CORRESPONDENCE

Natural history of recurrent erosion syndrome

EDITOR,—I read with interest the recent article by Heyworth and coworkers.1 In their paper there is no specific mention of, or discussion of, the role of oral tetracycline in the treatment of recurrent corneal erosions. In their results they state that 53% of patients who were symptomatic were taking some form of treatment, which included topical drops or ointment. They do not mention whether any patients were using systemic treatment in the form of oral tetracycline or any other systemic treatment. In the discussion there is no reference to the possible role of oral tetracycline in the management of these patients. They refer to topical treatment and possible surgical treatments. They also do not indicate whether any of the patients in the review are using a bandage contact lens to manage their symptoms. In their introduction they state there have been no randomised controlled trials of treatment in the management of recurrent corneal erosion. This is in fact incorrect and our paper in 1994 on the role of oral tetracycline in the treatment of recurrent corneal erosions reported the results of a prospective randomised controlled trial.2

PETER J MCDONNELL
Birmingham and Midland Eye Centre, City Hospital
NHS Trust, Dudley Road, Birmingham B18 7QU

Reply

EDITOR,—McDonnell is correct in stating that no mention was made regarding the role of systemic tetracycline in the management of recurrent corneal erosions. Our study1 looked at a group of patients who were initially treated for recurrent corneal erosions using topical lubricants. This group of patients was recruited over 5 years ago before the results of Hope-Ross and McDonnell's valuable study were known.2 Our study was a telephone questionnaire which was not investigating different treatment modalities in the management of recurrent erosions but merely reporting the symptomatology of a well documented group 4 years after the original study. We can say with some certainty that among those who were using some form of treatment those who were self medicating (67%) were not taking systemic tetracyline, but with regard to the remainder it is unlikely that those attending their general practitioner (26%) were taking systemic tetracyline. We do not have the data available for the remaining two patients who were continuing to attend an ophthalmologist.

Although we accept Hope-Ross and McDonnell's study findings our continued clinical experience with tetracycline has been less encouraging than theirs. Only two patients from this study continue to attend an ophthalmologist. One had certainly used a bandage contact lens in the past but had subsequently undergone phototherapeutic keratectomy and was still symptomatic, although to a lesser degree. Bandage contact lenses certainly have a role in the management of recurrent erosions in patients who are sufficiently troubled by symptoms to seek medical advice—something that the vast majority of these patients were not doing.

PETER HEYWORTH
JOHN DART
 Moorfields Eye Hospital, City Road,
London EC1V 2PD

Topical ointment does not prevent recurrent symptoms following traumatic corneal abrasion

EDITOR,—We would like to expand on comments by Heyworth et al.1 regarding the use of topical lubricating ointment for prophylaxis of symptoms of recurrent corneal erosion. The authors make the point that there are very few available data as to the prevalence of symptoms following traumatic corneal abrasion. We have addressed this specific issue in an ongoing prospective study. The study was designed to assess symptoms following uncomplicated traumatic corneal abrasion, and to assess the effect on symptoms of using a topical lubricant ointment. The project has the approval of our local research ethics committee.

All patients presenting with traumatic corneal abrasion in a previously healthy eye were treated with our standard regimen of cyclopentolate ointment 1% immediately and then atropine ophthalmic eye drops four times daily for 5 days; eyepads were not used.2 Injuries caused by a fingernail are felt to be at higher risk of progressing to recurrent corneal erosion,3 so the patients were randomised to one of two treatment groups. One group received our “standard regimen” alone, the other group continued with a “prophylactic regimen” of lubricating ointment (Lacrilube, Allergan) at night for 2 months. Patients were followed up after 3 months by telephone, using a symptom based questionnaire. Recurrent symptoms were graded as: (i) none or minimal, (ii) mild, (iii) moderate (difficulty with some daily activities, or sought further advice from a health professional), and (iv) severe (macroform recurrent erosion). Case notes were reviewed at 2 years. Three year follow up, again by telephone questionnaire, is due to take place later this year.

