

## Letters

### Candidal infection is uncommon in acute oesophagitis: evidence from a non-selected DGH population

Mucosal candida infection of the lower oesophagus is unusual except in certain groups of patients who are either immunosuppressed or who have other recognised causes of candidal infection.<sup>1</sup> Invasive oesophageal candidiasis occurs most often in the immunosuppressed, occurring in 10–20% of patients with myeloproliferative disorders or leukaemia and in up to 74% of patients with AIDS, with an increased frequency of infection in patients with endocrine disorders such as hypoparathyroidism.<sup>1</sup> Previous studies have shown that the incidence of candidal infection in 22 000 consecutive hospital admissions was 0.1% (27 cases), whereas it was found in less than 5% of a general population presenting with gastrointestinal complaints.<sup>2</sup> It is important to exclude invasive candidiasis as this is a major risk factor in the development of candidal septicaemia, which can result as a direct effect of visceral wall invasion. Complications of oesophageal candidiasis also include oesophageal stenosis and perforation, which may occur in the acute phase of infection, and which can be life threatening. Less commonly, pseudodiverticulosis may also result.<sup>1</sup>

Candidal oesophagitis is caused most commonly by *C. albicans*, *C. tropicalis*, and *C. krusei*.<sup>3</sup> The diagnosis of invasive candidiasis requires a combination of clinical suspicion and laboratory investigation. Difficulties in diagnosis arise where the clinical presentation is non-specific or serology produces false positive results because of vulvovaginal candidiasis. Oesophageal brushings are useful for identifying mucosal surface candidal colonisation but are poor at detecting fungal invasion.<sup>4,5</sup>

Here we present the results of a retrospective review of 60 cases of acute oesophagitis, with reassessment for candida by D-PAS staining.

Sixty consecutive oesophageal biopsies coded on the laboratory computer SNOMED database as acute inflammation with or without ulceration were examined from the period 1997–1998. In our hospital few specimens are sent for mycological culture, and brush cytology is not performed for the diagnosis of candida.

**Candidal staining**—All cases had remaining tissue available. Additional sections were cut if no spare unstained sections were available and then the sections were stained with PAS-D. Sections were pretreated with fresh diastase solution (0.5 cm<sup>3</sup> diastase in 50 ml deionised water) followed by treatment with periodic acid Schiff reagent and Carrazzi's haematoxylin, with tapwater washes in between each stage. The original H&E sections were re-examined to identify the presence of squamous mucosa or gastric mucosa and the nature of inflammation present (acute or chronic). The sections were also re-examined for evidence of ulceration. The minimum criterion required for oesophageal ulceration was the presence of squamous mucosa with epithelium and inflammatory granulation tis-

sue representing the ulcer bed, and/or squamous mucosa with fibrinopurulent and necrotic exudate representing the surface of an ulcer crater. The PAS-D stained sections were examined by both of us for evidence of candidal hyphae and spores, looking for mycelial forms of the fungi and for pseudo-hyphae, which were considered the minimum criteria for diagnosis of invasive candidiasis.<sup>3</sup>

**Results**—Nine of the 60 patients (15%) showed acute ulceration of the oesophagus; the remainder showed acute inflammation with Barrett's change in many cases but no evidence of acute ulceration. Of the 60 oesophageal biopsies examined, no candidal hyphae or spores were identified, either on initial haematoxylin and eosin examination or during this study, after restaining of all the cases with D-PAS. Two of the biopsies did contain some D-PAS positive material, but this material did not have the appearances of fungal spores and we both considered it to be artefact. No mycelial forms or hyphae were present in the sections of any of the cases examined.

**Comment**—Assessment of endoscopic biopsies for fungi using only haematoxylin and eosin staining may be difficult. The differential diagnosis of eosinophilic bodies or hyphae-like tissue in areas of acute oesophageal ulceration may include food debris, degenerate material from the base of an ulcer, herpetic ulceration, reflux oesophagitis, glycogenic acanthosis, other artefacts, and carcinoma. It is widely recognised that the use of D-PAS or Grocott stains may assist in the recognition of fungal hyphae and spores. More elaborate methods have also been used for detection of candida, such as immunostaining for *C. albicans*<sup>6</sup> and polymerase chain reaction.<sup>7</sup>

The aim of our study was to examine the method of routine reporting currently used in our laboratory when dealing with inflamed oesophageal biopsies—that is, without routine additional fungal stain—and to examine the efficacy of detecting candida on routine haematoxylin and eosin stained slides with an additional PAS or PAS-D stain. We showed that the addition of a routine fungal stain for endoscopic biopsies is unlikely to be of benefit in the detection of candida if the patient is not in an at risk group. If the patient is at risk of candida then combined endoscopic biopsy and brush cytology is likely to be much more sensitive than biopsy alone for the detection of the organism.<sup>5</sup>

