

BjO

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Editorials

Change at the *BjO*

The *BjO* has prospered for the past seven years because of the editorial leadership of Professor John Forrester. He brought intellectual vigour and honesty as well as creativity to this task. The journal is now both a highly regarded scientific publication as well as a thought provoking and interesting journal to peruse. During the tenure of John Forrester the *BjO*'s impact factor has increased, the quality of its scientific papers was outstanding, and the appearance and readability of the journal were first class. Regrettably, we must now thank Professor Forrester for his service and wish him all the best in his new endeavours as he steps down from the position of editor.

I am proud to have been appointed John Forrester's successor although I realise it will be difficult to match his successes. I have no intentions of reinventing the wheel and will build on the already strong model left by him. I am also pleased to say that there will be continuity in the editorial board that assists me in this task. I am particularly pleased to announce that Professor Andrew Dick, who will shortly assume his responsibilities in Bristol, has agreed to remain as the editor for the United Kingdom. His expertise and intellectual standards will be a great attribute in our task of trying to make the *BjO* even better. I am also pleased to say that most of the editorial board have agreed to remain. Although there may be a few new members added to the board, its essential structure will remain as it has been in the past with the majority of its members being from the United Kingdom but with a worldwide contribution from other members.

No successful journal can afford to not move forward and bring new formats to its structure. This is particularly true in this age of electronic publishing that is just beginning to make an impact in the world of scientific journals. Most of you are already aware of the fact that the *BjO* has already established an active and attractive website. We will be putting much of our energy and creativity into expanding this website and hopefully making it one of the leaders among clinical journals. To

this end I have appointed Robert Bhisitkul, MD, PhD, a colleague of mine at the University of California, San Francisco, as the website editor. He brings unique talents to this task. He has a PhD in neuroscience from Yale University as well as retinal training at Harvard Medical School. We hope to expand the website, bring new quality material to it, and ultimately have it stand on its own as a unique and distinct resource separate from the published hard copy of the *BjO*. In the next few months we hope to bring video tapes of surgical procedures and complications to the website. In addition, we will establish a quick response feature which will allow readers to comment on either the content of the published journal and/or the website. Although we believe it essential to expand and enrich the quality of the website, we do not plan to ignore the published hard copy of the *BjO*. We are currently redesigning the cover of the journal and in the next few months we'll add a new feature to the journal entitled "Point-counterpoint," a format in which experts can debate some of the controversial aspects and therapies of our subspecialty.

Undoubtedly, the journal will evolve and change in ways that are not yet apparent. We can only hope to use as our model during this evolutionary period that of Professor John Forrester. We hope that each new feature of the journal will have the same high scientific content that was established under John's leadership. While we wish to make the journal interesting and provocative, we in no way want to compromise the high intellectual standing established by him. All the members of the editorial board and I wish to thank John Forrester for the opportunity to work with him during his tenure as editor. It was a pleasure and an honour to do so. We are all committed to publishing a journal every bit as good as the one published under his leadership.

CREIG S HOYT

Editor, *BjO*

Herpes simplex virus in the human cornea

Herpes simplex virus (HSV) infection is prevalent throughout the world. An estimated 60–70% of children aged 5 and close to 90% of adults exhibit seropositivity (neutralising antibody) to HSV antigens. Despite this widespread prevalence, only 20%–30% present with clinical disease, and ocular manifestations develop in less than 1%.¹

Traditionally, the diagnosis of herpes simplex keratitis (HSK) has been based on clinical evaluation, occasionally complemented by viral culture. Immunohistology and, relatively recently, polymerase chain reaction (PCR) and in situ hybridisation (ISH) techniques have been employed to detect viral DNA in corneal buttons removed at the time of penetrating keratoplasty or in corneal biopsy specimen taken from patients with undetermined corneal inflammation.^{2–7} The deployment of these techniques, however, has largely been as part of studies or projects, rather than a routine clinical service. The sensitivity and specificity of these techniques is variable and the detection of viral DNA does not necessarily correspond with presence of infective virus, as only a part of the viral DNA may be present. Only viral culture is 100% specific, but its sensitivity is rather low. Like many diagnostic tests, these tests are not mutually exclusive but complementary. In the paper by Kaye *et al* in this issue of the *BJO* (p 563) the authors have compared the sensitivity and specificity of viral culture, immunohistology, PCR, and ISH in detecting virus in 110 human corneal buttons removed at penetrating keratoplasty and 19 eye bank donor eyes not suitable for corneal transplantation. They concluded that both PCR and immunohistology were sensitive for detection of HSV-1 in the human cornea and, when combined, the specificity for the diagnosis of HSK reached 97%. The clinical definition of HSK, as a history of recurrent dendritic or geographic corneal ulceration and the development of stromal scarring, was used as a standard to measure sensitivity and specificity.