Seventy four patients completed the 3 month follow up questionnaire (Table 1). Symptoms were considered to be due to recurrent corneal erosion if they were reported as frequent and significant pain, grittiness, photophobia, or watering of the injured eye only. A total of 21 patients (28%) reported such recurrent symptoms at 3 month follow up. We found no significant difference in symptom prevalence between “fingernail” and “non-fingernail” injuries which had been managed with our standard regimen (χ2 test: p = 0.54). Treatment of fingernail injuries with additional nightly ointment was associated with a higher prevalence of symptoms at 3 months (significant to χ2 test, p = 0.016).

Despite the high prevalence of symptoms in all groups at 3 months, only two patients had re-presented with macroform recurrent corneal erosion by 2 years. Both had been injured by a fingernail: one presented 3 months after treatment with our standard regimen, the other presented 7 months after a similar injury which was treated with additional nightly ointment.

These early results suggest that nightly lubricating ointment does not prevent recurrent symptoms when used following uncomplicated traumatic corneal abrasion. Instead, the reverse appears to be true, in that the group receiving additional ointment had significantly more symptoms at 3 month follow up. We were surprised at the high prevalence of recurrent symptoms in all groups. These early results may lead us to reconsider the place of both ophthalmic and ointment in our initial management. Future studies of treatment for corneal abrasion or erosion should pay close attention to patient symptoms.

TOM EKE
DANNY MORRISON
DAVID L J AUSTIN
Leicester Royal Infirmary NHS Trust
Correspondence to: Dr Danny Morrison, Department of Clinical Genetics, Molecular Medicine Centre, Western General Hospital, Edinburgh EH4 2XL


Table 1 Prevalence and severity of recurrent symptoms, 3 months after treatment for traumatic corneal abrasion. Symptoms were assumed to be due to recurrent corneal erosion if they were described as frequent and significant pain, grittiness, photophobia, or watering of the injured eye only.

<table>
<thead>
<tr>
<th>Cause of injury and treatment group</th>
<th>No symptoms (confirmed)</th>
<th>Moderate symptoms (difficulty with daily activities, or sought further opinion)</th>
<th>Severe symptoms (macroform recurrent corneal erosion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fingernail: standard regimen (test)</td>
<td>17 (85%)</td>
<td>2 (10%)</td>
<td>0 (5%)</td>
</tr>
<tr>
<td>(n=20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fingernail: additional nightly ointment (see text) (n=22)</td>
<td>11 (50%)</td>
<td>7 (32%)</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Other causes: standard regimen (n=32)</td>
<td>25 (78%)</td>
<td>3 (10%)</td>
<td>4 (12%)</td>
</tr>
</tbody>
</table>
Horner's syndrome in infancy

EDITOR,—Eke et al have addressed the issue of symptoms following an acute traumatic abrasion and demonstrate that 28% of patients were still symptomatic 3 months after the event. In our discussion we suggest that what is required is a study examining the symptomatology of patients with established recurrent erosion syndrome before deciding what treatment modalities would be appropriate. Eke et al's series represents a small group of patients (21) who are still symptomatic 3 months following an acute corneal abrasion, not long after the initial healing phase. This surely does not represent the group of patients that we are interested in—namely, those who have recurrent erosions some time following the initial injury. When Eke's group report the results regarding symptomatology at 3 years (due later this year) this will better represent a group of patients with recurrent erosion syndrome albeit limited to a small subgroup of these patients with a traumatic aetiology and whose numbers may be considerably less than those reporting symptoms at 3 months.

