Microbial keratitis

B H Jeng, S D McLeod

Shifting trends in the epidemiology of infectious keratitis demand that we approach all cases thoughtfully

Microbial keratitis is a potentially vision threatening condition that requires prompt diagnosis and treatment to prevent untoward outcomes. The incidence of this condition varies from 11.0 per 100 000 person years in the United States1 to 799 per 100 000 person years in the developing nation of Nepal.2 Microbial keratitis is thus a significant public health problem, and numerous studies have been performed describing the microbiology of corneal infection. As would be expected, there are regional differences in the organisms that are cultured from infected corneas, but for the most part, in the United States, Staphylococcus species seem to predominate.

On a global level, predisposing risk factors for microbial keratitis vary tremendously with geographical location. Although non-surgical trauma to the eye accounted for 48.6–65.4% of all corneal ulcers in the developing countries of Nepal and India,3,4 at a large county trauma referral centre in the United States, non-surgical eye trauma accounted for only 27% of all cases.5 In the United States, it is contact lens wear that has emerged as a major risk factor for microbial keratitis. The reported percentage of corneal ulcers associated with contact lens wear has increased in the general population from 0% in the 1950s and 1960s, to 31% in the 1970s, and to 52% in the 1980s.6 In our own community based population study during the late 1990s, we found a continuation of this upward trend with 55% of corneal ulcers treated with contact lenses in 1998.7 In a random sampling of non-cornea fellowship trained ophthalmologists performed by Bourcier et al,8 they estimated that 75% of corneal ulcers were contact lens related as well. In a similar study performed by Klintworth et al,9 they reported that 86% of ocular trauma cases were contact lens related with the incidence of trauma and corneal ulcers directly proportional when comparing patients with and without contact lens wear.

In this issue of the BJ O (p 834), Bourcier et al have reported that contact lenses were responsible for over half of all cases of bacterial keratitis in their study. Although the study originates from a large ophthalmic centre that provides tertiary care, most (76%) of the cases presented for the first time in their emergency room, and only 24% were referred by either general practitioners or ophthalmologists. In this mostly non-referral based population, the finding of over 50% of cases of bacterial keratitis being contact lens related is consistent with the previously mentioned community based studies from the United States. The authors discuss, however, some of the suspected cases of contact lens related bacterial keratitis may actually include contact lens related sterile inflammatory infiltrates that resolve spontaneously upon discontinuation of contact lens wear, rather than true cases of bacterial keratitis. Thus, the authors may have undercalculated the culture positivity rate and overcalculated the percentage of cases of bacterial keratitis with contact lens wear as a risk factor.

Emerging resistance to fluoroquinolones continue to mount within and outside the sphere of ophthalmology

It is interesting that in this study, while there were more culture positive contact lenses and/or storage cases than culture positive corneal scrapings, similar bacteria were isolated from the two sources in only 25% of all cases. This demonstrates that while organism recovery from a lens or case may be easier than from the cornea, the identity of organisms recovered from the contact lens and case cannot be considered a reliable guide for directing antimicrobial therapy. As shown in this study and has been demonstrated by previous studies, contact lens storage containers are frequently contaminated, commonly with Gram negative organisms. While it has been recognised that Gram negative organisms such as Pseudomonas aeruginosa are associated with contact lens related corneal ulcers, Gram positive organisms such as Staphylococcus species and Streptococcus species have also often been shown to be responsible for a significant portion of these ulcers even when Gram negative organisms are recovered from the lens and case. Indeed, the current study reports a higher incidence of Gram positive organisms than Gram negative organisms recovered from infections associated with contact lens wear. Thus, exclusive reliance on culture data from contact lenses and/or cases may result in suboptimal treatment of corneal ulcers.

Bourcier et al, as well as most authors of studies from academic referral centres, followed the textbook practice of scraping of all suspected cases of microbial keratitis for smear and culture. Since the Gram stain might fail to reveal culpable organisms and it is inadvisable to delay treatment while awaiting the results of cultures, it is common practice to begin empirical treatment with broad spectrum antibiotic drops. Treatment can then be modified later based on clinical response and, if necessary and available, on culture results. Traditionally, specially prepared fortified combined antibiotics were used to provide broad spectrum coverage, but the limited availability, cost, and inconvenience of these fortified preparations have led many academic and community based ophthalmologists to embrace the use of the commercially available topical fluoroquinolones (ciprofloxacin, ofloxacin, and, more recently, levofloxacin) since their introduction in the 1990s.6 These antibiotics have good ocular penetration and provide broad spectrum coverage against most aerobic Gram negative and Gram positive bacteria. They also are safe, do not require refrigeration, and are easily available. In addition, many clinical studies have demonstrated excellent efficacy of these drugs in treating bacterial keratitis.10-17 In a questionnaire based study, 82% of a random sampling of non-cornea fellowship trained ophthalmologists reported that they would treat less severe cases of suspected bacterial keratitis with a single fluoroquinolone, and 62% reported that they would treat more severe cases in this manner.18 Our own study of corneal ulcers in a non-referral based population found that 75% of corneal ulcers were in fact treated with a single fluoroquinolone agent (unpublished data).