Causes of candidal infection of the lower oesophagus include use of antibiotics, which may allow overgrowth or colonisation by *Candida* species, inhaled corticosteroids, reduced gastric acid output from H<sub>2</sub> receptor blockers, proton pump inhibitors, or prior vagotomy. Alcoholism, diabetes, malnutrition, advanced age, and abnormal oesophageal motility associated with conditions such as scleroderma and achalasia have also been associated with candida oesophagitis. Strictures, obstructing tumours, or diverticula which cause stasis are also associated with fungal oesophagitis, as is also chronic mucocutaneous candidiasis syndrome. Nine patients (15%) in our study had D-PAS stains performed at the time of biopsy by the reporting pathologist and the majority of these additional stains were requested when there was evidence of acute ulceration, not just inflammation.

The use of routine stains for candida is not justified unless the patient is immunosuppressed or falls into an at risk group. Routine

investigation for oesophageal candidal infection should also include brush cytology.

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- 1 Wilcox CM, Karowe MW. Esophageal infections: etiology, diagnosis and management. *Esophag Gastric Dis* 1994;2:188–206
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### Dihydrate birefringent calcium oxalate or Weddellite calcification

I read with interest the recent article by Singh and Theaker about calcium oxalate crystals within the secretions of ductal breast carcinoma in situ<sup>1</sup> and would like to comment on the eponym “Weddellite calcification.”

The term Weddellite is used because originally calcium oxalate was extracted from the Weddell sea. The British explorer and seal hunter James Weddell (1787–1834) on the brigantine “Jane of Leith” (*The Jane*) of 160 tons, manned by 22 men, in search of fur seals, explored the southern seas (Falkland Islands, Cape Horn, and its neighbourhood). He discovered a “still sea, perfectly clear of field ice” in the furthest south position of 74° 15' S, which he reached on 20 February 1832. It was a record southing that would not be broken until Wilhelm Filchner passed it nearly 100 years later in 1911. Weddell gave the name of George IV to this sea, but the name was abandoned when in 1890 it was proposed the sea be named after its discoverer.

Weddell published a book of the trip called *A Voyage Towards the South Pole*. This book is interesting not only as a record of the trip to what was then, and for long after, the highest southern latitude reached, but also because he gave an account of the South Shetlands and South Orkney Islands, which he had discovered on a previous voyage.

Weddell also discovered the non-migratory earless seal (Weddell seal, *Leptonychote weddelli*). This marine mammal grows to about three metres in length and about 400 kg in weight and is found around the south pole near the coast of Antarctica.

Little is known about Weddell's life. He was born on 24 August 1787 in Ostend, a son of a working upholsterer, a native of Lanarkshire, who had settled in London. At a very early age, the young Weddell showed affinity for the sea. With no education beyond the little that his mother had herself been able to give him, he was bound to the master of a coasting vessel, a Newcastle collier. He read widely on the subject of boats and navigation and rendered himself a capable and efficient navigator. He died unmarried in London in relative poverty on 9 September 1834 at the age of 47.<sup>2</sup>

Although the purpose of Weddell's trip was not discovery, his name has been retained by three eponyms: the Weddell seal, the Weddell sea, and Weddelite (calcium oxalate).

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**The risk of infection transmission by blood transfusion in England**

The review by Soldan and Barbara<sup>1</sup> on the risks of infection transmission by blood transfusion is an interesting and comprehensive article. However, there is little reference of prion disease and in particular new variant Creutzfeldt-Jacob disease (nvCJD) and the recently recommended control measures for blood donated in the United Kingdom. The only mention is in the last paragraph where they state “whether prion disease can be transmitted by transfusion is currently uncertain.”

From 1995 to the end of March 1999, 40 cases of nvCJD had been reported in the United Kingdom,<sup>2</sup> and it is currently not known how many people may be incubating it asymptotically. A recent working party report<sup>3</sup> considers that the distribution of infectivity of nvCJD may be different from that of other forms of CJD, as in the former there may be more involvement of lymphoreticular tissues, possibly involving circulating lymphocytes. Evidence of nvCJD has previously been found in human tonsillar tissue.<sup>4</sup>

In Britain donated blood supplies are to be treated to reduce the risk of patients being infected with nvCJD because of the theoretical risk that it could be transmitted by white blood cells.<sup>5</sup> Plasma which is used to manufacture plasma products—for example, as used in haemophilia—is currently obtained outside Britain.<sup>5</sup> Also from November 1999 all cellular blood products will undergo leucodepletion,<sup>6</sup> a method which removes up to 95% of white blood cells.<sup>5</sup>

Hopefully, further research will resolve these uncertainties about the infectivity of blood products and allow an accurate determination of risk.

