

**Microbial keratitis:
Treatment recommendations**

Presented by
Professor Stephanie Watson
Save Sight Institute

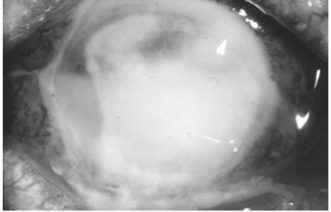
Maria Cabrera-Aguas, Pauline Khoo,
Monica Lahra

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Disclosure

MICROBIAL KERATITIS

- Sight threatening
- Elderly
 - 10% loss eye
 - 40% loss vision
- Children
 - Amblyopia



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Diversity of Microbial Species Implicated in Keratitis: A Review

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Abstract: Background: Microbial keratitis is an infectious disease of the cornea characterised by inflammation and is considered an ophthalmic emergency requiring immediate attention. While a variety of pathogenic microbes associated with microbial keratitis have been identified, a comprehensive review identifying the diversity of species has not been completed.

Methods: A search of peer-reviewed publications including case reports and research articles reporting microorganisms implicated in keratitis was conducted. Search engines including PubMed, Scopus and Web of Science with years ranging from 1950-2012 were used.

Results: 222 different species from 142 genera, representing 60 families were found to be implicated in microbial keratitis. Fungi exhibited the largest diversity with 144 species from 92 genera. In comparison, 77 species of bacteria from 42 genera, 12 species of protozoa from 4 genera and 4 types of virus were identified as the infectious agents. A comparison of their antigenicities shows reports of similarities between genera.

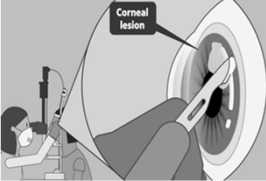
Conclusions: The diversity of microbial species implicated in keratitis has not previously been reported and is considerably greater than suggested by incidence studies. Effective treatment is heavily reliant upon correct identification of the responsible microorganisms. Species identification, the risk factors associated with, and pathogenesis of microbial keratitis will allow the development of improved therapies. This review provides a resource for clinicians and researchers to assist in identification and readily source treatment information.

Keywords: Microbial Keratitis, *Staphylococcus*, Amoebic Keratitis, *Acanthamoeba*, Mycotic keratitis, *Fusarium*, *Candida*, Herpetic keratitis, HSV-1.

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TREATMENT STRATEGIES
Simplified initial management of keratitis

- Corneal scrape & culture
- Document baseline indices
- Choose antimicrobial
- Initiate sterilisation phase
- Modify antimicrobial
- Determine end point



<https://vimeo.com/184614216>

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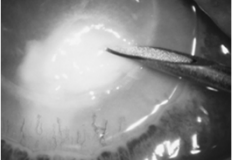

Ngo J, Khoo P, Watson S. Curr Eye Research. 2019

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Corneal scrape

16 STEPS

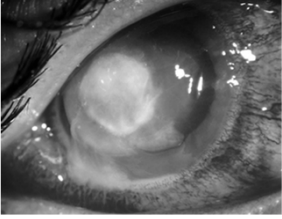
1. Arrange 7 blades/needles, anaesthetic eye drop, acanthamoeba and viral swabs, gloves and mask
2. Draw a circle on the back of the slide
3. Label slide with patient and sample details
4. Wash hands
5. Wear mask
6. Wear gloves
7. Instil anaesthetic eye drop
8. Stabilise the visual axis during sample collection
9. Inoculate the plates with cross-hatched streaks
10. Do not touch the plates
11. Place label on side of agar plate
12. Place sample into Sabouraud's agar slope
13. Stir blade/needle thoroughly in cooked meat medium
14. Dispose of blade/needle after sample collection
15. Swab the cornea not conjunctiva for viral and acanthamoeba swab
16. Pack specimens in bag to be ready for the laboratory

Ngo J, Khoo P, Watson S. Curr Eye Research. 2019
Samarawickrama C, Li Y-C, Cant N, Wilcox M, Dutta D, Watson S.
BMJ Open Ophthalmology. 2017

Document baseline indices

1. Thinning
2. Epithelial defect
3. Epithelial infiltrate
4. Hypopyon

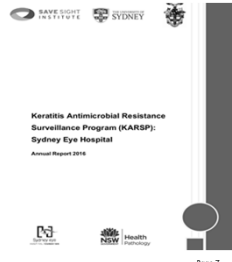


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Simplified initial management of keratitis

- Choose antimicrobial
 - Use local epidemiological data
 - Monotherapy with quinolones
 - Consider dual therapy

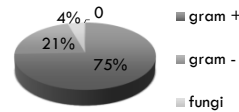


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Keratitis isolates: Sydney 2012 - 2016

1051 eyes: 66% positive culture rate



	n = 689
CoNS	59% (407)
Staph aureus	16%
MRSA	2%
Corynebacterium	6% (38)
Strept pneumoniae	4% (29)
Pseudomonas aeruginosa	55% (110)

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Cabrera-Aguas M, Khoo P, George CRR, Lahra MM, Watson S. Clin Exp Ophthalmol 2019

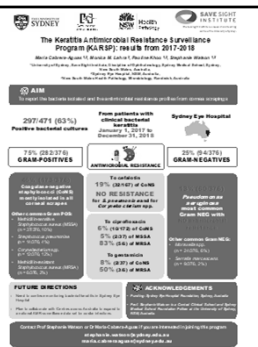
KARSP: 2017-2018

75% (282/376)
GRAM-POSITIVES

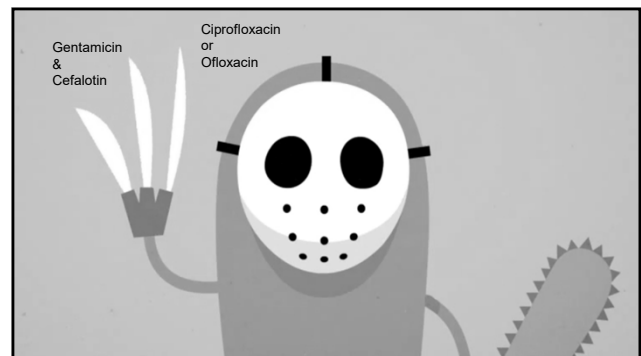
46% (173/376)
Coagulase-negative staphylococci

20%
Coagulase-negative staphylococci
resistant to cefalotin

INCREASING
Resistance of MRSA to
ciprofloxacin and gentamicin

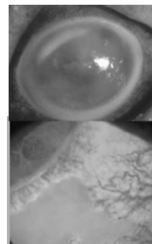


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Fortified antibiotics vs Fluoroquinolones

- Chemical conjunctivitis
- Ocular discomfort increased risk up to 78%
- ? Delayed epithelialisation

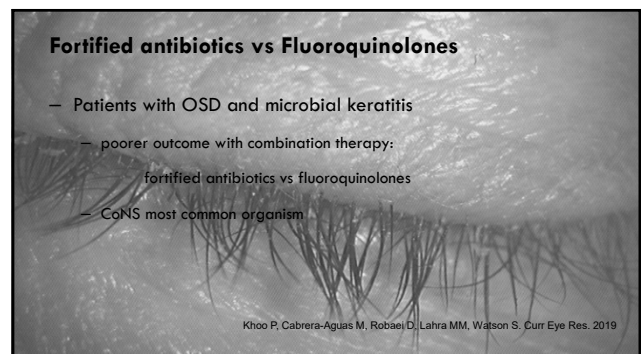


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McDonald EM, Ram FS, Patel DV, McGhee CN. Br J Ophthalmol. 2014

Fortified antibiotics vs Fluoroquinolones

- Patients with OSD and microbial keratitis
 - poorer outcome with combination therapy:
 - fortified antibiotics vs fluoroquinolones
 - CoNS most common organism



Khoo P, Cabrera-Aguas M, Robaei D, Lahra MM, Watson S. Curr Eye Res. 2019

AAO Bacterial keratitis: Preferred Practice Pattern

- Most community acquired infection resolves with empiric Rx
- Scrape
 - Infiltrate >2 mm
 - History of corneal surgery
 - Atypical features
- Cycloplegia
 - Decrease pain
 - Inhibit synechia for substantial AC inflammation



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Simplified initial management of keratitis

- Initiate sterilisation phase
 - Hourly for two days day only or day and night for severe ulcers
 - Continue hourly for three days after assessment

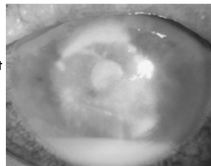


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Simplified initial management of keratitis

- Modify antimicrobial
 - Review at 48 hours
 - Alter if culture & sensitivity results suggest primary therapy inappropriate

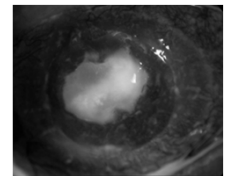


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Simplified initial management of keratitis

- Determine end point (sterilisation usual by 5 days):
 - Improvement at 5 days
 - Enter healing phase
 - Deterioration at 5 days
 - Exclude compliance failure
 - Reassess microbiology
 - Enter algorithm for progression

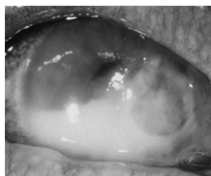


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Progressive keratitis

1. Ensure adequate therapy
2. Establish microbiological diagnosis
 - Cultures & stains for rare causes
 - Biopsy to obtain larger sample
3. Eliminate toxicity
4. Treat host response

