Microbial keratitis

B H Jeng, S D McLeod

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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,3–5 at a large county trauma referral centre in the United States, non-surgical eye trauma accounted for only 27% of all cases.6 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late 1990s, we found a continuation of this upward trend with 55% of corneal ulcers associated with contact lens wear (unpublished data). Similarly, in academic referral institutions in the United States, there was a well documented upward trend in the incidence of contact lens related corneal ulcers from 9% in the late 1970s to 44% in the late 1980s.6–11 However, later reports showed a declining trend to 9–18% in the late 1990s.12–14 This reduction in corneal ulcers seen at academic referral centres coincident with an increase in the community might be attributed to more successful community treatment of ulcers since the introduction of the topical fluoroquinolones ciprofloxacin and ofloxacin in the 1990s.15–17

In this issue of the *BJO* (p 834), Bourcier *et al* have reported that contact lens wear accounted 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. As 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 both within and outside the sphere of ophthalmology

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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, 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 properties; (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 persistent HPV infections were the most significant risk factor in cervical cancer.

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 to be debated. However, if one can propose that the “optimal” management of microbial keratitis is that which is the most convenient for both the patient and the physician, the most cost effective, and the most efficacious, then the “optimal” management strategy is as yet undefined. In spite of the advances in antibiotic pharmacology, shifting trends in the epidemiology of infectious keratitis demand that we approach all cases thoughtfully. Studies such as that provided by Bourcier et al provide most valuable information to this end.

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between ultraviolet light and a low risk (non-mutagenic) papillomavirus in 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 degrada- tion of p53 protein through the ubiquitin mediated pathway. This HPV infection mechanism leads to a damaged p53 dependent programmed cell death pathway,11 which is similar to that caused by mutations in the p53 gene. Low levels of normal nuclear p53 protein permit mutations in other genes to accumulate and allow the multistep development of tumours. Also, reduced bioavail- ability of p53 protein has been shown to be a key regulatory event in perturbation of CD95 signalling in HPV16 immortal- ised keratinocytes.23 HPV and p53 over-expression also commonly coexist in oropharyngeal carcinomas,11 penile carcinomas,12 grade III cervical intraepi- thelial neoplasia,3 and invasive squamous cell carcinomas of the cervix.3 Since increased nuclear p53 expression without apoptosis was found in the limbal epithelium of pterygia, limbal tumours, and most pingueculae,3 this would be consistent with HPV playing a part in the formation of pterygia.

The paper by Piras et al, in this issue of the BJO (p 864), shows a 100% incidence (17/17) of HPV in pterygia from Italian cases and a 21% (5/24) incidence from Ecuadorian cases. A recent study by Gallagher et al32 showed a 50% (5/10) incidence of HPV in pterygia in the United Kingdom. Detorakis et al33 found 15 pterygia contained type 18 HPV, for a total of 30% (15/50) in Greece. In addition they found that 8% of the associated conjunctiva contained HPV (4/50). In other studies Dolmetsch et al34 found HPV-16 in 100% of their pterygia (16/16) from Canada using immunohistochemical techniques. The above results are in contrast with the results of McDonnell et al35 who found HPV-16 in 88.1% (37/42) of their patients with conjunctival epithelial neoplasia but none in six pterygia from America. Dushku et al36 also found no evidence of HPV in 13 pterygia and 10 limbal tumours from American cases. McDonnell et al35 also found HPV in tissue swabs from eyes with no visible lesions in 66.7% (4/6) of patients with unilateral conjunctival epithelial neoplasia and in one patient who showed a persistence of infection many years after successful eradication of the lesion. This is consistent with the finding of Karci- oglu and Issa37 who found HPV in 57% of in situ squamous cell carcinomas, 55% of invasive squamous cell carcinomas; however they also found HPV in neoplastic lesions (20% of dichtmic droplet keratopathy and 35% of scarred corneas) as well as 32% of normal conjunctival tissue obtained during rou- tine cataract extractions. Thus, it would appear that HPV is not required for a pterygium and that even in its presence it cannot act alone in the development of conjunctival epithelial neoplasia.

At the moment several companies and research laboratories are carrying out preclinical and clinical trials of vaccines against high risk HPV.22–26 Since experiments with purified papillomavirus structural proteins as vaccines showed protection against the primary infection of dogs and rabbits, an effective prevention model can also be expected for the human vaccine. If this is true it may allow us to know whether prevention of HPV decreases or blocks the incidence of different cancers. It would also be of interest to see whether vaccinated individuals show a lower incidence of ptery- gia.

Since Koch’s postulates cannot be ful- filled and unless more definitive results are obtained such as those from future HPV vaccine trials, we can only make the following statements for the role of HPV in the occurrence of pterygia: (1) HPV is not necessary for the formation of a pterygium; (2) it is unlikely that HPV can act as the sole cause of a pterygium; (3) HPV may have a role in the formation of some pterygia; (4) pterygia and limbal dysplasias in the interpalpebral area, which regress after topical antiviral treatment with interferon α2b, may be due to HPV.29–31

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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.

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.

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