A large number of studies on human^{3–6 8 9} and animal^{10 11} corneal buttons, obtained during the quiescent stage of HSK, have reported the detection of viral DNA using PCR and immunohistology (ISH was not found to be as sensitive⁸). Holbach *et al*⁶ were able to detect viral DNA with equal frequency from vascularised and non-vascularised HSK corneas but noted a significantly higher detection of viral antigen, by immunohistology, in the avascular specimen. These studies show that the yield of viral DNA from both animal and human corneal tissue obtained from quiescent post-HSK eyes tends to decline with time. The longer the duration following the active episode, the less likely it is to detect viral DNA. This is probably related to the decline in the amount of viral DNA present. Interestingly, all the above studies, like the one reported by Kaye *et al* in this issue, also reported detection of viral DNA from non-HSK corneal buttons. The detection rate was not as high but was nevertheless significant. Furthermore, several studies have shown the presence of HSV DNA in normal and eye bank donor corneas,^{3 12–16} Primary graft failure and massive loss of endothelium in stored eye bank corneas, has been associated with viral DNA in the affected corneal tissue.^{12 17}

The presence of viral DNA in corneas, long after the active HSK episode has subsided, has led to the hypothesis of extraneuronal herpetic latency in the cornea. This concept is rapidly gaining popularity but is not yet totally convincing. The presence of viral DNA does not correspond with viral infectivity of the tissue.

This has been borne out both in cell culture studies and in vivo, after transplantation of viral DNA positive corneas to non-herpetic recipients. Morris *et al*¹³ analysed the spent culture media of 80 donor corneas and detected HSV DNA in three cell pellets; however, follow up of patients receiving these corneas did not reveal HSV eye disease or graft failure. In one study in rabbits, aimed at establishing HSV latency, only 10% of eyes contained virus that could be reactivated in culture while an additional 55% contained viral DNA.¹⁰

What then is the take home message for the practising clinical ophthalmologist? The diagnosis of HSK is still essentially clinical. Although it is always reassuring to have laboratory confirmation of a clinical diagnosis, one must not lose sight of the fact that the standard against which the sensitivity and specificity of the above tests was measured, was the clinical definition (diagnosis) of HSK. The apparent “widespread” presence of viral DNA in HSV, non-HSV, and even normal corneas is cause for concern but the mere presence of viral DNA does not automatically equate to its ability to cause infection. Corneal latency, however real or otherwise that might be, is not the same as neuronal latency. The comparatively low levels of viral DNA which is transcriptionally dormant, the lack of adequate numbers of latency associated transcripts, the possibility of presence of incomplete viral genome and its attenuation with time in corneal tissue, all serve to diffuse any concern over transplanting “infected normal corneas” to healthy recipients, at least at the present state of our knowledge. One question remains. If the amount of viral DNA and its detection rate declines with time in HSV infected corneas, does its detection in donor corneas imply viral reactivation in the period immediately preceding death? If so, then should these not be potentially infective?

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The efficacy of occlusion for strabismic amblyopia. Can an optimal duration be identified?

Patching carried out during the sensitive period is thought by clinicians to be an effective treatment for amblyopia.^{1,2} Success rates of patching vary but one study has reported success rates of 90% of patients improving to 6/12 or better within 3 months.³ Parents not uncommonly report difficulty in persuading their children to wear a patch.⁴ Inpatient treatment by supporting the parents and encouraging the children frequently achieves success.

A recent systematic review⁵ was unable to find any randomised controlled trials of treatment of amblyopia and concluded that there was no evidence that treatment worked. They relied heavily on the results of a study which suffered from many flaws in its design.^{6,7} Nevertheless, if the highest standards are applied, there is no evidence from a randomised controlled trial that patching works as a treatment for amblyopia. It follows that if treatment is ineffective there is no justification to screen for amblyopia and indeed this was the conclusion of the systematic review. Most ophthalmologists do not need to be convinced of the efficacy of patching treatment for amblyopia.

Cleary (this issue, p 572) has taken advantage of the presence of both compliers and non-compliers in a group of children with amblyopia treated with glasses and patching to carry out a prospective but non-randomised control trial. The numbers are small (only 17 non-compliers) but the two groups are comparable in terms of density of amblyopia and other variables. The logMAR crowded test (Glasgow acuity cards) has been employed and this is ideal for measuring visual acuity in amblyopia; the non-amblyopic eye has been used as a control. The improvement in visual acuity was significantly less in those strabismic children who did not comply with treatment. It is impossible to say that differences between the groups of compliers and non-compliers do not account for the difference in results but, nevertheless, given the paucity of

good quality data in this field, these results are of considerable interest. There are several other questions that need to be answered with regard to treatment of amblyopia. Is full time occlusion more effective than part time?⁸ What is the role of atropine penalisation as opposed to using an eye patch? When should treatment be stopped? What are the reasons for non-compliance with treatment and how can we best measure this? Is there anything more that we can do to help improve compliance? There is considerable research activity under way to address these issues. It is healthy for paediatric ophthalmology to have our assumptions challenged and provides impetus for the construction of a valuable evidence base. At present, a randomised controlled trial of occlusion therapy for anisometropic amblyopia is under way (Wright C, Clarke M, A multicentre randomised controlled trial of treatment of amblyopia detected at pre-school vision screening, personal communication) and the results of this study are awaited with interest.

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