Although there has always been a known gap in coverage for Streptococcus species by the second generation fluoroquinolones, emerging resistance of Staphylococcus aureus to ciprofloxacin and ofloxacin19-20 has raised concern over the use of monotherapy with these agents for suspected cases of bacterial keratitis. This is especially true given the high rates of microbial keratitis caused by Gram positive organisms. It is well recognised that the levels of drugs in the cornea obtained with topical therapy far
Human papillomavirus

Does human papillomavirus cause pterygium?

T W Reid, N Dushku

HPV is not necessary for the formation of a pterygium

Human papillomavirus (HPV) is the only DNA tumour virus where a large body of evidence implicates it in human cancers. The evidence for a causative role of HPV in human cervical cancer, was recently reviewed by zur Hausen,1 and is the following: (1) expression of specific HPV genes (such as E6 and E7) were shown in cervical cancer cell lines and cancer biopsies; (2) viral DNA was shown to have immortalisation properties4; (3) viral oncogene expression was shown to be required for the maintenance of the malignant phenotype in specific cervical cancer cell lines; (4) a substantial number of epidemiological studies have been performed which point to high risk HPV as a primary risk factor for cervical cancer. In addition, large case-control and prospective epidemiological studies supported this idea, and indicated that persisting HPV infections were the most significant risk factor in cervical cancer.7

Different types of HPV have been identified in a high percentage of non-melanoma skin cancers (basal and squamous cell carcinomas). However, these basal and squamous cell carcinomas occur preferentially in light exposed sites. This could suggest an interaction...
between ultraviolet light and a low risk (non-mutagenic) papillomavirus in dogs could make it a possible candidate in pterygia, which are thought to have aetiology involving ultraviolet irradiation.

The binding to the p53 protein of the E6 oncoprotein, encoded by HPV types 16 and 18, results in the rapid degradation of p53. This process regulates the ability of p53 protein to inhibit cell proliferation and induce cell cycle arrest, apoptosis, and immune surveillance. HPV E7 oncoprotein can interact with the p53 tumor suppressor protein and inhibit its function, leading to sustained expression of E6 and E7 proteins, which can promote cellular transformation.

In summary, while the exact role of HPV in the development of pterygia remains to be fully elucidated, the presence of HPV in conjunctival tissues and the potential for HPV to alter cellular functions involved in apoptosis and cell cycle regulation make it a plausible candidate in the pathogenesis of this condition. Further research is needed to better understand the role of HPV in the development of pterygia and to explore potential therapeutic strategies targeting HPV and p53 interactions.
Responding to readers’ and authors’ needs

Andrew D Dick, Creig Hoyt

Future changes to the BJO

As editors, keeping a pace with changes in publishing, pleasing both readers and authors without creating chaos or anarchy is challenging. We continue to respond to the voices of both readers and authors alike and will continue as such to change the journal format to maintain and fulfill its mission of supplying high quality information in its most relevant and readable form. We acknowledge that the readers and authors may have different expectations of the journal. Firstly, readers wish to be assisted in their continual professional development and revalidation and require easy access to information that is readable and succinct. Secondly, there is a need to assist researchers with information pertinent to their individual needs and, thirdly, of course, we need to give the authors the medium to present their findings and views in the most expeditious manner and which will sell to the widest audience.

As such, the BJO is committed, along with the rest of the BMJ Publishing Group, to provide a medium to satisfy all. Although the BJO has seen a dramatic increase in submissions, now over 1300 articles a year, with an acceptance rate of 34%, going online has enabled our mean time to decisions on papers to be cut drastically to three weeks. We aim to please authors further within the next 12 months as we launch the capability to publish manuscripts as soon as they are accepted—on the website—followed in print by the technically edited version a few months later. This will provide immediate dissemination of up to date work to all. In addition, this will hopefully create fruitful correspondence, which will be all web based; you will be asked to submit your correspondence (Mailbox) directly to eBJO. We will also increase page provision in the print journal to ensure that print publication time is around four months from acceptance.

What about the readers? The BMJ has reiterated from its studies that readers do not read traditional long full original articles, and the need for such articles to be so long has been questioned. We wish to encourage articles that are written succinctly and, in time, we will be providing a modified “Instructions to authors” that will have link sites to assist prospective authors less experienced in writing. The articles will be divided into Clinical science and Laboratory science as is the case at present and, within each section, there will be the opportunity to submit either extended or scientific reports. There will be strict word counts of 3000 and 1500 words, respectively, and we will be encouraging authors where appropriate to submit their work in the shorter version. Letters to the editor will remain but we will be focusing our attention, because of priority and space, on case series, genetic reports, and clinicopathological reports. Perspectives will also remain but again will be limited strictly to 4000 words. We still encourage and solicit editorials, commentaries, and world views and maintain our commitment towards globalisation, publishing work from, and provision of information to all.

Br J Ophthalmol 2003;87:808

Authors’ affiliations
A D Dick, C Hoyt, Editors; choyt@itsa.ucsf.edu


BJO

www.bjophthalmol.com
Microbial keratitis

B H Jeng and S D McLeod

*Br J Ophthalmol* 2003 87: 805-806
doi: 10.1136/bjo.87.7.805

Updated information and services can be found at:
http://bjo.bmj.com/content/87/7/805.1

These include:

**References**
This article cites 20 articles, 2 of which you can access for free at:
http://bjo.bmj.com/content/87/7/805.1#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
- Cornea (524)
- Ocular surface (618)
- Eye (globe) (708)
- Epidemiology (1075)
- Conjunctiva (216)
- Public health (479)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/