Joint Ophthalmology and Microbiology Microbial Keratitis Guidelines

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Microbial Keratitis is a blinding infection of the cornea. Urgent assessment, investigation and treatment are required to prevent potentially blinding complications. In order to conform to Royal College of Ophthalmologists guidelines, a pathway to aid diagnosis and treatment has been developed for doctors and nurses working in the hospital eye service.

Lead Clinician(s)

Geraint Williams	Consultant Ophthalmologist, Ophthalmology
Approved by Countywide Ophthalmology Audit Meeting on:	25th March 2019
Review Date: This is the most current document and is to be used until a revised version is available	25th March 2021

Key amendments to this guideline

Date	Amendment	Approved by:
Dec 2016	New guideline	
5th December 2017	Sentence added in at the request of the Coroner	
13th February 2019	Document extended for three months whilst review of document is completed	Geraint Williams
25th March 2019	Adjusted the dosing e.g. for Acanthamoeba in keeping with recent practice and Ganciclovir gel becoming 1st line for Herpetic keratitis reflecting the cessation of Aciclovir ointment	Geraint Williams

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Introduction

Microbial Keratitis is a blinding infection of the cornea. Urgent assessment, investigation and treatment are required to prevent potentially blinding complications. In order to conform to Royal College of Ophthalmologists guidelines, a pathway to aid diagnosis and treatment has been developed for doctors and nurses working in the hospital eye service.

Background

Microbial keratitis is a relatively common albeit potentially blinding corneal infection. [1] The majority of cases will have a bacterial aetiology in the United Kingdom but less common causes include fungal and acanthamoeba must be considered in the context of identifiable risk factors, outlined below.[2]

Common bacterial causes include:

Gram Positive cocci - *Coagulase-negative Staphylococci MSSA, Streptococcus pneumonia, α-haemolytic Streptococci*
Gram positive bacilli - *Corynebacterium spp. Propionibacterium*
Gram negative cocci - *Moraxella catarrhalis*
Gram negative bacilli - *Pseudomonas aeruginosa Other Pseudomonas spp. Serratia marcescens*

It is critical that early identification, investigation and treatment is instigated and coupled with a high index of suspicion of the causative organism. Furthermore the severity of the presentation will influence the decision to treat as an outpatient or give rise to consideration for admission for intensive antimicrobial therapy.

History

Although not an exhaustive list, common risk factors include:

Contact Lens Wear
Contact with non-sterile water
Storage and cleaning of contact lens solution
Washing eyes with tap water
Trauma including foreign and vegetable matter
Local immunosuppression
Systemic Immunosuppression
Entropion
Exposure
Neurotrophic
Lid Margin Disease
Corneal transplantation
HSV keratitis

Examination

Specific

Visual Acuity (VA)
Size and shape
Depth including perforation
Distance from limbus
Vascularisation (deep or superficial, number of clock hours of involvement)

AC activity
Intra-Ocular Pressure (IOP)
Evidence of intra-ocular infection i.e. endophthalmitis. A high index of suspicion must be assumed in the context of perforation.

General
Evidence of co-existing risk factors e.g. lid margin disease, malposition

Documentation
Microbiology Ophthalmic Group (MOG) proforma
Consider photography where possible

Investigation
Scrape: Under topical anaesthesia, with assistant or speculum as required a scrape should be taken gently with a no. 11 blade or a 21 gauge green needle, smeared and the blade discarded. This should be repeated for all samples including:

i. Gram Stain – glass side (same day evaluation)
ii. Blood
iii. Chocolate
iv. Sabauraud [1]

- Suspicion of acanthamoeba –

PCR (acanthamoeba and HSV) +/- In Vivo Confocal Microscopy (IVCM) in New Cross Hospital Wolverhampton.[2] [3] Suspend corneal scrape material in ampoule of sterile saline (at least 200 µl) and send to microbiology for Acanthamoeba PCR

- Suspicion of fungal keratitis –

Calcafluor white stain – glass slide (for fungal hyphae). IVCM has a role in make the diagnosis

- Suspicion of herpetic keratitis –

Always swab epithelial disease for PCR (dry swab and place in sterile universal container)

- Please mark the side of the slide the scrape has been smeared on
- Please put patient labels on the base of the agar plates, not the lids. Lids can fall off and potentially make the culture unidentifiable.
- It would be very helpful for microbiology to know if the patient is on antimicrobial drops, and if so what they are on or what is proposed on the request form

Please contact microbiology to inform of scrapes, send urgently and check results within same working day.

