www.nature.com/eye

npg

Evidence-based medicine audit as a tool for improving emergency ophthalmology

Abstract

Aim To audit the proportion of interventions in emergency ophthalmology that are evidence based and to determine whether the quality of care can be improved.

Methods Audit of diagnosis-intervention pairs was carried out retrospectively in March 2003. The outcomes were assessed for evidence level reached in the Medline database 1966–2003 and the Cochrane Database of Systematic Reviews. Locally agreed guidelines were issued and the study repeated prospectively in March 2004, when new medical staff were at a similar level of experience. The participants had no prior knowledge of the study to avoid prescribing bias (Hawthorne's phenomenon).

Results In the first part of the audit in 2003, 71% of interventions were evidence based, with 36% derived from systematic reviews, meta-analysis or randomised controlled trials (evidence levels 1-3). After guidelines for care were implemented in 2004, there was an improvement in the number of evidence-based interventions to 82% (P = 0.04), and levels 1–3 were reached in 60% (P = 0.02). The proportion with no evidence or against evidence dropped from 29 to 18% (P = 0.04). An additional benefit was to reduce the number of re-attendances required. Conclusion Evidence-based medicine can be used to improve the quality of care in the acute ophthalmic setting, both in refining the standard of interventions and in reducing the number of hospital visits.

Eye (2009) **23**, 368–375; doi:10.1038/sj.eye.6703029; published online 26 October 2007

Keywords: evidence based; emergency; ophthalmology; audit

MS Sagoo and J Raina

Introduction

Evidence-based medicine is defined as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.¹ The aim is to provide quality care, minimise medical error, and to ensure equitable provision of services. In specialties other than ophthalmology, there is a body of literature evaluating the proportion of clinical interventions that are evidence based. For example, in general medicine, 53% of interventions were based on randomised controlled trials and 29% on observational evidence.² The range across specialties is between 71 and 97%.^{3–8}

Emergency ophthalmology requires not only clinical skill but also knowledge of management options for best quality care and suitable outcome of the patient. Lai *et al*⁹ examined the quality of interventions in an emergency eye clinic in Hong Kong and reported that 77% of interventions were evidence based. The question still exists, however, as to whether quality of interventions can be improved by such evaluations. We aimed to answer this question by judging the quality of interventions made in a busy eye casualty facility in a mixed inner city area at the Ophthalmology Department of North Middlesex University Hospital, London in one period in 2003, to issue guidelines and recommendations for treatment based on the findings, and to re-evaluate the effects of these 1 year later.

Methods

The first phase of the audit was carried out retrospectively in March 2003. To minimise the risk of bias from Hawthorne's phenomenon (changing prescribing habits due to prior knowledge that outcomes are being monitored),

Department of Ophthalmology, North Middlesex University Hospital, London, UK

Correspondence: MS Sagoo, Moorfields Eye Hospital, City Road, London EC1V 2PD, UK Tel: + 020 7253 3411; Fax: + 020 7566 2062. E-mail: sagoo@ doctors.org.uk

Received: 16 June 2007 Accepted in revised form: 2 October 2007 Published online: 26 October 2007

Financial/competing interests: none This project was presented for the John Glyn Young Fellows Audit Prize (2007) at the Royal Society of Medicine the senior house officers staffing the eye casualty were kept unaware of the timing or nature of the study. The first 300 attendees in the eye casualty were identified and every third case file requested, to examine the evidence base for outcomes for 100 patients. An electronic database was used to record information on patient demographics, symptoms, diagnosis, visit details (number of visit, level of doctor examining the patient, and senior opinion sought by discussion or consultation), and management of the condition (details of treatment and medical or surgical nature). For assistance with resource planning, the final outcome of the patient (discharge, casualty review, and referred to outpatient or other specialty) was also recorded. The evidence level for each intervention was checked in a similar method to Lai *et al*⁹ using evidence levels for different types of study as follows:

Level 1 =Systematic review Level 2 =Meta-analysis Level 3 =Randomised controlled trial (RCT) Level 4 =Prospective study Level 5 =Retrospective study

Each intervention was searched for in the Cochrane Database of Systematic Reviews and in Medline from 1966 to March 2003. The highest level of evidence was recorded for each outcome and checked by the senior author (JR). Data were then analysed by each evidence level.

