MAILBOX

Use of polymerase chain reaction in detection of *Mycobacterium tuberculosis* complex DNA from vitreous sample of Eales' disease

EDITOR,-Eales' disease, first described by Henry Eales in 1880 is a primary retinal perivasculitis that predominantly affects the peripheral retina of young and otherwise healthy adults in the age group 15-40 years. Of the several aetiologies proposed, most favoured are tuberculosis and hypersensitivity to tuberculoprotein.1 Since polymerase chain reaction (PCR) using primers for the insertion sequence of IS6110 consisting of upstream primer: 5' CCTGCGAGCGTAGGCGT CGG3' and downstream primer: 5'CTC GTCCAGCGCCGCTTCGG 3' coding for 123 bp product, has found a universal acceptance for detection of Mycobacterium tuberculosis complex DNA in clinical specimens,2 we applied it on vitreous fluid samples obtained from clinically diagnosed patients with Eales' disease and controls (undergoing vitreous surgery for proliferative diabetic retinopathy and proliferative vitreoretinopathy).

Uncontaminated vitreous fluid from 12 cases of Eales' disease and 45 non-Eales' disease control patients collected at the beginning of vitrectomy were subjected to PCR using IS6110 primers for the presence of M tuberculosis complex DNA.2-4 PCR was found to be specific and sensitive enough to detect 2.5 pg of M tuberculosis complex DNA. Five (41.6%) among 12 vitreous fluid samples from Eales' disease (Fig 1) and only one (2.2%) out of 45 vitreous fluid samples from the control group were positive by PCR and this difference was statistically significant (Pearson- χ^2 <0.001). Vitreous fluid from both groups of patients did not reveal the presence of acid fast bacilli by direct smear and culture by standard conventional techniques.

The presence of *M tuberculosis* complex DNA in a statistically significant number of vitreous fluid samples of Eales' disease patients compared with the control group leads us to hypothesise the presence of sequestrated mycobacterium in the eyes of Eales' disease patients and a probable role of this bacterium in the pathogenesis of this enigmatic clinical condition.

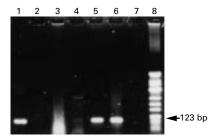


Figure 1 Results of PCR using IS6110 primers on vitreous aspirates of Eales' cases. Lanes: 1, case 1 (positive); 2, case 2 (negative); 3, case 3 (negative); 6, positive control (H37Rv); 7, negative control (reagents); 8, molecular weight marker (Phi x 174 Hinf 1 digest).

Part of the study has been presented at the annual meeting of the Association of Research in Vision and Ophthalmology, 1997.

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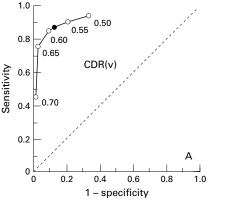
Vertical cup/disc ratio in relation to optic disc size

EDITOR,—In a recent paper,¹ the vertical cup/disc ratio (CDR) in relation to optic disc size was evaluated as an aid in the identification of optic discs with glaucomatous optic neuropathy. Two methods of using the vertical CDR were assessed, one method independent of disc size and the other dependent on disc size.

