Allo-limbal transplantation in patients with limbal stem cell deficiency

Editor,—We read with great interest the recent article by Dua and Azuara-Blanco, describing the use of a new immunosuppressive agent FK-506 in patients achieving allo-limbal transplantation. The authors also describe a modified surgical approach. Although FK-506 appears to be a safe and effective treatment option in these patients, the follow-up is longer than 1 year in only two of the six patients. These two patients experienced a limbal graft rejection episode in the postoperative period and we therefore feel that longer follow-up is necessary before the efficacy of FK-506 can be established. It would also be interesting to compare FK-506 with cyclosporin A in future studies to assess the relative safety and efficacy of the two drugs.

The potential advantage of HLA matching was cited in the discussion by the authors. Although a recent study indicates that HLA matching may not totally obviate the need for immunosuppression, we believe that it will allow reduction of dosage and or duration of treatment with these potentially toxic drugs. In countries with a paucity of corneal donor tissue, where even hepatitis B positive donor tissue is sometimes used, live related donor tissue is a valuable source of stem cells. However, the modified surgical technique described by Dua and coworkers would not be suitable for live related transplantation, as extent of tissue excision would prove detrimental to the donor eye.

We concur with the authors that adequate reconstitution of the ocular surface microenvironment is critical to the success of limbal transplantation procedures. We feel that the use of amniotic transplantation would have helped achieve this goal during surgery. We feel also that there are still many unanswered questions in limbal grafting for ocular surface reconstruction including the best surgical approach, the optimum amount of limbal stem cell transfer, the ideal microenvironment for survival of the transplanted limbal cells, the usefulness of HLA matching, and the role of newer immunosuppressive agents like FK-506. We suggest that before new information is available, the use of HLA matched live related limbal tissue, combined with amniotic membrane transplantation and long term immunosuppression of the patient would be a viable option in the treatment of advanced ocular surface disease.

Financial and proprietary interest: Nil.

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Reply

Editor,—The authors have commented on the use of FK-506 as an immunosuppressive agent in patients with allo-limbal transplantation. Our experience with tacrolimus (FK-506, Prograf, Fujisawa Ltd, London) has been very good thus far. Since publication of the preliminary experience with one drug, we have been followed for over 1 year now. Attempts to reduce FK-506 (with a view to stopping treatment) have resulted in rejection reactions in two patients (one of which is described in the paper), but resolved on increasing the dose. Young et al have expressed concern over the two patients who had developed rejection while on treatment with FK-506. They have underappreciated the superior efficacy of the drug. While we agree that the efficacy of this drug does need to be evaluated over a longer period of time, it needs to be emphasised that in one of these patients, where the reaction was observed 4 months after transplantation, it corresponded with a very low trough level of the drug and responded to an increase in the drug dose. The second patient experienced rejection after stopping the drug, 13 months post-surgery and responded to reinstating FK-506 therapy. Thus, in both instances it was not the efficacy of the drug that was in question. A third patient (patient 3) had a similar experience on reducing drug dosage 6 months post surgery, emphasising the need for long term treatment with immunosuppressive agents.

We have also used this drug in the treatment of several “high risk” corneal transplants with excellent results (unpublished observations). Young et al have suggested a prospective comparison of FK-506 with cyclosporin. Our preliminary experience with the two drugs, in the treatment of posterior uveitis, showed some advantages of FK-506 over cyclosporin. In theory, however, both drugs should be effective and should perhaps be used in a complementary manner, if onset of side effects with one drug dictate cessation of therapy.

There is no doubt that the use of HLA matched material from living related donors will provide the advantages of “fresh” tissue and “matched tissue”. Unfortunately, however, not all patients have willing, living related donors. When cadaveric limbal allografts have to be used, the advantage of “freshness” is preferred over the potential benefit of a “close match” and the associated delay. Tsunoda et al have demonstrated the viability of limbal stem cells (SCs) harvested from C-S rims stored in Optisol GS for up to 5 days. The surgical method described by Dua and Azuara-Blanco positions the limbal allograft posterior to the anatomical limbus in the host. The 150 µm thick donor limbal graft can result in a stepped ocular surface, which can be detrimental to long term survival of the transplanted epithelium. Splitting the ring of limbal tissue and interposing a separate piece of corneal stroma or limbus theoretically allows chinks in the reconstructed limbal barrier. Finally, the technique described does not allow sufficient flexibility in titrating the thickness of the donor tissue used. Since an important goal of ocular surface reconstruction is to achieve a smooth surface, surgeons often have to use donor limbal grafts of differing thickness in individual recipient eyes. This flexibility is possible if the limbal graft is fashioned from a C-S rim. In eyes undergoing combined penetrating keratoplasty and limbal tissue reconstruction, applying the donor limbal and corneal graft without an intervening gap is preferable.