Departmental guidelines based on evidence in the literature were written specifically taking into account local circumstances, and an agreement was reached by all consultant ophthalmologists in the unit. These were issued to the incoming senior house officers and throughout the department in February 2004. For any conditions not covered in the guidelines, the recommendation was either to consult the Wills Eye Manual¹⁰ or to seek the opinion of a more senior member of staff. One calendar year after the initial phase, the audit was repeated using exactly the same methodology, in the first week of March 2004, 1 month after guidelines were introduced. This timing was decided because the incoming senior house officers would have a similar level of experience to those in the 2003 study, and so this would give a better idea of whether the guidelines were making a difference to the quality of interventions. Exactly, the same methodology as the 2003 phase of the study was used: case notes for every third patient attending the emergency clinic from 1 March 2004 for 300 cases were requested and analysed in the standardised way. Fisher's exact test was used for the statistical analysis, to evaluate the difference between proportions of interventions between the independent data sets, where some of the observed frequencies are small.

Results

The results of the initial audit are shown in Tables 1–7. In 2003, 88 case notes were obtained; 3 of these had been misrecorded and had not actually attended the eye casualty and so were excluded, and a further 5 had no diagnosis made in the ophthalmology emergency visit, so these were also excluded from the analysis of interventions. Therefore, there were 80 diagnosisintervention pairs who were evaluated in the Cochrane Database of Systematic Reviews and Medline. The mean age of the patients was 38.8 years (median 38.5, range: 1 week-80 years), and 55% were men. Most consultations (99%) were with a senior house officer, and 10% of consultations were discussed with or seen by a more senior ophthalmologist. Table 1 shows the number and proportion of interventions for each evidence level in 2003 and those found by Lai et al9 in Hong Kong. The percentages for each evidence level correspond closely,

Evidence level	Number (%) in 2003, N = 80	Number (%) in 2004, N=82	Number (%) from Lai et al,9 N = 252
Level 1: systematic review	6 (8)	15 (18)	26 (10)
Level 2: meta-analysis	2 (3)	3 (4)	2 (1)
Level 3: randomised controlled trial	28 (35)	31 (38)	80 (32)
Level 4: prospective study	9 (11)	15 (18)	34 (14)
Level 5: retrospective study	12 (15)	3 (4)	52 (21)
Total with levels 1–3	36 (45)	49 (60)	108 (43)
Total with levels 1–5	57 (71)	67 (82)	194 (77)
No evidence	19 (24)	9 (11)	
Against evidence	4 (5)	6 (7)	
Total no or against evidence	23 (29)	15 (18)	58 (23)

105	
370	

Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Bacterial conjunctivitis	Topical antibiotic	6	7	11
Bell's palsy, corneal exposure	No oral steroid, topical lubricant drops	—	4	12
Cataract	Referred for cataract surgery	_	2	13
Microbial keratitis	Topical antibiotics, no steroid	_	1	14
Transient ischaemic attack	Referred for systemic evaluation to start oral anticoagulants	—	1	15

 Table 2
 Evidence-based medicine audit: interventions based on evidence level 1 (systematic reviews) in 2003 and 2004

Table 3 Evidence-based medicine audit: interventions based on evidence level 2 (meta-analysis) in 2003 and 2004

Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Age-related macular degeneration	Fundus fluorescein angiogram	_	3	16
Primary open-angle glaucoma	Topical β -blocker	1	_	17
Primary open-angle glaucoma	Topical latanoprost	1		17

Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Acute anterior uveitis	Topical steroid	5	3	18
Adenoviral keratitis	Topical lubricants	1	_	19
Allergic conjunctivitis	Topical steroid	4	2	20
Blepharitis	Topical antibiotic	2	_	21
Branch retinal vein occlusion	Blood tests, blood pressure, no laser photocoagulation		1	22
Central serous retinopathy	Observation, no laser	1	_	23
Congenital nasolacrimal duct obstruction	Lacrimal sac massage	—	1	24
Corneal abrasion	Topical antibiotic, no patching	8	7	25
Corneal foreign body	Topical antibiotic, no patching	3	7	25
Diabetic vitreous haemorrhage	Panretinal photocoagulation, no vitrectomy	—	1	26
Dry eyes	Topical lubricant		1	27
Episcleritis	Topical nonsteroidal anti- inflammatory	—	1	28
Herpes simplex dendritic ulcer	Topical antiviral		1	29
Herpes simplex stromal keratitis	Topical antiviral + topical steroid		1	30
Marginal keratitis	Topical steroid-antibiotic combination	—	1	31
Optic neuritis	Referred to neurology for further evaluation	1	—	32
Papilloedema, pilocytic astrocytoma	Referred to neurosurgery for further evaluation	—	1	33
Recurrent corneal erosion syndrome	Topical antibiotic	1	_	34
Recurrent corneal erosion syndrome	Topical lubricant		1	34
Scleritis	Oral nonsteroidal anti- inflammatory	1	_	35
Vernal keratoconjunctivitis	Topical steroid + topical mast cell stabiliser		1	36
Viral conjunctivitis	Topical lubricant		1	37
Visual-field defect	Automated perimetry	1	_	38



Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Chalazion	Incision and curettage		2	39
Chalazion	Topical antibiotic	2	1	39
Contact lens keratitis	Topical antibiotic	2	1	40
Hypertensive uveitis	Topical steroid + topical β -blocker	_	1	41
Posterior vitreous detachment	No retinal break, retinal detachment warning	4	6	42
Retinal detachment repair post- operative flat retina	Normal examination, reassure	1	—	43
Subconjunctival haemorrhage	Blood pressure control	_	1	44
Subconjunctival haemorrhage	Blood clotting tests		1	45
Traumatic vitreous haemorrhage	Close observation	—	2	46

Table 5Evidence-based medicine audit: interventions based on evidence level 4 (prospective studies) in 2003 and 2004

Table 6 Evidence-based medicine audit: interventions based on evidence level 5 (retrospective studies) in 2003 and 2004

Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Anterior ischaemic optic	Blood pressure management,	1		47
neuropathy	blood tests			
Chemical injury	Topical antibiotic	4	_	48
Chemical injury	Topical steroid–antibiotic combination	2	—	48
Congenital glaucoma	Topical β -blocker	_	1	49
Dacryocystitis	Oral antibiotics	1	—	50
Panuveitis	Topical steroid	1	_	51
Preseptal cellulitis	Intravenous antibiotics	_	1	52
Preseptal cellulitis	Oral antibiotics	1	_	53
Retinal detachment	Immediate referral for repair	2		54
Retinal macroaneurysm	Blood pressure control	_	1	55

 Table 7
 Evidence-based medicine audit: interventions based on no evidence or against evidence in 2003 and 2004

Diagnosis	Intervention	Number in 2003	Number in 2004	Reference
Acute anterior uveitis	Topical steroid-antibiotic combination	3		_
Allergic conjunctivitis	Topical steroid-antibiotic combination	4	_	_
Chalazion	Oral antibiotics	2	2	
Conjunctival mucus retention cyst	No treatment	1	_	_
Conjunctival mucus retention cyst	Topical lubricant drops	1	—	
Dacryocystitis	Topical steroids	1	_	_
Herpes simplex stromal keratitis	Topical steroid-antibiotic combination	1	_	
Phthisis bulbi	Topical steroids	1	_	_
Photokeratopathy	Topical antibiotic		1	
Subconjunctival haemorrhage	Oral analgesia	1	_	_
Subconjunctival haemorrhage	Topical antibiotic		2	
Subtarsal foreign body	Remove foreign body, topical antibiotics, no patch	1	2	
Superficial punctuate keratitis	Topical antibiotic	1	_	_
Superficial punctuate keratitis	Topical lubricant drops	1	1	_
Trichiasis	Epilation	1	1	_
Allergic conjunctivitis	Oral antihistamine	1	_	56
Herpes zoster ophthalmicus	Topical antiviral		1	57
Optic neuritis	Oral steroid, normal dose	1	_	58
Subconjunctival haemorrhage	No blood pressure check	2	2	44
Viral conjunctivitis	Topical antibiotic		3	59

and Fisher's exact test for the differences between proportions did not show a significant difference between our data and those of Lai *et al.*⁹ Tables 2–7 show a breakdown by level of evidence the number of patients for each diagnosis and intervention, and a citation from the literature search that supports that intervention. Medical interventions comprised 91% and surgical interventions 9%. The outcome of the patients was 35% discharged, 38% to be reviewed in casualty again, 25% to be seen in ophthalmic outpatient clinics, and 3% referred to another hospital specialty.