Please inform the on call ophthalmology consultant of any results that may require action that evening/weekend.

Please inform corneal nurse practitioner (NP) of scrapes via clinic nurses. An ongoing spreadsheet is maintained by the corneal NP for follow up of scrape results.

[1] The provision of an impression membrane combined with instillation in to Brain Heart Infused (BHI) broth is the subject of ongoing consideration with the microbiology department
[2] Unavailable in trust currently but may need onward referral
[3] Precise culture/PCR availability is subject of ongoing evaluation by microbiology

Treatment

Generic

- G. Ciprofloxacin (drops) hourly day and night pending review [3]
- Topical dilatation, preferably g Cyclopentolate 1% minims tds
- Consider oral ciprofloxacin for limbal disease and in cases of impending/actual perforation
- All patients must have their Gram stain confirmed the same day by the initiating doctor to guide further treatment
- If unusual organisms e.g. gram positive cocci then discuss with microbiologist regarding the introduction of suitable gram positive cover e.g. topical penicillin 1:5000 or 1% Teicoplanin [3]

Patients who cannot administer their own drops themselves or with family support and/or those with perforation require admission

Specific

1. Acanthamoeba [1]

1st Line: Polyhexamethylene biguanide (PHMB) 0.02% [4] , Propamidine 0.1% and Chlorhexidine 0.02%
2nd Line (if unavailable) Chlorhexidine 0.02% until PHMB and Propamidine available
Refractory Disease: Consider PHMB 0.06%

- [1] PHMB can penetrate slough and biofilms, has good tissue compatibility with no reported resistance.

Use is currently empirical:

- Hourly day and night for 1 day
- Hourly day only for 6-10 days
- Then reduce to 6-8 x daily
- Taper to 4x as disease is brought under control

Drug toxicity more common with diamidines e.g. Brolene **not** PHMB [4]

STOP 1 month off ALL therapy (including steroids) without signs of inflammation, or of inflammation so minimal as not to require treatment (Dart et al. 2009)
Steroids (only to be initiated by corneal team)

- Defer topical steroids for 2 weeks or more
- Only for deteriorating inflammation & pain
- Continue anti-amoebics for 4 weeks after steroids discontinued

Steroids do not exacerbate outcomes **IF** used with effective therapy
Risk of a poor outcome increases about 4x when steroids are used before the correct diagnosis of AK [5, 6]
Outcomes are better if diagnosis is made less than 3 weeks after onset

2. Fungal Keratitis [1, 7]

Fungal keratitis while rare, is more commonly seen in those who are immunosuppressed, have prolonged contact lens wear or history of foreign travel to tropical climates. Although historically yeast infections have been more common in UK populations, filamentary organisms are becoming more common.

1st Line Natamycin 5% [1,7, 8]

2nd Line
Chlorhexidine 0.02%
Voriconazole 1%
Amphotericin 5%

Deep stroma or uncommon fungal keratitis - dual therapy with consideration of oral Voriconazole.

Intensive treatment regime as per acanthamoeba should be considered but NOT with accompanying topical steroids.

Intra-stromal injection of Voriconazole and intra-cameral can be considered but needs discussion and initiation by the corneal team.

Oral Voriconazole should also be considered following discussion with the cornea team and microbiology and full history for risk factors including liver disease and baseline liver function tests/renal function tests.

Suggested Treatment Summary Table (excluding HSV) [1]

Organism	**Primary Treatment**	**Alternative Treatment**
Bacteria	Fluoroquinolone	Cefuroxime 5% and Gentamicin 1.5%
Acanthamoeba	Polyhexanine (Polyhexamethylene biguanide; PHMB) 0.02% or Chlorhexadine 0.02%	Hexamadine Brolene
Fungi	Natamycin 5%	Chlorhexidine 0.2% Voriconazole 1%

Second line treatments not kept in KTC acutes may be obtained via WRH pharmacy and if necessary dispensed via Accident and Emergency. Please discuss with the senior duty/on call pharmacist at WRH.

These include:

Gentamicin 0.3%
Levofloxacin 0.5%
Fusidic Acid
Chloramphenicol 0.5% non-preserved and Chloramphenicol ointment
Cefuroxime 5%
Penicillin 1:5000

Teicoplanin 1% can be specially ordered with notification

3. HSV keratitis

Epithelial disease

Topical Antiviral: Oc Ganciclovir 0.15% x5/day

NB Acyclovir 3% is no longer commercially available.

