

# Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America

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## Abstract

**Purpose** To establish the incidence, etiology and risk factors for microbial keratitis (MK) in Hong Kong.

**Methods** Two hundred and twenty-three new cases of presumed MK were recruited over a period of 17 months and comprehensive microbiologic studies performed. A nested case-control study was pursued for patients wearing contact lenses (CLW) to determine risk factors for MK with regards to types of CLW and hygiene practice.

**Results** Of the 223 patients recruited, 59 (26%) wore contact lenses. Corneal scrapes yielded positive cultures from 77 patients (35% overall, 56 non-CLW, 21 CLW). Two hundred and six CLW volunteers were recruited to participate in the case-control study, of whom 135 were matched with 45 CLW patients. The annual incidence of MK was 0.63 per 10 000 population and 3.4 per 10 000 CLW with rates for daily, extended and rigid lens wear of 3.09, 9.30 and 0.44 per 10 000 CLW respectively. *Pseudomonas aeruginosa* was the dominant bacterial pathogen. Six cases of *Acanthamoeba* keratitis occurred, five in CLW (incidence 0.33 per 10 000 CLW) and one following corneal abrasion. Non-CLW developed MK at a peak age of 73, which is 10 years younger than expected for Scotland and USA.

**Conclusions** Previous ocular surface disease and trauma were the main risk factors for MK in Hong Kong. CLW appears at least as safe as that found in Scotland and the USA. *Acanthamoeba* keratitis was detected but with an incidence rate five times lower than Scotland. Factors predisposing hydrogel

CLWs to MK, that were statistically significant, included overnight wear, poor hygiene and smoking.

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**Keywords:** microbial keratitis; incidence; contact lens; risk factors

## Introduction

Ulcerative and non-ulcerative keratitis due to infection is a potentially blinding condition that is generally only found in eyes with a predisposing element. Contact lens (CL) wear is recognized as an increasingly common risk factor in otherwise healthy eyes.<sup>1–3</sup> When not associated with CL use, it may be diagnosed in patients of all age groups and trauma may be a predisposing factor. With the growth of the CL user population since the 1980s, this factor has increased as the primary predisposing cause for microbial keratitis (MK) in the USA but not for Scotland and England.<sup>2,3</sup> Risk factors such as extended wear of the lens, especially sleeping with the lens in the eye, have been described<sup>4,5</sup> but have never been investigated in a subtropical Far East climate.

Microbial keratitis has been reported due to infection with a wide range of organisms. There are regional variations in the predominance of different microbes, reflecting different patient populations and climatic effects. Fungi are important in the tropical regions, such as South India and Ghana.<sup>6,7</sup> *Acanthamoeba* has been identified among CL related infections in many parts of the world.<sup>8</sup>

There is little information on MK and/or CL-related infections in Asia, although the

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number of CL wearers is expected to increase rapidly, particularly among the young. This is especially likely in China where the prevalence of myopia is on a rising trend. MK caused by unusual pathogens requires specific and often expensive diagnostic methods and therapies. A cost-effective approach in the diagnosis, management and prevention of this condition is only possible when the incidence, relative importance of different microbial agents and predisposing factors are known. The cause of such infection has never been fully investigated in South China, in particular in the semi-tropical urban climate of Hong Kong.

### Materials and methods

A prospective study of MK was conducted between April 1997 and August 1998 with patients from the two hospitals with Eye Units—Hong Kong Eye Hospital (HKEH) and the Prince of Wales Hospital (PWH)—serving our territory of Kowloon and New Territory East, who presented with such a clinical diagnosis and gave oral consent. MK was defined as the clinical presentation of a corneal stromal infiltrate >1 mm<sup>2</sup> usually but not necessarily with an overlying

epithelial defect. The onset of pain, redness, blurred vision, foreign body sensation, photophobia & discharge were all recorded as was the visual acuity on presentation. In addition, the size of the overlying defect and the position in the cornea (axial, paraxial or periphery) were recorded. Typical inflammatory keratitis such as marginal keratitis, and viral keratitis due to herpes and adenoviruses were excluded. Risk factors such as ocular trauma, previous ocular surface disease (OSD), contact lens wear (CLW) and history, application of steroid or antibiotic(s) and history of herpetic infection were recorded on presentation. The characteristics of the ulcer/infiltrate (size in square mm, shape, site and anterior chamber activity) were noted.