Guidelines agreed within the department were issued as detailed above. These were written with the knowledge of the results of the 2003 study, but included other common conditions. The conditions for which guidelines were written included ocular trauma, anterior and posterior segment pathology, glaucoma, oculoplastic, orbital, inflammatory, and neuroophthalmic diseases. The timing of the repeat study was not disclosed to prevent bias from Hawthorne's phenomenon.

In the 2004 audit assessing the impact of issued guidelines, 90 case notes were obtained from the 100 requested; 7 were miscoded and had not attended the ophthalmology department and 1 had no diagnosis made in the eye casualty. Therefore, 82 pairs of diagnosis–intervention were available for analysis and comparison to our previous study of 2003 to evaluate whether the quality of emergency ophthalmology could be raised. The mean age of patients seen was 47.6 years (median 48 years, range: 2–86 years), 54% were men. All patients were seen by a senior house officer, and 13% of cases were also discussed with or seen by a senior colleague, similar to the numbers for 2003.

Table 1 also shows the number of interventions in each evidence group for 2004. Overall, 82% of interventions in 2004 had some evidence, and 60% reached levels 1–3. Tables 2–7 also show a breakdown by level of evidence the number of patients for each diagnosis and intervention for 2004, and a citation from the literature search that supports that intervention. Medical interventions comprised 82% and surgical interventions 18%. The outcome of the patients was as follows: discharged in 55% (in 2003, 35%), review in the emergency clinic again in 22% (in 2003, 38%), ophthalmology outpatient clinic referral in 20% (in 2003, 25%), and referred to another specialty in 4% (in 2003, 3%).

Comparing the proportion of interventions by different evidence levels before and after departmental use of guidelines gave some interesting results. In 2003, 71% of interventions had some evidence compared to 82% in 2004 (P = 0.04, Fisher's exact test), and 60% reached levels 1–3 compared with 45% previously (P = 0.02).

There was also a shift in the quality of interventions by evidence level. There were 8% with evidence level 1 in 2003 and 18% in 2004 (P = 0.02, Fisher's exact test). Level 5 evidence was attributed to 15% in 2003 but was reduced to 4% in 2004 (P = 0.009, Fisher's exact test), suggesting the improvement in quality. There was no significant difference for interventions reaching evidence levels 2, 3, or 4. Although the proportion of interventions against evidence stayed steady between our two studies, there was a significant reduction in those interventions with no evidence. When the proportion with no evidence or against evidence are grouped, as in the methodology of Lai *et al.*⁹ there is a significant difference between our results in 2003 (29%) compared to 2004 (18%).

Discussion

Evidence-based medicine is a concept that has been embraced over the last decade. We present the results of our audit in an effort to examine whether the use of evidence-based guidelines could improve the quality of care given to patients in an acute ophthalmic setting.

In the initial reports from general medicine, it was thought that the proportion of interventions based on evidence was low. Subsequent studies of interventions in a range of specialties showed that most medicine was in fact evidence based and included general medicine,^{2,3} surgery,^{5,8} anaesthesia,⁷ and dermatology.⁶ In a landmark report in our specialty, Lai *et al*⁹ showed that ophthalmic interventions reached a similar level. None of these reports, however, have attempted to use the knowledge gained from auditing their interventions to devise ways of improving outcomes for patients. We therefore examined our outcomes using the same methodology as the previously published report⁹ and used this information to improve the quality of care.

Lai *et al*⁹ collected data from 252 interventions in July 2002 for seven sessions in the eye casualty at their tertiary referral centre in Hong Kong and found that 77% were based on evidence, and 43% of their interventions were grade 3 or better. They concluded that interventions in ophthalmic emergency care were comparable to other specialties.⁹ The results of our initial-phase study in a primary eye care facility in London were comparable to all their measures in a tertiary referral centre in Hong Kong (Tables 1 and 2). Overall, 71% of our interventions were evidence based compared to 77% of theirs, and 45% of our interventions were attributed to levels 1–3 *vs* 43% of theirs. Interventions without or against evidence were also similar in this comparison.

