

## EXTENDED REPORT

## Severe infective keratitis leading to hospital admission in New Zealand

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**Aim:** To identify key risk factors and the management and outcome of severe infective keratitis leading to public hospital admission in New Zealand.

**Methods:** Over a 2 year period, all admissions of presumed infective keratitis to Auckland Hospital were identified. The clinical records of all 103 cases were retrospectively reviewed with respect to clinical features, risk factors, management, and outcomes.

**Results:** The mean time from first symptoms or signs and presentation to hospital was 8.9 (SD 15.5) days. The majority of subjects, 88%, had at least one of the risk factors commonly associated with infective keratitis including previous ocular surgery (30%), contact lens wear (26%), topical corticosteroid use (25%), and ocular trauma (24%). Corneal scraping was performed in 92% and of a total of 105 scrapes, 71% were positive. Bacteria were isolated in all these cases, the majority being Gram positive organisms (72%). The most common isolates identified were coagulase negative *Staphylococcus* (16%), *Propionibacterium acnes* (14%), *Staphylococcus epidermidis* (11%), and *Streptococcus pneumoniae* (9%). In addition, yeasts were isolated in 5%, fungi in 4%, virus in 2%, and chlamydia in 1%. Importantly, polymicrobial infection accounted for 33% of culture positive cases. Antimicrobial treatment was changed on the basis of culture results in 17 cases (16.5%). Median initial visual and final best corrected visual acuity was 6/36–6/48 (logMAR 0.86) (IQR 0.39–2.00) and 6/12–6/15 (logMAR 0.360) (IQR 0.15–1.70), respectively. Previous ocular surgery and topical corticosteroid use were significantly associated with poorer visual acuity. The mean hospital stay was 5.8 days and the median 4.0 (IQR 2.0–8.0) days. Longer duration of stay was associated with the presence of hypopyon, larger ulcers, previous ocular surgery, and poor visual acuity.

**Conclusions:** Infectious keratitis is an important cause of ocular morbidity. A significant proportion of cases have potentially modifiable risk factors. Previous ocular surgery and topical corticosteroid use, in particular, were associated with poorer visual outcomes. Many cases of severe keratitis might be avoided, or their severity reduced, by appropriate education of patients and ophthalmologists.

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Microbial keratitis is an important cause of ocular morbidity and avoidable visual impairment in all age groups, and is commonly encountered by ophthalmologists worldwide.<sup>1</sup> Despite advances in treatment, infective keratitis remains clinically challenging and although the outcome can be favourable with appropriate management, there is potential for significant and permanent visual impairment in addition to social and healthcare costs.<sup>1,2</sup>

Although a number of studies, both retrospective and prospective, have considered the aetiology, management, and outcome of infective keratitis, the morbidity from severe keratitis remains high. Morbidity has been assessed in terms of loss of vision, duration of inpatient management, and surgical intervention.<sup>1–20</sup> A number of aetiological factors that predispose to severe keratitis have been identified including dry eye disease, neurotrophic cornea, topical corticosteroids, previous ocular surgery, trauma, and poor contact lens care.<sup>2–4,11</sup> None the less, despite this expanded knowledge base, potentially avoidable, severe microbial keratitis continues to be a significant drain on limited healthcare resources in ophthalmology.<sup>21</sup> The purpose of this study was twofold: firstly, to identify features of infective keratitis that led to hospital admission in the New Zealand public healthcare system and, secondly, to ascertain the preferred management and outcome of these cases.

## SUBJECTS AND METHODS

Auckland Hospital is located near the central business district of Auckland. It is a major teaching and training hospital with 22 consultant ophthalmologists who provide an ophthalmology service to the greater Auckland area (population approxi-

mately 1.3 million) with more than 50 000 outpatients being assessed each year. In most cases, the ophthalmology department acts as a secondary and tertiary referral centre; however, some patients self refer to the ophthalmic accident and emergency. The public health system in New Zealand is essentially similar to, but predates, the UK National Health Service (NHS).

All cases of presumed infective keratitis were identified using ward discharge records. Relevant case notes were assessed using a standardised pro forma. Between 1 March 1999 and 28 February 2001, there were 103 admissions with presumed infective keratitis. All charts were available. Five of these cases were repeat admissions. Therefore, the clinical records of 98 patients were retrospectively reviewed. These patients were managed by 14 consultant ophthalmologists, three of whom have subspecialist training in cornea and external disease. Criteria for admission were primarily the severity of the keratitis—that is, potentially sight threatening, and the need for intensive topical antimicrobials.

