ORIGINAL ARTICLE

# Review of *Acanthamoeba* keratitis associated with contact lenses in Hong Kong Chinese people

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## Abstract

**Aim:** To review the management and outcomes of *Acanthamoeba* keratitis associated with contact lenses in Hong Kong Chinese people.

**Methods:** This was a retrospective review performed at the subspecialty eye clinics at a tertiary hospital. Consecutive patients with presumed *Acanthamoeba* keratitis who were treated at the Prince of Wales Hospital, Hong Kong, from August 2005 to August 2007 were included. Medical interventions included corneal scraping, confocal microscopy, and intensive anti-*Acanthamoeba* eye drops. Surgical intervention included corneal gluing. Risk factors, clinical features, culture results, confocal microscopy results, treatment responses, and visual outcomes were analyzed.

**Results:** Nine eyes of seven patients with clinical *Acanthamoeba* keratitis were identified. The use of Complete® MoisturePlus™ solution, overnight contact lens wear, and swimming with contact lenses were found to be risk factors for *Acanthamoeba* keratitis. Ocular pain and perineural infiltrates were important clinical features of *Acanthamoeba* corneal ulcer. The culture-positive rate for *Acanthamoeba* was 22.2%. Confocal microscopy was positive for 44.4% of eyes. Eight (88.9%) of the treated eyes had improvement of vision after medical treatment. Eight eyes had vision better than 20/50 and 6 eyes had vision better than 20/30.

**Conclusions:** Contact with contaminated fluids was an important risk factor for contact lens–related *Acanthamoeba* keratitis. The recognition of clinical features, acquisition of corneal specimens for *Acanthamoeba* culture, and identification of intrastromal cysts by confocal microscopy were important for early diagnosis and subsequent treatment. Prompt initiation of a combination anti-*Acanthamoeba* treatment regimen was conducive to good visual recovery.

*Key words:* Acanthamoeba *keratitis, Contact lenses, Risk factors, Treatment outcome*

## Introduction

*Acanthamoeba* keratitis (AK) is a vision-threatening corneal infection caused by a free-living amoeba. *Acanthamoeba* spp are ubiquitous and can be isolated from various environments, including public water supplies, swimming pools, fresh water streams, sea water, hot tubs, ventilation ducts, soil, bottled water, eyewashes, and contact lenses and lens cases. Microcorneal trauma during contact lens wear and exposure to contaminated fluids could result in AK. *Acanthamoeba* spp exist in 2 forms, trophozoites and cysts. Trophozoites are motile and feed on bacteria. In unfavorable conditions, trophozoites will encyst. Cysts have a double wall containing cellulose, and are resistant to many chemical agents.[1] As a result, *Acanthamoeba* spp is difficult to eradicate.

AK is an uncommon cause of corneal infection. Recent reports from Japan[2] and India[3] have demonstrated that AK accounts for only 1% of microbial isolates of ulcerative keratitis. In a local study done in 1997 by Lam et al,

6 patients (2.7%) with AK were identified among 223 patients with microbial keratitis — 5 were contact lens users and 1 had had a previous corneal abrasion.[4] The reasons for this seemingly higher incidence of AK in Hong Kong could be related to 3 factors. First, the prevalence of myopia in the adult Hong Kong population is high (71%).[5] Second, contact lens wear is a preferable to spectacle wear in the adult population in Hong Kong. Third, orthokeratology contact lens wear has been promoted among Hong Kong children to temporarily reduce myopia.

Contact lens wear is an established risk factor for microbial keratitis[3,6-9] Severe complications of corneal infection such as corneal scarring or perforation may lead to permanent loss of vision. Among contact lens–related microbial keratitis, AK is one of the most challenging conditions to diagnose and manage clinically.

Following the recent USA Food and Drug Administration (FDA) Public Health Notification in May 2007 that AK may be related to Complete® MoisturePlus™ (Advanced Medical Optics, Santa Ana, USA), and the Hong Kong Centre for Health Protection release of May 2007 to local doctors on the same subject, this study was performed to review the patients with AK treated at the Prince of Wales Hospital, Hong Kong, a tertiary referral centre. The purpose of the study was to identify the common clinical features and risk factors, and to illustrate the management outcomes for contact lens–related AK in Hong Kong Chinese people.

