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Self-study CPD activity 2021

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Topic

Microbial keratitis

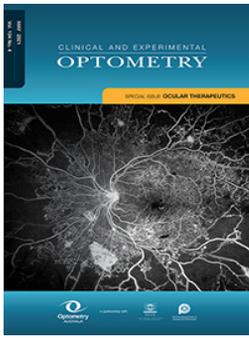
Article(s)

Microbial keratitis in a tertiary centre in Queensland, Australia (1999-2015)

Profession(s)

Optometrist / Medical Practitioner

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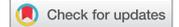


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RESEARCH



Microbial keratitis in a tertiary centre in Queensland, Australia (1999-2015)

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ABSTRACT

Clinical relevance: Keratitis is common and studies of blindness throughout the world have found that corneal disease is the second most common cause of blindness.

Background: Microbial keratitis a bacterial, fungal, or protozoan disease of the cornea, characterised by a corneal infiltrate with an overlying epithelial defect and associated anterior chamber reaction.

Methods: Patients were identified through the hospital pathology database and a retrospective chart review of all patients with a positive corneal culture between 1999 and 2015 at Princess Alexandra Hospital was carried out.

Results: There were 895 records from 779 patients included and additional 107 records excluded. The average age of the included patients was 58.9 years (SD 21.0). Males made up 498 (55.6%) of the included patients. Contact lens microbial keratitis (CLMK) was the most common risk factor for MK and was significantly more common in younger patients. CLMK was significantly associated with cultures positive for *Pseudomonas aeruginosa* ($p < 0.001$) while MK secondary to ocular surface disease and prior ocular surgery were more commonly associated with gram-positive organisms ($p < 0.001$). Monotherapy with a fluoroquinolone was the most common treatment for patients with MK. Good outcomes were seen in 57% of patients.

Conclusion: In this patient group, contact lens wear was the most common risk factor for MK. *Pseudomonas aeruginosa* was the most common isolate.

ARTICLE HISTORY

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KEYWORDS

Australia; microbial keratitis; tertiary referral

Introduction

Microbial keratitis can be caused by a range of bacteria, including frequently reported gram positive or gram-negative bacteria¹ to rare opportunistic infections that may be caused by less virulent organisms in immunocompromised patients.² Audits of corneal pathogens in Australia have been done regularly over the last 35 years (Table 1). They consistently show a predominance of gram-positive bacteria (51-83%). The virulent organisms that are frequently cultured are *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*. Audits from warmer northern cities have increased rates of *Pseudomonas aeruginosa*.¹⁰

The treatment of bacterial keratitis is focused on eradicating the causative organism using antibiotics. The initial choice of antibiotics is often challenging because it is made prior to the availability of microbiology results and is based on clinical and demographic information. Topical antibiotics are typically administered hourly during the first few days and nights to deliver extremely high doses of antibiotics.¹¹ This is subsequently tapered according to the patients' improvement, while the addition of a systemic antibiotic is generally ineffective as the cornea is an avascular tissue.

Traditionally, practitioners would use a combination of fortified antibiotics to attain the broadest possible antibiotic cover against both gram-positive and gram-negative bacteria.¹²⁻¹⁴ The most common combination was a fortified cephalosporin or vancomycin and gentamicin. The commercial release of fluoroquinolone antibiotics led to an increase in popularity of monotherapy with a fluoroquinolone because these eyedrops allow practitioners to prescribe a single off the shelf agent

which provides close to the same extremely broad coverage of duotherapy.^{11,15,16}

Controlled comparative studies of treatment of bacterial keratitis have shown that ofloxacin and moxifloxacin as monotherapy to have similar outcomes in treating bacterial keratitis as duotherapy with fortified antibiotics.^{11,17} Studies of the trends in antibiotic use in Queensland have shown that monotherapy with fluoroquinolones is becoming more common than duotherapy with fortified antibiotics.¹⁸ However, some centres note that this can create a clinical challenge because of the increasing resistance to fluoroquinolones.¹⁹

Organisms resistant to empirical antibiotics decrease the likelihood of successful treatment with antibiotics²⁰ and a consequent increased risk of vision loss.²¹ Consequently, knowing the sensitivity profile of common pathogens, and the trend of these sensitivities in a community is crucial to the effective management of bacterial keratitis. Additionally, the popularity of monotherapy with fluoroquinolones in Australia makes the resistance pattern to fluoroquinolones of particularly important.