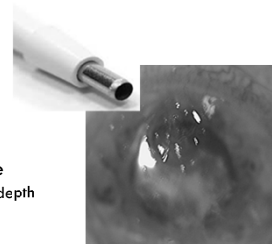


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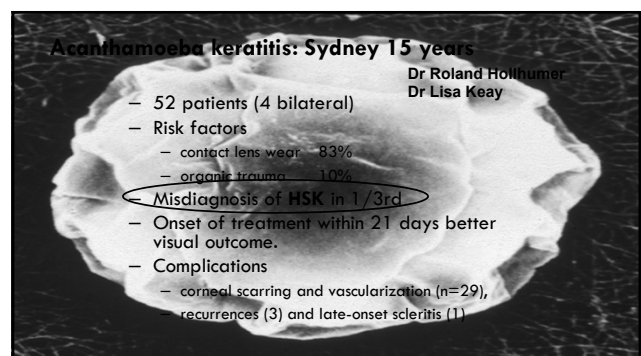
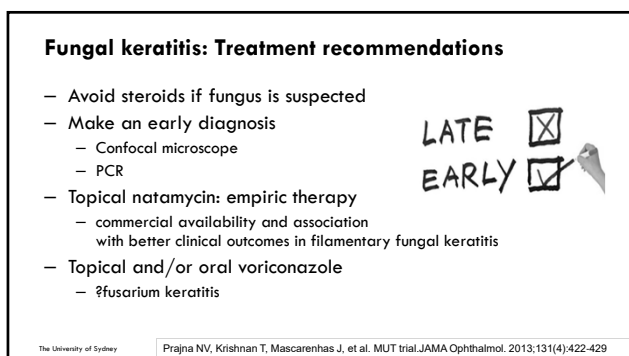
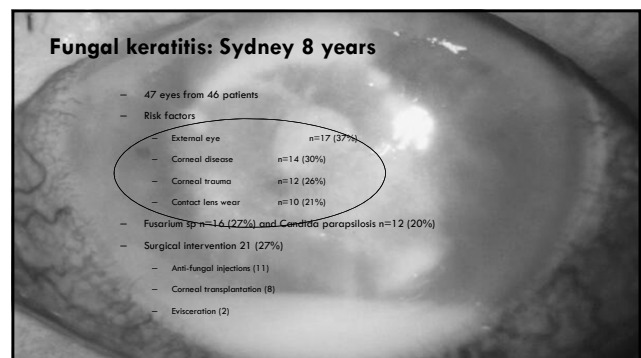
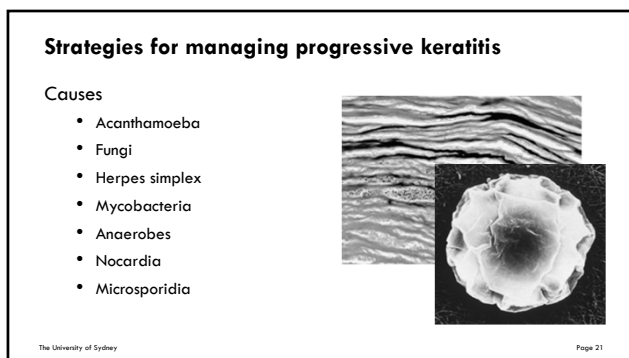
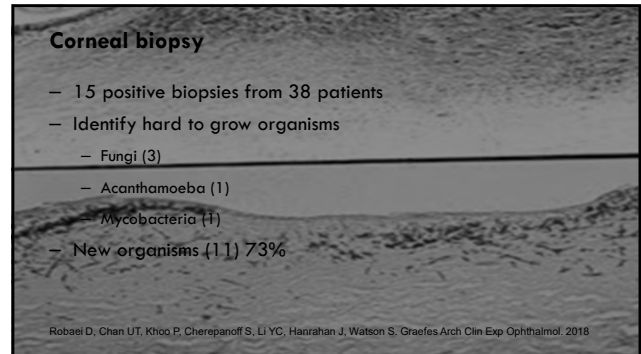
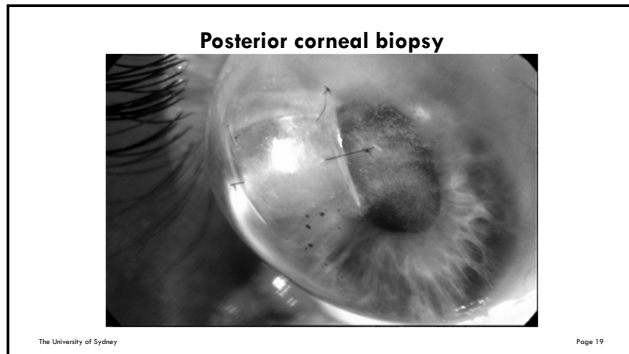
Corneal biopsy

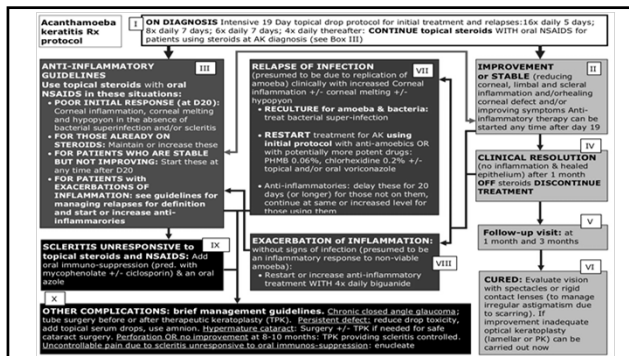
1. Trephination
 - Skin biopsy punch 3 -5 mm
 - Depth 0.2 to 0.3 mm
 - Remove large portion of lesion
 - Avoid visual axis
2. Free lamellar dissection with knife
 - Knife to outline area and shape to depth
3. Posterior biopsy



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Eliminate toxicity

- Aminoglycosides
- Preservatives
- Topical acyclovir
- Antifungals
- Antiacanthamoeba agents



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Treat host response

- Steroids in keratitis controversial
- Benefit:
 - decrease inflammation, reduce scarring and stromal melt
- Risk:
 - delayed epithelial healing, promote infection