In order to assess how many cases of MK (excluding classical inflammatory, herpetic and adenovirus infection) existed in Hong Kong private practice, a questionnaire was sent to all the 27 private ophthalmologists in our area on two occasions during the study period. They were asked to estimate the number of cases they had seen and the number they had referred to the two study centers in the previous 3 months. All Hong Kong ophthalmologists and the Hong Kong Optometric Association were informed of

**Table 1** Demographic information for patients with presumed microbial keratitis

	Contact lens wearers (CLW) (n = 59)		Non-contact lens wearers (Non-CLW) (n = 164)		Total (n = 223)		P value*
	n	%	n	%	n	%	
Age (years) <20	18	31%	7	4%	25	9%	0.0000 <sup>a</sup>
21–39	35	59%	36	22%	71	34%	
40–64	6	10%	56	34%	62	28%	
>65	0	0%	65	40%	65	29%	
Male	20	34%	93	57%	113	51%	0.0043 <sup>b</sup>
Female	39	66%	71	43%	110	49%	**0.39 (0.2–0.76)
Right eye	30	51%	82	50%	112	50%	0.9680 <sup>b</sup>
Left eye	29	49%	82	50%	111	50%	**0.97 (0.51, 1.83)
Previous eye disease	4	7%	79	48%	83	37%	0.0000 <sup>b</sup> **0.08 (0.02–0.23)
History of trauma	3	5%	44	27%	47	21%	0.0009 <sup>b</sup> **0.15 (0.03–0.49)
Use of antibiotic prior to hospital referral	34	58%	66	40%	100	45%	0.0271 <sup>b</sup> **2.06 (1.08–3.95)
Use of steroid prior to hospital referral	2	3%	11	7%	13	6%	0.2325 <sup>c</sup> **0.49 (0.05, 2.35)

\*P value: CLW vs non-CLW.

\*\*Matched odds ratio (95% exact confidence limits).

<sup>a</sup>Mann–Whitney U-test exact P-value.

<sup>b</sup>Chi-square test.

<sup>c</sup>Fisher's exact test.

this study and asked to help refer patients with MK that could be considered due to bacteria, fungi or amoebae to one of the two hospitals mentioned above for investigation and treatment.

Using preservative-free amethocaine eye drops for local anesthesia, corneal scrapings were performed in all cases with a Kimura spatula. Microscopy was performed on Gram-stained smears of the corneal sample. Inoculation of blood and chocolate agars and thioglycolate broth for bacteria, Sabouraud's agar for fungi and non-nutrient Page's saline agar for *Acanthamoeba* was carried out at the time of the procedure. Incubation took place at 37°C for 48 h for bacteria, 1 week for *Nocardia* and 3 weeks for fungi. Culture plates were examined using routine laboratory techniques. Culture plates for *Acanthamoeba* were incubated at 30°C, wrapped in plastic bags, and examined intermittently for up to 4 weeks for the presence of characteristic double-walled star-shaped cysts. This was precisely the same method as that used for the Scottish Cohort Study.<sup>2</sup>

The prevalence of CLW in Hong Kong has been investigated by Cho *et al* and recorded as 6% with 13% wearing rigid lenses.<sup>9</sup> The population by age group for our area in 1998 was provided by the Census and Statistics Department, Hong Kong Special Administrative Region. This census recorded a total of 2 489 701 persons, with 2 048 630 over the age of 15. This latter figure was used as the reference number for the total population who could be wearing contact lenses.

To determine the risk factors for CL-related MK, a nested case control study was carried out by recruiting 206 asymptomatic CLW volunteers with oral consent. One hundred and thirty-five matched our CLW patients for age (<25, 26–35, 36–45, and >45), sex (male or female) and educational status (graduate/non-graduate). One hundred and twenty of these 135 controls were community-based with 102 coming from our LASIK (Laser *in-situ* keratomileusis) Clinic, 12 from the Eye Screening 2000 Clinic and six from Kowloon optical practices (with the help of the Hong Kong Optometric Association). Fifteen matched controls were hospital-based lens-wearing asymptomatic staff recruited at PWH. These 135 CLW volunteers were not known to represent any specific bias. The research assistant face-to-face interviewed both the 45 CLW patients and 135 volunteer controls using the same questionnaires to establish their types of CLW and hygiene practice. Questions included the duration of time of use and use in sleep during daytime or nighttime.

For patient and matched control groups, potential risk factors such as extended wear of the lens were

evaluated for their association with MK by univariate and multivariate conditional logistic regression analyses.<sup>10</sup> All risk factors were first assessed individually, and matched odds ratios, the corresponding 95 percent confidence intervals and *P* values were calculated. Risk factors with *P* < 0.25 were analyzed by multivariate analysis<sup>10</sup> using a forward stepwise selection strategy. In general, the process added the most significant risk factor (ie the one that would result in the largest likelihood ratio statistic) to the model at each step, and would continue until no risk factor not in the model made a significant (*P* < 0.05) contribution. Whenever two or more potential risk factors were highly correlated or *P*-values were similar, the factor that was the more clinically or biologically important was selected for entry. Analyses were performed using the LogXact logistic regression software featuring exact methods, version 1.3 (CYTEL Software Corporation, Cambridge, MA, USA). To explore the association between possible characteristics and the type of CLW for the type of person who wears a CL overnight, the test for homogeneity odds ratios, Zelen statistic and Wilcoxon–Mann–Whitney test were used for the stratified 2 × 2 and 2 × 3 comparisons respectively (StatXact 4 for Windows: User Manual. Cytel Software Corporation, 2000).