The Princess Alexandra Hospital (PAH) is a large tertiary hospital in Brisbane, Australia. The PAH Ophthalmology department is one of the largest in the state with 19 consultants. All major sub-specialities are represented and there a specialised ophthalmology emergency clinic for acute presentations. Brisbane has a humid subtropical climate with hot, wet summers and dry, moderately warm winters. The temperature varies between an average minimum of 16 degrees and a maximum of 26 degrees. Yearly rainfall is on average just over 1,000 mm and rainfall occurs on an average of 125 days.²²

This audit provides a snapshot of the presentation and treatment of patients with microbial keratitis at the PAH.

Table 1. Culture results from Australian microbial keratitis audit studies.

Location	Year of Publication	Total cases	Culture Positive (%)	GP (%)	CNS (%)	SA (%)	SP (%)	GN (%)	PA (%)	F (%)
Adelaide ^{†3}	1987	87	-	51.7	13.8	23	5.7	22.3	10	9
Sydney ^{‡4}	1989	107	37.4	67.5	22.5	15	2.5	25	10	5
Perth ^{‡5}	1996	53	71	51.2	14.6	14.6	-	48.8	12.2	-
Sydney ^{‡6}	2005	190	62.8	75.9	47.2	20.4	5.6	25.9	11.1	3.7
Adelaide ^{‡7}	2005	211	63.5	66.4	29.8	18.7	6	28.3	12.7	5.2
Melbourne ^{‡23}	2006	266	49	55	35	7.6	3.1	22	7.6	5.3
Sydney ^{†8}	2006	112	42	-	38	11	1.9	-	21	-
Brisbane ^{†10}	2008	253	65	50.6	13.4	11.5	6.7	34.8	26.7	7.9
Sydney ^{†9}	2019	224	75	83	57	11	6	17	15	-

[†]listed as the proportion of isolates.

[‡]listed as the proportion of culture-positive cases.

CNS: coagulase-negative staphylococci; F: total fungi; GN: total gram negative; GP: total gram positive; PA: *Pseudomonas aeruginosa*; SA: *Staphylococcus aureus*; SP: *Streptococcus pneumoniae*.

Patient demographics, microbiology results, treatment, and outcomes of keratitis are described from the records included in this audit.

Methods

A retrospective patient medical record review was performed for all patients with a positive corneal scrape identified through the local microbiology database at the PAH. All available records were reviewed, between January 1999 and December 2015.

Microbiology results were used to identify cultured organisms. Cultures were collected on horse blood agar, sabouraud plates, and broth. The minimum criteria for a positive culture were the growth of three colonies on a solid medium.

Patient records were used to gather information about demographics (age and sex), risk factors for keratitis, clinical presentation, antibiotic treatment, and surgical interventions. The length of the review was measured in months from the date of corneal scraping until final recorded review, at the time of chart review. Prior ocular surface disease was recorded as a risk factor for keratitis if the patient had a prior history of herpetic keratitis (herpes simplex or herpes zoster), exposure keratopathy, corneal decompensation, Sjogren's disease, recurrent corneal erosions, marginal keratitis, trachoma, or neurotrophic keratopathy.

The outcome of an episode of keratitis was classified as good if final visual acuity was 6/12 or better; poor if it was 6/60 or worse or required a corneal transplant, otherwise average.

Ethics approval was gained from the Metro South Human Ethics Research Committee. Statistical tests were Chi-squared tests unless stated otherwise.

Results

Patient demographics

There were 895 records from 779 patients included and additional 107 records excluded (Figure 1). The average age of the included patients was 58.9 years (SD 21.0). Males made up 498 (55.6%) of the included patients. Males predominated in the younger age-groups, while females became more common in the older age-groups (Figure 2).

Risk factors for MK at PAH

Contact lens wear was the most common risk factor for microbial keratitis during the study. However, ocular surface disease, recent ocular trauma, and prior ocular surgery were also associated with the disease (Figure 3). Contact lens microbial keratitis

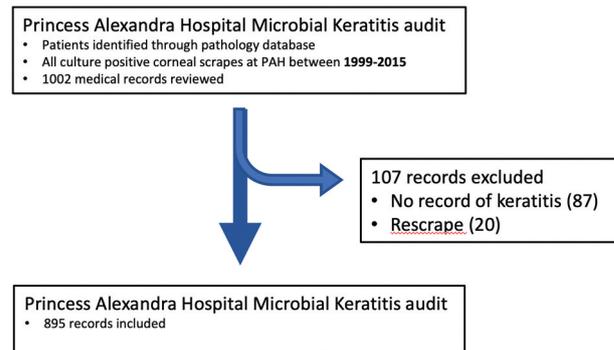


Figure 1. Princess Alexandra Hospital Microbial Keratitis audit patient inclusion.

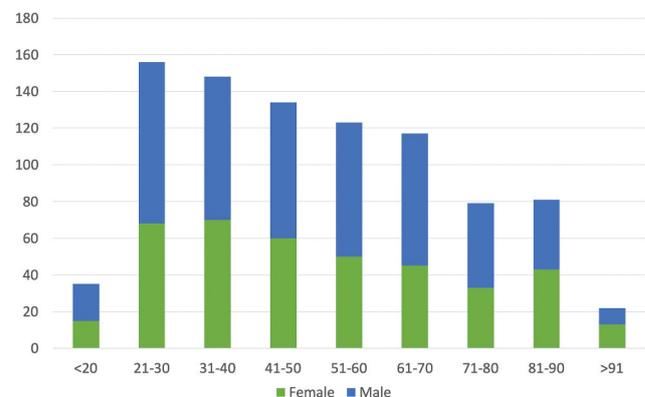


Figure 2. Age and sex distribution of patients with microbial keratitis at Princess Alexandra Hospital.

(CLMK) was significantly more common in younger patients, while prior ocular surgery or ocular surface disease was more common in older patients (Table 2, Figure 4).

The clinical features are shown in Table 2. There was a significant difference in the age of patients with MK related to different risk factors. However, there was no significant difference in the vision at presentation or final review, or in the length of review of patients with MK related to different risk factors.

Corneal culture results at Princess Alexandra Hospital

The majority of the included pathology records cultured only one organism (74.6%), although a significant number were polymicrobial (25.4%). In total there were 1,153 organisms cultured from the 895 included records. Table 3 shows that *Pseudomonas aeruginosa* was the most common single organism, although gram-positive organisms were more

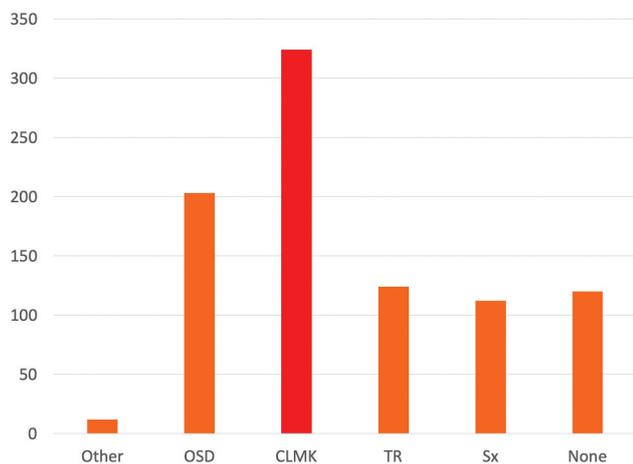


Figure 3. Risk factors for patients with microbial keratitis at Princess Alexandra Hospital.

