Chapter 8

EYE INFECTIONS

The eye and its adnexae can be subject to infection at different sites, as summarised below:

SITE	INFECTION	POSSIBLE ASSOCIATED RISKS
Eyelid: margin	Blepharitis	If prolonged, secondary changes to conjunctiva and cornea
Eyelid: glands	Hordeolum	Recurrence
Conjunctiva	Conjunctivitis	Usually trivial; if prolonged, shrinkage and poor tear film
Cornea	Keratitis	Scarring, opacification; when severe: ulceration, perforation
Lacrimal system	Dacryocystitis	Recurrence, nasolacrimal duct obstruction
Intraocular	Endophthalmitis Retinitis	Retinal damage, blindness
Orbit	Orbital cellulitis	Local and distant spread

Most superficial infections are benign and can be adequately managed in the community. However, in certain predisposed individuals, infection can be severe, prolonged and potentially sight-threatening. Such patients include contact lens wearers, immunocompromised patients and those in whom the natural defences of the eye have been breached (via disease process or trauma, including surgery). These infections need to be treated in a specialist unit. Organisms involved may be commensals or exogenous (bacteria, viruses, fungi and intracellular parasites).

EYELID

BLEPHARITIS

Blepharitis is a chronic eye condition characterised by inflammation of the eyelids. Blepharitis can be either anterior or posterior.

- Anterior: characterised by inflammation at the base of the eyelashes
- Posterior: characterised by inflammation of the inner portion of the eyelid, at the level of the meibomian glands.

INFECTIVE CAUSES	NON-INFECTIVE CAUSES
Bacterial: *Staphylococcus aureus*, *Staphylococcus epidermidis*	Seborrhea Rosacea Dry eye
Viral: herpes simplex, varicella zoster	
Parasitic: Demodex eyelash mites	

TREATMENT: BLEPHARITIS

- **Good lid hygiene** is the mainstay of treatment for all forms of blepharitis and should be emphasised in both the acute and maintenance phases of treatment.
- **Warm compresses:** Patients are advised to soak a washcloth in warm (not scalding) water and place it over the eyes. As the washcloth cools, it should be re-warmed and replaced for a total of five to ten minutes of soaking time. This is recommended two to four times a day during the acute phase and at a decreased frequency in the maintenance phase of treatment.
- **Lid massage:** Should be performed immediately following application of a warm compress. Either the washcloth that was used for compressing or a clean fingertip should be used to gently massage the edge of the eyelid towards the eye with a gentle circular motion.
- **Lid washing:** Either warm water or very diluted baby shampoo can be placed on a clean washcloth, gauze pad or cotton swab. The patient is then advised to gently clean along the lashes and lid margin to remove any accumulated material on the lashes, taking care to avoid contact with the ocular surface. Vigorous washing should be avoided as this may cause further irritation of the sensitive eyelid skin.
- **Topical antibiotics e.g.** sulfacetamide or chloramphenicol. May be helpful in reducing the bacterial load of the lashes and conjunctiva. The ointment is placed directly onto the lid margin up to four times a day for the first week then twice daily for two weeks. Many prefer to use the antibiotic once daily at bedtime only, since the ointment can cause significant blurring of vision for 10–15 minutes after application.
- **Oral antibiotics:** Long-term oral antibiotics, especially tetracyclines, may be helpful in severe cases of blepharitis. Treatment can be given intermittently according to the severity of the blepharitis and tolerance of the medication.

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ADULTS

PRIMARY REGIMEN	ALTERNATIVE REGIMEN	PREGNANT/NURSING WOMEN
Doxycycline 100 mg PO daily, tapered to 50 mg daily after improvement (often 2–6 weeks) OR Tetracyline 250 mg PO 6 hourly, tapered to 250–500 mg daily after improvement (often 2–6 weeks)	Erythromycin 250–500 mg PO daily OR Azithromycin 250–500 mg PO one to three times per week OR Azithromycin 1g per week for 3 weeks	Erythromycin 250 mg PO 6 hourly, tapered to 250 mg once or twice daily according to clinical response

CHILDREN: < 12 YEARS OF AGE

Erythromycin 10 mg/kg/dose PO 6 hourly (decreased gradually according to the clinical response)

- **Topical glucocorticoids:** There may be a role for topical glucocorticoid use in the short-term treatment of acute blepharitis exacerbations. Patients should generally be evaluated by an ophthalmologist prior to initiation of topical glucocorticoids.
  - Framycetin/gramicidin/dexamethasone/phenylethanol (Sofradex®)
  - Tobramycin/dexamethasone (Tobradex®)
- **Artificial tears:** Can be used to restore comfort and rebuild the tear film during and after medical treatment.
- **Refractory blepharitis:** Ivermectin has been used off-label to lessen the number of *Demodex folliculorum* (a species of face mite) found in the lashes.

HORDEOLUM

There are two types of hordeolum:

- External (stye): infection of the superficial sebaceous gland (eyelash follicle)
- Internal: infection of the meibomian glands (acute meibomianitis)

A hordeolum is usually caused by *Staphylococcus aureus* (MSSA or MRSA) infection.