## Results

Demographic information for the 223 patients with MK who presented to the two Ophthalmology Units between April 1997 and August 1998 (17 months) is given in Table 1 and clinical information is given in Table 2. A surprisingly high number (27%) of patients with MK without CLW had suffered previous ocular trauma. Microbes isolated from each group are given in Table 3. The incidence of MK for patients with OSD (non-CLW) at different age groups is shown in Figure 1.

Of the 223 patients with presumed MK, 197 patients were either referred by their private doctors, optometrists or were self-referred. This explains why 58% of lens wearers and 40% of those with OSD were receiving antibiotics on arrival at the hospital (Table 1). By estimation, the private ophthalmologists in our catchment area saw a total of 167 patients during the study period with ulcerative keratitis of all natures from viral to presumed microbial. Of these 167 patients, 26 (16%) were referred to the two study centers over 17 months as probable cases of infectious (bacterial, fungal or amoebal) MK, a serious condition usually requiring investigation and treatment in specialist centers. Their other 141 patients (84%) were not referred and managed as keratitis of other causes

**Table 2** Clinical information for patients with presumed microbial keratitis

	Contact lens wearers (CLW) (n = 59)		Non-contact lens wearers (Non-CLW) (n = 164)		Total (n = 223)		P*
	n	%	n	%	n	%	
<b>Chief complaint<sup>†</sup></b>							
Pain	26	44%	67	42%	93	42%	
Redness	18	31%	31	19%	49	22%	
Blurred vision	10	17%	30	19%	40	18%	
Foreign body sensation	3	5%	28	17%	31	14%	
Photophobia & discharge	2	3%	5	3%	6	3%	0.122 <sup>a</sup>
<b>Onset (days)<sup>‡</sup></b>							
<7	34	69%	86	67%	120	67%	
8–30	13	27%	41	32%	54	30%	
>31	2	4%	2	2%	4	2%	0.860 <sup>b</sup>
<b>Visual acuity<sup>§</sup></b>							
6/6	5	9%	12	8%	17	8%	
6/9	16	29%	35	23%	51	24%	
6/12–6/36	18	32%	30	19%	48	23%	
1–6/60	5	9%	24	15%	29	14%	
LP/HM/CF	12	21%	44	28%	56	26%	
No light perception	0	0%	11	7%	11	5%	
<b>Size of ulcer (mm<sup>2</sup>)<sup>¶</sup></b>							
< 4 mm <sup>2</sup>	38	66%	89	55%	127	58%	
> 4 mm <sup>2</sup>	20	34%	73	45%	93	42%	0.210 <sup>c</sup>
<b>Ulcer position<sup>  </sup></b>							
Axial	20	34%	46	28%	66	30%	
Paraxial	18	30%	58	36%	76	34%	
Peripheral	21	36%	58	36%	79	36%	0.673 <sup>c</sup>

\*P-value: CLW vs non-CLW.

<sup>†</sup>Information on three controls missing.

<sup>‡</sup>Information on 10 patients and 35 controls missing.

<sup>§</sup>Information on three patients and eight controls missing.

<sup>¶</sup>Information on one patient and two controls missing.

<sup>||</sup>Information on two controls missing.

<sup>a</sup>Chi-square exact test. <sup>b</sup>Mann-Whitney test exact P-value. <sup>c</sup>Chi-square test.

that included mainly herpetic and inflammatory causes such as marginal keratitis. Thus, 26 patients were referred by ophthalmologists and 197 from other sources, giving a total number with presumed MK of 223.

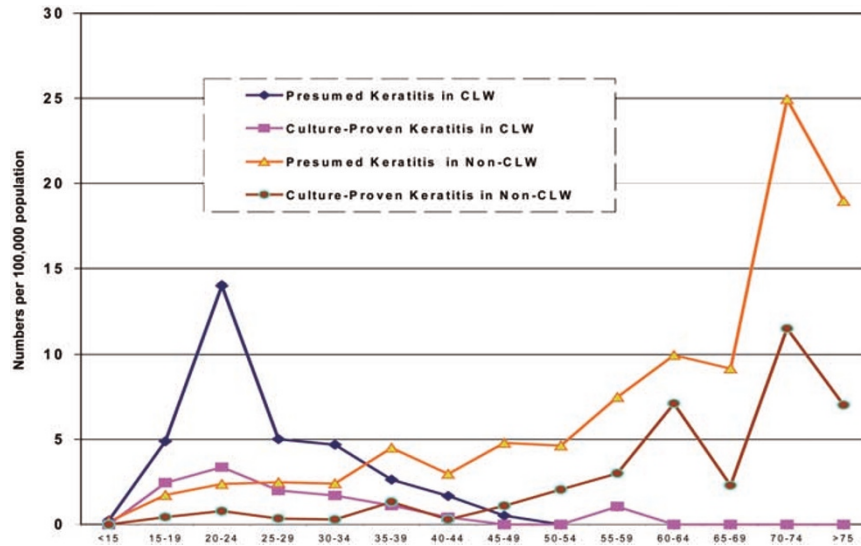
Of the 164 non-CLW patients, there were 86 cases of OSD with bullous keratopathy (19 cases; 22.1%), trachoma / trichiasis (13 cases; 15.1%), blepharitis (12 cases; 14.0%), dry eye (11 cases; 12.8%), previous herpes infection (11 cases; 12.8%), exposure keratopathy (nine cases; 10.5%), corneal scar (seven cases; 8.1%) and corneal thinning (four cases; 4.7%). Ten patients had systemic disease with seven suffering from diabetes, one had systemic lupus erythematosus and two had chest infections of whom one had tuberculosis. Eleven patients were using topical

corticosteroids when they presented to us. Three patients' eyes were totally blind (no light perception), two of them due to glaucoma and one due to previous retinal detachment. A history of trauma in a previously normal eye was given by 44 patients with a male to female ratio of 3.4:1. Only 10 patients had an apparently normal eye with no previous ocular disease or trauma on presentation to the hospitals with MK; their average age was 59.4 (standard deviation ± 15.0). Patients with MK wearing contact lenses did not have an associated ocular surface disease.

Corneal scrapings from 35% of patients yielded positive cultures listed in Table 3. *Staphylococcus aureus* and *Streptococcus pyogenes* infections were not found in those patients wearing contact lenses, only in those with OSD. *Pseudomonas aeruginosa* was the most

**Table 3** Microbes associated with keratitis in 77 patients, 56 non-CLW and 21 CLW

	Total	Ulcer site			
		Axial/Paraxial		Peripheral	
		Non-CLW	CLW	Non-CLW	CLW
Total number of isolates including polymicrobial cultures	90	45	26	17	2
Gram-positive bacteria (37)					
<i>Staphylococcus aureus</i>	9	6	–	3	–
<i>Streptococcus pyogenes</i>	3	2	–	1	–
Other cocci and diphtheroids	24	13	4	7	–
<i>Nocardia</i> sp	1	–	1	–	–
Gram-negative bacteria (42)					
<i>Pseudomonas aeruginosa</i>	28	11	11	5	1
Other non-fermenting rods	5	2	3	–	–
Coliforms	6	4	2	–	–
<i>Haemophilus, Moraxella, Neisseria</i>	3	3	–	–	–
Fungi (5)					
<i>Fusarium</i> sp	3	3	–	–	–
<i>Penicillium</i> sp	1	–	–	–	1
<i>Candida</i> sp	1	–	–	1	–
Protozoa (6)					
<i>Acanthamoeba</i> sp	6	1	5	–	–



**Figure 1** Annualized incidence rates of presumed and culture-proven microbial keratitis in Hong Kong for lens wearers (CLWs) and non-lens wearers.

frequently isolated pathogen in both groups of patients for central and peripheral ulcers. Four non-CLW patients with OSD had fungal infection, three with *Fusarium* sp and one with *Candida parapsilosis* while *Penicillium* sp was isolated from one CLW. Five cosmetic CL-wearing patients yielded *Acanthamoeba* as did one non-CLW patient who gave a history of washing his face with water from a puddle during an outdoor trip on a hot day. Surprisingly, *Nocardia* sp

was isolated from one lens wearer. Details of polymicrobial culture, antibiotic sensitivities and lens storage case microbiology are given elsewhere.<sup>11</sup>

For all patients, lesions  $\geq 4$  mm<sup>2</sup> were significantly associated with a positive culture, irrespective of the presence or absence of cells in the anterior chamber. For CLW with a lesion size of  $< 4$  mm<sup>2</sup>, and an absence of cells in the anterior chamber, a positive culture was obtained on only 7% of occasions (two out of 29)



**Table 4** Comparison of the use of contact lenses by the 45 patients with contact lens-microbial keratitis and 135 matched controls

Practice	Patients	Controls	Matched OR (95% CI)*	P**
<b>Soft lenses — extended wear type<sup>a</sup> (not a user)***</b>				
Yes	13	29	1.29 (0.57, 2.84)	0.6199
<b>Average number of days of lens use per week (5–7 days)</b>				
< 5 days	1	23	0.11 (0.003, 0.73)	0.0119
<b>Overnight use<sup>b</sup> (none)</b>				
yes	25	19	8.91 (3.26, 30.40)	< 0.0001
<b>Compliance of cleaning procedures<sup>b</sup> (Yes — scores 4 &amp; 5)</b>				
No (scores 1 to 3)	9	4	8.46 (2.11, 48.64)	0.0012
<b>Smoker<sup>c</sup> (not a smoker)</b>				
Yes	14	12	5.20 (1.80, 16.96)	0.0013

\*Matched OR (95% CI)—Matched odds ratio (95% confidence limits).

\*\*P—Univariate conditional logistic regression exact P-value.

\*\*\* ( ) indicates the reference group used.

<sup>a</sup>Excluded two control subjects using hard lenses.

<sup>b</sup>Information on 16 controls missing.

<sup>c</sup>Information on 15 controls missing.

making this a useful prognostic sign. This is less reliable in non-CLW as 19% were culture-positive (12 out of 62) in similar circumstances. The lesion sizes (mean: 10.9 mm<sup>2</sup>; range: 2–30 mm<sup>2</sup>) in the 14 patients who used corticosteroids prior to presentation were significantly larger than those who did not (mean: 6.4 mm<sup>2</sup>; range: 0.25–49 mm<sup>2</sup>).

Altogether, 45 of the 58 patients with CLW-MK had complete sets of medical records, follow-ups and filled questionnaires. Two hundred and six CLW volunteers were recruited to take part in the study of whom 135 were matched with these 45 CLW patients for age, sex and educational status. There was *no significant difference* in alcohol consumption, history of chronic illnesses or medication, income, housing type, duration

of contact lens use, and visual acuity of the right eye between the case and control groups. However, lens-wearing patients were significantly more likely to be smokers, wear their lenses overnight and fail to conduct proper lens hygiene (Tables 4 and 5). A comparison of overnight wear of the lens by controls and CLW patients with microbial keratitis for sex, social and hygiene factors is given in Table 6. No statistically significant results were found.

The total number of cases of culture-proven and presumed MK occurring over 17 months is given in Tables 7 and 8, for the overall number of patients and those in different categories of soft and rigid CLW. This includes expressing numbers of cases of CLW in the adult population over 15 years old, similarly considered by the other three cohort studies, since this is the age that CLW begins. The population for each sub-group (Table 8) has been estimated from the Hong Kong census previously described. From these data, collected over 17 months, the annualized incidence rate per 10 000 populations has been calculated (over 12 months). Data from the three previous cohort studies have been similarly listed in Table 8.

## Discussion

This work represents the first prospective incidence study of both presumed and *culture-proven* MK outside the USA and Europe. The overall incidence of presumed MK in the Hong Kong population was 0.63 per 10 000 that is slightly higher than that in Scotland of 0.36 per 10 000<sup>2</sup> (Table 8). The incidence of presumed MK for CLW (soft and rigid combined) was 3.4 per 10 000 lens wearers which is similar to that found in a recent study from Holland of 2.67 per 10 000<sup>4</sup> and 2.44 per 10 000 in Scotland,<sup>2</sup> albeit in the

**Table 5** Multivariate conditional logistic regression estimates for significant variables between 41 lens-wearing patients with keratitis and 116 matched asymptomatic lens-wearing controls<sup>a</sup>

Variables	Matched OR (95% CI)*	P**
<b>Smoker<sup>b</sup> (not a smoker)***</b>		
Yes	7.02 (1.10, 57.46)	0.0001
<b>Overnight use<sup>c</sup> (not an overnight user)</b>		
Yes	10.41 (2.62, 62.21)	0.0371
<b>Compliance of cleaning procedures (good compliance — scores 4 &amp; 5)</b>		
No (scores 1 to 3)	11.04 (1.87, 132.56)	0.0031

\*Matched OR (95% CI)—Matched odds ratio (95% confidence limits).

\*\*P—Univariate conditional logistic regression exact P-value.

\*\*\* ( ) indicates the reference group used.

<sup>a</sup>Excluded 11 disposable contact lens users (four cases and seven controls), and 12 unmatched controls.

<sup>b</sup>Information on 15 controls missing.

<sup>c</sup>Information on 16 controls missing.