Table 2. Clinical features of patients with microbial keratitis at Princess Alexandra Hospital.

		Age	First visual acuity (logMAR)	Last visual acuity (logMAR)	Visual improvement (logMAR)	Length of Review (months)
OSD	Mean	62.8	1.4	1.1	0.3	14.5
	SD	20.4	0.9	1.0	0.7	22.9
CL	Mean	36.5	0.6	0.2	0.4	6.9
	SD	13.8	0.7	0.5	0.7	16.5
Tr	Mean	45.6	0.7	0.2	0.4	5.6
	SD	15.2	0.8	0.5	0.6	9.8
Sx	Mean	65.3	1.6	1.2	0.3	21.4
	SD	17.4	0.8	0.9	0.6	32.1
None	Mean	53.5	0.9	0.6	0.3	8.1
	SD	20.6	0.9	0.8	0.7	14.0
Other	Mean	70.2	0.7	0.9	0.0	4.5
	SD	16.4	0.9	0.9	0.2	6.5
Total	Mean	50.1	1.0	0.6	0.4	10.3
	SD	20.8	0.9	0.8	0.7	20.3
p-value		< 0.001	0.2	0.2	0.8	0.6

CL: contact lens wear; OSD: ocular surface disease; Tr: recent ocular trauma; Sx: prior ocular surgery.



Figure 4. Age group and risk factor distribution of patients with microbial keratitis at Princess Alexandra Hospital.

common as a group. CLMK was significantly associated with *Pseudomonas aeruginosa* while MK secondary to ocular surface disease and prior ocular surgery were more commonly associated with gram-positive organisms. The most common fungal species isolated was *Fusarium*.

Figure 5 shows that there was seasonal variation in the isolation of *Pseudomonas aeruginosa* and presentation of cases of CLMK.

Antibiotic treatment of patients with microbial keratitis at PAH

Monotherapy with a fluoroquinolone was the most common treatment for patients with microbial keratitis at PAH (Table 4). The rate of treatment with monotherapy with fluoroquinolone steadily increased throughout the study, while treatment with duotherapy decreased throughout the study (Figure 6). Despite this overall trend of decreasing use of duotherapy, the subgroup of a fluoroquinolone and a fortified cephalosporin had a slightly increased rate of use towards the end of the study.

Patient outcomes

The outcome of 816 patients with keratitis treated at PAH is shown in Table 5. This shows that 57% of all patients had a good outcome while only 32% of patients had a poor outcome. Univariate analysis showed that good outcomes were significantly associated with keratitis caused by contact lens wear or recent ocular trauma ($p < 0.001$). Poor outcomes were significantly associated with keratitis related to ocular surface disease and prior ocular surgery. Figure 7 shows that the rate of good and poor outcomes were fairly stable during the period of study.

On average, there were 15 cases of poor outcome per year, so 15 cases of monocular blindness related to microbial keratitis per year. Additionally, there were 48 cases of patients in the database that were bilaterally at their final review blind (2.8 patients per year; vision of $< 6/60$ in both eyes).

Because the pre-keratitis vision was not recordable in the records, microbial keratitis may not have been the sole factor causing poor vision in these cases. The microbial keratitis might have occurred in patients with pre-existing poor vision due to advanced age-related macular degeneration, amblyopia, diabetic retinopathy, cataracts, or a failed corneal transplant. This may have impacted the ocular surface disease and prior ocular surgery group more than the younger groups with trauma or contact lens wear.

Discussion

Overall, the pattern of MK in this patient group is similar to that seen in other centres around Australia. MK was most commonly caused by contact lens wear, with a corneal culture positive for *Pseudomonas aeruginosa*. Monotherapy with a fluoroquinolone is the most common form of treatment, and the majority of patients had good outcomes.