TREATMENT: HORDEOLUM

EXTERNAL INFECTION

Can be treated with warm compresses, placed for about 15 minutes at a time approximately four times per day. It will drain spontaneously.

INTERNAL INFECTION

- Rarely drains spontaneously: may need incision and drainage; send pus for culture and sensitivity testing
- Methicillin-sensitive (MSSA): Cloxacillin 250–500 mg PO 6 hourly AND warm compresses
- Methicillin-resistant, community-associated (CA-MRSA): Cotrimoxazole 2 double strength tablets PO 12 hourly
- Methicillin-resistant, hospital-acquired (HA-MRSA): Linezolid 600 mg PO 12 hourly. Treat for 7–10 days.

CONJUNCTIVITIS

BACTERIAL CONJUNCTIVITIS

Causes include *Staphylococcus aureus* (more common in adults), *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.

Most acute bacterial conjunctivitis infections are self-limiting within one to two weeks. Topical antibiotics reduce the duration of the disease. Most practitioners prescribe a broad-spectrum agent on an empirical basis without culture for a routine, mild-to-moderate case of bacterial conjunctivitis. Always be aware of the differential diagnosis, and instruct patients to seek follow-up care if the expected improvement does not occur or if vision becomes affected.

TREATMENT: BACTERIAL CONJUNCTIVITIS

Treat with a topical fluoroquinolone ophthalmic solution:

Ciprofloxacin 3 mg/mL (Ciloxan®)

Day 1–2: 1–2 drops 2 hourly while awake

Day 3–7: 1–2 drops 4–8 hourly

OR

Gatifloxacin, moxifloxacin and ofloxacin drops are alternatives

HYPERACUTE BACTERIAL CONJUNCTIVITIS

Neisseria gonorrhoeae can cause hyperacute bacterial conjunctivitis that is sight-threatening as it can progress to keratitis and corneal perforation. The organism is usually transmitted from the genitalia to the hands and then to the eyes. Concurrent urethritis is typically present. Confirm the diagnosis by means of a PCR on a swab specimen. Hyperacute bacterial conjunctivitis requires immediate ophthalmologic referral. Sexual partners of the patient should be referred for evaluation and treatment, as should mothers of affected neonates, and the mother's sexual partners.

TREATMENT: HYPERACUTE BACTERIAL CONJUNCTIVITIS

ADULT

Ceftriaxone 1 g as a single intramuscular dose

Saline lavage of the eye

PAEDIATRIC

Ceftriaxone 25–50 mg/kg IM/IV (not to exceed 125 mg) as a single dose

Saline lavage of the eye

Treatment for presumptive *Chlamydia* co-infection should be considered: azithromycin 1 g PO as a single dose (adults)

ADULT INCLUSION CONJUNCTIVITIS

This is the most common manifestation of ocular chlamydial infection in sexually active young adults. Usually unilateral together with genital tract infection. History of sexual activity and previous sexually transmitted infection is important. May be complicated with corneal neovascularisation and/or conjunctival scarring. Conjunctival follicles or corneal infiltrates may persist for months. Confirm the diagnosis by means of a PCR on a swab specimen and test for genital tract gonorrhoea as co-infection is common.

TREATMENT: ADULT INCLUSION CONJUNCTIVITIS

PRIMARY REGIMEN

Azithromycin 1 g PO as a single dose

ALTERNATIVE REGIMEN

Doxycycline 100 mg PO 12 hourly for 7 days

Treat concomitant gonorrhoea with ceftriaxone 250 mg IM as a single dose if confirmed or if not specifically tested for.

NEONATAL CONJUNCTIVITIS (OPHTHALMIA NEONATORUM)

The age at onset suggests the cause:

AGE OF ONSET	CAUSE	LABORATORY DIAGNOSIS
Day 1	Chemical reaction due to silver nitrate prophylaxis	Not applicable
Day 2–5	*Neisseria gonorrhoeae:* often very purulent	Gram stain and culture or PCR
Day 5–14	*Chlamydia trachomatis:* pneumonia may be present	PCR of conjunctival scraping
Day 2–16	Herpes simplex virus	PCR of conjunctival swab

TREATMENT: NEONATAL CONJUNCTIVITIS

Onset day 1: no therapy indicated

GONOCOCCAL INFECTION (ONSET DAY 2–5)

Ceftriaxone 25–50 mg/kg IV as single dose (not to exceed 125 mg)

Topical treatment is inadequate

Treat neonate for concomitant *C. trachomatis*

Treat the mother and her sexual partner

CHLAMYDIAL INFECTION (ONSET DAY 3–10)

Erythromycin base or ethyl succinate syrup 12.5 mg/kg PO 6 hourly for 14 days

OR

Azithromycin suspension 20 mg/kg PO given daily for 3 days

Treat the mother and her sexual partner

HERPES SIMPLEX VIRUS (ONSET DAY 2–16)

Evaluate for systemic and CNS disease with PCR on blood and CSF

Acyclovir 20 mg/kg IV 8 hourly for up to 21 days. The dose of acyclovir must be adjusted for neonates with renal failure. Intravenous acyclovir should be administered at the time the diagnosis of neonatal HSV is suspected and before laboratory confirmation. Prompt administration improves outcome.