The surgical failure in case 4, who underwent limbal allograft transplantation 3 weeks after severe alkali burns, corroborates our

This figure is admittedly empirical, and further experience with this technique is needed for more definite information.

Finally, in the last paragraph, Young et al contrast themselves by, firstly, rightly pointing out the present limitations of limbal transplantation procedures and secondly by making a very definitive statement in proposing use of HLA matched live related tissue, combined with amniotic membrane transplantation and immunosuppression as a viable option. Amniotic membrane transplantation combined with limbal transplantation has been shown to give good results but there is no evidence to show that it is superior to any technique that does not employ the use of this membrane. Controlled randomised studies are also needed to sort out this issue.

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Limbal allografting using FK-506

Editor,—While we agree with Dua and Azuara-Blanco that the use of “fresh” donor eyes for limbal transplantation is preferable, social and surgery scheduling limitations may force surgeons to use stored corneoscleral (C-S) rims. Tsunoda et al have demonstrated the viability of limbal stem cells (SCs) harvested from C-S rims stored in Optisol GS for up to 5 days. The surgical method described by Dua and Azuara-Blanco positions the limbal allograft posterior to the anatomical limbus in the host. The 150 µm thick donor limbal graft can result in a stepped ocular surface, which can be detrimental to long term survival of the transplanted epithelium. Splitting the ring of limbal tissue and interposing a separate piece of corneal stroma or limbus theoretically allows chinks in the reconstructed limbal barrier. Finally, the technique described does not allow sufficient flexibility in titrating the thickness of the donor tissue used. Since an important goal of ocular surface reconstruction is to achieve a smooth surface, surgeons often have to use donor limbal grafts of differing thickness in individual recipient eyes. This flexibility is possible if the limbal graft is fashioned from a C-S rim. In eyes undergoing combined penetrating keratoplasty and limbal tissue reconstruction, applying the donor limbal and corneal graft without an intervening gap is preferable.

The surgical failure in case 4, who underwent limbal allograft transplantation 3 weeks after severe alkali burns, corroborates our

4 Dua HS, Azuara-Blanco A. Autologous limbal tissue transplantation in patients with unilateral corneal stem-cell deficiency. Br J Ophthalmol (submited)

recent report on the optimal timing of limbal transplantation after ocular surface burns. We feel that complex procedures such as limbal autografting or allografting are best performed after resolution of ocular surface inflammation and limbal revascularisation. While limbus tears is beneficial, ostensibly by providing biologic factors promoting epithelial health, corneal immunoglobulin deposition has been reported in a patient with persistent epithelial defect.

Four of the eyes in this report have a follow up of less than 1 year. Both eyes with follow up greater than 1 year experienced a graft rejection episode—during FK-506 therapy in one eye and after cessation of the drug in the other eye. This emphasises our limited understanding of the immunology of this procedure. Despite the initial encouraging report by Tan et al., our experience in a larger cohort with longer follow up, indicates that HLA matched limbal transplants from live related donors have poor long term survival, in the absence of systemic immunosuppression. We thus, agree with Dua and Azuara-Blanco that cadaver limbal transplantation offers the advantages of longer term survival, and is probably the procedure of choice despite the need for systemic immunosuppression of the recipient. A controlled clinical trial is difficult in the UK for instance, and reports like that of Dua and Azuara-Blanco are required to improve our understanding. We congratulate them on their use of FK-506 in limbal allografting.

Reply

Editor,—Rao et al have raised several issues with regard to limbal stem cell transplantation. The use of fresh versus preserved donor tissue remains unresolved. Empirically it is generally considered that fresh limbal tissue is better than stored. Storage conditions vary in different countries. In the UK for instance, by far the largest supply of donor material is stored in organ culture medium (Eagle’s MEM) with dextran added to deturgesc the tissue before use. This material has proved to be excellent for corneal transplantation (up to 4 weeks in storage) but has not been used for allo-limbal transplantation. Although corneal epithelial cell cultures can be derived from such donor rims, its efficacy as a source of limbal stem cells remains to be tested. The thickness of 150 µm includes 50 µm or more of limbal epithelium. The thickness of stromal tissue is therefore less than 100 µm. This is largely to facilitate handling and suturing of tissue. In our experience, the development of a “space” by the limbus was not an issue. In fact, over a period of several months, the tissue thinned and merged imperceptibly with the host. The “long term survival” of the epithelium was never compromised by the thickness of the donor limbus. The titration of donor tissue thickness is only relevant if a recipient bed is being fashioned to receive the donor tissue. This is often the case in auto-limbal transplantation. Placement of the donor limbus posterior to the “perceived” anatomical limbus of the host (often it is not possible to absolutely certain where the original limbus of the host is), has the advantage of allowing use of a wider limbal rim, to include limbus and peripheral cornea. “Transient failure” have been reported to be present in the peripheral cornea. Posterior placement also makes it technically easier to perform a corneal graft should one be required at the time.

The risk of introducing “chinks in the limbal barrier”, allowing ingress of conjunctival epithelium, is only theoretical as the authors themselves have stated. The use of a “spacer” or an extra bit of limbus from the other donor eye has proved to be quite successful. Even if a complete donor limbal ring is used, it is important to watch the healing conjunctival epithelium from the recessed conjunctiva. At times, although the ring may be complete, the underlying limbal epithelium may be missing in sectors. Conjunctival epithelium can cross over such a defect and encroach on to corneal surface. In such a situation, the principles laid down by Dua should be employed in the management. We agree with the authors that the chances of failure are high when allo-limbal transplantation is undertaken during the acute stages of a chemical insult. This is particularly relevant when living related donor tissue is available. Such material must be used as soon as possible, and after the acute inflammatory process has subsided. If limbal transplantation is considered essential in the early stages, serious consideration must be given to use of cadaveric donor tissue only.

Our experience with tacrolimus (FK-506, Prograf, Fujisawa Ltd, London) has been very good thus far. Several of our patients have been followed for over a year now. Attempts to reduce FK-506 (with a view to stopping treatment) have resulted in rejection reactions in two patients (one more since publication of the paper), but resolved on increasing the dose. In one patient where a rejection reaction was observed 4 months after transplantation, it corresponded to a very low trough level of the drug. We have also used this drug in the treatment of uveitis and several “high risk” corneal transplants with excellent results (unpublished observations). There is no doubt, like the authors have mentioned, that the therapy has to be continued long term.

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Anniotic membrane transplantation in ophthalmology (fresh v preserved tissue)

Editor,—Research on amniotic membrane transplantation in conjunctival and corneal disorders has been gaining popularity for the past 5 years.1 ‘Though the concept is as old as six to twelve centuries, it has recently become more popular owing to unmentioned/unidentified factors.’ In 1996, we performed our first amniotic membrane transplant following surgery for recurrent pterygium with successful results. The procedure was described by Tseng et al in 1998.2 We followed the method of preparation of the graft as mentioned by Sorsby et al in 1947.3 We are strictly following the conventional method of tissue harvesting and preservation for clinical use.4 However, we conducted a small study in six monkeys by using fresh amniotic membrane in six eyes, and in the contralateral eyes preserved (−80°C) amniotic membrane (control) was used. Tissue harvesting was from elective caesarian section delivery. Processing of the tissue was by the conventional procedure followed worldwide in both the groups. An intentional 7 × 7 × 0.2 mm anterior keratectomy was made in all eyes. In one eye freshly obtained amniotic membrane was transplanted, while in the fellow eye −80°C preserved tissue was transplanted after opening the first eye. The eyelids were closed for 2 weeks. All the animals received intramuscular antibiotics for 1 week and intramuscular dexamethasone and ceftriaxone for 2 weeks. The eyes were opened after 2 weeks. All the defects were healed and the corneas looked normal. From our small study it was evident that there was no difference in healing irrespective of method of preservation. However, to date no report has appeared on utilisation of freshly prepared amniotic membrane tissue transplantation. Though we routinely transplant amniotic membrane using the conventional method of preserved tissue, I would like to know the experience of other corneal surgeons who perform the procedure frequently, about the possibility of using fresh tissue clinically. I strongly feel that the procedure of amniotic membrane transplantation in a very safe, simple, and satisfactory method for treating conjunctival and corneal disorders; it can be practiced by all corneal surgeons, even those who do not have access to −80°C facility.

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References


Reply

EDITOR—Dr Panda’s letter essentially asks the question whether fresh amniotic membrane would be as good as preserved amniotic membrane. An amniotic membrane may act as a biological bandage, as a basement membrane (substrate) transplant, or via several favourable growth factors and cytokines that promote healing and epithelial cell migration. If the last of these mechanisms of action of the membrane is important, then theoretically, fresh membrane should work better than a preserved membrane. There is, however, no hard evidence to support this view yet. The experiment on monkeys, quoted in the letter by Dr Panda, suffers from the drawback, as do several published papers on use of amniotic membrane, of having no controls. It is very possible that the experimental epithelial defects created in healthy corneas of monkeys would have healed just as well without the use of either fresh or preserved membrane. Could it be that the monkeys would have a very favourable influence on corneal epithelial wound healing.

The issue, whether fresh is as good as (or better than) preserved, is somewhat sidelined by the risk of HIV infection. One of the main reasons for using preserved tissue is to enable one to perform a test for HIV infection, on the donor, at the time of harvesting the membrane and 6 months later, to cover the window period. As one harvested membrane can be used for several recipients, there is a risk of widespread infection in case of contamination. For this reason and other issues related to amniotic mem- brane transplantation, we would like to draw attention to the review by Dua and Azuara-Blanco.

Ocular abnormalities in a cohort of children born prematurely: effects of selection bias and possible confounding

EDITOR—Studying children born prematurely, Pennefather and colleagues1 showed that the prevalence of several ocular abnormalities at the follow-up examination at 2 years differed significantly between children who belonged to families who attended follow ups as a routine (group 1) and those who were classified as very reluctant for assessment (group 3). These differences were of relatively high magnitude, with relative risks (actually odds ratios) varying from 5.54 for strabismus to 10.91 for cicatricial retinopathy of prematurity. The authors claim that they used multiple logistic regression in their statistical analysis, but if the figures shown in their study are adjusted odds ratios they are, according to my calculations, identical to the crude odds ratios, which means that there were no confounders to any of the studied associations. This apparently contradicts the findings of the study of Campbell and colleagues2 quoted by the authors, that level of prematurity of the children and age and marriage status of the mothers were correlated with non-attendance. If these variables are also associated with the ocular abnormalities of Pennefather et al’s study, and not intermediate variables between the exposures and outcomes of interest, they are confounders, and should have been adjusted for in the multivariate analysis. This point needs further exploration.

Very interesting was the finding that the overall prevalence of abnormalities was similar between the total cohort (13.4%) and group 1 (11.3%). This small difference is explained because the proportion of losses to follow up that would have occurred under routine conditions was relatively small (9.5%), and did not have an important impact. It is an empirical demonstration that in cohort studies, for obtaining valid relative risk estimates it is very important to keep losses to follow up to a minimum, thereby minimising the role of selection bias.

Reply

EDITOR—We thank Dr Hollo for his interest and comments. Our results do show a higher value for the mean total thickness of the retinal nerve fibre layer (RNFL) in the macular hole group but we did not suggest in any way a statistical or clinically significant differ- ence between the two groups. We attempted to explain the apparently thicker peripapillary nerve fibre layer in macular holes on the basis of previous and relevant observations made by different authors. These include the presence of intraretinal fluid around the hole3 and vitreous traction on Henle’s fibre layer.4 On the other hand, we have stated that our controls were matched to the macular hole patients for age, sex, and side of the affected eye. The mean age (73.1 years) and the standard deviation (7.92) are exactly the same for both groups. Dr Hollo’s suggestion that the macular hole group is more heterogeneous on the basis of a different standard deviation value is therefore not valid. Although the number of subjects in our study is small, our data seem to suggest that the higher standard deviation value in the macular hole group might be related to alterations associated with long standing macular holes.

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BOOK REVIEWS

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This hardback full colour photographic atlas is the first of a three volume series of atlases from the renowned ocular oncology service at Wills Eye Hospital, Philadelphia. The format is appealing with a left hand page of succinct text on each condition with choice references. The facing page is a plate of colour photographs, including clinical photographs, intraoperative photographs, radiographs and photographs of gross pathological specimens, and photomicrographs. Full colour drawings, 18 in total, 4 of surgical techniques are also presented.