In this study, contact lens wear was the most common risk factor. This is similar to other studies from Australia and other developed countries which show a similar risk factor profile.^{23,24} Young patients are more likely to have worn contact lenses or be affected by recent ocular trauma, whereas older patients are more likely to have an ocular surface disease or prior ocular surgery. The young age of patients with CLMK is significant because it demonstrates the public health issue associated with contact lens wear. This is because CLMK is an avoidable disease and affected patients have a greater morbidity due to their greater longevity and the effect it has on their work-life.

Table 3. Corneal culture results of patients with microbial keratitis at Princess Alexandra Hospital.

Organism	Risk Factors (%)														p-value*
	CLMK	%	OSD	%	Tr	%	Sx	%	Other	%	None	%	Total		
Gram positive	195	48.6	197	74.6	130	75.1	95	68.3	12	85.7	109	74.7	738	< 0.001	
<i>Staphylococcus aureus</i>	10	2.5	30	11.4	6	3.5	24	17.3	3	21.4	13	8.9	86	< 0.001	
MRSA	1	0.2	1	0.4	0	0.0	3	2.2	0	0.0	2	1.4	7	0.135	
Coagulase negative staphylococcus	114	28.4	87	33.0	83	48.0	35	25.2	4	28.6	52	35.6	375	0.001	
<i>Streptococcus pneumoniae</i>	1	0.2	10	3.8	2	1.2	8	5.8	3	21.4	5	3.4	29	< 0.001	
Other gram positive	69	17.2	69	26.1	39	22.5	25	18.0	0	0.0	36	24.7	199	0.232	
Gram negative	191	47.6	59	22.3	18	10.4	37	26.6	2	14.3	20	13.7	327	< 0.001	
<i>Pseudomonas aeruginosa</i>	179	44.6	32	12.1	10	5.8	19	13.7	1	7.1	10	6.8	251	< 0.001	
Other gram negative	12	3.0	27	10.2	8	4.6	18	12.9	1	7.1	10	6.8	76	0.004	
Fungi	9	2.2	8	3.0	25	14.5	7	5.0	0	0.0	17	11.6	50	< 0.001	
Protozoa (<i>Acanthamoeba</i>)	6	1.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	6	0.059	

CLMK: contact lens microbial keratitis; MRSA: Methicillin-resistant *Staphylococcus aureus*; OSD: ocular surface disease; Sx: prior ocular surgery; Tr: recent ocular trauma. *p-values represent a comparison of the rate of each organism group between different risk factor groups.

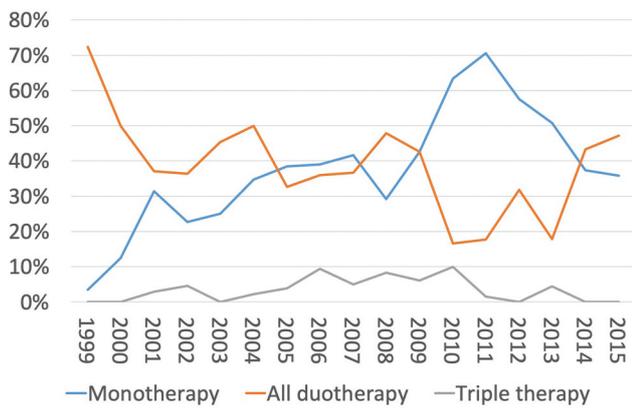


Figure 5. Monthly variations in contact lens keratitis and *Pseudomonas aeruginosa*.

Table 4. Antibiotic treatment of patients with microbial keratitis at Princess Alexandra Hospital.

Treatment type	Total	
	n	%
Monotherapy (Fluoroquinolones)	369	41%
All duotherapy	330	37%
Triple therapy	33	3.7%
Other	164	18.3%

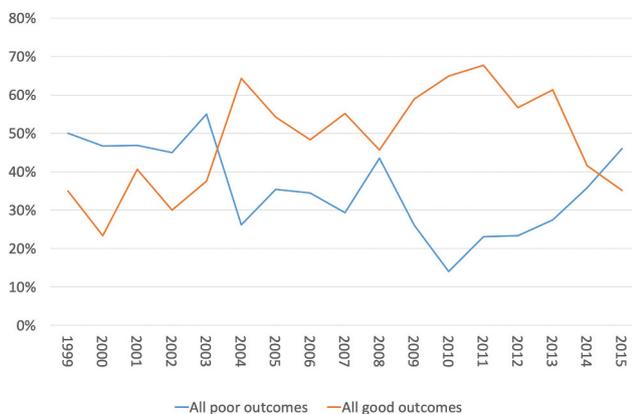


Figure 6. Yearly trend in antibiotic treatment of patients with microbial keratitis at Princess Alexandra Hospital.

