TTT and CNV

Editor,—The article by Newsom et al. on transpupillary thermotherapy (TTT) raises more questions than it is able to answer. Although TTT is definitely a method which seems to show a certain efficacy in occult choroidal neovascularisation (CNV) and thus warrants further investigation, we must take issue with the authors’ conclusions concerning its use in classic CNV.

The authors state that 78% of the predominantly occult membranes and 75% of the predominantly classic membranes were closed as a result of TTT. This seems to have, in particular because only 24 of 44 patients had angiographic follow up, which is the criterion for determining CNV closure. Furthermore, how is the irradiance used to be understood? On the one hand, the authors state—without providing any evidence—that smaller lesions need a higher irradiance, but on the other hand larger lesions—which are presumably requiring only lower irradiance—received confluent treatment with several overlapping spots of TTT, which implies that the amount of irradiance necessary on a cumulative basis might be similar to the irradiance needed to treat smaller lesions!

The authors also state that TTT compared well with the results of the TAP study group for predominantly classic CNV. They imply that their results are better than those of their cases which showed stabilised vision (nine eyes with a visual loss of less than 3 lines) can be compared with the TTT results at 1 year (246 eyes with a visual loss of less than 3 lines). Firstly, the TTT study was a small, single-centre controlled multicentre study performed on 609 patients which, without doubt, has a much higher statistical value than the present study with 12 predominantly classic membranes.

Secondly, Newsom et al. cannot compare their visual results adequately as the TTT study used a standardised testing procedure employing Early Treatment for Diabetic Retinopathy charts as well as masked and certified vision examiners in comparison to the Snellen values mentioned in the above study, which were obtained by unmasked, and therefore biased, examiners. Furthermore, on closer examination of the results, not one of the 12 patients showed any improvement for visual acuity at 12 months after TTT; in comparison, in the TAP study 5.7% of all verteporfin treated patients showed an improvement of more than 15 letters (approximately 3 lines) at the 12 months visit.

While we recognise the potential of the TTT method, we would like to warn against extrapolating the data of this study in a relatively small patient cohort to make conclusions on the efficacy in treating classic CNV.

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Further pathophysiological insights into age related macular degeneration

Editor,—We read with great interest the excellent editorial by Ciulla,1 which describes pathophysiological paradigms for age related macular degeneration (ARMD) and the development of choroidal neovascular membranes (CNVM). We were particularly pleased to note that Ciulla considered that “whatever the initial stimulus for CNVM formation, it is clear that angiogenic growth factors are ultimately involved.” Furthermore, he observed that primary vascular changes in the choroid may also be responsible.

In light of these observations, we had hypothesised a relation between abnormal vascularisation (angiogenesis), haemorrhheological factors, and endothelial dysfunction in patients with ARMD. We felt that abnormalities in the systemic and choroidal vasculature, may relate to the release of angiogenic factors and subsequent proliferation of choriocapillaris through a defect in Bruch’s membrane in susceptible individuals. To investigate this hypothesis further, we recently reported a cross sectional study2 of patients presenting with ARMD and measured plasma levels of VEGF (an index of angiogenesis), haemorrhheological factors (fibrinogen, plasma viscosity), and von Willebrand factor (an index of endothelial damage/dysfunction) from these patients. Median plasma VEGF (225 ± 195 pg/ml, p = 0.0004), mean von Willebrand factor (124 ± 99 IU/ml, p = 0.0004) levels were higher in ARMD patients compared with healthy controls. Mean plasma fibrinogen and plasma viscosity levels were also higher in the patients (both p < 0.0001). Our observations would therefore suggest further pathophysiological insights into ARMD, with an association between this disorder and markers of angiogenesis (VEGF), haemorrhheological factors, haemostasis, endothelial damage/dysfunction.

Rather than the existence of individual pathogenic processes,1 perhaps a close interaction between abnormal angiogenesis and the components of Virchow’s triad for thrombogenesis may contribute to the pathogenesis of ARMD and the development of CNVM. Indeed, the availability of a blood marker for ARMD could have potential value, as measurement of such a marker could be a non-invasive way of perhaps predicting individuals at high risk of developing ARMD. We have recently applied such a concept (that is, a blood marker to monitor the progression of eye disease) in a study of plasma VEGF in diabetic proliferative retinopathy, where the high plasma levels were normalised at the 4 month follow up, after treatment with panretinal laser photocoagulation.1

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A new colour vision arrangement test to detect functional changes in diabetic macular oedema

Editor,—We refer to the interesting article by Maar et al. published in the BJ O. The authors should be congratulated for presenting a new method of screening for diabetic macular oedema. However, the paper contains some statistical errors, and we believe the results can be interpreted in other ways.

Firstly, there are some internal inconsistencies with some of the results reported in the paper. Specificity of the Mollon T test (score >1) for detecting clinically significant macular oedema (CSMO) was reported as 88.9% and specificity was reported as 99.3%. These values could not possibly be obtained with the subject numbers specified, as we believe they have been erroneously published.

From other data provided by Maar et al. we are able to reconstruct values for these statistics. The mean Mollon T score and SD for non-CSMO patients implies 28 non-CSMO patients passed the test (true negatives) and one failed (false positive). The number of eye with CSMO was 10 and there were 29 eyes without CSMO. Table 1 can be constructed.

It is apparent from this table that the sensitivity of the test is 8/10 or 80.0% and not 88.9% and the specificity of the test is 28/29 or 96.6% and not 99.3% as quoted in the paper.

These values are of course only estimates of the true specificity and sensitivity and are based on fairly small numbers of subjects. It is good practice to report such figures accompanied by the 95% confidence intervals of these proportions.3 For the purpose of assessing the practical value of a screening tool the lower limit or 5% confidence limit of the proportion is of clinical interest because it reflects the sensitivity and specificity of this test in the “worst” scenario. Various methods could be used to calculate or approximate such an interval. For example, using the Wilson’s score method incorporating continuity correction,4 the 95% CI of the sensitivity is 44.2%–99.1% and the specificity is 80.4%–99.8%. The clinician will be quick to notice the wide confidence interval for the sensitivity. This is an inherent problem in such studies, where the absolute number of cases of CSMO is relatively small. Thus it is possible that the Mollon test is only a mediocre indicator of the presence of CSMO and the high sensitivity was obtained by chance.

The authors have mentioned that “the Mollon-Reffin test was a better predictor than the other tests because it had a lower false
positive rate (1 − specificity)" in the legend to the Figure 3 of their paper. It is quite possible that this entry is pointing that practical advice on coping with low or reduced vision is not included as it could be assumed that many people buying this book would be looking for this type of information. Instead a considerable portion of the book is taken up with accounts of famous people and their eye problems. Although very interesting to read, the usefulness of its inclusion is debatable, especially when considering the likely audience. The book concludes on a slightly political note with a discussion of world blindness and the issue of training overseas ophthalmologists in the United Kingdom where they may not receive an experience appropriate to their local population. A brief overview of future developments in eye care is outlined and an extensive glossary, further reading list, and addresses of useful agencies complete the volume.

I found the book an interesting and enjoyable read. It will probably appeal more to healthcare professionals interested in a career in ophthalmology than members of the general public who may require more practical information. In conclusion, I am still waiting for my colleagues to comment on the sudden improvement in my ophthalmic knowledge; however, I was able to correctly answer that Nelson was blind in his right eye at the hospital quiz night!

HELEN JULIAN


Scleritis is part of a book series Fundamentals of Clinical Ophthalmology to update general ophthalmologists in specific areas and also, most probably, for ophthalmologists in training. Each book has been edited by a specialist, in this case Peter McCluskey in Australia, with expertise in each chapter from individual authors.

Overall, I think the book is good and achieves its aim if directed to the ophthalmic trainee as an introduction to scleritis and its differential diagnosis. However, as a result of frequent collating problem of multi-author books, it does not read fluently and is sometimes frustrating. This, however, should not discourage any trainee reading this book. It takes the reader logically through the anatomy and biochemistry of the sclera, highlighting reasonably up to date knowledge on cellular components and extracellular matrix and their steady state in relation to matrix metalloprotease and corresponding tissue inhibitors. If we were then to read chapter 3, which is the pathology of scleritis, it would have been more rewarding to have some link between the basic science and the pathology. That is the relation of the inflammatory response to the breakdown of the steady state and the extracellular matrix. As it stands both chapters are excellent in their own right, but do fail to be linked.

The rest of the book is clinical with good figure representation of both anterior segment and posterior segment disease. The reading is easy and encourages constant thinking of the differential diagnosis.

There are also chapters on the investigation and management of scleritis. Again these chapters might have been more informative if they were linked to the overall cell biology, biochemistry, and pathology so as to educate us in why we may be undertaking such investigations. There is a lack of explanation as to the serology assays performed to look for antinuclear antibodies or ANCA and its specific antigenic components. I think this slightly disjointed approach may still leave the ophthalmic trainee confused regarding what is being present. The section on treatment is well presented and highlights the requirement for pretreatment assessment, prevention of side effects, and overall management of patients on immunosuppression.

Overall, the book is an enjoyable read and certainly useful for the trainee. For a small book it would have benefited from greater editorial licence to merge the information in all the chapters more coherently.

ANDREW DICK


This is a concise, well-written reference for students, residents, and clinicians interested in gaining a better understanding of electrophysiologic tests of the visual system.

The book is divided into five chapters, each devoted to one of the following electrophysiologic tests: the electroretinogram (ERG), the electro-oculogram (EOG), the focal and multifocal ERG, the pattern electroretinogram (PERG), and the visual evoked potential (VEP). Each chapter begins with a description of the physiology underlying each test and the specific techniques used for responses. The chapters then include examples of the results commonly seen in different hereditary and acquired disorders, with accompanying fundus photographs in many cases. The book also explains the molecular basis of diseases which have been genetically characterised.

The authors have made significant improvements to the second edition of this book. The first edition included only a page each on focal and pattern ERG. In response to the development of the multifocal ERG, the current edition devotes an entire chapter to both the focal and multifocal ERG. The multifocal ERG holds promise in early diagnosis of many diseases, including glaucoma, and both of these techniques will probably become increasingly important in future investigations of macular disorders. The section on pattern ERG has been greatly expanded and includes a lucid description of clinical applications for which the PERG is useful. In addition, the description of the PERG is integrated with the section on VEP, explaining how these tests can best be used to differentiate between macular and optic nerve dysfunction. The authors have included numerous clinical photographs and examples, making the text particularly relevant and easy to comprehend.

This textbook successfully meets the authors’ stated objectives to “provide a background on the physiology that underpin the measurement of various electrophysiologic components, describe the clinical phenotypes of various disorders . . . for which electrophysiologic investigations are of potential use, discuss the various electrophysiologic findings . . . anticipated in different disorders . . .” and (to) clarify how the enlightened use of various procedures can be of value in the diagnosis and monitoring of patients with hereditary or acquired disorders of the retina,

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optic nerve, and visual pathway.” It is a valuable reference for anyone interested in obtaining a clear understanding of the objective measurement of visual function in a variety of diverse clinical disorders.

JACQUES L DUNCAN

NOTICES

Affordable eye care

The latest issue of Community Eye Health (37) discusses affordable eye care. For further information please contact Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL. (Tel: (+44) (0) 20-7608 6909/6910/6923; fax: (+44) (0) 7250 3207; email: eyeresource@ucl.ac.uk) Annual subscription £25. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medicines, Equipment, Instruments and Optical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (Tel: (+44) (0) 20-7608 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, will be sending volunteer surgeons to India early in 2001. Details can be found at the charity website at www.secondsight.org.uk or by contacting Dr Lucy Mathen (email address lucymathen@yahoo.com).

American Institute of Ultrasound in Medicine—Millennium Ultrasound Course Series

A course entitled “Obstetrical and Gynecological Ultrasound” will be held in New York City, NY, on 24–26 August 2001. Further details: Stacey Bessling, Public Relations Coordinator, AIUM, 14750 Sweitzer Lane, Suite 100, Laurel, MD 20707-5906, USA (tel: 301-498-4100; email: sbessling@aium.org).

14th World Congress of the International Society for Laser Surgery and Medicine

The 14th World Congress of the International Society for Laser Surgery and Medicine is to be held on the 27–30 August 2001 at Sri Ramachandra Medical College and University Hospital, Chennai, India. The American Society of Lasers in Medicine and Surgery has indicated that it will designate the 14th World Congress of ISLSM as its society’s co-sponsoring meeting. A pre-conference course and separate sessions in ophthalmology will be held as a part of this international meeting. Further details: Dr B Krishna Rau, President, 14th World Congress of the International Society for Laser Surgery and Medicine, Department of Surgery, D2 Ward, Sri Ramachandra Medical College and Research Institute, Porur, Chennai - 600 116, India (tel: 91-44-4765856, 4768027-28, 8527776, 8594804; fax: 91-44-8594578, 4767008; email: krishnar@giiasm01.vsnl.net.in and website: www.medindia.net/islsm2001).

31st Cambridge Ophthalmological Symposium

The 31st Cambridge Ophthalmological Symposium will be held 3–5 September 2001 at St John’s College Cambridge. The subject is Retinal Detachment. Further details: COS Secretariat, Cambridge Conferences, The Lawn, 33 Church Street, Great Shelford, Cambridge CB2 5EL, UK (tel: 01223 847464; fax: 01223 847465; email: b.ashworth@easynet.co.uk).

1st Asia Pacific Forum on Quality Improvement in Health Care

The 1st Asia Pacific Forum on Quality Improvement in Health Care will be held from 19–21 September 2001 in Sydney, Australia. Presented by the BMJ Publishing Group (London, UK) and Institute for Healthcare Improvement (Boston, USA), with the support of the Commonwealth Department of Health and Aged Care (Australia), Safety and Quality Council (Australia), NSW Health (Australia) and Ministry of Health (New Zealand). Further details: quality@bma.org.uk; fax +44 (0) 7383 6869.

41st St Andrew’s Day Festival Symposium on Therapeutics

The 41st St Andrew’s Day Festival Symposium on Therapeutics will be held on 6–7 December 2001 at the Royal College of Physicians of Edinburgh. Further details: Ms Eileen Strawn, Symposium Co-ordinator (tel: 0131 225 7324; fax: 0131 220 4393; email: e.strawn@rcpe.ac.uk; website: www.rcpe.ac.uk).

4th International Conference on the Adjuvant Therapy of Malignant Melanoma

The 4th International Conference on the adjuvant therapy of malignant melanoma will be held at The Royal College of Physicians, London on 15–16 March 2002. Further details: Conference Secretariat, CCI Ltd, 2 Palmerston Court, Palmerston Way, London SW8 4AJ, UK (tel: + 44 (0) 20 7720 0606; fax: + 44 (0) 20 7720 7177; email: melanoma@onfcomm.co.uk: website: www.onfcomm.co.uk/Melanoma).

XXIXth International Congress of Ophthalmology

The XXIXth International Congress of Ophthalmology will be held on 21–25 April 2002 in Sydney, Australia. Further details: Congress Secretariat, C/- ICMS Australia Pty Ltd, GPO Box 2609, Sydney, NSW 2001, Australia (tel: +61 2 9241 1478; fax: +61 2 9251 3552; email: ophthalm@icmsaust.com.au; website: www.ophthalmology.aust.com).

International Society for Behçet’s Disease

The International Society for Behçet’s Disease was inaugurated at the 9th International Congress on Behçet’s Disease. Professor Shigeaki Ohno represents the ophthalmology division (Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Sapporo, Japan: tel: +81-11-716-1161 (ext 5944); fax +81-11-736-0952; email: sohno@med.hokudai.ac.jp). The 10th International Congress on Behçet’s Disease will be held in Berlin 27–29 June 2002. Further details: Professor Ch Zouboulis (email: zoubbere@zedat.fu-berlin.de).