This atlas is comprehensive in its coverage with 95 different disease entities of the eyelids and conjunctiva described and illustrated. These include common and important diseases such as malignant melanoma and basal cell carcinoma as well as less common entities such as phacomatosi choristoma. The contents are organised into 25 chapters, the first 15 of which are lesions of the eyelids with the remaining 10 (Part II) covering the conjunctiva. Within each part, tumours are logically grouped according to patterns of differentiation/presumed histogenesis. Therefore, for the eyelids, separate chapters exist—for example, for tumours of the epidermis, sebaceous glands, sweat glands, melanocytes, neural tissues, vascular tissues, etc. A strength is the inclusion of chapters covering inflammatory, infectious, developmental and other lesions, such as amyloidosis, that can simulate neoplasia. Interestingly, the authors have chosen to collect benign cystic lesions of the eyelids into a separate chapter rather than, for example, covering conjunc-tival hidrocytoma in the chapter on sweat gland tumours. The final chapter of each section discusses the surgical management of lesions at those sites.

This volume is remarkably authoritative, lavishly illustrated (1056 figures), and commendably succinct, in keeping with the aim of an atlas rather than a textbook. Valuable clinicopathological correlation is found for almost all lesions illustrated. Although this book is produced in the USA, its terminology and applicability are suitably international. Only a few examples of potentially troublesome nomenclature are present, including the use of the term “benign lymphoma” and the classification of epithelial papillomas of the lacrimal drainage apparatus as “squamous” without reference to their nature.

In summary, this is a superb atlas reflecting the outstanding experience and expertise of its authors. Its format and content ensure that it is equally at home as a reference text in the clinic setting, the library, the ophthalmic pathology laboratory or within a personal collection. It will be of value to general ophthalmologists and dermatologists, as well as specialists in external diseases, ocuoplastics, oncology, and oculoplastics.

Reviewing this volume has made it determine to obtain the companion volumes on intraocular tumours and orbital tumours.

BRIAN J CLARK


This is a well presented and easily assimilated book. It has high quality colour reproduction and the examples of the various videokeratographic maps are very clear if at times larger than they need be solely for the sake of clarity. The book follows a logical progress from basic principles through the normal cornea and contact lens practice to the corneal appearance in disease and after corneal surgery. Each chapter is extensively, even zealously, referenced and I suspect that this is more than the average reader wants.

For the general reader or for someone who wants to get an overview of topography and topographical systems this book is probably as useful as any other than I have seen. It is readable and many will like the highlights in text boxes and tables. This is good communication.

There are, however, frustrating omissions. It is decidedly uncritical. I looked in vain for a realistic discussion on the imperfections and difficulties encountered in videokeratography—for example, the smoothing that takes place over the central cornea. There is no discussion about the manufacturers’ algorithms—at least the manufacturers are secretive on this point but most readers would I think be interested in understanding better how the pretty isodioptric maps are produced. It would have been helpful, too, if some of the information that is not adequately covered by the manufacturers, but is available, could have been discussed. For instance how can the user extract data from his device to permit statistical analysis?

The authors also fail like many before them to justify the need for expensive topographical devices. Reading the test it is difficult to get away from the impression that computer assisted topography is nothing more than pretty pictures and phenomenology. I would like to have seen the chapter on contact lenses expanded.

The book is like a meal entirely consisting of canapés, very enjoyable but leaving one unsatisfied and wanting more.

COLIN M KIRKNESS


This paperback edition of a book, first produced in 1985 and revised for reissue in 1997, is aimed at the contact lens practitioner seeking information regarding the effect of contact lenses on the eye. It not only offers chapters covering the anatomy of the eyelids, conjunctiva, tear film, anterior limbus, and cornea, but it also reviews various aspects of corneal and anterior segment physiology such as corneal swelling, epithelial behaviour, and sensation and the way these are affected by contact lens wear. Chapters discussing lens spoliation, infection, and cornea are contributed by other experts in the field. While the text is a useful discussion of the pharmacology, both qualitative and quantitative, it also shows their relevance to clinical aspects of contact lens wear to the practitioner. Some chapters are in more detail than others, but the style is clear and accessible. The text is amply supported by illustrations, graphs, tables, and photographs. The discussion in each chapter is supported by scientific argument based on experimental evidence and the published literature. Some of the references quoted, however, are fairly historical and I was a little surprised that all of the references in some chapters were from before the mid-1980s. I think the reader will also find that some of the data regarding pharmacological treatments have advanced since the time of writing.

