

## MAILBOX

### Accuracy of glaucoma referrals: need to report precision of estimates

EDITOR.—Referral accuracy is an important measure of primary care effectiveness. It is defined as the proportion of patients referred for a particular condition who are subsequently diagnosed as having that condition (that is, the true positive proportion). Statistically, it estimates the probability that a patient who is referred will have the disease (positive predictive value) and, as with all statistical estimates, the value calculated in any sample will be subject to error, the magnitude of which decreases as the sample size increases. In recent years there has been an increase in the number of publications on the accuracy of referrals by optometrists to ophthalmology clinics. This letter has been prompted by reading some of those concerned with referrals for suspected glaucoma,<sup>1-12</sup> but the issue applies generally to estimates of referral accuracy for any disease condition and, indeed, to all measures of screening effectiveness that involve calculation of sample proportions, such as sensitivity, specificity, and so on.

The majority of reports of estimated referral accuracy give no indication of the precision (standard error) of the estimates. Although some reported estimates of accuracy are obtained from relatively large samples of referred patients, others are based on samples of 10 patients or less. For example, Dayan *et al*<sup>4</sup> and Newman *et al*<sup>6</sup> each report samples of referred patients (sample sizes 11 and 10 respectively) in which there were no positively diagnosed cases. Using these data to estimate referral accuracy in the population gives 99% confidence intervals of 0 to 38% and 0 to 40% respectively. This means that if one sample of 10 patients shows referral accuracy of zero, then the referral accuracy in 99% of samples drawn from the same population would not necessarily be zero but would be expected to lie between 0 and 40%. Newman *et al*,<sup>6</sup> in subdividing referrals according to the mode of screening, obtain some accuracy estimates from even smaller samples. They report, for example, that two out of five patients referred on the basis of optic disc + visual field assessment gave a positive diagnosis of glaucoma; referral accuracy of 40%. For this sample the 99% confidence interval ranges from 8 to 83%. Awareness of the lack of precision in small sample estimates of referral accuracy is important for correct clinical interpretation. The comparative effectiveness of different referral strategies or modes of screening should not be judged on the basis of estimates from very small samples. Clinicians should keep in mind the fact that population values for referral accuracy may in some situations be much higher, or indeed lower, than those observed.

It is therefore recommended that authors should routinely report 95% or 99% confidence intervals (CI) for all measures of diagnostic accuracy. When these measures are simple proportions, as is referral accuracy, the general equation for the confidence interval is  $CI = \text{proportion} \pm (z \times \text{standard error of proportion})$ . In this equation  $z$  is the standard normal deviate;  $z = 1.96$  for a two sided 95% CI, or  $z = 2.58$  for a 99% CI. The common simple formula<sup>13</sup> for the standard error  $s_p$  of a proportion  $p$  is

$$s_p \approx \sqrt{\{p(1-p)/n\}}$$

where  $n$  is the sample size; and the confidence interval is then

$$CI = p \pm z \sqrt{\{p(1-p)/n\}}$$

However a problem with this formula, which is based on a binomial approximation to the normal distribution, is that it can in some circumstances produce confidence limits of less than 0 or greater than 1, when clearly the population proportion must always lie between 0 and 1. This common approximation should therefore be avoided in favour of exact binomial confidence intervals which are available in many statistical software packages. Alternatively, a formula which always gives confidence intervals within the natural limits of 0 and 1, and is also easy to calculate is<sup>14</sup>:

$$CI = \{2np + z^2 \pm z \sqrt{(z^2 + 4np(1-p))} / 2(n + z^2)\}$$

JIM GILCHRIST

Department of Optometry, University of Bradford,  
Bradford, West Yorkshire BD7 1DP

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### Topical steroid use in the treatment of ocular alkali burns

EDITOR.—The article by Davis *et al*<sup>1</sup> mentions the use of 10% vitamin C eye drops with a pH 5.5-6.5 and the authors specify potassium ascorbate. Preparing for a future emergency I made vitamin C eye drops in my office by putting ordinary Norwegian vitamin C tablets in 10 ml saline and found the pH to be 3! I then realised that my vitamin C tablets were ascorbic acid. Therefore, ophthalmologists should be warned: vitamin C could be

ascorbic acid or acetate. The ophthalmologist need not prepare homemade vitamin C eye drops in the emergency room. The pharmacist should prepare the eye drops, using either potassium or sodium ascorbate.

ANDERS OETHER

Astrups Gate 3, Box 776, N-6501 Kristiansund,  
Norway

- Davis AR, Ali QH, Aclimandos WA, *et al*. Topical steroid use in the treatment of ocular alkali burns. *Br J Ophthalmol* 1997;81:732-4.

### Reply

EDITOR.—Dr Oether makes two important points with regard to the treatment of ocular alkali burns. We would agree that it is crucial to optimise outcome that topical potassium ascorbate drops are readily available for emergency use. Equally, we would agree that pharmacists, in an appropriately controlled environment,<sup>1</sup> should perform the manufacture of these drops.

ALISON DAVIS

- Manufacturing Chemists Association. *Rules and guidelines for pharmaceutical manufacturers and distributors*. London: Stationery Office, 1997.

### Orbital lymphangioma

EDITOR.—Tunç *et al* published a thorough analysis of the course and management of orbital lymphangiomas. They state that besides careful and sometimes repeated surgery there is little convincing evidence of other promising treatment options: "... few patients have been treated with other modalities including ... sclerosing agents but there are sparse data with those approaches".<sup>1</sup> The latter fact might be the result of failures, which have not been published. Therefore, we would like to communicate our disappointing results. Recently, the intralésional application of OK 432 (Picibanil, Chugai Pharmaceuticals Co, Tokyo, Japan) has been used successfully in the treatment of lymphangiomas in various body sites.<sup>2</sup> Usually, OK 432 is injected in one of the cystic spaces of the tumour, leading to an inflammatory reaction and finally to complete shrinking of the tumour within 4-8 weeks. Encouraged by our own good experiences in the treatment of childhood lymphangiomas of the neck or trunk, we decided to choose this approach in the case of a 22 year old young woman suffering from a histologically proved lymphangioma of the left conjunctiva and anterior orbit. The tumour initially presented in early childhood but did not show significant growth until end of the second decade. One surgical debulking procedure had not led to a satisfactory result. Therefore, we performed two injections of OK 432 within 4 weeks. Though we observed the expected inflammatory reaction and swelling, this was not followed by an involution of the tumour. Three months after OK 432 treatment the prolapse of the conjunctival part of the tumour had even increased. A second and now more successful surgical reduction of the mass was necessary. While we have no explanation for the failure of OK 432 in our case, we believe that, though very successful in other localisations, this treatment might be inappropriate in cases of orbital lymphangioma.

SUSANNE PITZ

Department of Ophthalmology, University Hospital,  
Langenbeckstrasse 1, 55131 Mainz, Germany

MATTHIAS DITTRICH  
Department of Paediatrics

Correspondence to: Dr Pitz

- 1 Tunç M, Sadri E, Char DH. Orbital lymphangioma: an analysis of 26 patients. *Br J Ophthalmol* 1999;**83**:76–80.
- 2 Ogita S, Tsuto T, Nakamura K, et al. OK 432 therapy in 64 patients with lymphangioma. *J Pediatr Surg* 1994;**29**:784–5.

### Reply

EDITOR.—There is a paucity of data on the use of OK 432 in this condition. I have also seen one case with the orbit involved in which this treatment was unsuccessful. Perhaps the Japanese centres will present data from a controlled trial, but from my case and anecdotal reports (including the current one) I have not been impressed. The obvious concern is not to reinvent the wheel regarding minimally effective therapies. In both orbital haemangiomas and lymphangiomas several treatments were advocated for many years with minimal effect; hopefully this will not be another one.<sup>1</sup>

DEVRON H CHAR  
Tumori Foundation, Department of Ophthalmology,  
Stanford University, California Pacific Medical Center,  
Davies Campus, San Francisco, CA 94114, USA

- 1 Char DH. *Clinical ocular oncology*. 2nd ed. Philadelphia: Lippincott, 1997.

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## NOTICES

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### 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: eyesource@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.

### 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 Founda-

tion, Bismarckstrasse 55, 45128 Essen, Germany (tel: 0201 87910-87; fax: 0201 87910-99; email: jk-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 Insitut 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@stpaulhosp.bc.ca; website: www.interchange.ubc.ca/bceio/isgeo).

### Leonhard Klein Foundation

The Leonhard Klein Foundation in the Donors' Association for the Promotion of Sciences and Humanities in Germany is to bestow the Leonhard Klein Award 2000 of DM 30 000 for innovative work in the development and application of microsurgical instruments and microsurgical operating techniques. Deadline for applications is 31 March 2000. Further details: Stifterverband für die Deutsche Wissenschaft e V, Herrn Peter Beck, Postfach 16 44 60, D-45224 Essen, Germany.

### 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).

### XXII Tuebingen Detachment Course

The XXII Tuebingen Detachment Course, retinal and vitreous surgery, will be held in the congress centre Incheba, Bratislava, Slovak Republic 6–7 April 2000 preceding the congress on retinal detachment of the Slovak Ophthalmological Society 8–9 April 2000. Further details: Professor Peter Strmen 81369 Bratislava, Miczkiewiczova 13 (tel/fax: 00421-7-52964641; email: strmen@faneba.sk).

### Vith Mediterranean Ophthalmological Society

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

The Vith 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 Hadassah 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, Hadassah Hebrew University Hospital, PO Box 12000, Jerusalem 91120, Israel.

### 5th International Vitreoretinal Meeting—IIV 2000

The 5th International Vitreoretinal Meeting—IIV 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@ipr.univ.cce.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, Hamraborg 1–3, Is-Kopavogur, Iceland (tel: +354 554 1400; fax: +354 554 1472; email: incentiv@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: MCN Medizinische Congress-organisation Nuremberg AG, Zerbabelshofstrasse 29, D-90478 Nuremberg, Germany (tel: +49-911-3931621; fax +49-911-3931620; email: doerflinger@mcn-nuermberg.de).

### 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).