The following information was identified for all subjects included in the study: date of birth, age, sex, and date of admission. Documented presence of predisposing risk factors included the following specific factors: dry eye, contact lens wear (both soft and hard), previous ocular trauma, previous ocular surgery, loose suture, previous herpes simplex virus infection, previous herpes zoster ophthalmicus infection, previous topical steroid use, trichiasis or entropion. The size of the lesion (measured along the greatest dimension), location of lesion, presence of associated clinical features including hypopyon, epithelial defect, ocular discharge, uveitis, elevated

intraocular pressure (>21 mm Hg), initial best spectacle corrected visual acuity (BSCVA), and duration of symptoms before presentation to hospital, were noted.

In addition, the following were documented: treatment at presentation and following assessment at hospital, both first line and second line treatments, and changes in treatment according to microbial sensitivities (including use of antibiotics, steroids, antivirals, lubricants, and other drugs). The following were also noted: initial provisional diagnosis, whether or not a corneal scrape was performed, whether and what pathogen was isolated, sensitivities to antimicrobials, whether a rescrape was performed, and any other relevant microbiological results. All notes were assessed to identify surgical procedures including the following specific procedures: biopsy, corneal graft, and application of glue. The total number of days in hospital, final diagnosis, and final BSCVA were recorded.

Visual acuity was recorded in patient notes according to Snellen chart convention. For the purposes of statistical analysis these values were also converted to logMAR values. Visual acuity recordings for "counting fingers," "hand movements," "light perception," and "no light perception" were also dealt with similarly once Snellen chart values were assigned, following the schedule of Steinberg *et al* in assessing visual impairment in patients with cataract.<sup>22</sup>

Where corneal "scrape/biopsy" was performed, specimens were routinely obtained with a sterile blade or needle and smeared onto slides for Gram stain as well as inoculated directly onto media for isolation of bacteria (tryptose blood agar base, brain heart infusion agar, GC agar base, cooked meat phyton medium), virus (veal infusion broth), fungi (Sabouraud dextrose agar and brain heart infusion broth) and where appropriate, amoeba (Page's amoebic saline (PAS) agar). While Gram stain results were usually available the same day, the various media were routinely incubated for a total of 10 days or 2 weeks depending on the media, before giving a final report. All microbiological testing was carried out by the microbiology laboratory at Auckland Hospital.

### Statistical analyses

Differences between continuous outcome variables for established and putative risk factors were sought using the Wilcoxon two sample test, the Kruskal-Wallis test, or Student's *t* test for independent groups where appropriate. Categorical data were examined using Fisher's exact test and the  $\chi^2$  procedure (without continuity correction). Spearman rank correlation was used to test for linear univariate association. All tests were two tailed and a 5% significance level was maintained throughout.

### RESULTS

A total of 98 patients (103 episodes in 98 eyes), 56 male (57%) and 42 female (43%) were included in the study. The patient age ranged from 2 months to 88 years with a mean of 45 (SD 24) years. There did not appear to be any seasonal variation in the numbers of patients admitted during the study with the mean number of subjects admitted per month being 4.3 (SD 2.2). Between two and six admissions were identified every month of the study except for March 2000 and February 2001 in which there were nine and 11 respectively.

The time interval between first symptoms and signs and presentation to hospital ranged from same day presentation—that is, 0 days, to 90 days; however, the mean time interval was 8.9 (SD 15.5) days.

At the time of hospital admission, 42 patients had not been on topical therapy, 39 had been prescribed topical antibiotics, and 18 were using topical corticosteroid drops (Table 1). In the group who had used topical steroids before admission, there was an even distribution of male and female patients. Thirteen

**Table 1** Topical treatment at time of admission

Treatment	No (103 admissions)	%
Antibiotics	39	37.9
Corticosteroids	18	17.5
Antibiotics and antivirals	2	1.9
Antivirals	10	9.7
Antibiotics and lubricants	4	3.9
Lubricants	8	7.8
Other	10	9.7
No topical medication	42	40.8

Topical treatment being used by patients before, or at the time of presentation, either for keratitis or pre-existing ocular condition (n = 103). In 39 patients, no topical ophthalmic agents were used. NB: percentages do not add up to 100% because of overlap of subgroups.

