# Correspondence

## The value of Toxoplasma specific IgA in diagnosis

We agree with the conclusions of Takahashi and Rossi[1] that the sensitivity of their immunosorbent agglutination assay (ISAGA) makes it an ideal screening test and that detection of IgA is a useful indicator of early infection. However, the relative usefulness of IgA and IgM has not been considered as all of the acute toxoplasmosis serum samples tested were positive for both.

In their paper only 51 patients with acute toxoplasmosis were tested. All were IgM positive but none had documented duration of illness.[1] We have developed a toxoplasma specific IgA-ISAGA based on an in-house IgE-ISAGA.[2] Our assay differs in that a semiquantitative result is obtained by titrating the amount of antigen used not the patient serum. Our IgA-ISAGA has been found to be highly specific, with only one in 583 (0·17%) false positive results. Using this assay, 120 serum samples from 68 patients with acute toxoplasmosis with known duration of symptoms have been tested. All except three contained toxoplasma specific IgA. As found previously, peak levels of specific IgA were detected after approximately two months.[1,3] Serum samples which were IgA negative were all taken less than two weeks[2] and 1·4 months[1] after the onset of symptoms. Two of these samples had detectable IgM (Toxo-M ISAGA, BioMerieux, France) one of which was positive; the third was IgM negative. Positive reactions were detected up to about 11 months, the longest duration sample available. In contrast, 25 of 120 were Toxonostika ELISA-IgM (Organon Teknika, Cambridge, UK) negative and seven of 25 were also Toxo-M ISAGA negative. This suggests that specific IgA is in fact a less specific indicator of acute infection than specific IgM. In a group of 11 pregnant women all IgM positive IgA positive reactions were recorded in 37 of 38 serum samples, confirming that IgA may not be advantageous over IgM in acquired infection. However, IgA is more sensitive than IgM as an indicator of congenital toxoplasmosis and is therefore diagnostic when detected in fetal or neonatal samples.[3]

Persistence of specific IgM also causes problems in diagnosis of non-pregnant individuals. In patients[2] with persistent IgM for three and five years, respectively, specific IgA was negative in one; in the second specific IgA fell during the five year period but remained borderline positive even after five years. This confirms previous indications that, like IgM, persistence of IgA appears to be variable.[3]

In our experience, detection of specific IgE is a better indicator of acute infection than either specific IgM or IgA.[2] Therefore measurement of specific IgA should be used as an adjunct to established techniques and not replace them.

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## Systemic absorption of vancomycin

Further to the recent marked upsurge in the United Kingdom of *Clostridium difficile* infections,[1] we report our findings from a recent study of systemic absorption of vancomycin administered orally in 10 patients with bacteriologically confirmed pseudomembranous colitis (PMC). The patients ranged in age from 14 to 81 years. Renal function varied between normal and severely impaired. Most patients were treated with oral vancomycin in a dosage regimen of 125 mg four times daily for 10 days but in one case of relapsing disease the patient was given oral vancomycin 500 mg four times daily in two five day pulses separated by an interval of two days. Vancomycin serum concentrations were measured by immunoassay, the first five by the enzyme multiplication immunoassay technique (EMIT) and the remainder by TDX. It should be noted that results obtained with the TDX may be artificially high as it also detects vancomycin crystal line degradation product 1, which may accumulate in patients with impaired renal function. In seven of the 10 patients the vancomycin concentrations were unrecordably low at <1 mg/l. This included one patient with mildly impaired renal function (urea 13·0 mmol/l, creatinine 209 μmol/l) and the patient being treated with 500 mg four times daily vancomycin pulses mentioned above. Four patients had recordable serum vancomycin concentrations ranging from 1·0 to 3·1 mg/l. In only one of these patients was renal function impaired (table).

These findings confirm that treatment of PMC with oral vancomycin may result in some absorption of the drug through the inflamed colonic mucosa,[2,3] with four of these 10 patients showing detectable concentrations in their serum.

However, with the usual dosage of 125 mg four times daily, the resulting concentrations are generally low and are unlikely to reach potentially toxic concentrations (>50 mg/l), even in patients with moderate to severe renal impairment.[4] Routine monitoring of serum vancomycin concentrations is therefore not generally indicated in patients with PMC being treated with oral vancomycin, except perhaps when larger doses than normal are being used (for example, 500 mg four times daily) in patients with severe renal failure, when there may be a small risk of accumulation of absorbed drug.

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*Serum vancomycin concentrations in patients with bacteriologically confirmed PMC*

| *Patient No.* | *Day of therapy* | *Vancomycin concentration (mg/l)* | *Day of therapy* | *Urea* | *Sodium* | *Postassium* | *Creatinine* |
|---|---|---|---|---|---|---|---|
| 1 | 2 | 3·1 | 0 | 8·0 | 148 | 3·1 | 107 |
| | 4 | <1 | | | | | |
| | 13 | <1 | 12 | 5·4 | 143 | 3·8 | 102 |
| 2 | 4 | 1·0 | 6 | 1·8 | 135 | 3·4 | 55 |
| 3 | 6 | 2·5 | 5 | 7·1 | 129 | 3·7 | 84 |
| | 8 | 1·9 | 8 | 6·3 | 135 | 3·3 | 75 |
| 4 | 10 | 1·6* | 8 | 19·2 | 132 | 5·4 | 1243 |

* This result was obtained with the TDX and may be elevated for the reasons discussed.

## A rapid and safe method to fix India ink on specimen resection margins

India ink is a useful aid to the evaluation of specimen resection margins. The ink is usually applied with a brush before sectioning and allowed to dry, after blotting off any excess, for a few minutes. Alternatively, the inked specimen may be immediately immersed in Bouin's solution for a short time (20–30 seconds) to fix the ink to the surfaces.[1–4]

With all specimens, including large specimens (for example, breast or neck dissections), fresh tissue for special processing or frozen sections, it is possible to reduce the time required to fix the ink on the specimen before freezing or further sectioning by using Bouin's solution.

Problems may be encountered by the routine use of large quantities of Bouin's solution because of its content of picric acid (2,4,6-trinitrophenol). This chemical has been used as an explosive and also as a component of matches, in the leather industry, and as a chemical reagent. Because of its extensive use, mostly military in the past, it is now considered to be a potential contaminant of the environment, mostly of the groundwater.[5] Exposure to picric acid or its salt is primarily through inhalation of dust or through skin contact causing a sensitisation dermatitis. The latter situation may occur in a histopathology laboratory dealing with the commercially available picric acid as a fixative. To reduce the use of this toxic chemical and to limit it to essential needs, a different solution to fix the India ink on specimens has been developed and used. It is composed of 40% formalin (10 ml), glacial acetic acid (5 ml) and distilled water (85 ml). The pH of this solution ranges from 2·69 when fresh and unused to 2·78 after one week of use.

The time needed to fix the ink is even shorter than with Bouin's solution, being less than 10 seconds, and the staining effect obtained with Bouin's solution, sometimes unwanted, is avoided. The solution must be changed weekly.

No microscopical artefacts have been seen and no tissue damage at the histochemical or immunohistochemical level have been revealed after four months of routine use. The solution has now been permanently introduced in our dissection room.

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## Necrobiotic granulomas of the urogenital system

We agree with Dr Agel[1] that the granulomatous tissue response associated with diathermy and laser treatment warrants wider diagnostic recognition. Unfortunately, however, Dr Agel appears to have overlooked our own contribution[2] to the nature and origin of diathermy pigment in such specimens. We also believe that the potential biohazardous nature of diathermy pigment, because of the nature of its metallic composition, is poorly appreciated and deserves greater emphasis.

In our study 14 cases of postsurgical granulomatous inflammation within the urinary tract were investigated using electron microscopy and energy dispersive analysis of *x* rays (EDAX). The findings were then correlated with the composition of diathermy instruments which had also been subjected to metallurgical analysis. The brown staining material, observed on light microscopy by ourselves and Dr Agel, appeared amorphous ultrastructurally and was found to contain iron, calcium, aluminium, phosphorous, sulphur, and chlorine by EDAX. This material was interpreted as necrotic tissue with absorbed metallic salts from the surrounding body fluids. By contrast, darker particulate material present appeared electron dense and contained variable combinations of three different groups of elements. These comprised pure tungsten, from tungsten wire cutting loops, copper, zinc, nickel, manganese, and iron from nickel silver coagulation "roller balls" and iron, chromium, nickel, manganese, molybdenium, copper, and vanadium from the stainless steel supporting wires. Whereas tungsten is probably biologically inert, evidence indicates that nickel, chromium, copper, and zinc are immunogenic. Also, in certain circumstances, both nickel and chromium can be carcinogenic. Consequently, on the basis of these observations, we have suggested that it is probably advisable to discontinue the use of nickel, chromium, zinc, and copper in the manufacture of diathermy electrodes. A strengthened tungsten electrode, possibly in a ceramic mount, would seem to offer a more biocompatible alternative.

It would also appear desirable that the granulomatous response following later treatment is subjected to a similar, extensive microanalytical study. Aluminium oxide, possibly derived from the laser housing, has been found in one case.[3]

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*Dr Agel comments:*
I thank Dr Slater and Professor Henry for their comment on my letter.[1] My letter described the presence of "diathermy pigment" in most of the granulomas found in uteri and urinary bladders following either laser or diathermy resection. The recognition of such a pigment should be of help to diagnostic histopathologists when investigating granulomatous conditions of the urogenital system. It was not my intention to discuss the nature of the pigment; such discussion will appear in a detailed paper which describes our cases where the work of Henry *et al*[2] will be appropriately quoted.

## Audit of tumour pathology reviewed by a regional oncology centre

I was very encouraged to read of the audit of tumour histopathology referred by a district general hospital and received by the regional oncology centre.[1] It includes my own areas of difficulty, lymphomas, sarcomas and grading of ovarian epithelial neoplasms. I also note a statement in the introduction, which should perhaps be given greater emphasis, that a copy of the pathological findings is sent back from the oncology centre to the district general hospital.

Patients from our hospital are referred to several specialist oncology and radiotherapy centres, and slides and reports are sent. Long before the advent of any formal external quality assessment schemes, I have found a copy of the reviewing pathologist's report to be an extremely helpful, routine form of quality control. It enables any major or minor diagnostic discrepancies to be considered, reveals what classification is being used and suggests what prognostic histological features should be mentioned. There is a second important practical consideration. The patient will return to the district hospital for follow up and possible further biopsies. If there is a significant discrepancy between the report of the referring pathologist and the diagnosis given back to the clinician, the potential exists for future confusion unless the pathologist is aware of it.

Over the years I have found that some pathology departments are extremely punctilious about sending their reports. Some rely on a single conscientious individual who may leave and occasional hospitals cannot seem to manage it with any degree of reliability.

Most departments are now computerised. I would like to make a plea that it becomes routine practice that referral centres generate an extra copy of the report on all reviewed histology for dispatch to the referring histopathology department. This practice is much less contrived than external quality assessment schemes, and is both courteous and useful to the referring pathologist.

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# Book reviews

**Atlas of Gynecologic Pathology.** 2nd edn. JD Woodruff, TL Angtuaco, TH Parmley. (Pp 325; $170·50.) Raven Press. 1993. ISBN 0-7817-0056-6.

The objective of this atlas, as stated in the preface to the first edition, is to present gynaecological pathology in broad terms giving the novice a general introduction. The text on the back flap claims that the atlas is an essential diagnostic tool for every pathologist and gynaecologist. Does this atlas achieve these goals which appear prima facie to be mutually incompatible?

A strong correlation between clinical and pathological appearances is achieved in this work. Embryological development and normal histology are described at the beginning of the chapters. This book contains clinical pictures, many colour photomicrographs and also, new to this edition, many radiological illustrations. Annotated drawings accompany photomicrographs and radiological images to facilitate their interpretation. The text on the back flap mentions state-of-the-art electron micrographs; I did not find any, although a few photomicrographs of immunohistochemical stains are included.

It is a pleasure to browse through this atlas as the photomicrographs are almost all of good quality. The text is generally well integrated with the pictures. The balance of text and numbers of photomicrographs follows the authors' stated objective. Nine pages including 20 photomicrographs are devoted to placental development. Borderline serous and mucinous ovarian tumours are dealt with briefly and the accompanying text does not clearly indicate the histopathological criteria of borderline malignancy. The absence of rare but well described lesions and general lack of histopathological differential diagnostic considerations limits the usefulness of this atlas for the diagnostic histopathologist.

This book does, I think, achieve the stated aim of an introduction to gynaecological pathology though some parts of the text could well lead to confusion. To achieve the prime object has led, as the authors' accept, to selection of material. Though the pictures are delightful, I cannot recommend this atlas as a histopathology bench book.

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