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*Authors' response*

We agree with the author of this letter that more comment about nvCJD and the adoption of measures to try to control its possible transmission by blood donated in the United Kingdom is warranted. The situation with regard to nvCJD, as described by Dr Dawson, was evolving during and since the time we wrote our review, and we welcome its addition to the record in this manner.

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**An assessment of the artefacts introduced by mounting two parallel sections from each histological level of cervical punch biopsies.**

A previous study<sup>1</sup> that compared different methods of orienting cervical biopsies has been extended to determine the optimal method of mounting the sections, cut from these biopsies, on the slide to ensure that they are clearly visible for histological examination under the coverslip.

In this department six levels have traditionally been cut from each cervical biopsy, with two adjacent sections from each level being mounted on either side of the midline along the long axis of the slide. This practice places the sections in close proximity to the edge of the coverslip where they may not be protected if the coverslip moves medially or where they may become obscured if mountant is squeezed from between the slide and the coverslip, and becomes smeared over the edge of coverslip.

Two hundred routine cervical punch biopsies in which duplicate sections from each level were mounted on either side of the midline were assessed prospectively up to July 1999. They were compared with 47 biopsies, mainly gastric, duodenal, and rectal, in which a single section from each level was mounted at the midline of the slide. The slides were reviewed by a single pathologist who assessed the following features.

- (1) Is part of one or more of the the sections from each level incompletely covered by the coverslip leaving it at least partially unprotected?
- (2) Is part of one or more of the the sections from each level completely or incompletely covered by the mountant? As a result of being covered by mountant, are
- (3) one or more of the sections from each level partially or completely obscured?

This category was included to distinguish those cases in which, despite mountant having been smeared over the coverslip, it had retained its transparency, permitting the features in the underlying section to be assessed from those cases in which the mountant was no longer transparent and obscured the section.

- (4) In each case the number of levels at which both sections from any particular level were obscured or uncovered was also assessed, because it could be argued that the above only presents difficulties if both sections from each level are obscured or uncovered, as each section has a duplicate cut at only 4 µm from it, which can also be assessed.

Cases were only included in the “obscured” categories if the tissue was covered. Slides in which mountant was present on a part of the coverslip which did not sit over tissue were considered adequate for diagnostic purposes and not included, although it is recognised that they may not meet technical standards of perfection.

Statistical analyses were performed using the Mann Whitney U test. A p value of less than 0.05 was considered to be significant.

The results are presented in table 1. In 16% of cases in which duplicate sections had been mounted from each level, one or more section was not protected by the coverslip as opposed to 2% of cases where a single section was mounted at each level. At least one section was covered (62.5%) or obscured (53.5%) by mountant when duplicate sections were mounted from each level; the corresponding percentages when a single section was mounted at each level were 16.3% and 4.7%. Where duplicate sections from a given level had been mounted, both sections were at least partly obscured by the mountant representing a potentially serious limitation in the diagnosis of such cases in 21% of cases.

Biomedical scientists should be discouraged from mounting parallel sections from histological levels because of the difficulty in ensuring that a section of adequate technical quality will be produced.

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- 1 Heatley MK. A comparison of three methods of orienting cervical punch biopsies. *J Clin Pathol* 1999;52:149–50.

*Table 1 The number of sections not covered by the coverslip that were covered by balsam, and the number of levels where material was obscured by balsam; if two levels were mounted the level was only considered to be obscured if both sections were obscured*

	Number of sections										p Value	
	0	1	2	3	4	5	6	7	8	9		10
<i>Number of sections not protected by the coverslip</i>												
Two sections/level	158	15	9	4	2	1	1					0.016
One section/level	42	1	0	0	0	0	0					
<i>Number of sections covered by mountant</i>												
Two sections/level	75	31	41	24	14	5	4	1	1	3	1	<0.0001
One section/level	36	3	1	1	0	1	1	0	0	0	0	
<i>Number of sections obscured by mountant</i>												
Two sections/level	93	33	41	15	12	3	2	0	1			<0.0001
One section/level	41	2	0	0	0	0	0	0	0			
<i>Number of levels with both sections obscured by mountant</i>												
Two sections/level	158	36	3	2	1	0	0					<0.001
One section/level	43	0	0	0	0	0	0					

## Book reviews

**Basic Tests for Drugs, Pharmaceutical Substances, Medicinal Plant Materials and Dosage Forms.** (Sw fr 26; Sw fr 18.20 in developing countries.) Geneva: World Health Organisation, 1998. ISBN 92 4 154513 5.

This book updates two related WHO publications, *Basic Tests for Pharmaceutical Substances* (1986) and *Basic Tests for Pharmaceutical Dosage Forms* (1991), and gives information on tests for a further 23 substances, 58 dosage forms, and four medicinal plant materials. The drugs/preparations listed are mainly from the WHO *Model List of Essential Drugs* (1997). Reagents, test solutions, and volumetric solutions not listed before are detailed in the present volume, although there is nothing on suppliers, and little on reagent stability, storage conditions, and so on. There is a cumulative index to the three books.

The tests are confined to a physical description of the material and simple colour and other reactions, and aim to facilitate identity testing of bulk supplies, for example when labelling is unclear, and to indicate whether gross degradation has occurred in certain substances. A lot of work has gone into this relatively short publication, as evidenced by the list (more than a page) of acknowledgements of individuals and collaborating centres. Is the book of interest to clinical/forensic laboratories? Probably not, except that some laboratories might find a few of the tests useful if asked to identify powders, and so on (see Flanagan RJ, *et al. Basic analytical toxicology*. Geneva: WHO, 1995). There are simpler ways of identifying tablets (for example, Ramsey JD, Woolley JM. *TICTAC—a CD-ROM for the identification of tablets and capsules*. The International Association of Forensic Toxicologists: Proceedings of the 35th Annual Meeting, Padova, 1997:174–82).

The tests are supplemented by a review of recent published non-WHO work on simple methods for identifying pharmaceuticals, including volumetric, spectrophotometric, and thin layer chromatographic (TLC) methods. It seems that more than 150 TLC procedures were developed by WHO collaborators in the early 1980s using some 40 different

mobile phases, but this work was not published as it was thought necessary to try to reduce the number of mobile phases used. Publishing and updating books, data sheets, and so on is becoming easier as desk top and even electronic publishing become the norm. It remains to be seen how WHO will respond to this challenge—there is not even an email address for comments in the present volume.

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**Leukaemia Diagnosis (2nd ed).** By B J Bain. (£49.50.) Blackwell Science, 1998. ISBN: 0 632 051 655.

The first edition of this book was published in 1990 with the subtitle *A guide to the FAB classification*. (The FAB group had by then published proposals for the classification of the acute leukaemias, the myelodysplastic syndromes and the chronic lymphoid leukaemias.) “This book is much more than an atlas,” quoted from a review of that edition, advertises this new volume from its back cover. How true. Much more than just a guide to the FAB classification too. It has been comprehensively revised and updated to include current immunophenotypic, cytogenetic, and molecular developments, and also consideration of scatterplot data from the new generation of automated counters. The book is both a comprehensive atlas of clearly reproduced photomicrographs of a whole range of common and rare leukaemic material, and an elegant and enthusiastically written treatise on leukaemia classification.

No classification of leukaemia can be perfect. The often competing criteria of easy and reproducible applicability, clinical relevance, and biological plausibility necessitate compromises. This work does not seek to champion or defend the FAB classifications, but explains them critically, and sets them in contemporary context in the light of the newer technological developments. Cytogenetic and molecular discoveries have clarified many biological entities. Meanwhile, generations of careful morphologists, for whom Dr Bain is a contemporary standard bearer, have gone back to the microscopic appearances to find that much of the information was there for the want of looking. Thus we can predict from the preliminary appearances when we are going to find an 8;21 translocation or a 16 inversion, whether or not a Philadelphia negative case is going to be found to have a bcr rearrangement, and many more examples. For the clinical haematologist this is not only rapidly available free

information, it is also fun, and there’s little enough of that around these days. Even the developing “Bugger the cytochemistry, what do the markers show?” school of haematology should be enticed back to their microscopes by this enthusiastic writing, and I commend this book unreservedly to all haematologists and trainees.

PETER CAREY

## Notices

### Practical Adult Cardiovascular Pathology Course

Royal Brompton Hospital,  
Imperial School of Medicine

6–7 March 2000

A “hands on” course approaching in detail the problems facing the diagnostic pathologist when dealing with cardiovascular pathology. Approaches to cardiac necropsy and sudden death will be emphasised. The course is aimed at trainees studying for the MRCPath.

*Further details:* Short Course Officer, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, UK; tel +44 (0)2073518172; fax +44 (0)2073518246; email: shortcourse.NHLI@IC.ac.uk

### British Society for Clinical Cytology BSCC Spring Tutorial: Cervical Cytology

Guy’s Hospital, London

7 April 2000

Lectures and workshops including “Invasive squamous cell carcinoma” (W Gray), “Borderline changes” (P Smith), and “Atrophic smears” (L Turnbull).

*Further details:* BSCC Office, EMI, Central Research Laboratories, Dawley Road, Hayes, Middx UB3 1HH, UK; tel +44 (0)181 6062511; fax +44 (0)181 6062563; email: lesley.couch@psilink.co.uk