**Table 6** Contact lens overnight wear comparisons: controls, MK patients (cases), and controls vs MK patients

		Contact lens-wearing control Overnight wear of lens					Contact lens-wearing MK patient Overnight wear of lens					Control vs MK case
		No		Yes		P	No		Yes		P	
		n	%	n	%		n	%	n	%		
Sex	Female	80	80.0%	11	57.9%	<b>0.0415</b>	18	90.0%	17	68.0%	0.0782	1.0000
	Male	20	20.0%	8			2	10.0%	8	32.0%		
Education	Primary	69	69.0%	13	68.4%	0.5779	14	70.0%	16	64.0%	0.4595	1.0000
	Secondary or above	31	31.0%	6	31.6%		6	30.0%	9	36.0%		
Income (HK\$)	≤10,000	26	26.5%	5	26.3%	1.0000	9	47.4%	8	33.3%	0.2176	0.3229
	10001 – 20 000	53	54.1%	10	52.6%		9	47.4%	10	41.7%		
	≥30 001	19	19.4%	4	21.1%		1	5.3%	6	25.0%		
Smoke	No	92	92.0%	15	78.9%	0.0995	15	75.0%	16	64.0%	0.3217	0.6302
	Yes	8	8.0%	4	21.1%		5	25.0%	9	36.0%		
Alcoholic	No	97	97.0%	14	73.7%	<b>0.0026</b>	16	84.2%	20	80.0%	0.5190	0.0714
	Yes	3	3.0%	5	26.3%		3	15.8%	5	20.0%		
Average number of days of lens use per weeks (days)	< 1	1	1.0%	0		0.7763	0		0		0.5556	0.9261
	2–4	16	16.0%	2	10.5%		0		1	4.0%		
	5–7	83	83.0%	17	89.5%		20	100.0%	24	96.0%		
Eye disease in the past 6 months	No	76	76.0%	11	57.9%	0.0914	16	80.0%	12	48.0%	<b>0.0280</b>	0.6783
	Yes	24	24.0%	8	42.1%		4	20.0%	13	52.0%		
Use of eye drops or ointment in the past 2 months	No	84	84.0%	13	68.4%	0.1035	13	65.0%	21	84.0%	0.1306	0.0508
	Yes	16	16.0%	6	31.6%		7	35.0%	4	16.0%		
Source of eye drops/ointment	Doctors	10	66.7%	3	50.0%	0.1574	1	14.3%	2	50.0%	0.6818	0.614
	Optometrist	2	13.3%	3	50.0%		1	14.3%	0			
	Over the counter	3	20.0%	0			5	71.4%	2	50.0%		
Disinfectant	Multipurpose	45	48.9%	12	66.7%	0.4567	3	18.8%	5	25.0%	0.8069	0.163
	H <sub>2</sub> O <sub>2</sub>	40	43.5%	5	27.8%		9	56.3%	12	60.0%		
	Other types	7	7.6%	1	5.6%		4	25.0%	3	15.0%		
Compliance of cleaning frequencies	Scores 1–3	7	7.4%	4	22.2%	0.0730	6	35.3%	11	45.8%	0.3634	0.327
	Scores 4–5	88	92.6%	14	77.8%		11	64.7%	13	54.2%		
Compliance of cleaning procedures	Scores 1–3	10	10.6%	4	22.2%	0.1632	4	22.2%	10	41.7%	0.1608	1.000
	Scores 4–5	84	89.4%	14	77.8%		14	77.8%	14	58.3%		
Use of tap water to clean lenses or cases	N	78	83.0%	16	88.9%	0.4130	17	89.5%	15	62.5%	<b>0.0458</b>	0.147
	Y	16	17.0%	2	11.1%		2	10.5%	9	37.5%		
Use of tap water to store lenses	N	93	98.9%	17	94.4%	0.2968	17	89.5%	19	79.2%	0.3157	1.000
	Y	1	1.1%	1	5.6%		2	10.5%	5	20.8%		
Weekly use of protein tablets	N	21	22.8%	4	25.0%	0.5352			2	11.1%	0.3085	0.511
	Y	17	77.2%	12	75.0%		14	100.0%	16	88.9%		
Care of the empty storage cases	Not air-dried	5	5.3%	5	27.8%	<b>0.0094</b>	5	27.8%	10	43.5%	0.2401	0.310
	Air-dried	89	94.7%	13	72.2%		13	72.2%	13	56.5%		

**Table 7** Comparative population study data of microbial keratitis assessed prospectively in cohort studies in Hong Kong (1997/8), Holland<sup>1</sup> (1996), Scotland<sup>2</sup> (1995) and New England,<sup>5</sup> USA (1985)

	Hong Kong 1997/8	Holland 1996 <sup>1</sup>	Scotland 1995 <sup>2</sup>	New England 1985 <sup>5</sup>
Population	2 489 701	–	2 945 810	>9 000 000
	Over age 15: 2 048 630	Over age 12: 3 188 000	Over age 15: 2 372 567	Over age 12: 8 021 000
All types of contact lens wear (CLW):	122 918	1 400 000	166 080	637 550
Rigid CLW:	16 225	639 000	24 980	108 172
Soft (hydrogel) CLW on a daily wear basis only:	93 783	713 000	141 100	399 843
Soft CLW on an extended wear basis only:	12 910	24 000	approx. 850 (bandage only)	129 535

latter study the number of expected cases of culture-negative MK was estimated from previous work in Glasgow.<sup>12</sup>

CLW patients with presumed MK were much younger (90% <40 years) than the non-CLW patients (75% >40 years) and were more likely to be female (2:1 ratio). Distribution between left and right eyes was similar. Only 7% CLW had previous eye disease, except myopia, compared to 49% of non-CLW. Trauma was more common amongst non-CLW (27%). Symptoms and onset of MK were remarkably similar between the two groups, as was the size and position of the lesion and visual acuity on presentation.

*Pseudomonas aeruginosa* was the single most important bacterial species in culture-positive cases for both CLW and non-CLW. This is typical of a tropical climate but very different to that of a temperate one.<sup>2,7,8,12</sup> Patients with presumed MK, returning from a hot tropical climate to a temperate one, should always be treated for a possible *Pseudomonas aeruginosa* infection before culture results are known, as it is the commonest expected bacterium. Fungal infection occurred less commonly than expected, with one fungal case for every 17 bacterial cases. This compares favorably with equatorial tropical climates when the ratio can reach 1 for 1.<sup>6,7</sup> The probable explanation for this result lies in the urbanization of Kowloon and the adjacent New Territory of Shatin in which the study was conducted. In contrast to rural surroundings, it is a modern development of concrete construction, which does not produce a high airborne count of fungal spores, grown from vegetable matter, that can infect a compromised eye. More detailed aspects of this microbiology are considered elsewhere.<sup>11</sup>