Review within 1 week and refer to corneal service if failure to respond to treatment.
HSV melts need urgent assessment and treatment including the prevention or intervention for perforation e.g. with glueing or other surgical intervention

Stromal disease

i. No epithelial disease: Topical Prednisolone 0.5% minims x4/day

ii. Epithelial disease: Commence topical antiviral and when resolved commence topical steroids x4/day as above and continue topical antiviral until epithelial disease resolved/no evidence of recurrence.

Do not taper topical antiviral treatment or maintain prolonged topical therapy beyond 2 weeks without corneal team input.

Review within 1 week and refer to cornea service for further management

If suspicions of secondary microbial keratitis – scrape and follow MK pathway with antiviral cover

Endothelial Disease

This is a rare complication of HSV and is seen more commonly in Asian populations secondary to CMV virus. [9, 10] It can masquerade as endothelial dystrophy and needs investigating by aqueous PCR and systemic antiviral. This needs discussion with corneal team and microbiology.

Oral Acyclovir has a role in prevention, immunocompromise, children and severe disease only. [11-15]

Acyclovir resistance is becoming a recognized problem, in particular those with >12 months oral therapy. [16, 17] Please consider these in refractory or atypical cases as sampling for resistance (via microbiology) and alternative topical and systemic treatment may need to be considered.

Corneal HSV melts will require consideration for high dose oral Acyclovir e.g. 800mg po x5/day. Baseline urea and electrolytes should be requested and renal input requested if eGFR <20mL/min/1.73m^2. [18]

Follow up

Review within 72 hours (preferably 48 hours within the working week and on prolonged weekends e.g. bank holidays).

An opportunity for second review within the week in the nurse practitioner clinic on a Monday PM in KTC acute clinic.

At first review gram stain result and culture sensitivities/PCR must be documented in notes even if negative. At this time point the lab must be contacted to verify any updates.

In light of a gram stain/microbiology information coming to light over the weekend/bank holidays requiring an urgent change in treatment e.g. gram positive cocci necessitating Penicillin then the on call consultant will need to initiate this change. Furthermore in this circumstance of a prolonged weekend requiring such a change and/or need for early review, this will need to be arranged in an appropriate clinical setting e.g. accident and emergency.

Gram negative results are not routinely called through to the on call doctors the same evening or KTC acutes during the week. Gram positive organisms that may require change in therapy to Penicllin or Cefuroxime or hyphae will be communicated.

This is not a substitute for the attending doctor ensuring that patients gram stains are chased during the working day and treatment plans revised, and appropriate handover prior to the weekend/bank holiday taking place.

All must be referred to cornea service that are not responding to treatment within 1 week.

Discuss large/deep ulcers/ any suspected of fungal or acanthamoeba/uncertaintanty about severity or need for early review/admission within this time frame. Early advice is preferable.

Notes

1. Immunosuppressed patients may not have infiltrate and need high index of suspicion
2. Autoimmune corneal melts may have a mixed infective/autoimmune component and must be investigated and treated for infection [19]
3. Do not diagnose HSV keratitis in contact lens wearer until acanthamoeba excluded
4. 5% will be acanthamoeba or fungal keratitis
5. 10% will have mixed bacterial and other organism
6. Do not initiate topical steroid drops without discussing with corneal team due to risk of exacerbating infection and unclear benefit. [20]
7. Patients with corneal transplant must be discussed with the corneal team

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
Investigation (3) Treatment (4-5) Follow Up (6)	Ensure compliance with guidelines	Audit	Annual	Miss. Janine Smith (audit lead for RCOphth clinic standards)	Mr. Geraint Williams Consultant Body at departmental audit meeting	Annual

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Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Mr. Geraint Williams (Consultant Ophthalmologist)
Dr. Hugh Morton (Consultant Microbiologist)
Miss Julia Sen (Consultant Ophthalmologist, Lead for Risk)
Mr Malcolm Woodcock (Consultant Ophthalmologist, Clinical Director)

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Geraint Williams
Countywide Ophthalmology Audit Meeting

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
1.	**Does the policy/guidance affect one group less or more favourably than another on the basis of:**		
	• Age	No	
	• Disbility	No	
	• Gender reassignment	No	
	• Marriage and civil partnership	No	
	• Pregnancy and maternity	No	
	• Race	No	
	• Religion or belief	No	
	• Sex	No	
	• Sexual Orientation	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the policy/guidance likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the policy/guidance without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	**Yes/No**
1.	Does the implementation of this document require any additional Capital resources	Yes
2.	Does the implementation of this document require additional revenue	Yes
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	Agreed by David Burrell

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval.