Letters

Colonic angiodysplasia

I was very interested by the suggestion by Roskell *et al* that colonic angiodysplasia may be related in some way to abnormalities in vascular basement membrane.¹

The idea is appealing, and the illustration of staining for type IV collagen does indeed appear to show a difference between the strong positivity in submucosal vessels (fig 1A) and absence in the lamina propria vessels (1B). However, in colonic mucosa there is a basement membrane between the columnar epithelium and the stroma. This contains type IV collagen. If we are to trust the apparent absence of staining of the vascular basement membranes in the lamina propria, can the authors explain why the adjacent epithelial basement membranes also appear to be completely negative in their illustrations?

P N FURNESS

Department of Pathology, University of Leicester,
Leicester LE5 4PW, UK

- 1 Roskell DE, Biddolph SC, Warren BF. Apparent deficiency of mucosal vascular collagen type IV associated with angiodysplasia of the colon. *J Clin Pathol* 1998;51:18-20.

Authors' response

Dr Furness is correct in pointing out that the epithelial basement membrane in the colon would be expected to stain for type IV collagen, and indeed in all of our cases and controls some staining was seen. However, at the antibody concentration used in our study the epithelial basement membrane staining was very weak and focal compared to the strong staining of the submucosal blood vessels. Indeed epithelial basement membrane staining compared in intensity to the weak staining of the mucosal vessels seen in angiodysplasia.

Our observation of apparent deficiency of type IV collagen in the mucosal vessels is presented as a relative deficiency compared to the strong submucosal vascular staining, and is not compared to the epithelial basement membrane. If we had used a concentration of antibody high enough to result in strong epithelial basement membrane staining sufficient for photography, the differences in vascular staining would not have been visible.

DEREK ROSKELL
SIMON BIDDOLPH
BRYAN WARREN

Nuffield Department of Pathology, John Radcliffe
Hospital, Oxford OX3 9DU, UK

Immunofluorescent patterns associated with ANCA

We would like to comment on a number of issues raised by Savige *et al* in their recent paper in the Journal.¹

First, they state that dual positivity for anti-MPO (myeloperoxidase) and anti-PR3 "usually indicates non-specific binding"—that is, a false positive. Our experience is different. We find dual positivity is a relatively rare phenomenon and tends to represent true positivity. This may in part result from our practice to include a control (uncoated well) to check for non-specific ELISA binding. Reviewing our last 500 referred samples reveals only one dual positive. This sample was from a 50 year old female with long standing biopsy proven Wegener's granulomatosis. Immunofluorescence was C-ANCA pattern.

Next, we agree that antibodies such as antimitochondrial and anti-smooth muscle can stain neutrophils, but with the exception of antinuclear antibody (ANA), these rarely mimic true ANCA and seldom cause recognition problems in routine analysis. With regard to the problem of ANA interference, we still find the use of formalin fixed neutrophils helpful in the differentiation of ANA and P-ANCA, though the method has its critics.² In our hands, anti-MPO antibodies are rarely formalin negative. A recent review of our data shows that, in a three month period, 0/56 sera showing nuclear stain on ethanol fixed neutrophils and negative on formalin fixed neutrophils (that is, ANA or atypical P-ANCA) were anti-MPO positive. Thus in the context of necrotising vasculitides it offers a quick and useful method for selecting sera for anti-MPO ELISA.

Lastly, Savige *et al* mention a range of atypical immunofluorescence staining patterns, such as the so called "flat cANCA." We are strongly of the view that, while these are of research interest, they should be communicated clearly to ward doctors not as ANCA positive but instead as atypical reactivity of doubtful clinical significance.

R J LOCK

D J UNSWORTH

Immunology, Southmead Hospital,
Bristol BS10 5NB, UK

- 1 Savige JA, Paspaliaris B, Silvestrini R, *et al*. A review of immunofluorescent patterns associated with antineutrophil cytoplasmic antibodies (ANCA) and their differentiation from other antibodies. *J Clin Pathol* 1998;51:568-75.
2 Spickett GP, Broomhead V. Formalin fixation and patterns of antineutrophil cytoplasmic antibodies. *J Clin Pathol* 1995;48:89-90.

Authors' response

Thank you for the opportunity to reply to Drs Lock and Unsworth. Their letter has highlighted some of the difficulties with ANCA testing that have been addressed by a group of clinicians and scientists in the *International consensus document on ANCA testing and reporting*.¹

The Consensus document states that the minimum requirements for ANCA testing in new patients are the indirect immunofluorescent (IIF) examination of all sera on normal neutrophils. Sera that contain ANCA, any other cytoplasmic fluorescence, or an ANA that results in a homogeneous or peripheral nuclear pattern should then be tested promptly in ELISA for both proteinase 3 (PR3)- and MPO-ANCA.

The Consensus document recommends that reports use the terms "C-ANCA" for cytoplasmic granular fluorescence with interlobular accentuation, "C-ANCA (atypical)" for other types of cytoplasmic fluorescence, "P-ANCA" for any type of perinuclear or granulocyte specific nuclear fluorescence, and "atypical ANCA" for other less common patterns, such as mixed cytoplasmic and perinuclear fluorescence. Antigen specificities are described as PR3- and MPO-ANCA. Reports should indicate that positive neutrophil IIF alone is not diagnostic for Wegener's granulomatosis or microscopic polyangiitis, and that decisions about treatment should not be based solely on the ANCA results.

In reply to specific points raised by Drs Lock and Unsworth:

The ability to distinguish between ANCA and other autoantibodies that stain neutrophils depends very much on the quality of the neutrophil preparation and the skill of the observer. Because of this variability, the con-

sensus document has indicated that all sera that produce positive IIF should be tested in PR3- and MPO-ELISA. The absence of binding in these assays will indicate that the diagnosis of Wegener's granulomatosis and microscopic polyangiitis is unlikely.

With respect to IIF patterns, the consensus document recommends that a "flat ANCA" is called a "C-ANCA atypical." However, it is not always possible to distinguish this from a "C-ANCA" and for this reason ELISA for PR3- and MPO-ANCA should be performed to diagnose Wegener's granulomatosis and microscopic polyangiitis.

The consensus document does not suggest formalin fixation to differentiate between an ANA and P-ANCA. This is because the success of this technique varies in different laboratories, ANA and P-ANCA may occur together, the procedure involves another "run" of IIF, and an ELISA is still necessary if the IIF remains positive, at least to determine the antibody level.

Finally, most laboratories, in Australia at least, use commercial kits for PR3- and MPO-ANCA and do not subtract the binding to uncoated wells for individual sera. Under these conditions "dual positivity" usually represents non-specific binding and is often "borderline" in amount. If background binding is subtracted, then "dual positivity" is more likely to represent a "true" ANCA.

JUDY SAVIGE (on behalf of the other authors)

University Department of Medicine,
Austin and Repatriation Medical Centre,
Heidelberg, VIC 3084, Australia

- 1 Savige J, Gillis D, Davies D, *et al*. International consensus statement on testing and reporting of antineutrophil cytoplasmic antibodies (ANCA). *Am J Clin Pathol* (in press).

CD-ROM reviews

Topley and Wilson's Microbiology and Microbial Infections, 9th edition (CD-ROM). Edited by L Collier, A Balows, and M Sussman. (£995.00.) Edward Arnold, 1997. ISBN 0 340 70015 7.

Long before the influence of Calman on training, my only guidance for preparation for MRCPath was "read Topley from cover to cover." There were two volumes then. Now there are six. New in the 9th edition are the international authorship, coverage of mycology and parasitology, and the CD version. This is now a massive text to review. I would not expect to find factual fault with any of the contributions from experts, nor did I, even in the areas on which I am qualified to opine. I shall concentrate on the new electronic format.

The CD offers the advantage at least of saving shelf space, but the book becomes "virtual" and there is no feeling of where one is in the text—nor indeed how much of it there is. I find it uncomfortable to read more than a small amount of text from the screen.¹ It was easier to print individual sections that I wanted to study (you can do this for up to 50 paragraphs).

The software allows text searches with varying degrees of complexity, rapid jumps, and personalised electronic annotation and colour highlighting of text. One can cut and paste text (for example references) into personal documents. This does facilitate plagiarism but that is more of a problem in students' assessed work

than in professional skullduggery. However, all the otherwise hidden tags that allow the jumps and popups are carried too.

The quality of the graphics varies from poor to acceptable. Electron micrographs were generally clear and fungal cultures looked good (fuzziness helps). The blood films of malaria did not adequately show dots and clefts. Some of the "extra illustrations exclusive to the electronic version" turned out to be very poor quality line drawings. This was a disappointment. Large tables were particularly tricky to navigate if they did not fit into one screen, and vertical labels were very hard to read. I got round that by highlighting columns in colour blocks—very useful in following a long vertical list of biochemical reactions in the identification of bacteria.

Where the paper reviewer can delight in finding typos, the electronic reviewer has the additional opportunity to look for bugs (even more fun in a book on infection). There are lots. Searching for *Mycobacterium bovis* takes you to all the occurrences of that species but also to *Mycoplasma bovis*. Some jumps don't go anywhere. Eikenella is such a great bacterium that it receives full coverage in two chapters.

Publishers seem to find it convenient to take the word processed text of books and turn them into CDs. They fail to take full advantage of the opportunities presented by electronic publication. We are increasingly used to "point and click." It is a shame the CD version displays lists in almost the same format as the book. The first step has been taken to transform this reference text into electronic format, but as long as the CD version so closely matches the paper version its full potential will never be realised.

These are small gripes. This remains a standard text book that has been improved, expanded and updated. Some imaginative fine tuning would make the CD version clearly the one to buy.

W R GRANSDEN

¹ The CD was run as a single user application on the following equipment, which is about the minimum requirement:

Dell Optiplex PC
Windows 3.11
Ultrascan SVGA monitor 1024 × 768, 256 colours
16 MB RAM
Pentium processor

Atlas of Pathology: Spleen (CD-ROM).

By J Diebold, A le Tourneau, J Audouin, T Molina. (£116.04). Springer-Verlag, 1998. ISBN 3540146407

Images are the key ingredient for a histopathological diagnosis—and a picture tells more than a thousand words. Furthermore biology is so diverse that the number of morphological appearances is almost infinite. Therefore it is very helpful to have illustrations next to text on histopathology. An atlas on splenic pathology was badly needed and now there is an atlas on CD-ROM, by Diebold, le Tourneau, Audouin and Molina. These writers have a very long experience in splenic pathology and are therefore able to present an enormous diversity of cases, including very rare disorders. Since such images have not hitherto been available, this is a welcome addition.

The CD-ROM is well organised and one can search the images with an extensive user-friendly search system, based on ICDO codes or SNOMED codes and keywords. The number of search possibilities is probably even

larger than needed for this atlas. On the other hand several terms used in the REAL classification on lymphomas are not recognised.

The CD-ROM enables one to find images rapidly (depending on the system one uses) and gives one the opportunity to enlarge an image and add the provided text to it. Since this is basically an atlas, the amount of information with each picture is small. For instance, there is an interesting case diagnosed both as lymphoplasmacytic lymphoma and monocytoid B cell lymphoma. Both morphologies are shown and the following information is given:

M-96713 Malignant lymphoma, lymphoplasmacytic

M-97113 Monocytoid B-cell lymphoma, spleen
Lymphoplasmacytic lymphoma associated with a marginal zone lymphoma. Hematein-eosin. Diffuse infiltration by small lymphoid cells with a dark nucleus. At the periphery, a more pale area constituted by marginal zone cells, some with a monocytoid B cell morphology. Both cells belong to the same clone.

It remains unclear how to classify this case and why. For more information there are several textbooks of course, but some relevant references on each disorder would be very helpful. Only rarely are a few references given.

The quality of the images is overall quite good, although for some (rare) disorders a not very well handled specimen was all that was available. The quality of the images is dependent on the system used. I have tested the disk on several systems and some gave rise to problems in obtaining the correct colours. However, even on a notebook (with TFT screen) the picture was quite acceptable, though to obtain very detailed pictures with nuclear detail (important for some lymphomas) even an advanced high resolution screen was insufficient.

Who would benefit from this CD-ROM? The histopathologist who likes to work with atlases and computers who encounters an unusual spleen. He or she will need a textbook as well, to get information on differential diagnosis, clinical aspects, references, and so on.

J H J M VAN KRIEKEN

Book reviews

Inclusion-Body Myositis and Myopathies. Edited by V Askanas, G Serratrice, and W K Engel. (£80.00.) Cambridge University Press, 1998. ISBN: 0521 57105 7.