**Table 2** Factors predisposing to microbial keratitis

Predisposing risk factor	No of patients (n=98)	%
Ocular surgery	29	29.6
Contact lens wear	25	25.5
Topical corticosteroid use	24	24.5
Ocular trauma	23	23.5
Previous herpes simplex keratitis	13	13.3
Dry eye	7	7.1
Suture related	7	7.1
Previous herpes zoster keratitis	6	6.1
Trichiasis/entropion	5	5.1
Multiple risk factors	33	33.7
No risk factors	15	15.3

Factors predisposing to microbial keratitis (n = 98 subjects). Sum of the percentages of patients with each risk factor does not add up to 100% because of overlap of subgroups.

of the 24 steroid treated eyes had undergone previous ocular surgery, and nine of these procedures had been penetrating keratoplasty.

### Predisposing factors

The majority of patients, 88%, had at least one of the known risk factors predisposing to infective keratitis. Previous ocular surgery was the most common risk factor (30%) in the study group, followed by contact lens wear (26%), corticosteroid use (25%), and trauma (24%) (Table 2).

In the group of patients (n=29) who had undergone previous ocular surgery, the type of surgical intervention included penetrating keratoplasty (12), cataract extraction (13), trabeculectomy (four), retinal detachment repair (three), excimer laser photorefractive keratectomy (PRK) for myopia (two), lid procedures (two), and one case each of Molteno tube, conjunctival flap, strabismus surgery, and vitreous biopsy (some eyes underwent more than one procedure and one patient had also undergone a contralateral penetrating keratoplasty). The date of latest surgery could be ascertained in 25 of the 29 cases and these presented with keratitis at a mean of 3.0 (SD 3.7) years (range 3 days to 10 years) following ocular surgery. In seven of these cases (24.1%) the keratitis was thought to be related directly to a loose, or broken, corneal suture. In all seven cases, (five cases of penetrating keratoplasty and two of penetrating corneal trauma), the suture utilised was a 10/0 Nylon monofilament with a mean of 19.4 (SD 17.2) months since the most recent surgery (range 2–49 months, with four cases occurring more than 2 years after surgery)

Previous surgery was an important factor with respect to the number of days spent in hospital (Wilcoxon two sample test,  $p=0.001$ ). The median duration of stay for those who had

previous surgery was 5.5 days (interquartile range, IQR 4.0–11.0) compared with 3.0 days (IQR 2.0–6.0) in those who had not. It was also an important factor in relation to poorer visual acuity. The initial median visual acuity in the surgery group was approximately HM (logMAR 2.00) (IQR 0.54–2.00) compared with 6/30 (logMAR 0.70) (IQR 0.30–2.00) in the non-surgery group. Median final visual acuity was CF (logMAR 1.70) (IQR 0.38–2.00) and 6/12 (logMAR 0.30) (IQR 0.10–0.52) in the surgery and non-surgery groups respectively ( $p < 0.0001$ ).

Corticosteroid use was also statistically related to poorer initial ( $p = 0.033$ ) and final visual acuity ( $p = 0.006$ ). Median initial visual acuity in patients with previous corticosteroid use was HM (logMAR 2.00) (IQR 0.58–2.00), and in patients without this risk factor, 6/30 (logMAR 0.70) (IQR 0.30–2.00). Median final visual acuity in the corticosteroid group was 6/60 (log MAR 1.00) (IQR 0.30–2.00), whereas, in the non-steroid group it was 6/12 (log MAR 0.30). Steroids were also associated with the size of the ulcer, with the median diameter in steroid treated eyes (3.5 mm), being significantly greater than that of non-steroid eyes (2.0 mm) ( $p = 0.031$ ). In some cases initial visual acuity and dimensions of the ulcer could not be clearly defined because of photophobia and discharge.

There was no statistically significant difference in the vision at presentation ( $p = 0.43$ ) and final visual outcome ( $p = 0.22$ ), where trauma or contact lens wear were considered as predisposing causes.