With the disc size independent method, for a group of patients with primary open angle glaucoma (POAG) and a control group, the authors calculated the vertical CDR and, based on a histogram plot of the control group, concluded that the vertical CDR is not normally distributed. An empirical cut off for the upper limit of normal was taken as the 97.5 percentile. When this test criterion (vertical CDR = 0.682) was applied to the two groups, this method yielded a sensitivity of 56.6% and specificity of 97.7% for the identification of glaucomatous optic discs. The conclusion that the vertical CDR is not normally distributed is not disputed (Chernoff-Lehmann test,2 p<0.10). However, the optimal vertical CDR may be selected rationally (rather than arbitrarily) by plotting sensitivity against (1 - specificity) to produce a receiver operator characteristics (ROC) curve (Fig 1A). The optimal test criterion is the point on the ROC curve furthest from the line of zero discrimination³; from the authors' data, the optimal test criterion is a vertical CDR cut off of 0.587 (sensitivity 86.6%, specificity 87.5%). Having rationally selected the optimal test criterion, its value as a clinical aid is best assessed by the predictive power of a positive test (rather than by isolated sensitivity and specificity values). This predictive power (V+) is the proportion of true positives (by reference test) to total positives (true positives + false positives) and is a function not only of sensitivity and specificity but also of prevalence. V+ may be calculated from: V+ = $1/((((S - 1).(P - 1))/N.P)+1)^{-1}$, where N = sensitivity, S = specificity, and P = prevalence. The prevalence of glaucoma varies according to the population studied and the criteria used as the reference test, but is generally considered to be approximately 2% in adults older than 40 years of age. 4-6 With this prevalence and a sensitivity of 86.6% and a specificity of 87.5%, for an optimal vertical CDR cut off of 0.587, the predictive power of a positive test is 12.4%. This indicates that 87.6% of positives would be false. The corresponding predictive value for the authors' test criterion (vertical CDR cut off = 0.682) is 33.4%.

With the disc size dependent method, the authors calculated the 95% confidence interval of the linear regression of the relation between vertical cup diameter and vertical disc diameter, after appropriate magnification correction. It then appears that the authors used the upper waist of the 95% confidence interval as a straight line to calculate a linear intercept of -0.87. The simple relation between vertical cup diameter and vertical disc diameter was then used to calculate the upper limit of the 95% confidence interval of the vertical CDR as: (((1.193.vertical disc diameter) - 0.87)/vertical disc diameter). When this test criterion was applied to the two groups, sensitivity and specificity for the identification of glaucomatous optic discs were respectively 62.3% and 98.9%. The optimal confidence interval may be selected rationally using an ROC curve constructed from different confidence intervals: the optimal test criterion is a confidence interval of 72% (sensitivity 90.2%, specificity 92.3%) (Fig 1B) which yields a predictive value, V+ = 19.3%. The predictive value of the authors' test criterion of a 95% confidence interval is 53.6%.

We therefore agree completely with the authors that optic disc biometry provides useful data in the identification of glaucomatous discs: the authors' work has shown that the disc size dependent method (V+=19.3%) is superior to that which is disc size independent (V+=12.4%). Their disc size dependent



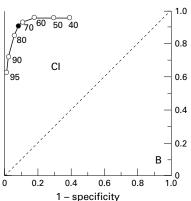


Figure 1 Receiver operator characteristics curves for vertical cup/disc ratio (CDR) (A) and confidence intervals of vertical CDR – vertical disc diameter regression analysis (B). Open circles = (sensitivity, 1 – specificity) points; solid circles = optimal test criteria. Diagonal line indicates zero discrimination. CDR(v) = vertical CDR; CI = confidence interval.

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method is reminiscent of the concept of the "rim index" (observed neuroretinal rim area/ expected neuroretinal rim area) first described in 1991 by Montgomery.

In general, the arbitrary selection of test criteria yield better predictive values but poorer sensitivities, whereas optimal selection of test criteria using ROC curves improves sensitivity but reduces predictive power. We therefore consider it important to appreciate that, in screening for a low prevalence disease with important health implications such as glaucoma, test criteria must be optimised to maintain a high sensitivity and steps taken to cater for a false positive rate of at least 80% which is inevitable in these circumstances.