We tested whether it would be possible to use guidelines to improve outcomes of clinical decisions beyond the published 'gold standard' for ophthalmology, by either increasing the total number of interventions that were evidence based, reducing the numbers that had no evidence or were against evidence, or increasing the quality of interventions. This report shows that evidencebased evaluation can be used to increase most of these facets. After introducing guidelines, the total number of evidence-based interventions increased significantly from 71 to 82% and their quality increased so that there were less with level 5 and more with level 1 interventions. Even measures of the total interventions with no evidence or against evidence showed a reduction. The only parameter that did not alter significantly was the proportion of interventions against evidence. This may imply that there are a certain number of difficult cases to which generalised studies cannot be applied or indeed that the evidence base from older studies may be out of date with current clinical practice.

The limitations of our study include the possibility of bias. Prescribing bias from prior knowledge of the study by the doctors involved (Hawthorne's phenomenon) was avoided by keeping the dates of both studies unknown to the participants. Bias from improvements in the clinical knowledge of the doctors involved was avoided by careful timing of the study when a new set of doctors would have similar clinical experience to the first set. There exists the possibility that after a year has elapsed, there is more evidence in the literature as a further year's worth of studies have been published. We avoided this potential bias by assessing the 2003 and 2004 interventions in Medline and Cochrane databases from 1966 to 2003 for both years.

However, bias may occur from the deliberately reductionist approach that this methodology takes, in that only the primary diagnosis and primary intervention were examined. Additionally, only two databases were searched, and other sources such as textbooks or case reports were ignored. The reason for this omission was for consistency with previously published studies to compare like for like. Similarly, there is some variation in the literature on which type of study should be assigned to a particular evidence level.^{2,8} Our aim was to audit our outcomes against the 'gold standard' published by Lai *et al*,⁹ so we chose to replicate their method of attributing evidence levels to the various types of studies.

It may also be the case that our study is applicable only to a particular set of circumstances, either the location or staffing of our service. It is encouraging that a primary care facility has the similar outcomes to those of a tertiary referral centre, and that this can be improved upon by a simple method. Perhaps this technique is only useful for relatively junior medical staff, and it would be interesting to see the evidence level of interventions by more senior staff. It is quite possible that with experienced clinicians, the use of guidelines becomes obsolete. In one study examining the evidence base for interventions in eye casualty in Wolverhampton (UK), 90% of interventions were found to have been led by scientific evidence.⁶⁰ In that study, 66% of interventions were carried out by nurse practitioners using departmental guidelines. This supports our view that locally agreed guidelines and protocols should be used for good quality ophthalmic care. However, it must be recognised that a proportion of clinical practice will exist for which there is little published or high-quality evidence. This includes interventions for rare conditions or surgical procedures, for both of which randomised controlled trials may be difficult to achieve.

The case mix between the study of Lai *et al*,⁹ and the two phases of our study is obviously different and is a potential confounding factor that is difficult to control for. This is related to the random nature of cases presented to an emergency service, and we recognise the limitation of this on the audit findings. This might be overcome by a larger clinical audit over a longer period, in an extension of the present study. Nevertheless, issuing guidelines on a wide range of conditions has had an impact on quality, in that there was a positive effect rather than no effect or a negative effect, and also has implications on patient outcomes with fewer return visits. Resource planning is an important issue in a nationally funded health service. A secondary aim of this study was to improve patient outcome and reduce the numbers of unnecessary casualty or outpatient reviews. Our use of guidelines was successful in achieving this with a discharge rate changing from 35 to 55% and a reduction in the number of review visits to the eve emergencies clinic. It is possible that this method gives relatively inexperienced medical staff the confidence to take such decisions, reducing the uncertainty that causes unnecessary re-attendance.

In summary, audit of evidence-based ophthalmology outcomes can be used to measure performance and to improve the quality of care by the use of locally agreed guidelines and has the added benefit of reducing the number of re-attendances required. It will be interesting to see whether other specialties in medicine can also refine their outcomes.

Acknowledgements

We thank Mr K A Thiagarajah, Mr G Palexas, and Dr L Jarrett for their comments on this study.

References

 Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ* 1996; **312**(7023): 71–72.