### Ophthalmic assessment

Considering the visual acuities recorded at presentation,  $n = 92$  (89%), the largest proportion,  $n = 37$  (40%) were poorer than 6/60. Poorer initial visual acuity was more commonly seen in older patients (Spearman correlation coefficient,  $p < 0.0001$ ), those with larger lesions ( $p < 0.0001$ ), and those presenting to hospital with longer duration of symptoms ( $p = 0.049$ ). This was also related significantly to poorer final visual acuity ( $p < 0.0001$ ), greater change in vision ( $p = 0.0003$ ), and longer duration as a hospital inpatient ( $p < 0.0001$ ).

The location of the corneal lesion was central in 50 cases, peripheral in 20 cases, and paracentral or spanning both central and peripheral domains in 33 cases. In 27 cases the exact size of lesion was not recorded. The median size of the lesion in greatest dimension, where recorded, was 2.4 mm; however, lesions ranged in size from 0.5 mm to 9.0 mm in diameter. Not unexpectedly, where measured, larger lesions were associated with poorer vision ( $p < 0.0001$  for both initial and final corrected acuity), longer duration of symptoms and/or signs before presentation ( $p = 0.015$ ), and protracted hospital admissions ( $p = 0.0002$ ). Anterior uveitis was a common feature, present in 61 (59%) cases with 21 subjects (20%) exhibiting a hypopyon at presentation.

### Microbiology results

Corneal scraping for microbiological identification was performed in 94 out of 103 (92%) admissions, and subsequently seven cases had a second scrape. A third scrape was performed in three cases, and one of these also had a fourth. Of the cases where a corneal scrape was not performed, the reviewers presumed this was thought to be a “reasonable” policy decision by the physician in five cases because the lesions described were relatively small or had intact epithelium. In the other four cases (4%) the subjects and presentation appeared appropriate for corneal scrape, and the reason this was not performed was not identified.

In total, 105 scrapes were performed. Of these, 75 (71%) were “positive,” being 69 of the first scrapes, four of the second, and two of the third. Bacteria were isolated from all of these culture positive cases. In addition, yeasts were isolated in 5%, fungi in 4%, virus in 2%, amoeba in 1%, and chlamydia in 1%. Presence of hypopyon was positively associated with a

**Table 3** Organisms isolated from culture of corneal scraping of patients ( $n = 98$ ) admitted with suspected microbial keratitis ( $n = 122$  isolates)

Organism	No of isolates
Coagulase negative <i>Staphylococcus</i>	20
<i>Propionibacterium acnes</i>	17
<i>Staphylococcus epidermidis</i>	14
<i>Streptococcus pneumoniae</i>	11
<i>Staphylococcus aureus</i>	7
<i>Pseudomonas aeruginosa</i>	7
<i>Corynebacterium</i>	6
<i>Moraxella</i> species	6
Gram +ve species, mixed	6
<i>Serratia</i> species	3
Aerobic bacillus	3
HSV type 1	2
Saprophytic yeast	2
Other organisms, single isolates	18

bacterial (Fisher’s exact test,  $\chi^2$  procedure,  $p = 0.027$ ) or viral ( $p = 0.005$ ) aetiology. Of the culture positive cases, the most common isolates were coagulase negative *Staphylococcus*, *Propionibacterium acnes*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* (Table 3).

Polymicrobial infection was identified in 25 out of the 75 culture positive cases (33%). Indeed, two organisms were detected in 15 scrapes, three organisms in four scrapes, four organisms in three, five organisms in two, and six organisms in one scrape.

There were 25 patients with “negative” first cultures. Of these, 12 had been on topical antimicrobial therapy before corneal scraping was performed, and six were contact lens wearers.

Other means of microbiological identification were carried out in a minority of cases instead of, or in addition to, corneal scraping. These included conjunctival swab (four), conjunctival biopsy (one), corneal biopsy (three), and culture of intraocular samples (two). Despite the high proportion of contact lens wearers (26%) in the current series, culture of contact lenses (three) or cases (four) was only carried out in five patients. Of the five subjects, the culture results from two eyes, from both corneal scrape and the contact lens/case, were similar. In two eyes no organisms could be isolated from the corneal scrape, whereas, organisms thought to be the likely pathogens were isolated from the contact lenses/cases. In the last of the five cases, different organisms were identified from the cornea and the contact lenses/cases, leading to a modified antibiotic regimen effective against both organisms in vitro.

### Treatment

Almost all patients (100, 97%) received antibiotics as a first line treatment following admission to hospital. The most common first line antibiotics used were the duotherapy combination of fortified cephalosporin 5% eye drops and tobramycin 1.36% eye drops ( $n = 64$ ), or ciprofloxacin 0.3% eye drops as monotherapy ( $n = 28$ ). Various other combinations of these three drugs and chloramphenicol 0.5% were used in a small minority of cases (Table 4). As second line treatment, one third of patients had a modification in antibiotic regimen.

Steroids were used as first line adjunct treatment in only 8%, whereas use of steroids increased as a second line treatment, once resolution had commenced, to 40%. Other forms of treatment included antivirals and lubricants and over half of all patients received other topical medication, predominantly cycloplegic drugs (Table 5).

Antimicrobial treatment was changed on the basis of sensitivities in 17 patients (16.5%). In 29 admissions, a procedure or surgical intervention was performed (Table 6).



**Table 4** Use of first line antibiotics. Of 103 admissions, 100 subjects were commenced on antibiotics as first line treatment

Antibiotic regimen	No (n= 100)
Cephazolin 5%/tobramycin 1.36%	64
Ciprofloxacin 0.3%	28
Chloramphenicol 0.5%	3
Ciprofloxacin 0.3%/chloramphenicol 0.5%	2
Cephazolin 5%/ciprofloxacin 0.3%	1
Tobramycin 1.36%	1

**Table 5** Topical treatment commenced following referral to hospital (n = 103 admissions)

	First line treatment	Second line treatment
Antibiotics	100	33
Antivirals	9	8
Steroids	8	41
Lubricants	3	19
Other	57	18

**Table 6** Procedures related to admission with presumed microbial keratitis (n=103 admissions). Forty two procedures were performed on 29 patients

Surgical procedure	Number (n = 42)
Tarsorrhaphy	10
Removal of suture	9
Examination under anaesthetic and scrape	7
Corneal biopsy	4
Penetrating keratoplasty	3
Tissue glue	3
Aqueous or vitreous sample	2
Botulinum induced ptosis	2
Tarsotomy	1
Vitreotomy	1

## Outcomes

At the time of chart review (mean 45 days, range 3–234 days following initial assessment), 86 patients had both initial and final visual acuity recorded. Fifty three of these had a significant change in visual acuity (defined as a change of two or more Snellen lines), whereas 33 had no significant change. Overall, the median initial visual acuity was approximately 6/36–6/48 (logMAR 0.86) (IQR 0.39–2.00) and the median final visual acuity was 6/12–6/15 (logMAR 0.36) (IQR 0.15–1.70). Of those who demonstrated 6/60 vision, or worse, at latest review, all but one had visual acuities of 6/60, or worse, at initial presentation.

The median duration of stay in hospital was 4.0 (IQR 2.0–8.0) days and ranged from 1 to 31 days. Longer hospital stays were significantly associated with the presence of hypopyon (Wilcoxon two sample test,  $p=0.006$ ) and previous ocular surgery (Wilcoxon two sample test,  $p=0.001$ ). Longer duration of stay was also correlated with larger ulcers (Spearman correlation coefficient,  $p=0.0002$ ), and poorer visual acuity, both at presentation ( $p<0.0001$ ) and at final assessment ( $p=0.0009$ ).

## DISCUSSION

Microbial keratitis is relatively common in ophthalmic practice; however, we were surprised at the frequency with

which severe microbial keratitis required hospital admission in this New Zealand population. In a 2 year period, 103 cases of presumed severe microbial keratitis were admitted to Auckland Hospital for intensive topical antimicrobial treatment. This study population is comparable to, or greater than, series published from other centres in the developed world, including Western Australia, Sydney, Sweden, and southern California.<sup>3–6</sup> Our study population includes all community cases, as all cases of microbial keratitis severe enough to warrant hospitalisation are admitted only via the acute ophthalmic service within Auckland Hospital. However, retrospective review of case notes has inherent inconsistencies and limitations because all items of interest sought in the records may not be included; fortunately, in this study all patient case notes were available for review and the standard of documentation was high.