The sporadic form of inclusion body myositis is stated to be the commonest muscle disease to strike those over 50 years of age. A good multiauthored book on both hereditary inclusion body myopathies (h-IBM) and sporadic inclusion body myositis (s-IBM) would therefore be a welcome addition to the library of any department dealing with muscle biopsies. This book is a collection of reviews about IBM and is divided into six sections. The first section deals with comparisons (both pathogenic and pathological) between the hereditary IBM (h-IBM) and the sporadic forms (s-IBM) of IBM. There is extensive discussion of the diagnostic features on both light microscopy (including immu-

nohistochemistry) and electron microscopy. Other sections deal with IBM viewed from a historical perspective, and there are also separate sections examining in detail the clinical and pathological aspects of both s-IBM and h-IBM (including atypical cases as well as other conditions characterised by basophilic rimmed vacuoles). The penultimate section deals with the mitochondrial abnormalities seen in IBM. Finally there is a section on possible treatment strategies. While reviewing the book I was examining a biopsy of a patient with possible IBM who also had evidence of HTLV-I infection. Not only did this book discuss a previous case and provide a reference; it also provided possible pathogenic mechanisms. Most chapters are well written and throughout the book the index appears to be helpful. In addition, there are up to date references. The majority of the 100 photographs are of very good quality.

My main criticisms are somewhat trivial. Figure 1.1 is placed in chapter 3, which is rather irritating. In addition, I feel that some of the introductions to chapters are a little repetitive and would have benefited from some editorial pruning. In summary, this is a well written book which I would certainly recommend to all those clinicians, pathologists, and researchers with an interest in muscle diseases. Although not primarily intended as a pathological bench book it does have some very useful contributions to make for any pathologist struggling with a possible case of IBM.

A KING

Introduction to the Blood-Brain Barrier: Methodology, Biology and Pathology. Edited by W M Pardridge. (£85.00.) Cambridge University Press, 1998. ISBN: 0 52158124 9.

The anonymous preface to this book claims that "adequate knowledge of the blood-brain barrier forms an essential component in the complete understanding of a large proportions of medical disciplines," and laments general ignorance on the structure, function, and investigative techniques appropriate for this important structure. The book itself attempts to redress this problem. To what extent does it succeed? The answer is almost completely, as both the contents and scope of the book belie a mere "introduction." The book comprises 50 chapters by a leading international group of basic and clinical scientists (including several distinguished pathologists!) and is divided into five sections concerning the methodology appropriate for the study of the blood-brain barrier, its transport biology, with more specific sections on signal transduction and biochemistry, and finally pathophysiology in disease states. The last of these sections proved to be the most instantly appealing, with a wide ranging series of excellent contributions, from microvascular abnormalities in dementia to multiple sclerosis and cerebrovascular disease with particularly interesting contributions on infectious diseases including HIV, cerebral malaria, and bacterial meningitis. The first section on methodology, containing a discussion of the clinical applications of barrier function methodology using MRI and PET technology, was particularly interesting and informative. The book has been well edited and produced, with numerous illustrations in monochrome. The index is excellent and the chapters are well

referenced up to 1996, with a few references from 1997.

I would recommend this book as an essential purchase for a library in a medical school or hospital with a basic or clinical neuroscience department. Individual pathologists with an interest in the brain from a biochemical, microbiological, or neuropathological background may wish to explore the book further—it has been widely used by clinical and non-clinical staff, reflecting its broad appeal and the relative monopoly it enjoys in its chosen field.

JAMES IRONSIDE

TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumours (4th edition). Edited by P Hermanek, R V P Hutter, L H Sobin, G Wagner, C Wittekind. (£15.50.) Springer-Verlag, 1997. ISBN: 3 540 62704 9.

No doubt the staging of a malignant tumour in a surgical resection specimen looms high in the top 10 of least favourite tasks of the surgical pathologist. Many a sigh of frustration is heaved when that much desired 15th lymph node defies detection in the gastrectomy specimen. Don't we all prefer sitting at our microscope, diagnosing rare and interesting diseases at a glance, because we are so very clever?