Nevertheless, the text maintains an authoritative and comprehensive discussion of the topics covered. In particular, the chapters regarding lens spoliation and contact lens related infection were very clear and concise reviews of the subjects. For those interested in basic sciences, there is a thorough study of corneal physiology including an examination, with relevant equations, of the forces involved in maintaining corneal hydration. I felt, however, that the description of the contemporary understanding of glycosaminoglycans and collagen arrangement could have been expanded and illustrated further with diagrams. In the chapter regarding recovery from contact lens wear, there was also mention of the topography of the cornea with a discussion or reference to modern topographical methodology which I am sure would have helped illustrate the points.

I was disappointed at standard of the proof reading; some of the pharmacological terms and lens types were misspelt, and some of the legends were difficult to interpret without the main text.

In all, this is an interesting book to read and use as a reference for basic understanding of the subject, but other readers must be mindful of modern trends in materials and clinical and investigational techniques not presented here. It does, however, review certain topics which are not easily available in other texts but are of great value to the contact lens specialist.

J ANGUS SCOTT
NOTICES

External eye infections
The latest issue of Community Eye Health (no 30) discusses external infections of the eye. Included are papers on conjunctivitis, corneal ulcer, and transmission and control of infection. 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) 171 608 6909/6910/6923; fax: (+44) 171 250 3207; email: eyeresource@ucl.ac.uk) Annual subscription £25. Free to workers in developing countries.

Residents’ Foreign Exchange Programme
Any resident interested in spending a period of up to one month in departments of ophthalmology in the Netherlands, Finland, Ireland, Germany, Denmark, France, Austria, or Portugal should apply to: Mr Robert Achelett, Secretary of the Foreign Exchange Committee, European Board of Ophthalmology, Institute of Ophthalmology, University College Dublin, 60 Eccles Street, Dublin 7, Ireland.

Jules François Prize
The 2000 Jules François Prize of $100 000 for scientific research in ophthalmology will be awarded to a young scientist who has made an important contribution to ophthalmology. All topics in the field of fundamental and/or clinical research in ophthalmology will be considered. The application should be sent jointly with a curriculum vitae, the list of all publications, and three copies of the candidate’s 10 most relevant publications to Jules François Foundation Secretary, Professor Dr M Hansens, Dienst Oogheelinke, de Pintelaan 185, B-9000 Gent, Belgium. Deadline for applications 31 December 1999.

Joachim Kuhlmann Fellowship for Ophthalmologists 2000
The Joachim Kuhlmann AIDS Foundation, Essen, Germany, is sponsoring two fellowships per year for ophthalmologists at a well known institute, who want to train in CMV retinitis and other HIV related ophthalmologic diseases. The fellowships are valued at £25 000 each. deadlines for applications are 31 January and 31 July. Detailed applications, including CV and publication list, should be sent to the Joachim Kuhlmann AIDS Foundation, Bismarckstrasse 55, 45128 Essen, Germany (tel: 0201 87910-87; fax: 0201 87910-99; email: jo-stiftung@t-online.de).

16th Congress of the International Society for Geographical and Epidemiological Ophthalmology (ISGEO)
The 16th Congress of the ISGEO will be held at the Institut D’Ophthalmologie Tropicale De L’Afrique (IOTA) in Bamako, Mali on 21–22 February 2000. Further details: Dr Paul Courtright, ISGEO Secretary, BC Centre for Epidemiologic & International Ophthalmology, University of British Columbia, St Paul’s Hospital, 1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada (email: pcourtright@spaulshosp.bc.ca; website: www.interchange.ubc.ca/bceno/isgeo).

American Institute of Ultrasound in Medicine
The American Institute of Ultrasound in Medicine will hold the 44th annual convention in San Francisco, California on 2–5 April 2000. Further details: AIUM Professional Development Department, 14750 Sweitzer Lane, Suite 100, Laurel, MD 20707-5906 (tel: 800-638-5353; fax: 301-498-4100; email: conv.edu@aium.org; website: www.aium.org).