Perhaps, unsurprisingly, in this New Zealand study, the size of the ulcer was significantly associated with the age of the patient, the duration of symptoms before presentation, the duration of stay in hospital, and poorer initial and final visual acuity. Ninety two per cent of eyes underwent a corneal scrape as primary inpatient management. Interestingly, 71% of these corneal scrapes were positive. This isolation rate is very similar to that in a recent study from Western Australia (71%), although other series have reported positive microbial results in 37% to 86% of cases.<sup>1–15</sup> Contributing to the culture negative cases may be the inclusion of sterile ulcers, the use of antibiotics before presentation to hospital, or the failure to stop antibiotics for 24–48 hours before scraping. Topical anaesthetic agents before sampling may also produce false negative results.<sup>12, 23</sup>

The prevalence of different organisms responsible for severe microbial keratitis varies in different geographic regions, reflecting differing populations and climate.<sup>1, 6, 7, 24</sup> Gram positive organisms made up the majority (72%) of positive isolates in our study, coagulase negative *Staphylococcus* being the most common (16%). The most common Gram negative organism isolated was *Pseudomonas aeruginosa* (6%). Fungal, viral, and amoebae isolates made up a small, but significant, proportion of positive cultures. Significantly, 33% of culture positive cases involved more than one organism, placing the rate of polymicrobial infection in our series among the highest reported.<sup>1, 2, 6, 7, 10, 15, 16</sup>

Acanthamoeba and fungi, while relatively uncommon, are important causes of keratitis because a delay in diagnosis may occur and visual loss can be severe.<sup>3, 25</sup> Acanthamoeba has been strongly associated with contact lens wear, particularly soft contact lenses and overnight wear of contact lenses.<sup>26, 27</sup> The single case of acanthamoeba keratitis in this series was a soft contact lens wearer who washed her lenses in tap water daily and wore these during recent hot tub bathing. Mycotic keratitis is more common in developing and tropical countries, because of climatic conditions and greater occurrence of agricultural injuries, with fungi being responsible for up to 44% of corneal ulcers.<sup>14</sup> However, only 4% of our series involved fungi. In one case this was thought to be a culture contaminant, whereas, the other three eyes were treated for the mycotic infection with amphotericin and/or natamycin with final BSCVA of 6/9, 6/7.5, and 6/6.

Standard treatment regimens for microbial keratitis usually involve duotherapy using fortified antibiotics (usually an aminoglycoside and a cephalosporin), or monotherapy using a fluoroquinolone.<sup>28</sup> The two treatment options most commonly chosen (92%) in this series were the combination of fortified preparations of tobramycin and cephazolin (64%) or ciprofloxacin alone (28%). Several studies have shown ciprofloxacin ophthalmic solution 0.3% to be as effective as a fortified antibiotic combination<sup>16–19</sup>; however, despite its broad spectrum antimicrobial coverage, ciprofloxacin may have gaps in Gram positive coverage that may make a fortified duotherapy combination more popular in severe, vision

threatening keratitis.<sup>13</sup> For less severe cases, it has the obvious advantage of convenience as a single, commercially available, agent, as opposed to combination therapy, and it is generally well tolerated with few adverse effects.<sup>17,28</sup> This study identified no statistically significant differences between cases treated with ciprofloxacin or the cephazolin-tobramycin combination in respect of the duration of hospital stay or final visual acuity.

In this study, previous use of topical corticosteroid was statistically associated with larger corneal lesions ( $p=0.031$ ) and poorer vision both at presentation ( $p=0.033$ ) and final assessment ( $p=0.006$ ). Use of topical corticosteroids in microbial keratitis remains controversial. Theoretically, their use is aimed at limiting the degree of structural damage caused directly by the micro-organisms—for example, by the lytic enzymes which degrade tissue, and damage caused by the host inflammatory response against these micro-organisms.<sup>29,30</sup> At the same time, suppression of inflammation also provides the potential for micro-organisms to reach higher tissue concentrations and therefore become more difficult to control. Generally it is recommended that steroids should not be used until the responsible microbe is identified, sensitivities reported, and a favourable response to antimicrobial treatment is evident.<sup>29,30</sup> Furthermore, steroids should not be used unnecessarily if the cornea and eye are improving without steroids, or if there is excessive corneal thinning. Corticosteroids are contraindicated in fungal keratitis and relatively contraindicated in acanthamoeba keratitis.<sup>29</sup>