PETER HEYWORTH
Adneal Service, Moorfields Eye Hospital, City Road, London EC1V 2PD

Horner's syndrome in infancy

EDITOR,—George et al1 recently undertook a review of 23 cases of Horner's syndrome presenting in the first year of life. They remind us of the difficulty in differentiating between congenital and acquired Horner's syndrome in this age group. In their introduction they state that, in both congenital and acquired cases, "heterochromia may appear to be progressive as the child develops normal pigmenta- tion in the fellow iris". Iris heterochromia would therefore appear to be of little value in distinguishing between congenital and acquired cases, the latter potentially being the result of a congenital abnormality. The authors conclude with a management protocol for the investigation of Horner's syndrome in infancy—namely, a full general examination and demonstration that almost any stable glaucoma patient would be appropriate. A computed tomograph of the thorax was subsequently performed and showed a ganglion- neuroma. We have therefore included increasing heterochromia in our series as an index of suspicion because this had prompted further investigation in this one patient.

N D L GEORGE
C S HOYT
Department of Ophthalmology, Clarendon Wing, Leeds General Infirmary, Leeds LS2 9NS

Improved immunoperoxidase techniques for the immunopathological diagnosis of superficial viral infections

EDITOR,—I read with great interest the paper by Thiel et al2 who applied immunoperoxidase and immunofluorescence techniques to diagnose viral infections of the ocular surface. Eleven years ago, we described a method of immunocytochemical staining for viral antigens on ocular surface cells collected on cellulose acetate strips.3 Thiel and coworkers should be congratulated for improving this methodology by the use of a Biopore membrane device that facilitates specimen collection and processing. Another advantage common to these diagnostic techniques is that sample collection simultaneously accomplishes debridement, which may be beneficial in herpetic keratitis and other viral infections of the ocular surface.

JAY S PEPOSE
Department of Ophthalmology and Visual Science, Washington University School of Medicine, 660 S Euclid Avenue, St Louis, MO, USA


progression was demonstrated with STATPAC 2 than with PROGRESSOR (unlike STATPAC 2) is not widely used in clinical practice. It is therefore important to know which treatment (if required) of an irreversibly progressing visual field test to be performed each year. With the criteria of Viswanathan et al., 60% of the simulated fields showed significant progression in at least one inner point and 29% showed progression in at least one outer point. This means that at least 72% showed false significance on at least one occasion. In fact, 55% of the simulated fields showed progression on two consecutive test occasions. If we had included the short term fluctuation, the number of false significances would have been even larger. This finding of 72% false significances is in agreement with our experience with the 10 glaucoma patients. Viswanathan et al. must have been fooled by their own selection of progressing patients, and the use of remaining statistical significance at the last visit as a criterion for reliability is incorrect. It is not surprising that many points in subjectively progressing visual field tests show significant progression at the end of the follow up period, and this yields no information as to the specificity of the analyses employed.

It is generally and correctly considered, because of the large random variability of glaucomatous visual fields, real progression can seldom be demonstrated in glaucomatous visual fields in only 1 year. In view of this we are quite satisfied that the mean time until progression was demonstrated with STATPAC 2 was more than 2 years. In fact, we recommend stricter progression criteria for STATPAC than those used by the authors, again in the interest of specificity. Linear regression analysis has advantages in visual field follow up, one is that all available data are used. Such analyses can be applied both properly and improperly. Analyses that lack specificity are only misleading, however, and may even result in improper clinical management. A more thorough analysis of regression analyses for visual field follow up is needed, and we will address this subject in a future article.

Specialty of the analyses employed.

We agree with Heijl et al. that the 5% significance level is likely to result in overdiagnosis of progression. In fact, even using the 5% level PROGRESSOR would be expected to produce less overdiagnosis than STATPAC 2 since PROGRESSOR has a a rate (that is, slope) criterion for progression which STATPAC 2 does not: this also mitigates against the “problem with mass significance testing” which “goes without saying”. When we first compared PROGRESSOR with STATPAC 2 (in terms of numbers of progressing points detected rather than speed of detection) we expected the 5% level to be an overly lax criterion for PROGRESSOR. We were surprised to find that this criterion had to be relaxed still further to the 10% level in order for PROGRESSOR to emulate STATPAC 2.

It is not surprising that Heijl et al. found a high rate of false progression using a rudimentary numerical significance criterion. This is to be expected when the 5% significance level is specified, and their simulation echoes research done on true clinical data.

