and transmit information? With the development of electronic storage media and the Internet, paper is not always the first choice but even if it is then there are other decisions to be made. Will the book be illustrated? Will it be written in fully expanded grammatical prose or will some information be contained in lists and tables? How will it be indexed? What degree of cross referencing will be included?

The authors of this textbook have taken the unusual step of producing a large (893 page) multi-author text on anatomical pathology with no illustrations and all the text presented as succinct bulleted lists. Because I come from the "picture is worth a thousand words" school of information presentation and assimilation, I was initially sceptical of this approach, but I spent some time investigating the usefulness of this format.

The book is divided into general pathology and organ systems. Each organ chapter is divided into the usual categories of congenital anomalies, inflammatory, and neoplastic conditions. Each condition has its features listed under headings such as clinical, macroscopic, microscopic, immunohistochemistry, electron microscopy, and differential diagnosis. However, these are pure lists with very little explanatory text. Any technical description of a histology appearance—for example, pineocytic rosettes or nuclear pseudoinclusions—will send trainee pathologists scurrying to a book that does contain a picture. Any list of immunohistochemical reactions given as only positive or negative sent me to other sources of information for the pattern of staining and the percentage of specific tumours that did or did not give a positive reaction. I discovered several anomalies in the text that required further explanation. Ductal intraepithelial of the breast is presented as though it is the universally accepted system of classification of epithelial proliferations in the breast. The reporting of oestrogen receptor status in breast cancer is said to be positive if greater than 10% of nuclei are positive, with no reference to the more sophisticated and widely used McCarty H score. There is no mention of Her 2 assessment in breast cancer or c-kit in gastrointestinal stromal tumours of the

oesophagus and stomach (it is mentioned as a diagnostic immunohistochemical stain in the intestinal chapter). Somewhat surprisingly, this book does not have an index so that information can only be found through the contents list at the start of each chapter.

Despite the best intentions of the authors of this book I cannot find any use for it within a diagnostic histopathology laboratory for either consultant or trainee pathologists. The absence of illustrations, the list format of the text, and the absence of an index mean that there are a multitude of more accessible and useful sources of this information.

S Cross

### Leucocyte Typing VII

Mason D, ed. (£225.00.) Oxford University Press, 2001. ISBN 019 263 25223.

This book is the edited proceedings of the seventh conference or international workshop on white cell differentiation antigens held in Harrogate UK in June 2000. Although originally confined to white cells like Topsy these meetings have grown to encompass many other related cell types, such as dendritic cells endothelial cells, platelets, and red blood cells. Originally, these meetings involved a wide range of interests from the basic science of the molecules through to their practical applications. Over the years, this has changed slowly towards the more scientific end of the spectrum and this is reflected in the contributions to this volume. In some ways it seems a little odd that pathologists, who as a group must be the biggest users of CD reagents, are little represented now at these meetings. I remember hearing a senior British pathologist, a most eminent immunocytochemist, being asked if he was attending the third or fourth meeting. Replying in the negative he cheerfully asserted that when the book arrived it would contain all he needed to know.

Well, the book of the seventh has arrived so what does it hold for pathologists? First, I don't think one is meant to attempt to read it. This is a heavyweight tome of nearly a thousand pages. It is very well laid out in 17 sections and has an excellent index, so it is no trouble to use it as a work of reference as and when needed. In particular there is a very useful summary guide to many CD antigens at the end. Every time I used a new antibody, obtained an unusual result, or read something new I looked up this section. For those CDs

covered the summary was usually good. It is a pity that it is not complete because it detracts from the comprehensiveness of this section as a reference. The chapters in the individual sections are well laid out and edited. The coverage and the detail available depends upon the individual contributions to the conference.

In summary, this is a good reference to the most recent CD conference. It is also probably the most up to date guide to these molecules and has many aspects that are of interest and use to practising pathologists. However, it is not a comprehensive work of reference and should not be bought in the hope that it could fulfil this task.

K Gatter

### Biochemical Investigations in Laboratory Medicine

Barth JH, Butler GE, Hammond P, eds. (324.00.) ACB Ventura Publications, 2001. ISBN 0 902429 34 5

I was considering buying this book but to my delight a gratis copy arrived on my desk to review. But would it have been worth purchasing?

The book, published in the form of a glossy surfaced ring binder, presumably for hands on laboratory use, gives diagnostic algorithms and protocols for various biochemical dynamic tests. Competitors would possibly include *Algorithms in Chemical Pathology*, by M Crook, Butterworth-Heinemann and *The Bart's Endocrine Protocols* by PJ Trainer and M Besser, Churchill-Livingstone. Not everyone will necessarily agree with the algorithms described by the authors. I found some possibly a little too simplistic but they nevertheless cover a range of conditions likely to be encountered by the hospital laboratory.

I found the book particularly useful regarding non-endocrine tests, such as the investigation of renal tubular acidosis or renal calculi. However, if there is a next edition then updating and clarification of some of the dynamic tests will be necessary—for example, oral glucose tolerance tests will need to include impaired fasting glucose.

At under 200 pages this was an easy and fruitful read. It would be a useful book for the chemical pathology department to have, close to hand, to help with those difficult queries. In response to my initial question this is a book worth buying for the clinical laboratory; although a little pricey at £24.

M Crook