Nonetheless, cancer staging is the most important single determinant of prognosis of a patient with a given type of malignant tumour. In most types of tumour, stage determines surgical curability, and within the groups of potentially surgically curable or irresectable disease, chances of survival are often directly related to tumour size and spread. As a consequence, the love's labour of minute examination and dissection of gross specimens looms equally high in the top 10 of our most important duties.

On our bookshelves and desks, our most important guide to standardising the staging of malignant neoplasms, the UICC "TNM Atlas" has, of course, been present from the publication of the first edition (1982) onwards. The fourth edition, which has recently become available and which contains a very large number of alterations, is of course indispensable! Who needs the advice of a reviewer? This is a booklet one simply cannot do without.

Therefore, rather than advising you to buy a copy, if you have so far omitted to do so, let me briefly eulogise and applaud, for congratulations and exclamations of admiration are in order. This is, indeed, an absolutely excellent little book. The text is precise, clear, and succinct (remember, you will not need the remark, repeated dozens of times, that "there should be histological confirmation of the disease," but there are others in the hospital, who will also be using the book, and for whom this remark is primarily intended) and the drawings are superb. As an extra, there is a very handy 24 page folder in which the criteria for each substage are summarised. All in all: a splendid book!

W J MOOI

Pathology of Occupational Lung Disease, 2nd edition. By A Churg and F H Y Green. (£72.00.) Williams & Wilkins Europe, 1998. ISBN 0 683 30386 4

The second edition of this classic book, largely written by two international experts in the field and with contributions by a further eight authors, many of whom are well known

experts themselves, offers a comprehensive and authoritative account of the morphology and pathophysiology of occupational lung disease. Important contributions on the clinical evaluation and on (American) legal aspects result in a broad perspective and make this book of interest also for others active in the management of patients suffering from these diseases.

The book provides a wealth of data, which are generally easily accessible through numerous tables and lists. Illustrations are also numerous and include a plethora of excellent micrographs of tissue sections, many chest radiographs, macroscopic specimen photographs, and scanning EM pictures and x ray spectra of a very large variety of inhaled dusts. The text is detailed, at times to such a degree that even the interested reader needs to make a conscious effort to finish reading the book in its entirety. Perhaps the layout of the book, which is a bit grey, and has a make up of text and tables which I personally consider rather uninviting, is partly to blame here. However, this should not interfere with our judgement of the essentials, to which these criticisms do not apply.

Pathologists with a special interest in lung disease should seriously consider buying this book. Basically, there is no competition: it is unique. One should, however, bear in mind that the large pulmonary pathology textbooks (Dail and Hammar, Spencer/Hasleton, Thurlbeck) also offer much detailed information on the pathology of occupational lung disease. Pathologists who do not have a special interest in this area may find that these more general texts are adequate for their requirements. Those, however, who wish to obtain a really detailed account of the pathology of this group of diseases and who are interested in the many additional bonuses of this text (chemical, clinical, mineralogical, forensic, legal) will not want to do without their personal copy of this extraordinary and outstanding book.

W J MOOI

Pathology of Viral Hepatitis. Edited by R D Goldin, H C Thomas, and M A Gerber. (£85.00.) Edward Arnold, 1998. ISBN: 0 340 59664 3

There are some excellent general liver textbooks on the market, some of which are quite slim, and suitable for those in training and also for the general pathologist dealing with the occasional liver biopsy or unexpected postmortem cirrhosis. Do we need specialised texts? If the answer is yes, the starting point has to be viral hepatitis, as discussed in this book. This is a slim and eminently readable volume with some complex molecular biology succinctly (and understandably!) explained. There are excellent chapters on pathogenesis and carcinogenesis which illustrate basic pathogenic principles in a far broader context, as does the chapter on the more specialised area of hepatitis in immunosuppressed patients. The chapter on uncommon viruses is one of the most exhaustive and up to date account I have seen. The addition of treatment responses is perhaps unexpected but very welcome, as many clinicians appear to expect considerable understanding, if not management advice, from their pathologist. Some niggles of discontent are the incredibly variable quality of the illustrations—virtually all purport to be H&E stained but the range is reminiscent of an armoury of special stains. The discussion on routine reporting of

chronic HCV infection could have been expanded, not least the pros and cons of routine scoring. I would have welcomed a few sentences on the historical aspects in the unravelling of the alphabet of hepatitis viruses.

These apart, I think there is much of interest to those in training, any pathologist wanting to have a broader grasp of the global problem of viral hepatitis, and also the interested clinician wishing to be involved in rewarding clinicopathological discussion.

SUSAN DAVIES

Notices

Gynecologic and Obstetric Pathology: 1999

April 5–9 1999

Boston, Massachusetts, USA

Directed by Robert E Scully MD, Robert H Young MD, and Christopher P Crum MD

The course is designed for pathologists and obstetrician-gynaecologists at resident and practitioner levels. Further details from: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston MA 02115; tel +1 617 1525; fax +1 617 432 1562; email: hms-cme@hms.harvard.edu

Urologic Surgical Pathology for the Practising Pathologist

May 7–9 1999

Cambridge, Massachusetts, USA

Directed by Robert H Young MD

The course provides a comprehensive review of urological surgical pathology with special attention paid to recent advances and newly recognized entities. Further details from: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston MA 02115; tel +1 617 1525; fax +1 617 432 1562; email: hms-cme@hms.harvard.edu

Correction

In the Leader "Classification of acute leukaemia: the need to incorporate cytogenetic and molecular genetic information" by B J Bain (vol 51, June, pages 420–3), the fusion gene in M3-like AML associated with the t(11;17)(q23;q21) is given incorrectly in the text. The correct fusion gene, PLZF-RAR α , is given in table 2.

Instructions for Authors

Papers for publication should be sent to the Editor, *Journal of Clinical Pathology*, BMA House, Tavistock Square, London WC1H 9JR (tel: 0171 383 6209/6154; fax: 0171 383 6668; email: jclinpathol@compuserve.com). Receipt of manuscripts will be acknowledged by the editorial office.

Submission of a paper will be held to imply that it contains original work not being offered elsewhere or published previously. Manuscripts should be prepared in accordance with the Vancouver style.¹ The Editor retains the right to shorten the article or make changes to conform with style and to improve clarity. All authors must sign the copyright form after acceptance.

Failure to adhere to any of these instructions may result in delay in processing the manuscript and it may be returned to the authors for correction before being submitted to a referee.

General

- Authors must submit four copies of the original manuscript typed in double line spacing. The journal is now produced electronically and revised manuscripts should be submitted as printed copy and on disk. A guide to submitting an article on disk will be sent when requesting a revision or on notification of an acceptance. Authors should not submit the original paper on disk.
- The names of the authors, with initials, should be followed by the name of the institution where the work was carried out. An indication of the position held by each author should be given in an accompanying letter to the Editor, and manuscripts should bear the name of one author to whom correspondence should be addressed. If available, a fax number and an email address should be supplied.
- Identifying information should not be published in written descriptions, photographs, or pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication; but patient data should never be altered or falsified in an attempt to attain anonymity. Informed consent should be obtained if there is any doubt. Masking the eyes in photographs of patients is inadequate protection of anonymity (for the full statement see the *BMJ*²).
- Authors should include the names and addresses of four experts whom the authors consider suitable to peer review their work.
- When submitting original manuscripts authors should send a copy of any of their other papers on a similar subject to assure the editors that there is no risk of duplicate publication.
- If requested, authors should produce the data upon which the manuscript is based for examination by the Editor.
- The number of authors should be kept to a minimum and should include only those who have made a contribution to the research: justification should be made for more than five authors. Acknowledgments should be limited to workers whose courtesy or assistance has extended beyond their paid work, and to supporting organisations.
- Sponsors of research must be declared.
- Authors should provide up to four keywords/phrases for the index.
- All measurements must be in SI units apart from blood pressure measurements, which should be in mm Hg, and drugs in metric units.

- Abbreviations should be used rarely and should be preceded by the words in full before the first appearance.
- In the statistical analysis of data 95% confidence intervals should be used wherever appropriate.
- Any article may be submitted to outside peer review and for statistical assessment.
- No free offprints will be provided; reprints may be ordered when the proof is returned.

Original articles

- Papers should be no more than 2000 words long and should report original research of relevance to the understanding and practice of clinical pathology. They should be written in the standard form: abstract; introduction; methods; results; and discussion.
- The journal uses a structured form of abstract in the interests of clarity. This should be short (no more than 250 words) and include four headings: *Aims*—the main purpose of the study; *Methods*—what was done, and with what material; *Results*—the most important results illustrated by numerical data but not *p* values; and *Conclusions*—the implications and relevance of the results.

Leaders/Editorials

- Leaders and Editorials are published by editorial invitation; unsolicited reviews or commentaries are unlikely to be accepted, though the Editor is always pleased to receive suggestions.

Short reports

- Single case reports of outstanding interest or clinical relevance, short technical notes, and brief investigative studies are welcomed and usually published in the form of a Short/Technical report.
- Length must not exceed 1500 words, including an unstructured abstract of less than 150 words, up to two figures or tables (or one of each) and up to 10 references. If more illustrations are required the text must be reduced accordingly.

Letters

- Letters must be typed in double line spacing, should normally be no more than 500 words, have no more than five references, and must be signed by all authors. Two copies should be provided.

Tables and illustrations

Tables should be presented separately in double line spacing without ruled lines; when presented on disk they should be in a separate file from the text.

- Letters and other marks which are to appear on the face of a photomicrograph should be made on a photocopy: they will be added in the Journal style in the editorial office when the manuscript is accepted.
- Legends for illustrations should be typed with double spacing on a separate sheet. The staining technique used should be stated. Magnifications should be given for electron micrographs but not for light micrographs except in cases where this is important.
- Photographs and photomicrographs should be on glossy paper for half tone reproduction. The printing process requires that prints are unmounted and unbacked, and of high quality, with full tonal scale. Illustrations that will not reproduce well will be returned and this may delay publication. Areas in which tissue does not appear ("background") should be as near white as possible. Three sets of prints must be supplied with each manuscript. Only salient features should be included to preserve detail.

- Colour reproduction of figures in papers is encouraged and is heavily subsidised by the Journal. Advice on costs and material to be submitted for colour work should be sought from the editorial office. The journal can accept colour images as TIFF files in the following media: zipped or unzipped files on floppy disks, compact disks, or optical disks. A hard copy of the image should be provided.
- If any tables or illustrations submitted have been published elsewhere, written consent to republication should be obtained by the author from the copyright holder (usually the publisher) and the authors. A copy of the letter giving consent must be included.

Descriptions of laboratory methods

- When a manufacturer's method is used in a study with a particular item of equipment or kit of reagents, the source of this method and reference to the scientific literature on which it was based should be given. Authors might consider it courteous to inform manufacturers that an article assessing their product has been submitted for publication.
- For quantitative methods, information on the sensitivity, precision, and accuracy in the hands of the authors should always be provided. When a well recognised method is used, these requirements could be met simply by providing the references to the methodology and discussing the performance in a recognised current quality assurance scheme. Modifications to methods that have not been previously published should be detailed in the text and supported by evidence of their efficacy.
- It is useful to indicate, either from personal observations or by reference, the working range of an assay and the normal reference range when it is used on samples from humans. When information is expressed as mean $\pm$ 2SD, the distribution of the range (normal, skew, or logarithmic) should be stated.

References

- References must be numbered in the order they appear in the text and include all information (Vancouver style; references with more than three authors should give only the first three followed by *et al*):
 - 1 Fletcher CDM, McKee H. Sarcomas - a clinicopathological guide with particular reference to cutaneous manifestations. I. Dermatofibrosarcoma protuberans, malignant fibrous histiocytoma and the epithelial sarcoma of Enzinger. *Clin Exp Dermatol* 1984;9:451-65.
 - 2 Washington JA. Conventional approaches to blood culture. In: Washington JA, ed. *The detection of septicemia*. West Palm Beach, Florida: CRP Press, 1978:41-87.
- References in the text should be identified by arabic numerals in brackets—for example, [1] [2].
- Information from manuscripts not yet accepted, or personal communications may be cited only in the text and not included in the references. References are not checked by us; authors must verify references against the original documents before submitting the article.
- 1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *BMJ* 1991;302:338-41.
- 2 International Committee of Medical Journal Editors. Protection of patients' rights to privacy. *BMJ* 1995;311:1272.

Manuscript checklist:

- Is there an abstract?
- Are the abbreviations spelt out?
- Are the measurements in SI units?
- Are the references in Vancouver style?

Revised January 1999