The frequency of gram-positive organisms and *Pseudomonas aeruginosa* is also similar to other studies around Australia.²³ In particular, the association of *Pseudomonas aeruginosa* (PA) and CLMK is widely reported,^{23,25} although the rate of PA in CLMK in

Table 5. Outcomes of different keratitis risk factor groups.

	Good		Average		Poor		Total
	n	%	n	%	n	%	
Contact lens wear	231	76.7	27	9.0	43	14.3	301
Ocular surface disease	64	34.6	18	9.7	103	55.7	185
Recent ocular trauma	89	75.4	13	11.0	16	13.6	118
Prior ocular surgery	17	16.5	19	18.4	67	65.0	103
No identifiable risk factor	59	60.2	10	10.2	29	29.6	98
Other	5	45.5	1	9.1	5	45.5	11
Total	465	57.0	88	10.8	263	32.2	816

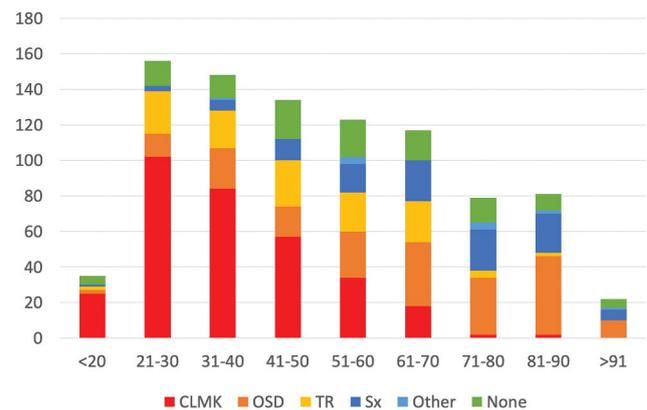


Figure 7. Yearly rate of outcomes in Princess Alexandra Hospital Microbial Keratitis database.

Queensland is higher than that reported from southern states. This is likely to be due to the tropical climate of Queensland and climatic factors, such as higher temperature and humidity.²⁶ This correlation is also shown by the seasonal variation in the isolation of PA in this study. Both of these factors are very important for practitioners to note to enable the correct selection of empirical antibiotics for the management of MK.

The frequency of use of fluoroquinolones in management of MK is similar to that noted in New Zealand,^{27,28} and the choice of mono-therapy with a fluoroquinolone is suitable based on the comparative studies showing efficacy with duotherapy with fortified antibiotics.^{11,17} However, practitioners should note that fluoroquinolones have only moderate efficacy against virulent gram-positive organisms. Consequently, mono-therapy with a fluoroquinolone should be used with caution in patients that have a higher risk of having keratitis secondary to a virulent gram-positive organism. This includes older patients or patients with the ocular surface disease or prior ocular surgery.

The high rate of good outcomes in keratitis management is encouraging. It implies that younger patients do well despite their potentially more severe pseudomonal CLMK. It should be noted that this data is skewed by the potential inaccuracy of the pre-keratitis vision, and the association of poorer vision with older patients.

Conclusion

In this patient group, the most common risk factor for keratitis is contact lens wear, the cultured organism is often *Pseudomonas aeruginosa*, and antibiotic treatment is monotherapy with a fluoroquinolone.

Disclosure statement

No potential conflict of interest was reported by the authors.

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QUESTIONNAIRE

I6 (21)

Microbial keratitis in a tertiary center in Queensland, Australia (1999-2015)

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer;** in which case you must mark **all** the correct answers.

Question 1: Is it **TRUE** or **FALSE** that microbial keratitis (MK) is caused by a range of bacteria?

- A: TRUE
- B: FALSE

Question 2: Which organisms frequently cultured in Australia can be linked to MK?

- A: *Staphylococcus aureus*
- B: *Streptococcus pneumoniae*
- C: *Pseudomonas aeruginosa*
- D: None of the above

Question 3: Which one of the following is the most popular form of treating MK?

- A: Debridement
- B: Corticosteroid eyedrops
- C: Fluoroquinolone eyedrops
- D: Antiviral medication

Question 4: Studies of treatment of bacterial keratitis have shown that and as monotherapy have similar outcomes in treating bacterial keratitis as duotherapy with fortified antibiotics?

- A: Ofloxacin
- B: Moxifloxacin
- C: Amoxicillin
- D: Phenoxymethylpenicillin

Question 5: Which of the following were common risk factors for MK at Princess Alexandra Hospital (PAH)?

- A: Contact lens wear
- B: Prior ocular surface disease
- C: Gender
- D: Age

Question 6: Which of the following options are **CORRECT** regarding corneal culture results at PAH?

- A: Contact lens microbial keratitis (CLMK) was significantly associated with *Pseudomonas aeruginosa*
- B: *Streptococcus pneumoniae* was the most common single organism
- C: The most common fungal species isolated was *Fusarium*
- D: There was no seasonal variation in the isolation of *Pseudomonas aeruginosa* and presentation of cases of CLMK

Question 7: Is it **TRUE** that more than half of the patients with keratitis treated at PAH had a good outcome?

- A: YES
- B: NO

Question 8: MK might have occurred in patients with pre-existing poor vision due to which of the following?

- A: Trachoma
- B: Advanced age-related macular degeneration
- C: Glaucoma
- D: Diabetic retinopathy

Question 9: The higher rate of *Pseudomonas aeruginosa* in CLMK in Queensland was possibly due to which of the following?

- A: Tropical climate
- B: Arid climate
- C: Temperate climate
- D: Steppe climate

Question 10: Which of the following should be used with caution in patients that have a higher risk of having keratitis secondary to a gram-positive organism?

- A: Polytherapy
- B: Pharmaceutical combination therapy
- C: Monotherapy with fluoroquinolone
- D: Fixed-dose combinations

END



PERSONAL INFO

(Complete the sections marked with an asterisk *)

*FOH Number		*HPCSA No	
*Time spent on activity	____ Hour ____ Min	If any of your personal details have changed please make a note here	
I hereby declare that the completion of this document is my own effort without any assistance.			SIGNED: _____ DATE: _____

ANSWER SHEET

I6 (21)

Microbial keratitis in a tertiary center in Queensland, Australia (1999-2015)

	A	B	C	D	E		A	B	C	D	E
1						6					
2						7					
3						8					
4						9					
5						10					

RATE THIS ACTIVITY

POOR 1		FAIR 2		AVERAGE 3		GOOD 4		EXCELLENT 5	
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IMPORTANT INFO

This activity is accredited for **TWO CLINICAL CEU'S**

You have to achieve 70% to pass this activity.

If you have chosen our "**online option**", you have to complete your answer sheet online.

If you have chosen our "**email or hard copy option**", you can return your answer sheet to us or complete it online.

Your results will be available immediately if you complete your answer sheet online. If you return your answer sheet for assessment you will receive feedback by email within 48hours.

RETURN ANSWER SHEET TO

FAX: 086 614 4200 / 012 653 2073

WHATSAPP: 074 230 3874

EMAIL: SAFOCUS@IAFRICA.COM

ONLINE: <http://foh-cpd.co.za/cpd-online/cpd-user>

(Username: FoH membership No & Password: ID)

(YOU WILL RECEIVE A CONFIRMATION OF RECEIPT SMS WITHIN 12-24 HOURS, IF NOT RECEIVED PLEASE SEND AGAIN)