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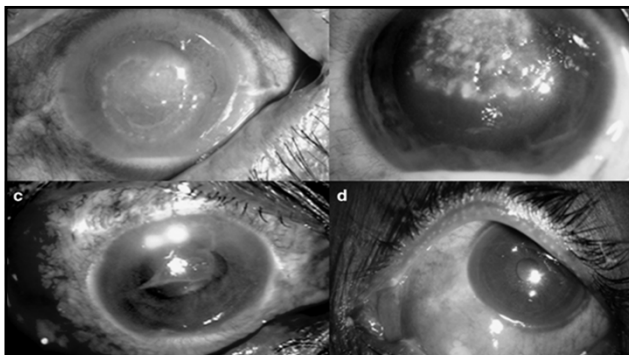
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Cochrane review: Steroids vs topical antibiotics alone

- 3 small RCT's:
 - VA, healing times the same
- **SCUT:** topical prednisolone sodium phosphate 1.0% after a 48-hour course of topical moxifloxacin 0.5%
 - 3-month visual acuity, 3-month scar size, rate of perforation the same

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Anticollagenases

- In vivo data
 - reduced perforation rate in pseudomonas ulcers
- No high quality human RCTs
- Side-effects
 - GIT upset
 - Sun-sensitivity
 - Skin pigmentation
 - Inactivates OCP

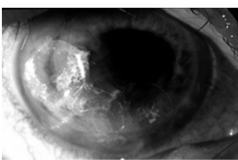


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Progressive keratitis

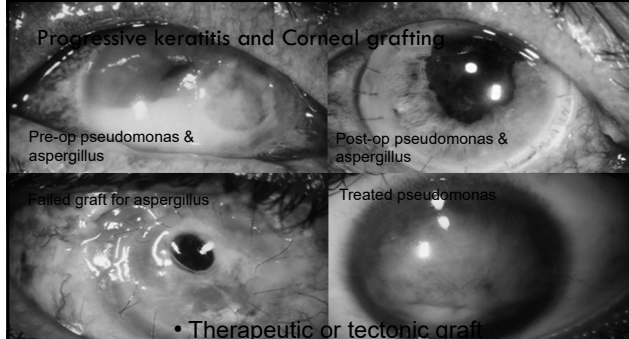
- Glue perforation
 - Temporary and antibacterial
- Therapeutic or tectonic graft
 - Fungus:
 - wide excision
 - topical cyclosporin to avoid steroids
 - Acanthamoeba:
 - where possible delay keratoplasty until the eye is uninfected and medically cured of Acanthamoeba.



Tan J, Li Y-C, Foster J, Watson SL. J Clin Exp Ophthalmol. 2015.
Robaei, Carrity, Minassian, Dart. Ophthalmology 2015

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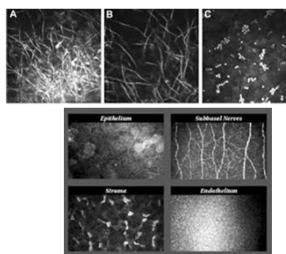
Progressive keratitis and Corneal grafting



- Therapeutic or tectonic graft

Special tools

- PCR and confocal for diagnosis
 - Acanthamoeba
 - Filamentous fungi
- CXL
- ? New antimicrobials

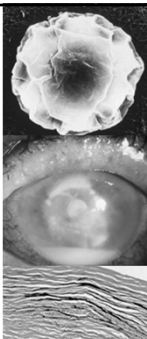


Chidambaram JD et al. Ophthalmology 2016

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MICROBIAL KERATITIS

- Most cases respond to simplified initial Rx
- Failure results from
 - Iatrogenic disease
 - Precipitating causes untreated
 - Ineffective or misdirected treatment
- Epidemiology and drug choice critical



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Thank you

Sydney Eye Hospital Foundation
 Sydney Medical School Foundation
 Corneal unit Sydney Eye Hospital
 National Health and Medical Research Council
 Professor John Dart, Moorfields Eye Hospital




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