## Methods

A retrospective case review of contact lens–related AK managed at the Prince of Wales Hospital between August 2005 and August 2007 was performed. Patients were identified from the microbiology department records for *Acanthamoeba* culture requests (thus both confirmed and clinical cases were identified). The criteria for inclusion were: positive *Acanthamoeba* culture from corneal scraping; and/or *Acanthamoeba* cyst identified by confocal microscopy; and/or typical clinical features together with clinical response to anti-*Acanthamoeba* treatment.

All patients were interviewed during one of their follow-up clinic visits, and a standard data sheet was completed together with the chart review. Risk factors such as history of trauma, contact lens wear, overnight contact lens wear, swimming or hot spring use with contact lenses inserted, and previous ocular diseases were documented. Contact lens details, including brand name, lens type, contact lens wearing schedule, disinfection solution used, and compliance to the recommended replacement schedule, were also obtained. Clinical signs at presentation and at follow-up, culture results, clinical treatment outcome, and visual outcome were examined.

## Results

Nine eyes of 7 patients were diagnosed with AK from August 2005 to August 2007. All of the patients were contact lens users, and were Hong Kong Chinese women. The average age at presentation was 23.1 years (SD, 7.2 years). The average degree of myopia was -3.2 D (SD, 0.9 D) [**Table 1**].

The most common contact lens type used was the monthly replacement soft contact lens. The most commonly used disinfection solution was Complete MoisturePlus. Five patients (71.4%) admitted using the contact lenses for a longer duration than the recommended time (**Table 2**). Overnight contact lens wear was reported by 3 patients (42.9%), and 4 patients (57.1%) reported swimming with their contact lenses in situ. None of the patients had a history of frank corneal trauma.

The most common presenting symptoms were intensive ocular pain (88.9%) and blurring of vision (44.4%). Patients mostly presented within 1 week of the onset of symptoms (**Table 1**). One patient presented 28 days after the onset of symptoms (patient 6). Her delayed presentation was due to masking of the symptoms by topical steroid use. At presentation, the most common clinical signs were epithelial defects (55.6%), perineural infiltrates (44.4%), ring infiltrates

**Table 1. Demographic data of 7 patients with *Acanthamoeba* keratitis.**

| Data | Number of patients (%) |
|---|---|
| Age (years) | 23.1 ± 7.2 |
| Sex | |
| Male | 0 |
| Female | 7 (100) |
| Laterality | |
| Right | 5 (55.6) |
| Left | 4 (44.4) |
| Myopia (D) | - 3 ± 0.9 |
| Duration of contact lens wear (years) | 4.3 ± 6.3 |
| Duration from onset of symptoms to presentation (days) | 7.6 ± 8.1 |
| Duration from onset of symptoms to initiation of anti-*Acanthamoeba* treatment (days) | 3.0 ± 4.3 |
| Follow-up (months) | 12.3 ± 7.4 |

**Table 2. Contact lenses and disinfection methods used.**

| Contact lenses and disinfection | Number of eyes (n = 9) |
|---|---|
| Type of contact lens | |
| Monthly replaced | 5 |
| Biweekly replaced | 1 |
| Non-disposable soft | 1 |
| Orthokeratology (n = 2) | 2 |
| Disinfection method | |
| Complete MoisturePlus | 6 |
| Normal saline | 1 |
| Oxsept | 1 |
| Three-steps | 1 |
| Compliance with replacement schedule | |
| Yes | 7 |
| No | 2 |

(33.3%), and dendritic epithelial erosion (11.1%) [**Figures 1** to **4**]. Only 1 eye (11.1%) had hypopyon at presentation. Visual acuity at presentation ranged from 20/20 to hand movements.

Corneal scraping was performed for each of the 9 eyes and the specimens were sent for bacterial, fungal, and *Acanthamoeba* culture. *Acanthamoeba* culture was positive in only 2 eyes (22.2%). Confocal microscopy was performed on 6 eyes, and intrastromal cysts were demonstrable in 4 eyes (**Figure 5**).

All the eyes were treated with one of, or a combination of, 3 drugs — polyhexamethylene biguanide (PHMB 0.02%; Leiter's Park Avenue Pharmacy, San Jose, USA), propamidine isethionate (Brolene 0.1%; Aventis Pasteur, Maidenhead, UK), and neomycin-polymyxin B-gramicidine (Neosporin; Glaxo Wellcome, Saint-Laurent, Canada) [**Table 3**].

The average duration from presentation to initiation of anti-*Acanthamoeba* treatment was 3.0 days (SD, 4.3 days) [**Table 1**]. Before the diagnosis of AK was made, 1 patient was diagnosed with herpetic corneal ulcer, and 3 patients were

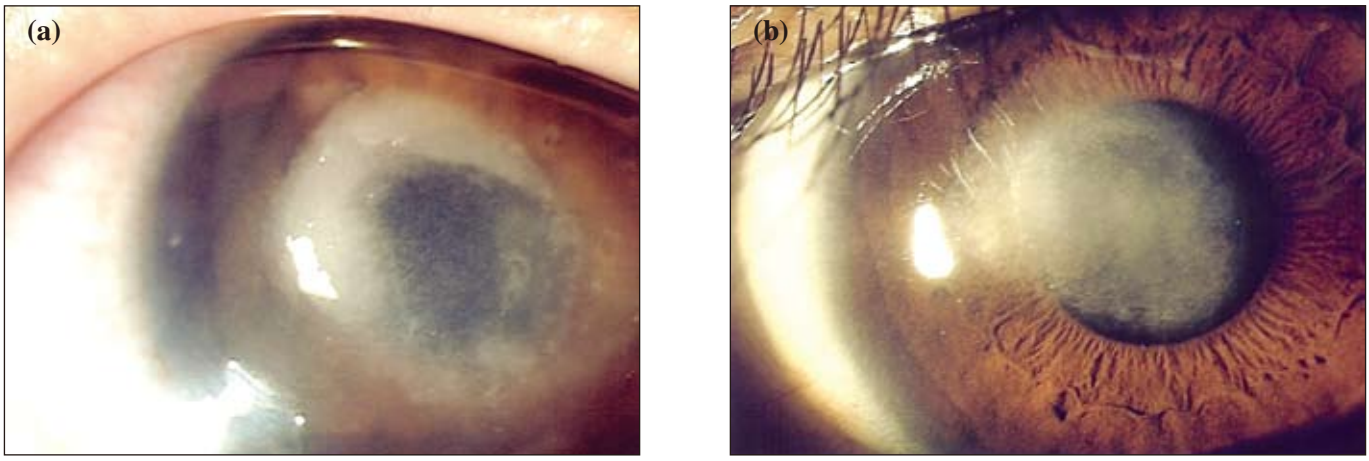


**Figure 1. Slit-lamp photograph of patient 1 with (a) a ring infiltrate at presentation; and (b) a central corneal scar after treatment.**

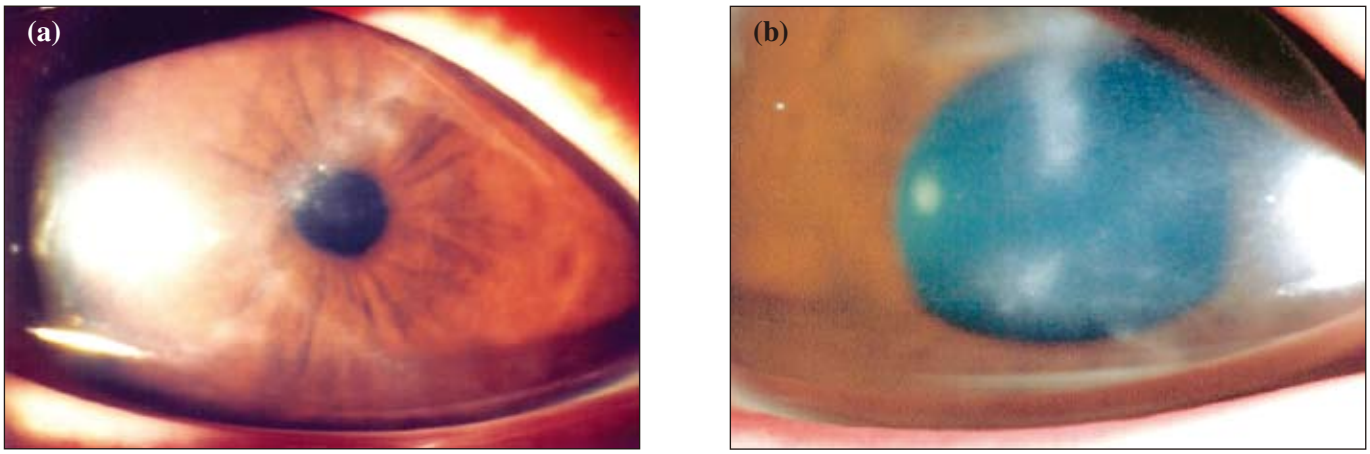


**Figure 2. Slit-lamp photograph of patient 3 with (a) elevated linear infiltrates; and (b) perineural infiltrates.**

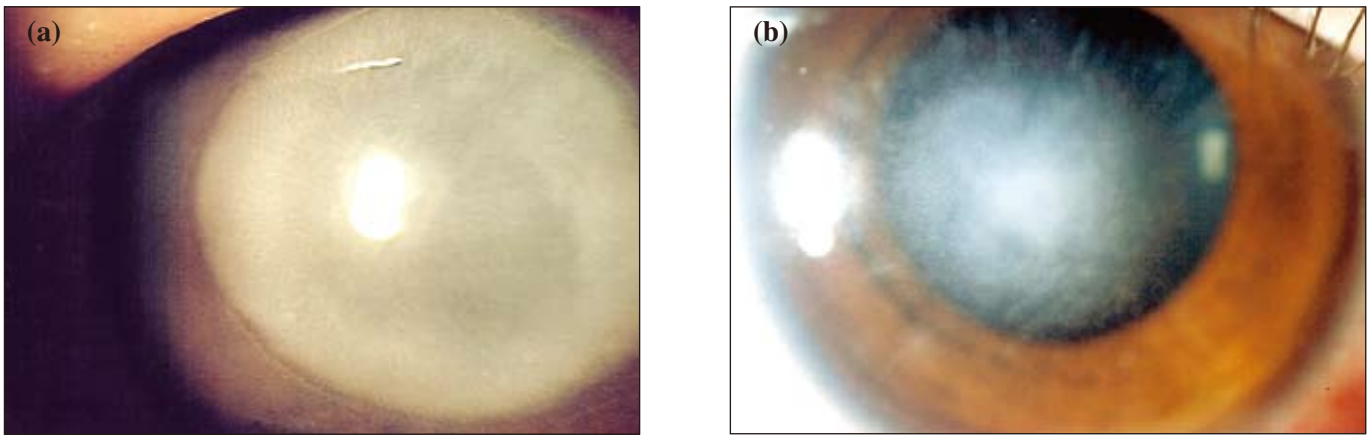


**Figure 3. Slit-lamp photograph of patient 6 with (a) dense ring infiltrate at presentation; and (b) glue was in situ with organized hypopyon.**

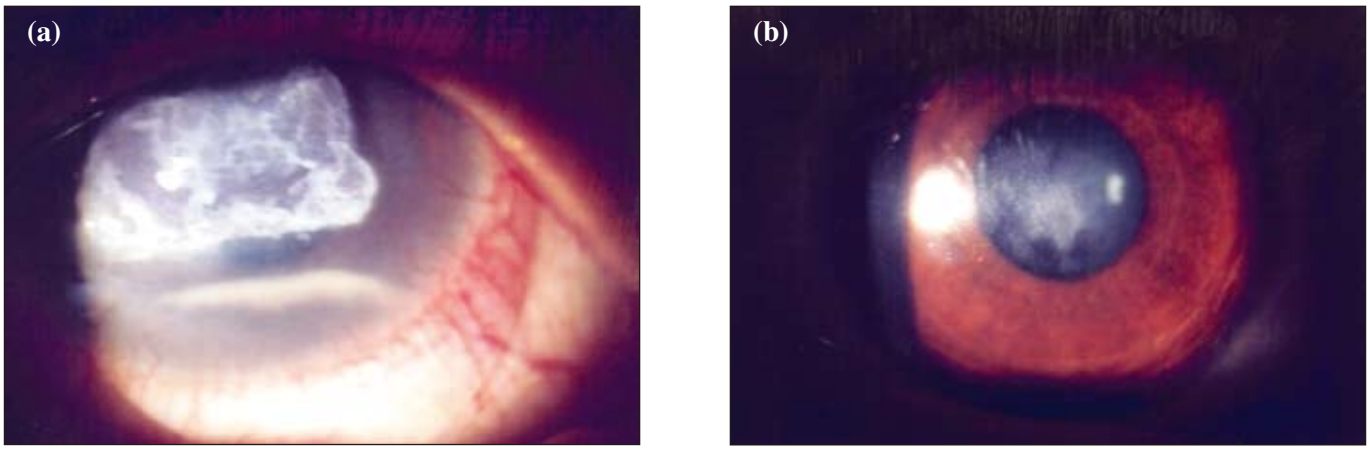


**Figure 4. Slit-lamp photograph of patient 7 with (a) radiating perineural infiltrates at presentation and (b) faint corneal scar after treatment.**

treated with fortified antibiotics. Patient 7 was diagnosed with AK at presentation. Initiation of anti-*Acanthamoeba* treatment was delayed for 2 days because the drugs had to be ordered from an overseas pharmaceutical company on a named patient basis. Prolonged treatment is required for AK and the patients were followed up for an average of 12.3 months (SD, 7.4 months).

A corneal scar of various densities persisted on the cornea of patient 1 (**Figure 1**). Eight of 9 eyes had final best-corrected visual acuity (BCVA) of better than 20/50, and 6 of 9 eyes final BCVA of better than 20/30. Visual acuity was measured at the time of data collection. When comparing pre- and post-treatment vision, visual improvement was noted in 8 eyes. Patient 6 presented with ring infiltrate with visual acuity of 1/200 (**Figure 3**). Despite intensive medical therapy with hourly PHMB, propamidine isethionate, and neomycin-polymyxin B-gramicidine, the cornea eventually perforated in a paraxial location. Emergency surgery was performed, and cyanoacrylate glue (Histoacryl®; Braun, Michigan, USA) was applied as a temporary tectonic graft. The patient's final BCVA was finger counting 10 months after treatment. Corneal graft surgery is planned after the initial rehabilitation period.

## Discussion

Myopia is a common ocular condition, affecting 25% of the population of the USA aged between 12 and 54 years.[10] The prevalence of myopia varies throughout the world, being higher in Asians (38.7%) than in Caucasians (17%).[11-15] Although excimer laser is gaining popularity, laser refractive surgery is not without limitations. Patients with thin corneas, large pupils, and high myopia may not be suitable candidates for laser refractive surgery. Therefore, contact lens wear remains a popular option for adults with myopia. Recently, there has been a resurgence of interest in orthokeratology contact lenses for the temporary reduction of myopia.[8,16] This approach has been promoted as being able to halt or even reverse myopic progression. This claim is particularly appealing to parents of children with myopia. As a result, orthokeratology contact lens wear has gained popularity amongst children and adolescents for freedom from spectacle wear.

In the study of 223 patients with microbial keratitis by Lam et al, 59 patients (26%) wore contact lenses.[4] Six patients (2.7%) were confirmed to have AK, 5 (2.2%) of which were contact lens related. AK is known to be a severe infection that can result in corneal scar formation, and even corneal perforation leading to severe visual impairment. Poor clinical outcome may result if there is a delay in diagnosis and initiation of treatment. Duguid et al classified diagnosis as 'early' (within 28 days), 'intermediate' (28 days to 2 months), and 'late' (>2 months).[17] Visual recovery was more favorable when patients were diagnosed early. The presentation of AK is variable and may be non-specific. Patients may present with mild red eye with a disproportionate degree of eye pain to the clinical appearance. Dendritiform epithelial

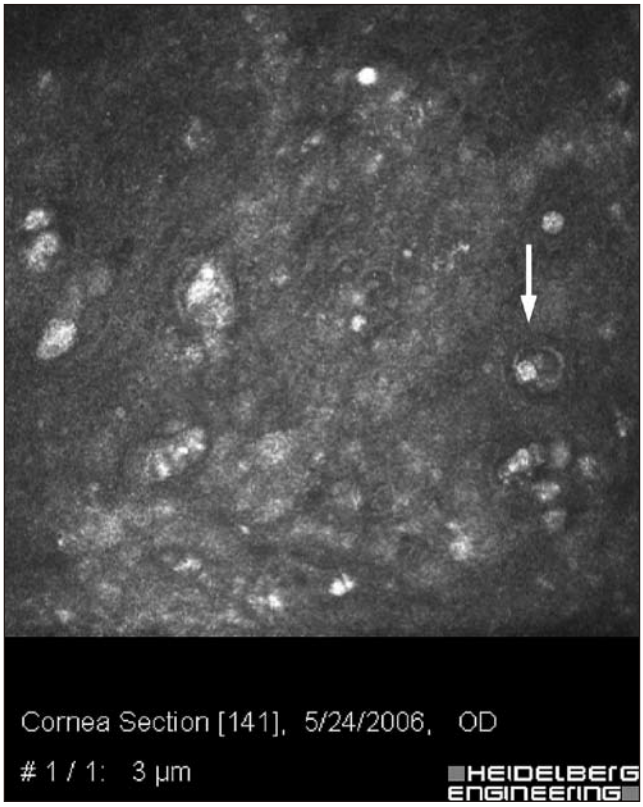


**Figure 5. Confocal microscopy of patient 3 demonstrating an intrastromal acanthamoeba cyst with hyperintense cell wall (arrow).**

**Table 3. Treatment outcomes.**

| Patient number | Sex/age (years) | Previous treatment | Treatment regimen | Presenting visual acuity | Final visual acuity |
|---|---|---|---|---|---|
| 1 | F/18 | Antibiotic | Steroid<br>Anti-herpetic<br>PHMB | 1/200 | 20/30 |
| 2 | F/28 | Antibiotic | Brolene | 20/20 | 20/15 |
| 3 | F/28 | Antibiotic | Brolene | 20/20 | 20/20 |
| 4 | F/22 | Nil | PHMB<br>Brolene | 20/30 | 20/30 |
| 5 | F/22 | Nil | PHMB<br>Neosporin | 20/60 | 20/40 |
| 6 | F/38 | Steroid | PHMB<br>Brolene<br>Neosporin | 1/200 | CF |
| 7 | F/14 | Nil | PHMB<br>Brolene | HM | 20/20 |
| 8 | F/19 | Antibiotics | PHMB<br>Brolene | 20/30 | 20/30 |
| 9 | F/19 | Nil | PHMB<br>Brolene | 20/100 | 20/30 |

*Abbreviation:* PHMB = polyhexamethylene biguanide.

pattern early in the course of AK may mimic herpes simplex keratitis.[18] Patients with intermediate presentation may have superficial corneal infiltrates distributed along the corneal nerves (perineural infiltrates). In this study, most patients had symptoms of a painful eye not controlled by oral analgesics, and perineural infiltrates and ring infiltrates were the most common presenting signs.

The confocal microscope enables in vivo optical examination of the cornea in axial sections.[19] Using this approach, the microscopic details of the cornea at the cellular level can be observed. In this study, confocal microscopy was used successfully to detect intrastromal cysts in 4 eyes.

Risk factors for AK in contact lens wearers include the type of contact lens worn, the disinfection procedure, overnight contact lens wear, and swimming while wearing contact lenses. The epidemiology of contact lens–related microbial keratitis was reported by Liesegang in 1997.[7] Different contact lens materials pose different risks for infective keratitis. The relative risk was 1.0 for rigid gas-permeable contact lenses, 0.5 to 2.7 for polymethyl methacrylate rigid contact lenses, 1.0 to 4.2 for daily-wear reusable soft contact lenses, 2.7 to 36.8 for extended-wear soft contact lenses, and 13.0 to 13.3 for reusable soft contact lenses.[7] In this study, the most common type of contact lens was the monthly or biweekly replacement soft contact lenses. None of the patients wore daily disposable contact lenses. Any deviation from the chemical disinfection procedures or insufficient duration results in heightened risks for infection, and this study documented poor compliance to the contact lens replacement schedule. Extended use of daily disposable contact lenses further increases the risk for corneal infection.[20]

Six (66.7%) of 9 patients used Complete MoisturePlus multipurpose solution only to disinfect the contact lenses. Multipurpose solutions are popular due to the convenience of disinfection by simply soaking the contact lenses in the solution for a fixed period of time. Attracted by the 'no rub' and 'one step' disinfection procedure, contact lens wearers prefer using these multipurpose solutions. However, in May 2007, the USA Centers for Disease Control and Prevention (CDC) reported an association of AK with the use of Complete MoisturePlus cleaning solution. The CDC and FDA notified the public and medical communities that the manufacturer had undertaken a voluntary global recall of the product. The Hong Kong Centre for Health Protection (CHP) also announced the recall of the solution on the CHP website and via the media.[21] Unfortunately, 1 patient in this study (patient 8) was still using this multipurpose solution when she presented in June 2007. To prevent any outbreak of contact lens–related microbial keratitis, proper contact lens handling procedures must be promoted. The Hong Kong CHP posted contact lens handling guidelines on the CHP website on 22 August 2005.[22]

Overnight contact lens wear (of any lens type or material) is associated with a higher risk than daily wear.[23] When sleeping with contact lenses in situ, the closed eyelids cause relative corneal hypoxia and epithelial edema. An edematous cornea is more susceptible to abrasion from minor trauma, thus microabrasions caused by contact lenses may lead to corneal epithelial defects. Any breach of the corneal surface as a result will increase the risk for infection.

The principle of orthokeratology lenses is to mechanically 'brace' and flatten the central cornea during the night. Patients using orthokeratology contact lenses are required to wear the rigid contact lenses for approximately 8 hours per night. This unphysiological practice has resulted in an ever growing number of publications about orthokeratology lens–related corneal infections, for both non-Acanthamoeba and AK in children and adults.[8-9,24] Patient 7 was a form 4 student at an elite secondary school. She was informed of the contact lens handling procedures but failed to comply with the recommendations. Therefore, should orthokeratology

contact lens wear be considered for children, parents must be informed of the risk for permanent visual loss and correct lens hygiene procedures must be taught to the most appropriate person (the lens wearer or their parents).

Four of 7 patients in this study reported wearing contact lenses in a swimming pool or spa. The soiling of contact lenses in a swimming pool or spa could lead to corneal infection by *Acanthamoeba*.[25]

*Acanthamoeba* infections are difficult to treat because of the ability of the organism to encyst in adverse conditions; cysts are considerably more resistant to treatment than are trophozoites. Furthermore, if there is a delayed treatment, the organisms invade progressively deeper into the stroma. This may further limit the success of topical agents, as drug concentrations may be reduced in the deeper target tissues.[26] The treatment outcomes in this study of AK are comparable to international studies. Duguid et al reported treatment outcomes for 111 patients and concluded that BCVA better than 20/30 was achieved for 79.3% of patients.[17] Butler et al found that 75% of 20 patients achieved BCVA of 6/12 or better.[27] In this study, BCVA better than 20/30 was achieved in 77.8% of patients and BCVA of 20/40 was achieved in 88.9% of patients. The main factors contributing to treatment success are early diagnosis and prompt initiation of anti-*Acanthamoeba* therapy.[17]

A limitation of this study is the lack of patients from other centers in Hong Kong. Therefore, this series might not be representative of the disease spectrum in Hong Kong.

In conclusion, it is hoped that this report will increase the awareness of this relatively uncommon ocular infection among the local medical community. Responsibility for awareness of the risks among the general public rests with the CHP and the medical profession. If a patient presents with a corneal infection and associated risks and findings, AK should be considered, and referral to an ophthalmologist for urgent assessment, tissue culture, and the prompt initiation of treatment may preserve the patient's vision. Topical steroids must be withheld for patients suspected to have corneal infection.

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