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 on, the role of oral tetracycline in the treatment of recurrent corneal erosions. In their results they state that 55% 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 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

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 chloramphenicol eye drops four times daily for 5 days; eyepads were not used. 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 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 suggest that we should reconsider the place of both eyepad and ointment in our initial management. Future studies of treatment for corneal abrasion or erosion should pay close attention to patient symptoms.

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</th>
<th>Minimal symptoms</th>
<th>Mild symptoms (non-disabling)</th>
<th>Severe symptoms (confirmed macroform corneal abrasion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fingernail: standard regimen (n=20)</td>
<td>17 (85%)</td>
<td>2 (10%)</td>
<td>0</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Fingernail: additional nightly ointment (n=22)</td>
<td>11 (50%)</td>
<td>7 (32%)</td>
<td>4 (18%)</td>
<td>0</td>
</tr>
<tr>
<td>Other causes: standard regimen (n=31)</td>
<td>25 (78%)</td>
<td>8 (26%)</td>
<td>8 (26%)</td>
<td>0</td>
</tr>
</tbody>
</table>

4 Kirkpatrick JNP, Hoh HB, Cook SD. No eye pad for corneal abrasion. Eye 1993;7:668–70.

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 study 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.1 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 tetracycline, but with regard to the remainder it is unlikely that those attending their general practitioner (26%) were taking systemic tetracycline. 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


TOM EKE
DANNY MORRISON
DAVID 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

2 Kirkpatrick JNP, Hoh HB, Cook SD. No eye pad for corneal abrasion. Eye 1993;7:668–70.
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
Adnexal Service, Moorfields Eye Hospital, City Road, London EC1V 2PD

Horner’s syndrome in infancy

EDITOR,—George et al 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 pigmentation 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 an underlying pathology. The authors conclude with a management protocol for the investigation of Horner’s syndrome in infancy—namely, a full general examination and whose numbers may be considerably less than those reporting symptoms at 3 months.

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

Improved impression cytology techniques for the immunopathological diagnosis of superficial viral infections

EDITOR,—I read with great interest the paper by Thiel et al 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. 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 herpes keratitis and other viral infections of the ocular surface.

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


Visual field progression in glaucoma

EDITOR,—We read with interest the article by Viswanathan et al.1 We were surprised by the authors’ progression criteria for the PROGRESSOR method; their criteria are extremely sensitive and non-specific: only one point needs to show significantly negative slope when tested on the 5% level, together with an observed slope of <−1 dB/year and <−2 dB/year for inner and outer points, respectively. With 74 test points, it goes without saying that one here faces a problem with mass significance testing, which explains the very low specificity. It is obvious that almost any stable glaucoma patient would be marked as progressing with the reported method.

To illustrate the effect, we studied 10 patients with manifest glaucoma which, after at least 5 year follow-up in each case, had shown false progression at eight visual fields, did not show visual field progression on the same clinical grounds as those used by Viswanathan et al. We had used the same type of visual field test as the authors—that is, Humphrey 30-2 full threshold. In order to eliminate the possibility of any significant subclinical progression, the order of field tests were randomised before tests were analysed by the PROGRESSOR method. This randomisation occurred that all significant progression would be the result of pure chance. Using the progression criteria of Viswanathan et al, stated above, five visual fields showed progression at the fourth visit, and already at the sixth visit eight eyes (80%) had shown false progression at one or more visits.

Further, we performed a Monte Carlo simulation study with the same criteria. 1 0000 fields were simulated and tested 10 times and the regression slope was tested at each point starting at the third test occasion. The field was divided into two regions with 50 inner points and 24 outer points, respectively, as stated by Viswanathan et al, and the field
generated by Gaussian variables with one homogeneous random component common to all points in the region (SD 1.1 dB), and with an independent inhomogeneous variation (SD 0.9 dB) between points. All fields were assumed to be stable, with constant mean at all test occasions. We therefore performed three tests 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 progression on at least one occasion. In fact, 35% 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 erroneous. 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 any of the statistical analyses employed.

It is generally and correctly considered that 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. More thorough analyses of regression analyses for visual field follow up is needed, and we will address this subject in a future article.

ANDERS HEIJL
BOEL BENGTSSON
Department of Ophthalmology, Malmo, 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 2 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.

Dr Heijl, Bengtsson, and Lindgren criticise us on our methodology and approach. Specifically they express concern at 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 implemented by STATPAC 2. With this in mind, we set out to compare PROGRESSOR and STATPAC 2 in as fair 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 by expert 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 employs a conservative 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”.3 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 2.4

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

A C VISWANATHAN
F W FITZKE
R A HITCHINGS
Department of Visual Science, Institute of Ophthalmology, University College London, 4–11 Bath Street, London EC1Y 9EL


Topical steroids and alkali burns

EDITOR,—In their recent report attesting to the safety of topical prednisolone in the treatment of alkali burns1 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 aqueous concentrations many times greater than prednisolone phosphate (Predsol) 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.

GORDON N DUTTON
Wit Glasgow Hospitals, University NIO Trust, Western Infirmary, Glasgow G11 6NT

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