- 2 Ellis J, Mulligan I, Rowe J, Sackett DL. Inpatient general medicine is evidence based. A-team, Nuffield Department of Clinical Medicine. *Lancet* 1995; **346**(8972): 407–410.
- 3 Michaud G, McGowan JL, van der Jagt R, Wells G, Tugwell P. Are therapeutic decisions supported by evidence from health care research? *Arch Intern Med* 1998; **158**(15): 1665–1668.
- 4 Gill P, Dowell AC, Neal RD, Smith N, Heywood P, Wilson AE. Evidence based general practice: a retrospective study of interventions in one training practice. *BMJ* 1996; 312(7034): 819–821.
- 5 Kenny SE, Shankar KR, Rintala R, Lamont GL, Lloyd DA. Evidence-based surgery: interventions in a regional paediatric surgical unit. *Arch Dis Child* 1997; **76**(1): 50–53.
- Jemec GB, Thorsteinsdottir H, Wulf HC. Evidence-based dermatologic out-patient treatment. *Int J Dermatol* 1998; 37(11): 850–854.
- 7 Myles PS, Bain DL, Johnson F, McMahon R. Is anaesthesia evidence-based? A survey of anaesthetic practice. Br J Anaesth 1999; 82(4): 591–595.
- 8 Kingston R, Barry M, Tierney S, Drumm J, Grace P. Treatment of surgical patients is evidence-based. *Eur J Surg* 2001; 167(5): 324–330.
- 9 Lai TY, Wong VW, Leung GM. Is ophthalmology evidence based? A clinical audit of the emergency unit of a regional eye hospital. *Br J Ophthalmol* 2003; 87(4): 385–390.
- 10 Rhee D, Pyfer M. The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease, 3rd edn. Lippincott Williams & Wilkins: Philadelphia, 1999.
- 11 Sheikh A, Hurwitz B, Cave J. Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database Syst Rev* 2000; (2): CD001211.
- 12 Salinas RA, Alvarez G, Alvarez MI, Ferreira J. Corticosteroids for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev* 2002; (1): CD001942.
- 13 Snellingen T, Evans JR, Ravilla T, Foster A. Surgical interventions for age-related cataract. *Cochrane Database Syst Rev* 2002; (2): CD001323.
- 14 Wilhelmus KR. Indecision about corticosteroids for bacterial keratitis: an evidence-based update. *Ophthalmology* 2002; 109(5): 835–842; quiz 843.
- 15 Algra A, de Schryver EL, van Gijn J, Kappelle LJ, Koudstaal PJ. Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin. *Cochrane Database Syst Rev* 2001; (4): CD001342.
- 16 Bressler NM, Arnold J, Benchaboune M, Blumenkranz MS, Fish GE, Gragoudas ES *et al.* Verteporfin therapy of subfoveal choroidal neovascularization in patients with agerelated macular degeneration: additional information regarding baseline lesion composition's impact on vision outcomes-TAP report No. 3. *Arch Ophthalmol* 2002; **120**(11): 1443–1454.
- 17 Zhang WY, Po AL, Dua HS, Azuara-Blanco A. Metaanalysis of randomised controlled trials comparing latanoprost with timolol in the treatment of patients with open angle glaucoma or ocular hypertension. *Br J Ophthalmol* 2001; **85**(8): 983–990.
- 18 Dunne JA, Travers JP. Double-blind clinical trial of topical steroids in anterior uveitis. *Br J Ophthalmol* 1979; 63(11): 762–767.
- 19 Laibson PR, Dhiri S, Oconer J, Ortolan G. Corneal infiltrates in epidemic keratoconjunctivitis. Response to double-blind corticosteroid therapy. *Arch Ophthalmol* 1970; 84(1): 36–40.

- 20 Abelson M, Howes J, George M. The conjunctival provocation test model of ocular allergy: utility for assessment of an ocular corticosteroid, loteprednol etabonate. *J Ocul Pharmacol Ther* 1998; **14**(6): 533–542.
- 21 Seal DV, Wright P, Ficker L, Hagan K, Troski M, Menday P. Placebo controlled trial of fusidic acid gel and oxytetracycline for recurrent blepharitis and rosacea. *Br J Ophthalmol* 1995; **79**(1): 42–45.
- 22 Argon laser scatter photocoagulation for prevention of neovascularization and vitreous hemorrhage in branch vein occlusion. A randomized clinical trial. Branch Vein Occlusion Study Group. *Arch Ophthalmol* 1986; **104**(1): 34–41.
- 23 Ficker L, Vafidis G, While A, Leaver P. Long-term follow-up of a prospective trial of argon laser photocoagulation in the treatment of central serous retinopathy. *Br J Ophthalmol* 1988; **72**(11): 829–834.
- 24 Kushner BJ. Congenital nasolacrimal system obstruction. *Arch Ophthalmol* 1982; **100**(4): 597–600.
- 25 Kaiser PK. A comparison of pressure patching versus no patching for corneal abrasions due to trauma or foreign body removal. Corneal abrasion patching study group. *Ophthalmology* 1995; **102**(12): 1936–1942.
- Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy. Four-year results of a randomized trial: Diabetic Retinopathy Vitrectomy Study Report 5. Arch Ophthalmol 1990; 108(7): 958–964.
- 27 McDonald CC, Kaye SB, Figueiredo FC, Macintosh G, Lockett C. A randomised, crossover, multicentre study to compare the performance of 0.1% (w/v) sodium hyaluronate with 1.4% (w/v) polyvinyl alcohol in the alleviation of symptoms associated with dry eye syndrome. *Eye* 2002; **16**(5): 601–607.
- 28 Liu CS, Ramirez-Florez S, Watson PG. A randomised double blind trial comparing the treatment of episcleritis with topical 2-(2-Hydroxy-4-methylphenyl) Aminothiazole Hydrochloride 0.1% (CBS 113A) and placebo. *Eye* 1991; 5(Part 6): 678–685.
- 29 Coster DJ, Wilhelmus KR, Michaud R, Jones BR. A comparison of acyclovir and idoxuridine as treatment for ulcerative herpetic keratitis. *Br J Ophthalmol* 1980; **64**(10): 763–765.
- 30 Wilhelmus KR, Gee L, Hauck WW, Kurinij N, Dawson CR, Jones DB et al. Herpetic Eye Disease Study. A controlled trial of topical corticosteroids for herpes simplex stromal keratitis. Ophthalmology 1994; 101(12): 1883–1895; discussion 1895–1896.
- 31 McGill JI, Easty DL, Levy I, Holt-Wilson AD, Shilling J. The aetiology and treatment of marginal corneal ulcers. *Trans Ophthalmol Soc UK* 1971; **91**: 501–507.
- 32 Optic Neuritis Study Group. The 5-year risk of MS after optic neuritis: experience of the optic neuritis treatment trial. *Neurology* 1997; **49**(5): 1404–1413.
- 33 Wisoff JH, Boyett JM, Berger MS, Brant C, Li H, Yates AJ et al. Current neurosurgical management and the impact of the extent of resection in the treatment of malignant gliomas of childhood: a report of the Children's Cancer Group trial no. CCG-945. J Neurosurg 1998; 89(1): 52–59.
- 34 Hykin PG, Foss AE, Pavesio C, Dart JK. The natural history and management of recurrent corneal erosion: a prospective randomised trial. *Eye* 1994; **8**(Part 1): 35–40.
- 35 Watson PG, Lobascher D. The diagnosis and management of episcleritis and scleritis. *Trans Ophthalmol Soc UK* 1965; **85**: 369–378.



- 36 Tabbara KF, al-Kharashi SA. Efficacy of nedocromil 2% versus fluorometholone 0.1%: a randomised, double masked trial comparing the effects on severe vernal keratoconjunctivitis. Br J Ophthalmol 1999; 83(2): 180–184.
- 37 Shiuey Y, Ambati BK, Adamis AP. A randomized, doublemasked trial of topical ketorolac versus artificial tears for treatment of viral conjunctivitis. *Ophthalmology* 2000; **107**(8): 1512–1517.
- 38 Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA *et al.* The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002; **120**(6): 714–720; discussion 829–830.
- 39 Jackson TL, Beun L. A prospective study of cost, patient satisfaction, and outcome of treatment of chalazion by medical and nursing staff. *Br J Ophthalmol* 2000; 84(7): 782–785.
- 40 Morlet N, Minassian D, Butcher J. Risk factors for treatment outcome of suspected microbial keratitis. Ofloxacin Study Group. Br J Ophthalmol 1999; 83(9): 1027–1031.
- 41 Ohno S, Ichiishi A, Matsuda H. Hypotensive effect of carteolol on intraocular pressure elevation and secondary glaucoma associated with endogenous uveitis. *Ophthalmologica* 1989; **199**(1): 41–45.
- 42 Tanner V, Harle D, Tan J, Foote B, Williamson TH, Chignell AH. Acute posterior vitreous detachment: the predictive value of vitreous pigment and symptomatology. *Br J Ophthalmol* 2000; 84(11): 1264–1268.
- Thompson JA, Snead MP, Billington BM, Barrie T, Thompson JR, Sparrow JM. National audit of the outcome of primary surgery for rhegmatogenous retinal detachment. II. Clinical outcomes. *Eye* 2002; 16(6): 771–777.
- 44 Fukuyama J, Hayasaka S, Yamada K, Setogawa T. Causes of subconjunctival hemorrhage. *Ophthalmologica* 1990; 200(2): 63–67.
- 45 Bartholomew JR, Salgia R, Bell WR. Control of bleeding in patients with immune and nonimmune thrombocytopenia with aminocaproic acid. *Arch Intern Med* 1989; **149**(9): 1959–1961.
- 46 Nischal KK, James JN, McAllister J. The use of dynamic ultrasound B-scan to detect retinal tears in spontaneous vitreous haemorrhage. *Eye* 1995; **9**(Part 4): 502–506.
- 47 Sawle GV, James CB, Russell RW. The natural history of non-arteritic anterior ischaemic optic neuropathy. J Neurol Neurosurg Psychiatry 1990; **53**(10): 830–833.
- 48 Brodovsky SC, McCarty CA, Snibson G, Loughnan M, Sullivan L, Daniell M *et al*. Management of alkali burns: an

11-year retrospective review. *Ophthalmology* 2000; **107**(10): 1829–1835.

- 49 Turach ME, Aktan G, Idil A. Medical and surgical aspects of congenital glaucoma. *Acta Ophthalmol Scand* 1995; 73(3): 261–263.
- 50 Mauriello Jr JA, Guzman C. Oral and topical antibiotic therapy of complete, primary acquired nasolacrimal duct obstruction in adults. *Ophthal Plast Reconstr Surg* 1999; 15(5): 363–365.
- 51 Dodds EM, Lowder CY, Meisler DM. Posterior segment inflammation in HLA-B27 + acute anterior uveitis: clinical characteristics. *Ocul Immunol Inflamm* 1999; 7(2): 85–92.
- 52 Sobol SE, Marchand J, Tewfik TL, Manoukian JJ, Schloss MD. Orbital complications of sinusitis in children. *J Otolaryngol* 2002; **31**(3): 131–136.
- 53 Uzcategui N, Warman R, Smith A, Howard CW. Clinical practice guidelines for the management of orbital cellulitis. *J Pediatr Ophthalmol Strabismus* 1998; 35(2): 73–79; quiz 110–111.
- 54 Laatikainen L, Harju H, Tolppanen EM. Post-operative outcome in rhegmatogenous retinal detachment. *Acta Ophthalmol (Copenh)* 1985; 63(6): 647–655.
- 55 Lewis RA, Norton EW, Gass JD. Acquired arterial macroaneurysms of the retina. *Br J Ophthalmol* 1976; **60**(1): 21–30.
- 56 Abelson MB, Kaplan AP. A randomized, double-blind, placebo-controlled comparison of emedastine 0.05% ophthalmic solution with loratadine 10 mg and their combination in the human conjunctival allergen challenge model. *Clin Ther* 2002; 24(3): 445–456.
- 57 Neoh C, Harding SP, Saunders D, Wallis S, Tullo AB, Nylander A *et al.* Comparison of topical and oral acyclovir in early herpes zoster ophthalmicus. *Eye* 1994; 8(Part 6): 688–691.
- 58 Kaufman DI, Trobe JD, Eggenberger ER, Whitaker JN. Practice parameter: the role of corticosteroids in the management of acute monosymptomatic optic neuritis. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2000; 54(11): 2039–2044.
- 59 Ward JB, Siojo LG, Waller SG. A prospective, masked clinical trial of trifluridine, dexamethasone, and artificial tears in the treatment of epidemic keratoconjunctivitis. *Cornea* 1993; **12**(3): 216–221.
- 60 Bhatt R, Sandramouli S. Evidence-based practice in acute ophthalmology. *Eye* 2007; **21**(7): 976–983.