The authors have seemingly fallen into the trap of equating statistical significance with clinical significance. Any change in the visual field must be placed in the context of the overall management of the patient (which will include consideration of intraocular pressure, optic disc features, current and previous therapy, together with the patient’s age and general medical condition) before the clinical implications may be ascertained. Statistical significance in visual field change, no matter how it is obtained, does not itself equate to clinical significance. The subject of which progression criteria correspond most closely to “true” clinically observed worsening of glaucoma is currently under investigation.

Because setting the progression criteria at the p<0.05 level will provide a large number of false positive responses, we do not recommend the use of this level for clinical use. As PROGRESSOR (unlike STATPAC 2) is not widely available the chance of “improper clinical management” is therefore negligible. This cannot be said to be the case for the widely available STATPAC 2 for the original criteria established by the authors (ref 20 in our paper) are considered by many as the gold standard for progression. We are interested that Heijl et al. now set stricter criteria for progression than is currently available on STATPAC 2 and would be interested to learn what these might be as they have not, to our knowledge, appeared in print.

We are surprised that Heijl et al. are quite satisfied with a detection time of more than 2 years for STATPAC 2. This seems a nihilistic approach when a more sensitive analysis such as PROGRESSOR, coupled with clinical perception, offers the hope of earlier detection and treatment (if required) of an irreversibly blinding condition.

Finally, we are delighted that Heijl et al. are engaged in “a more thorough analysis” of linear regression, particularly as they dismissed linear regression as “the best way to diagnose cataracts” at the open glaucoma meeting of the ICO in 1990. We await their results with interest.

ANDERS HEIJL
BOEL BENGTSSON
Department of Ophthalmology, Malmö, Sweden

GEORG LINDGREN
Department of Mathematical Statistics, University of Lund, Sweden

Reply

EDITOR—We thank Heijl et al. for their interest in our paper.1 Their letter raises a number of issues, all of which are worthy of discussion. Our paper was a continuation of previous work (ref 25 in our paper) comparing a new analysis program (PROGRESSOR) with the widely available visual field analysis program STATPAC 2. In the earlier paper we showed that the two programs identified the same locations in the visual field as “progressing”. In this paper we showed that “progression” as we defined it occurred much earlier with PROGRESSOR than STATPAC 2. As an uncontrolled outcome of glaucoma management is (further) visual field loss, any approach looking for earlier detection of visual field loss seemed to have merit.

Drs Heijl, Bengtsson, and Lindgren criticise us on methodology and approach. Specifically they express concern about the use of a significance level of p<0.05, suggest that our patient selection would bias the results, and express satisfaction that the mean time before STATPAC 2 can detect progression is more than 2 years.

We set the significance level for our study at the 5% level because this is the only significance level we are satisfied with. With this in mind, we set out to compare PROGRESSOR and STATPAC 2 as far as a trial as possible. Since there is no external “gold standard” for glaucomatous visual field progression it is impossible to measure the true specificity of any analysis.1,2 Our patient selection, which would have a bearing on the results, was from a cohort of patients with normal pressure glaucoma who had progression identified on clinical examination of a large series of visual fields. This group may well be unrepresentative of glaucoma patients as a whole but as examples of undoubted progression they allowed us to perform the study. We agree with Heijl et al. that the 5% significance level is likely to result in overdiagnosis of progression. In fact, even using the 5% level PROGRESSOR would be expected to produce less overdiagnosis than STATPAC 2 since PROGRESSOR has a rate (that is, slope) criterion for progression which STATPAC 2 does not: this also mitigates against the “problem with mass significance testing” which “goes without saying”. When we first compared PROGRESSOR with STATPAC 2 (in terms of numbers of progressing points detected rather than speed of detection) we expected the 5% level to be an overly lax criterion for PROGRESSOR. We were surprised to find that this criterion had to be relaxed still further to the 10% level in order for PROGRESSOR to emulate STATPAC 2.