*Acanthamoeba* was the second most important microbe in contact lens-associated MK. The incidence of *Acanthamoeba* keratitis was low (0.33 per 10 000 lens

wearers) similar to Holland (0.05 per 10 000 lens wearers but only one case identified) and that expected, but not proven, in the USA. This is much less frequent than Scotland where an incidence of 1.49 per 10 000 lens wearers has recently been recorded.<sup>2</sup> Our culture-positive findings in CLW, of five *Acanthamoeba* isolates compared to 21 bacterial isolates (a ratio of 1:5), compares with recent findings from Wills Eye Hospital, Philadelphia when a similar ratio of 1:6 was recorded recently.<sup>13</sup>

The relationship between lesion size in square mm (mm<sup>2</sup>) and culture-positivity has been found helpful previously in Scotland when a size of 4 mm<sup>2</sup> or greater was expected to be culture-positive associated with cells in the anterior chamber.<sup>12</sup> Rattanatham *et al*<sup>13</sup> have experienced a similar situation in Philadelphia, USA (Wills Eye Hospital) when they found that lesions of 2–4 mm<sup>2</sup> healed in 7 days but those >4 mm<sup>2</sup> required an average of 41 days. They recorded a worse prognosis for corneal lesion >4 mm<sup>2</sup> reflecting our experience and that of Scotland.<sup>12</sup>

The CLWs had a peak incidence of MK at age 22 while the non-CLW patients showed a peak increase for MK in the age range 70–74 (Figure 1). This trend in the non-CLWs is 10 years earlier than that found in Scotland<sup>2</sup> and the USA,<sup>1</sup> perhaps reflecting the socio-economic conditions. For the 44 trauma-associated cases, 25% of the total number of non-CLWs, 89% were work-related, particularly in metal and building work grinding that generates dust or fine metal chips impacting on the cornea. The use of goggles would have prevented such injuries and will be encouraged. Patients with existing OSD were also particularly susceptible to infection.

Wear of contact lenses for refractive purposes (myopia and/or astigmatism) was responsible for 26% of cases of MK overall, an encouragingly low rate, but



**Table 8** Comparison of incidence rates for microbial keratitis assessed prospectively in cohort studies in Hong Kong (1997/8), Holland<sup>1</sup> (1996), Scotland<sup>2</sup> (1995) and New England,<sup>5</sup> USA (1985)

Incidence type	Hong Kong			Holland			Scotland			New England		
	Cases over 17 months	Population	Annualized rate per 10 000	Cases over 3 months	Population	Annualized rate per 10 000	Cases over 8 months	Population	Annualized rate per 10 000	Cases over 4 months	Population	Annualized rate per 10 000
Culture-proven keratitis overall	77	2 489 701	<b>0.22</b>	– <sup>a</sup>	–	–	52	2 945 810	<b>0.26</b>	– <sup>a</sup>	–	–
Culture-proven keratitis among adults >15	77	2 048 630	<b>0.27</b>	–	–	–	52	2 372 567	<b>0.33</b>	–	–	–
'Presumed' microbial keratitis overall	223	2 489 701	<b>0.63</b>	–	–	–	71	2 945 810	<b>0.36</b>	–	–	–
'Presumed' microbial keratitis among all adults >15	221	2 048 630	<b>0.76</b>	–	–	–	71	2 372 567	<b>0.45</b>	–	–	–
Culture-proven keratitis For all types of CLW (soft and rigid)	21	122 918	<b>1.21</b>	30	1 376 000	<b>0.872</b>	20	166 080	<b>1.81</b>	– <sup>b</sup>	–	–
'Presumed' microbial keratitis for all types of CLW (soft and rigid)	59	122 918	<b>3.39</b>	92	1 376 000	<b>2.67</b>	27	166 080	<b>2.44</b>	–	–	–
'Presumed' microbial keratitis in all types of soft CLW	58	106 693	<b>3.84</b>	75	737 000	<b>4.07</b>	26	141 100	<b>2.76</b>	186	637 550	<b>8.75</b>
'Presumed' microbial keratitis for all cosmetic soft CLW	58	106 693	<b>3.84</b>	–	–	–	25	141 100	<b>2.66</b>	150 <sup>c</sup>	529 378	<b>8.50</b>
Culture-proven keratitis for daily soft CLW	15	93 783	<b>1.13</b>	–	–	–	18	141 100	<b>1.91</b>	–	–	–
'Presumed' microbial keratitis for daily cosmetic soft CLW	41	93 783	<b>3.09</b>	63	713 000	<b>3.54</b>	25	141 100	<b>2.66</b>	56 <sup>d</sup>	399 843	<b>4.20</b>
'Presumed' microbial keratitis for extended wear cosmetic soft CLW	17	12 910	<b>9.3</b>	12	24 000	<b>20</b>	–	–	–	94 <sup>e</sup>	129 535	<b>21.8</b>

Continued

**Table 8** Continued

Incidence type	Hong Kong			Holland			Scotland			New England		
	Cases over 17 months	Popu- lation	Annual- ized rate per 10 000	Cases over 3 months	Popu- lation	Annual- ized rate per 10 000	Cases over 8 months	Popu- lation	Annual- ized rate per 10 000	Cases over 4 months	Popu- lation	Annual- ized rate per 10 000
'Presumed' microbial keratitis for rigid gas permeable and/or hard lenses	1	16 225	<b>0.44</b>	17	639 000	<b>1.06</b>	2	24 980	<b>0.8</b>	9	108 172	<b>2.50</b>
Acanthamoeba keratitis in soft CLW	5	106 693	<b>0.33</b>	1	737 000	<b>0.05</b>	14	141 100	<b>1.49</b>	–	–	–

‘–’: Not performed in study.