Rapid diagnosis, detection, and identification of the causative agent, and immediate institution of the appropriate therapy are important for a successful visual recovery.<sup>1,3,12,14</sup> Routine culture of corneal lesions before antibiotic treatment is initiated is key to the management of infective keratitis. Laboratory results, while not immediately available, can subsequently guide appropriate modification of the antibiotic regimen in instances where resistant organisms are identified, multiple organisms occur, or infections fail to respond to the initial regimen.<sup>2,15,24</sup> Identifying and culturing the microbial organism after commencing treatment can be difficult and the staining characteristics of organisms can be altered by previous antibiotics.<sup>24</sup> In this study there was a mean of 8.9 days from commencement of symptoms to hospital admission, and 38% had been commenced upon topical antibiotics. None the less, as a principal management, 92% of eyes underwent a corneal scrape to identify the pathogens. Thereafter, 17 cases (16.5%) had treatment modification on the basis of these microbiological results. In a broader sense, microbial cultures also provide information on patterns in the spectrum of infective organisms, the susceptibility of these organisms to available antibiotics, and emerging antibiotic resistance.<sup>13,14</sup>

Culture of the lids and conjunctiva have been found to be of little diagnostic value because of low sensitivity and specificity,<sup>2,13,15</sup> and conjunctival swabs were taken in only four patients in this series. The results from these cultures did not alter management in any case. Although a quarter of subjects in this study were contact lens wearers (26%), culture of contact lenses or cases was only carried out in five cases, whereas some authorities suggest this should be routine in the management of sight threatening microbial keratitis in order to maximise isolation of responsible organisms.<sup>31</sup> In three of the five cases different organisms were identified from the cornea and the contact lenses/cases, leading to a modified antibiotic regimen. Although these data suggest a useful role for culturing contact lenses and cases in the current series, it must be noted that contact lenses are frequently contaminated with micro-organisms that may, or may not, be the causative agent in keratitis.

The length of hospital stay has many implications both for the patient and the public health service. For the latter this includes financial resources, staffing, bed space, and time. The mean hospital stay in this study was 5.8 days, the median stay

was 4.0 days. It is also of note, that the mean age of inpatients was 45, and 69% were between 16 and 65 years, emphasising the potential for impact on those of working age from severe infectious keratitis.

Severe infectious keratitis remains a leading cause of ocular morbidity worldwide, and New Zealand is no exception. With potentially devastating visual impairment and significant costs to the public health system, optimising the prevention and management of microbial keratitis is essential. One way of doing this is to target at-risk groups with educational measures. Importantly, in this study, 88% of subjects admitted to hospital had at least one predisposing risk factor, particularly previous ocular surgery, contact lens wear, topical corticosteroid use, and ocular trauma. In addition to patient education, clinical recommendations for ophthalmologists must include appropriate follow up for postoperative surgical patients with planned removal of all corneal sutures (four of seven suture related infections occurred more than 2 years after surgery), particular attention to identifying loose or broken sutures, patient education in respect of loose or broken sutures, and close monitoring of patients applying topical corticosteroids. In addition, the importance of lens hygiene and significance of the duration of contact lens wear should be continually emphasised to all contact lens wearers by eye care professionals and public education measures. An important factor in optimising management of infective keratitis remains the rapid initiation of appropriate microbiological testing and treatment. In this series, there was a mean of 8.9 days between symptoms and hospital admission with no eyes undergoing a corneal scrape as part of this initial management. While no significant difference was found in outcome between treatment with a fortified duotherapy combination compared to a monotherapy regimen, the high rate of polymicrobial infection in this New Zealand series may support the former as first line treatment on the basis of its broader antimicrobial coverage.

Regrettably, it is disappointing to note that although the principal risk factors for severe microbial keratitis have been well established over the past 20 years, the majority of subjects in this series exhibited potentially modifiable risk factors. As a group, infective keratitis places a significant burden on public hospital services ( $\approx 2\%$  of annual ophthalmic services in Auckland) and results in significant, potentially avoidable visual morbidity. Continual education, both of ophthalmologists and patients, is still required to minimise the incidence and severity of microbial keratitis.

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