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A C VISWANATHAN
W F FITZKE
R A HITCHINGS
Department of Visual Science, Institute of Ophthalmology, University College London, 1–11 Bath Street, London EC1Y 9EL

7 Schulzer M. Errors in the diagnosis of visual field progression in normal-tension glaucoma. Ophthalmology 1994;101:1589–94

Topical steroids and alkali burns

EDITOR—In their recent report attesting to the safety of topical prednisolone in the treatment of alkali burns,1 Davis and colleagues do not specify the type of prednisolone which was prescribed. Prednisolone acetate (Pred Forte) is absorbed into the human eye and reaches squamous concentrations many fold higher than prednisolone phosphate (Predsol)2 perhaps on account of an acetylating enzyme in the cornea. It is therefore important to know which form of prednisolone was employed in this study.

editor—In answer to Mr Dutton’s question, I have rechecked our data and the paragraph detailing treatment should now read:

“All patients with a grade 1 injury or greater were treated with a standard regimen which included . . . topical steroid (dexamethasone alcohol 0.1% or prednisolone sodium phosphate 0.5%, or betamethasone sodium phosphate 0.1%; in addition two patients had betamethasone sodium phosphate ointment at night)”

Of those who had prednisolone drops, none had prednisolone forte eye drops. The aim of our paper was to emphasise the safety of topical steroids when used in conjunction with vitamin C in the treatment of alkali burns. To compare the use of different types of steroids would require a prospective study.

Alison Davis
Eye Department, King’s College Hospital, Denmark Hill, London SE5 9RS

IN MEMORIAM

Fred Hollows
Fred Hollows died on 10 February 1993 in the age of 63 years after a short and valiant battle with kidney, lung, and brain cancer. In his remarkable career he had quickly risen to being a major international figure in the world of ophthalmic surgery.

In the 1950s Fred Hollows decided as a young medical student to become an ophthalmologist because this would give him a useful skill to work in Africa. As a postgraduate ophthalmology student in Wales, Hollows studied epidemiology so that he could link eye doctors with wide ranging community health programmes. In 1968 at Wattie Creek in northern Australia Hollows identified in an aboriginal community “dahlak blindness”, a hazy corneal condition first found in Eritrea. He began to lobby for funds and between the years 1976 and 1979 a “better vision for all” programme called the National Trachoma and Eye Health Programme treated the eyes of 100 732 people; 62 116 of these were indigenous Australians.

Eventually this led to series of eye health programmes in Eritrea, Nepal, and Vietnam, which have restored the sight of thousands, and to a struggle to lessen disparity in health and treatment between the “haves” and “have nots”.

When he went to Eritrea in 1988 during the height struggle for independence he taught the medical doctors in ophthalmological surgery. There were many patients with cataract who could not be treated in Eritrea at that time because of lack in experience and material. Many of the patients came from Danakel (south eastern Eritrea), said to be the hottest place on the earth.

From 1990 to 1992 Professor Hollows gathered the necessary capital to build the intraocular lens factory in Asmara; such a factory has been put to the test before in Australia.

His dream came true: The Foundation of Fred Hollows was officially opened on 20 January 1994 in Asmara by the president of the state of Eritrea, I Aferworki, the Australian senator of foreign affairs, Gareth Evans, and Mrs Gashi Hollows with her children. This laboratory is an expression of his admiration, understanding, and love of the people of Eritrea and their struggle to achieve independence and self reliance. The factory produces an estimated 60 000 intraocular lenses per year; in Eritrea there are 30 000 cataract patients per year.

His desire to help and identify himself with the suffering of the people of Eritrea did not end with the eye programme. He undertook the task of finding a solution to the removal of the millions of landmines scattered in Eritrea and other countries.

Fred Hollows was no dry, dusty academic but had considerable style and joie de vivre. He maintained an active family life with his wife and their five young children.

Fred Hollows will remain for a long time in our hearts and memories. We share deepest sympathy with his family.

Biniam Ghebremedhin

NOTICES

Avoidable blindness
The latest issue of the Community Eye Health (no 25) discusses the elimination of avoidable blindness. With an editorial by Bjorn Thyldufors, the director of the WHO Programme for the Prevention of Blindness and Deafness, the issue covers treatment of cataract in regions of India and the role of patient counsellors in increasing the uptake of cataract surgery and IOLs. 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 6910; fax: (+44) 171 250 3207; email: eyeresource@ucl.ac.uk)

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.

XVI Tuebingen Detachment Course
The XVI Tuebingen Detachment Course in retinal and vitreous surgery will be held 4–5 September 1998 at Odessa, Ukraine. Further details: Professor I M Logai, Director, The Filatov Institute, 49/51 Boulevard Francois. Odessa, 270061, Ukraine. (Tel: +38-0482-22 20 35; fax: +38-0482-68 48 51.)

International Agency for the Prevention of Blindness (IAPB)
The International Agency for the Prevention of Blindness (IAPB) will hold its next general assembly in Beijing, China on 5–10 September 1998. Further details: Gallapalli N Rao, Secretuary General, IAPB Secretariat, LV Prasad Eye Institute, LV Prasad Marg, Banjara Hills, Hyderabad 500 034, India. (Tel: 091-40-215389; fax: 091-40-248267; email: IAPB@latpeye.stph.net)

XI Tuebingen Angiography Course
The XI Tuebingen Angiography Course will be held 12 September 1998 at the auditorium university dental clinic, Tuebingen. Further details: Dr W Inhoffen, University Eye Clinic Department of Ophthalmology III, Schlichstrasse 12, D-72076 Tuebingen, Germany. (Tel: +49-(0) 7071-29268; fax: +49-(0)-7071-293746; email: ingrid.kreissig@uni-tuebingen.de; http://www.medizin.uni-tuebingen.de/~webagen/index.html)

ICOP 98
The next International Conference in Ophthalmic Photography (ICOP) will be held on 19–21 September 1998. Further details: Mrs Gillian Bennenhor, Senior Ophthalmic Photographer, Bristol Eye Hospital, Lower Maudlin Street, Bristol BS1 2LX. (Tel: 0117-928-4677.)

IV meeting of the European Society for Out-Patient Eye Surgery (ESOPES)
The IV meeting of the European Society for Out-Patient Eye Surgery (ESOPES) will be held in Vittel, France on 9–11 October 1998. Further details: Mrs Gillian Choron, Director, Palais des Congrès, Av Bouloumieux, BP 57, 8802 Vittel, France. (Tel: +33 329 08 18 30; fax: +33 329 08 6601.)

Vlth International Symposium on Graves’ Ophthalmology
The Vlth International Symposium on Graves’ Ophthalmology will be held on 27–28 November 1998 in Amsterdam. Further details: Amsterdam Thyroid Club, Department of Endocrinology, F5-171, Academisch Medisch Centrum, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands.

Hong Kong Ophthalmological Symposium 98
The Hong Kong Ophthalmological Symposium 98 on myopia will be held on 28–29 November 1998 at the Hong Kong Convention and Exhibition Centre. Further details: Dr Woon-ming Chan, Secretary, Organising Committee, Hong Kong Ophthalmological Symposium 98, University Eye Centre, 3/F, Hong Kong Eye Hospital, 147K Argyle Street, Kowloon. (Tel: (852) 2761 9128; fax: (852) 2715 0089; email: cokh@netigator.com)

Singapore National Eye Centre
The 3rd SNEC international meeting and 11th international meeting on cataract, implant, microsurgery and refractive keratoplasty (ICIMBRK) will be held in the Shangri-La Hotel, Singapore on 28–30 November 1998. Further details: Organising Secretariat, 3rd SNEC International Meeting and 11th ICIMBRK, Singapore National Eye Centre Pte Ltd, 11 Third Hospital Avenue, Singapore 168751. (Tel: (65) 2277-255; fax: (65) 2277-290/1)