<sup>a</sup> Study only related to contact lens wear.

<sup>b</sup> Study only included patients with presumed microbial keratitis (culture not performed).

<sup>c</sup> 150 derived from 128 infected cosmetic soft CLW plus 22 unknown types of soft CLW.

<sup>d</sup> 56 derived from 48 known daily use of CLW plus expected proportion of 22 unknown infected CLW to be practising daily use modality of wear ( $n = 8$ ).

<sup>e</sup> 94 derived from 80 known cases of presumed microbial keratitis with extended wear of cosmetic soft CL plus expected proportion of 22 unknown infected CLW to be practising extended wear ( $n = 14$ ).

this figure could be lower than elsewhere due to the large number of trauma-related cases in Hong Kong. The rate of CLW-MK is higher in Scotland at 38% of cases overall<sup>2</sup> but this figure included many cases of *Acanthamoeba* infection which are potentially preventable and for which the incidence is now believed to have reduced considerably.<sup>14</sup> In the USA, CLW has constituted up to 50% of cases of MK in the past,<sup>1</sup> but a much lower figure of 13% (range 10–18%, 37 out of 229 cases) has been recorded over the last 5 years in Philadelphia.<sup>13</sup> The latter USA figure could, however, have been skewed since the patients came from a referral centre rather than from a population-based study.

Both univariate and multivariate conditional logistic regression analyses (Tables 4 and 5) of the patients and matched controls have indicated that overnight wear of the contact lens, poor compliance with lens cleaning procedures and being a smoker are significant independent variables. No difference could be established however on the basis of sex, income, smoking, or hygiene compliance between the patients with MK and the controls for the type of CLW who would wear their lenses overnight. This means that it is not possible to predict the type of person who is likely to wear their lens overnight.

This is only the second time that smoking *per se* has been recorded as a significant risk factor for lens-associated microbial keratitis, with one in three CLW patients smoking compared to one in 11 matched CLW controls, 90% of whom were <40 years old. Smoking

varies in the Hong Kong population from 25% in men and 8% in women over the age of 70<sup>15</sup> to 7% of men and <1% of women under the age of 25.<sup>16</sup> This demonstrates the importance of using age-matched controls. Schein *et al* in 1989 first identified smoking as a risk factor for lens-wearing keratitis when smokers were estimated to have three times the risk of keratitis compared to non-smokers ( $P = 0.01$ ).<sup>17</sup>

The incidence of MK in the population of Hong Kong has been compared with other cohort studies in Europe (Holland<sup>4</sup> and Scotland<sup>2</sup>) and the USA<sup>5</sup> (New England) (Table 8). While these four studies have been conducted differently, with only those of Hong Kong and Scotland studying all types of MK as defined above, it is possible to show that extended (overnight) wear (EW) of soft hydrogel contact lenses has given a much higher incidence rate of MK, proven significantly in the case of each study, than for daily wear (DW) of soft lenses with incidence rates per 10 000 lens wearers as follows: Hong Kong DW 3.09, EW 9.3; Holland DW 3.54, EW 20; and USA DW 4.2, EW 21.8. In Scotland, EW was not practised but a similar incidence rate for DW was found of 2.66 per 10 000 lens wearers.

Microbial keratitis with rigid lens wear was much less frequent for all four studies with the incidence rate per 10 000 lens wearers as follows: Hong Kong 0.44, Holland 1.06, Scotland 0.8 and USA 2.5. For *Acanthamoeba* keratitis in lens wearers, Hong Kong had a low incidence (0.33 per 10 000) comparable to Holland (0.05 per 10 000 but only one case identified) and much less than Scotland (1.49 per 10 000). The incidence rate for the USA is unknown.

Our study suggests that eye protection with goggles in at-risk industries, which expose the subject's cornea to fine metal dust/chips, is required to reduce the large number of trauma-associated cases in Hong Kong. Education of the contact lens-wearing public with informed preventive measures, such as avoidance of overnight (sleeping) wear of hydrogel contact lenses, non-smoking and use of sterile multi-purpose solutions in lens storage cases without tap water,<sup>18</sup> should be cost-effective in reducing the incidence of lens-associated MK in Hong Kong and elsewhere. These measures will be complemented by new ideas such as the incorporation of salicylate into multipurpose solutions, to prevent the formation of biofilm on lenses and the adherence of microbes including *Acanthamoeba* to them within the storage case.<sup>19</sup>

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