Vlth Mediterranean Ophthalmological Society
The combined meeting of the Vlth Mediterranea Ophthalmological Society and the Vlth Michaelson Symposium on Ocular Circulation and Neovascularisation will be held in Jerusalem on 21–26 May 2000. Further details: Secretariat, c/o Tourotours Israel Ltd, PO Box 3190, 61031 Tel Aviv, Israel (tel: +972-3-5209999; fax: +972-3-5239099; email: meetings@unitours.co.il).

The Vlth Michaelson medal and award will be delivered on 24 May 2000 in Jerusalem. The medal and award ($15 000 monetary prize) are sponsored by the Israel Academy of Sciences and Humanities and by the Hadasah Hebrew University Hospital and Medical School of Jerusalem, Israel. Nominations are sought from the ophthalmic community at large. Suggestions and reasons for choice and CV highlights should be sent to Professor David BenEzra, Secretary for the International Nominating Committee, Pediatric Ophthalmology Unit, Hadasah Hebrew University Hospital, PO Box 12000, Jerusalem 91120, Israel.

5th International Vitreoretinal Meeting–IV 2000
The 5th International Vitreoretinal Meeting–IV 2000 will be held in Parma, Italy, on 26–27 May 2000. The main topics will include “Hypotony and glaucoma in vitreoretinal surgery”, “Internal limiting membrane surgery”, “Macula oedema”, “Open globe injuries”, and “News in retinal pigment epithelium”. Further details: C. Cantu, MA De Giovanni, or S. Tedesco, Scientific Secretariat, Institute of Ophthalmology, University of Parma, Via Gramsci 14, 43100 Parma, Italy (tel: +39 0521 259106; fax: +39 0521 292358; email: nuzzi@ipruniv.ccc.unipr.it).

XXXIV Nordic Congress of Ophthalmology
The XXXIV Nordic Congress of Ophthalmology will be held in Reykjavik, Iceland, 18–21 June 2000. This meeting celebrates the 100 year anniversary of the Nordic Ophthalmology Conference. Further details: Iceland Incentives Inc, Hambrborg 1–3, Is-Kopavogur, Iceland (tel: +354 554 1400; fax: +354 554 1472; email: incentives@itn.is).

13th Annual Meeting of German Ophthalmic Surgeons
The 13th annual meeting of German Ophthalmic Surgeons will be held on 15–18 June 2000 at the Meistersingerhalle, Nuremberg, Germany. Further details: MGN Medizinische Congress-organisation Nuremberg AG, Zerrzahlofstrasse 29, D-90478 Nuremberg, Germany (tel: +49-911-3931621; fax +49-911-3931620; email: doerflinger@mcn-nuremberg.de).

DB-2000, International Forum on Diabetic Retinopathy
The International Forum on Diabetic Retinopathy will take place on 7–9 September 2000 at the Palazzo Reale, Naples, Italy. Further details: Francesco Bandello, Secretary, MGR Congressi, Via Servio Tullio, 7-52964641; email: strmen@faneba.sk).
12th Afro-Asian Congress of Ophthalmology
The 12th Afro-Asian Congress of Ophthalmology (Official Congress for the Afro-Asian Council of Ophthalmology) will be held on 11–15 November 2000 in Guangzhou (Canton), China. The theme is “Advances of ophthalmology and the 21st century). Further details: Professor Lezheng Wu, Zhongshan Eye Center, SUMS, New Building, Room 919, 54 Xianlie Nan Road, Guangzhou 510060, PR China (tel: +86-20-8760 2402; fax: +86-20-8777 3370; email: lwuicv@gzums.edu.cn).

Singapore National Eye Centre 10th Anniversary International Congress
The Singapore National Eye Centre 10th Anniversary International Congress will be held in conjunction with 3rd World Eye Surgeons Society International Meeting on 2–4 December 2000 at the Shangri-La Hotel, Singapore. Further details: The Organising Secretariat, 11 Third Hospital Avenue, Singapore 168751 (tel: (65) 2277255; fax: (65) 2277290; internet: www.snec.com.sg).

The Hong Kong Ophthalmological Symposium 99
The Hong Kong Ophthalmological Symposium 99 will be held 4–5 December 2000 in Hong Kong, China. Further information: Miss Vicki Wong, Room 802, 8/F Hong Kong Academy of Medicine, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong (tel: (852) 2761 9128; fax: (852) 2715 0089; email: cohk@netvigator.com).