> D B BARR D J NOLAN

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- 1 Garway-Heath DF, Ruben ST, Viswanathan A, et al. Vertical cup/disc ratio in relation to optic disc size: its value in the assessment of the glaucoma
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Reply

EDITOR,-We thank Barr and Nolan for their observations. We agree that the ROC curve is indeed a useful way of presenting such data, allowing a ready comprehension of the relation between sensitivity and specificity over a range of possible cut off values. However, the statement that the "optimal test criterion" is the point on the ROC curve furthest from line zero is an oversimplification. The optimal test criterion depends entirely on circumstances in which the test is applied, not on an abstract mathematical concept. Specifically, in this context, the estimation of the cup/disc ratio (CDR) is not a "test" performed in isolation. The vast majority of new glaucoma referrals to the hospital eye service are from optometrists, who perform a number of tests for glaucoma: tonometry, ophthalmoscopy (estimation of the CDR and qualitative assessment) and, increasingly, visual field testing.1 2 The optometrist integrates the results of disc assessment with the other test results, and comes to a reasoned decision of "glaucoma probability".

The cut off values used in our paper were selected for high specificity, because the prevalence of glaucoma in the general population is low. In a population with a 2% glaucoma prevalence, application of our cut off values would yield the number of cases (per 1000 population) given in Table 1. For the disc size dependent method, there are 23.3 referrals per 1000, 53.6% of whom have glau-

In a population with a 2% glaucoma prevalence, application of Barr and Nolan's cut off values would yield the number of cases (per

Table 1 Case detection per 1000 population using cut off values given by Garway-Heath et

Disc size	True	False	False
	positives	positives	negatives
Independent	11.3	22.5	8.7
Dependent	12.5	10.8	7.5

Table 2 Case detection per 1000 population using cut off values given by Barr and Nolan

Disc size	True	False	False
	positives	positives	negatives
Independent	17.3	122.5	2.7
Dependent	18.0	75.5	2.0

1000 population) given in Table 2. For the disc size dependent method, there are 93.5 referrals per 1000, 19.3% of whom have glau-

Application of the latter cut off values would result in a huge burden of false positive referrals to the hospital eve service, to be added to the false positive referrals that result from the application of the other tests (tonometry and visual field testing).

The true false negative rate using the cut off values we propose will be much lower than suggested in Table 1. Our data set comprised glaucoma patients with minimal visual field loss (average MD -3.44). In reality, there will be a greater range of glaucoma severity in the undiagnosed population,45 making the test more sensitive. In addition, the results of disc biometry (of which estimation of the CDR is only a part) have to be taken together with the results of other tests. If it is assumed that half all individuals with glaucoma have raised IOP,6 then up to half the false negatives are likely to be referred for further assessment on that basis. Visual field testing would further reduce the false negative rate.

A more sophisticated application of the data is possible, with cut off values tailored according to the relative prevalence of glaucoma in subsets of the population. For instance, it is well established that the prevalence of glaucoma rises with the height of intraocular pressure (IOP).6 It would be possible to apply a cut off with high sensitivity to individuals with raised IOP and a cut off with high specificity to individuals with normal IOP. In this way, the overall pick up of cases can be maximised and the false positive rate kept to a minimum. A false positive rate of 80% is, therefore, by no means inevitable. However, making the method unnecessarily complicated would deter its use.

The method described in our paper was advocated as a simple adjunct to qualitative disc assessment. The great majority of cases not picked up by the CDR method (at our selected cut off) had focal changes in the neuroretinal rim,3 which can be detected by a careful qualitative examination. Over 90% of the more difficult cases to detect clinically, those with diffuse rim loss, were picked up by the method.

In summary, our selected cut off values were far from arbitrary, allowing CDR estimation to be integrated rationally with other aspects of the clinical examination, without resulting in unmanageable numbers of false positive glaucoma referrals.

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- 1 Harrison RJ, Wild JM, Hobley AJ. Referral patterns to an ophthalmic outpatient clinic by general practitioners and ophthalmic opticians and the role of these professionals in screening for ocular disease. *BMJ* 1988;**297**:1162–7.

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Suggestion for IL-2 treatment of conjunctival squamous carcinoma

EDITOR.—We refer to a recent publication of Poole, discussing the incidence of conjunctival squamous carcinoma in Tanzania, notably in HIV affected patients. We have extensively studied a similar condition (bovine ocular squamous carcinoma) with a comparable genesis in veterinary cases, in the Harare area (Zimbabwe).2 We treated such cases with intralesional IL-2 injections of 200 000 U IL-2 (Chiron) over 10 days. A large number of remissions and in 67% of the cases even complete cures (20 month observation period) were obtained. In fact, even tumours of over 6 cm in diameter may regress completely with this therapeutic regimen.3 This form of treatment is cheap, non-toxic, effective, and feasible even in basic situations. It might be worth considering such treatment in human patients, obviously with the appropriate prerequisites.

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Reply

EDITOR,-I thank Koten and Den Otter for their interest in my paper. Their experience with intralesional interleukin-2 in the treatment of bovine ocular squamous carcinoma makes very interesting reading. Regional low dose administration of interleukin-2 appears to be safe and is already used in other specialties: systemic toxicity is reduced and a high local concentration is achieved,1 and most adverse reactions are self limiting and can be managed on an outpatient basis.2 An appropriate clinical trial would be valuable if their good results in the bovine condition could be replicated in the human one.

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It would be hard to justify experimental treatment in an advanced condition where local excision or enucleation might be life saving. A careful trial in the treatment of early conjunctival tumours, however, with vigilant follow up (sometimes difficult in an African setting), might be worthwhile. Another application of their useful work, when attempting to preserve an otherwise normal eye, might be to inject interleukin-2 at the excision margins after tumour resection, to prevent recurrence.

To be of use in Africa any treatment needs to be cost effective. One vial of recombinant interleukin-2 contains 18 million units and costs £140.3 If this could be used for several patients the cost might not be prohibitive. To put this cost in perspective, many patients I saw in Tanzania could not afford the £15 for cataract surgery.

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- 1 Tartour E, Mathiot C, Fridman WH. Current status of interleukin-2 therapy in cancer. Biomed Pharmacother 1992;46:473–84.
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BOOK REVIEWS

Assessing Children's Vision. By Susan J Leat, Rosalyn H Shute, Carol A Westall. Pp 394. £35. Oxford: Butterworth-Heinemann, 1999. ISBN 0-7506-0584-7.

This text is written by optometrists and its main strengths are as a practical guide to vision assessment and refraction in infants and young children. It is a comprehensive review of the up to date literature on visual development and assessment in the child. A chapter on normal child development emphasises that vision develops a parallel with motor, sensory, social, and language skills. Practical tips to help gain the child's and parents' confidence and cooperation in examination and assessment abound. (We must always ask and explain the toddler's role in the examination if we are to expect cooperation and a meaningful result.)

There are a few omissions and inaccuracies in the medical section. A succinct review of congenital and childhood cataract management fails to mention examination of the red reflex with the direct ophthalmoscope for cataract as part of the routine neonatal examination of all newborns. Many paediatric ophthalmologists now utilise intraocular lens implants in the routine surgical management of childhood cataract, particularly after 1–2 years of age.

This book will be invaluable as a guide to vision assessment in childhood for optometrists, orthoptists, paediatricians, and ophthalmologists. The ophthalmologist will also find it an up to date source of the currently available knowledge on the development of vision in the infant and young child.

W H CHURCH

Atlas of Glaucoma. Ed Neil T Choplin, Diane C Lundy. Pp 304, £99.50. London: Martin Dunitz, 1998. ISBN 1-85317-375-4.

Ophthalmology is by definition a visual subject and this is evidenced by the fact that some of the best selling books in ophthalmology are colour atlases. As someone who always preferred to read comics at school rather than books I therefore looked forward to reading through this new atlas of glaucoma. The two editors have assembled a well known list of contributors to write chapters in this atlas under three broad headings: the basics of glaucoma, clinical entities, and treatment. A range of topics is covered from aqueous humour dynamics and ocular blood flow, through to various aspects of treatment.

As one would expect from an atlas there are many large, high quality colour illustrations. However, the format does vary and inevitably some chapters have rather more text than one would expect for a colour atlas. I very much enjoyed some of the colour drawings, and I felt the illustrations for the subject of aqueous humour dynamics help to bring a normally dry subject to life. The colour illustrations are surprisingly effective in helping to explain some of the subjects such as tonography. I also liked the chapter on angle closure glaucoma with accompanying high frequency ultrasound photographs to back up the anatomical concepts. The chapter by Fellman on gonioscopy was also particularly good because of the accompanying line drawings and the pictures of dynamic gonioscopy, viewing the same drainage angles with different examination techniques. Finally, it was nice to browse through the rest of the book looking at the illustrations and accompanying text, as there were some very good illustrations that I had not previously seen in other books or publica-

The book does suffer slightly from the fact that it has multiple authors, are therefore formatting of the chapters is rather variable, which the authors acknowledge in the foreword. Some of the chapters have, for an atlas, rather too much text and too few pictures. In the chapter on filtration surgery, all of the illustrations are in black and white, which rather lets the book down, compared with the excellent colour illustrations in the rest of the book. There were also one or two irritating features like incomplete references and mislabelled illustrations. However, these are minor details and should be easily remedied in the next edition.

In conclusion, this is a book I would certainly recommend to trainees in ophthal-mology and those with an interest in glaucoma because of some of the excellent illustrations, which are a good aid to learning.

P T KHAW

Vitreoretinal Disease: The Essentials. Ed Carl D Regillo, G C Brown, H W Flynn Jr. Pp 693, DM298, SFr 265. New York: Georg Thieme, 1999. ISBN 3-13-111371-5.

This textbook is intended to provide the ophthalmologist with an up to date source of information on medical and surgical vitreoretinal disease. The book follows many others in being subdivided into basic sciences covering embryology, anatomy, and physiology followed by a further section on techniques of fundus examination, angiography, ultrasonog-

raphy and electrophysiology. Finally, and fortunately, the most extensive section is clinical.

The editors have to be congratulated in ensuring that a multiauthor textbook manages to be consistent in its style. The quality of the illustrations is extremely high and there are many colour photographs which add, rather than detract, from the text. An innovation in this textbook is the use of highlighted paragraphs which the authors call "pearls" or 'controversial points". Some readers might find these somewhat distracting but the reviewer found them to be very useful. Obviously a book running to 690 pages cannot claim to be fully comprehensive but there were very few obvious omissions and there are useful references at the end of each chapter. A very useful appendix is included which summarises the major multicentre trials as they pertain to vitreoretinal disease. This section would be extremely helpful for juniors in training and those practising ophthalmologists who perhaps have not read the trials in detail.

Inevitably there are minor quibbles in such a book; for example, the management of retinal detachment fails to mention the D-Ace procedure, a fault found in many American textbooks. It is also a pity that the proof reading was not entirely up to scratch—for example, on page 190 the final paragraph ends in mid sentence.

Overall, however, this textbook is a valuable addition to the ophthalmic literature and the presentation is certainly different enough to make it an essential purchase for all departmental libraries and, if the pricing is correct, I am sure many ophthalmologists will buy a personal copy.

P S BAINES

Diabetic retinopathy. A guide for diabetes care teams. By William D Alexander. Pp 62, £14.95. Oxford: Blackwell Science, 1998. ISBN 0-632-05171-X.

Fear of eye disease is a major anxiety of individuals with diabetes. Monitoring the eyes of these individuals is a major anxiety of those charged with managing their diabetes. The situation is complicated by the fact that advanced diabetic retinopathy may have no effect on current visual function, but denied timely treatment it is likely to progress to irreversible visual loss. The need for efficient and reliable eye screening is therefore very considerable, as also is the need for the diabetic individual to participate in his own care and management.

This attractive and refreshingly unpretentious little volume embraces these central issues relating to the monitoring and treatment of diabetic eye disease in a concise 'Introduction and Aims" chapter. It proceeds to summarise the classification and natural history of diabetic retinopathy followed by a description of ocular examination and a discussion of options for methodology and organisation of screening. The next two sections consider the indications for referral from the primary screener to the specialist ophthalmologist, and the management of diabetic retinopathy. Then, true to the pragmatic theme of the book, it concludes with a very useful chapter on management of visual loss, followed by an annotated picture

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gallery of non-diabetic eye abnormalities which may be encountered on funduscopic examination.

The layout of short chapters and bullet pointed lists is excellent and easy to read and refer to. The liberal use of panels listing key points or summarising information is also very helpful. The widespread use of (a wide variety of) illustrations makes the book attractive to look at. The quality of reproduction of some of the retinal images, however, will be a particular disappointment to those who do not already know what they are trying to illustrate.

Bill Alexander is to be congratulated on producing this thoughtful and informative book at a time when the development of a variety of models for provision of diabetic services is contemporaneous with heightened awareness of a need to set and observe rigorous standards of practice. I am sure that for those wishing to increase their understanding of diabetic retinopathy it will be money well spent.

KEN MCHARDY

NOTICES

Ageing and the eye

The latest issue of *Community Eye Health* (no 29) discusses ageing and the eye. Included are papers on ageing and the eye from a global perspective; epidemiology; delivery of eye care to the elderly; and age related macular disease. 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 Acheson, Secretary of the Foreign Exchange Committee, European Board of Ophthalmology, Institute of Ophthalmology, University College Dublin, 60 Eccles Street, Dublin 7, Ireland.

4th Meeting of the European Neuro-Ophthalmology Society

The 4th meeting of the European Neuro-Ophthalmology Society will be held on 29 August–2 September 1999 in Jerusalem, Israel. Further details: Secretariat, 4th Meeting of the European Neuro-Ophthalmology Society, PO Box 50006, Tel Aviv, 61500, Israel (tel: 972-3-514000; fax: 972-3-5175674/972-3-5140077; email: Eunos99@kenes.com).

International Agency for the Prevention of Blindness

The sixth general assembly of the International Agency for the Prevention of Blindness will be held on 5–6 September 1999 at the Conference Centre, Beijing Friendship Hotel, Beijing, People's Republic of China. The theme is "The right to sight". Further details: IAPB Secretariat, LV Prasad Eye Institute, LV Prasad Marg, Banjara Hills, Hyderabad 500 034, India (tel: 091-40-215389; fax: 091-40-248271; email: IAPB@lvpeye.stph.net).

Ophthalmological Clinic, University of Creteil

An international symposium on the macula will be held on 1–2 October 1999 at the Ophthalmological Clinic, University of Creteil. Further details: Professor G Soubrane, Chef de Service, Clinique Ophtalmologique Universitaire de Creteil, Centre Hospitalier Intercommunal, 40 Avenue de Verdun, 94010 Creteil, France (fax: 01 45 17 52 27).

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 Hanssens, Dienst Oogheelkunde, 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 ophthalmological diseases. The fellowships are valued at \$US5000 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: jk-stiftung@t-online.de).

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, Hamraborg 1–3, Is-Kopavogur, Iceland (tel: +354 554 1400; fax: +354 554 1472; email: incentiv@itn.is).

5th International Viteoretinal Meeting-IIV 2000

The 5th International Viteoretinal Meeting—IIV 2000 will be held in Parma, Italy, on 26–27 May 2000. The main topics will include "Hypotony and glaucoma in viteoretinal 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.cce.unipr.it).

DR-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, Congress Secretariat, MGR Congressi, Via Servio Tullio, 4, 20123 Milano, Italy (tel: 39 02 430071; fax: 39 02 48008471; email: dr2000@mgr.it).

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@gzsums.edu.cn).