Neonates with ocular herpes simplex virus involvement, such as keratitis, should receive a topical ophthalmic solution (e.g. 1% trifluridine OR 3% vidarabine) in addition to systemic acyclovir therapy. They should also be referred to an ophthalmologist for consultation.

TRACHOMA

Trachoma is a chronic bacterial keratoconjunctivitis caused by *Chlamydia trachomatis* that is largely limited to endemic areas in underdeveloped regions.

TREATMENT: TRACHOMA

CHILDREN

Azithromycin 20 mg/kg PO as a single dose

ADULTS

Azithromycin 1 g PO as a single dose

OR

Doxycycline 100 mg PO 12 hourly for 21 days

OR

Tetracycline 250 mg PO 6 hourly for 21 days

VIRAL CONJUNCTIVITIS

Viruses cause up to 80% of all cases of acute conjunctivitis. Clinical accuracy in diagnosing viral conjunctivitis is very low – many cases are misdiagnosed as bacterial conjunctivitis. Viral conjunctivitis is typically caused by adenoviruses and is usually unilateral. Ocular pain and photophobia suggest a possible keratitis and these patients should be referred to an ophthalmologist.

TREATMENT: VIRAL CONJUNCTIVITIS

- No effective treatment exists; viral conjunctivitis is a self-limiting process
- Artificial tears may help to relieve symptoms

PREVENTION

- Viral conjunctivitis is highly contagious and is spread by direct contact with the patient and his or her secretions or with contaminated objects and surfaces.
- Hand washing, disinfection of contaminated areas/objects.

KERATITIS

BACTERIAL KERATITIS

Bacterial keratitis is a serious and sight-threatening process and warrants urgent evaluation by an ophthalmologist. Patients with bacterial keratitis usually complain of rapid onset of pain, photophobia and decreased vision.

BACTERIAL KERATITIS PRESENTATION	CAUSE
Acute with no co-morbidity	*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus* spp.
Contact lens use: overnight wear and daytime wear	*Pseudomonas aeruginosa.*
Dry cornea: patients with aqueous tear deficiencies, eye trauma, diabetes, topical steroid use and immunosuppression	*Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes,* Enterobacteriaceae*, Listeria* spp.

TREATMENT OF BACTERIAL KERATITIS

Bacterial keratitis requires urgent ophthalmological referral and prompt initiation of topical bactericidal antibiotics (ideally after obtaining cultures).

Topical broad-spectrum antibiotics with adequate coverage against both Gram-positive and Gram-negative pathogens should be started as the first line of treatment. These antibiotics are sometimes compounded in fortified concentrations not commercially available. Moxifloxacin or gatifloxacin is frequently used as first-line treatment. Alternatively, a combination of topical fortified antibiotics (such as cefazolin 5% and tobramycin or gentamicin 1.4%) can be used. Treatment has to be aggressive and given half hourly to hourly for several hours to enhance the therapeutic levels of drugs thereby bringing the infection under control. Frequency should be reduced based on the clinical response.

Oral or parenteral antibiotics have been shown to be of no benefit and are indicated only for ulcers with perforation, scleral involvement or endophthalmitis. Gonococcal infections require systemic ceftriaxone.

Topical glucocorticoids and topical drug combinations containing steroids should not be used in the initial treatment of suspected bacterial keratitis; their role is controversial and best left to the discretion of the consulting ophthalmologist.

The results of Gram staining should not be used to alter the initial therapy started. Initiate therapy with a broad-spectrum regimen and change it based on the clinical response and culture and sensitivity results. Drug concentrations achieved in the eye may be above the serum MIC levels and this may explain a good clinical response to an antibiotic to which the organism is not very sensitive to in-vitro. In these situations, a change in therapy is not warranted.

TREATMENT: BACTERIAL KERATITIS

ACUTE WITH NO CO-MORBIDITY

Moxifloxacin 0.5% OR gatifloxacin 0.3% eye drops: 1–2 drops every hour for 48 hours, then taper based on clinical response

CONTACT LENS USERS

Ciprofloxacin 0.3% drops OR levofloxacin 0.5% 1–2 drops hourly for 24–72 hours then taper based on clinical response

Alternative regime: Tobramycin OR gentamicin 0.3% 1–2 drops hourly for 24 hours then taper based on clinical response

DRY CORNEA, TRAUMA, DIABETES, TOPICAL STEROID USERS AND IMMUNOSUPPRESSION

Moxifloxacin 0.5% OR gatifloxacin 0.3% eye drops: 1–2 drops every hour for 48 hours, then taper based on clinical response

Alternative regimen: Fortified topical vancomycin (50 mg/mL) **AND** ceftazidime (50 mg/mL) hourly for 24 hours then taper based on clinical response

Adjust antibiotics based on the organism isolated.

FUNGAL KERATITIS

The prompt diagnosis and management of fungal keratitis is important because it can result in devastating ocular damage. Fungal keratitis warrants urgent evaluation by an ophthalmologist.

CAUSES

Aspergillus spp, *Fusarium* spp and *Candida* spp.

RISK FACTORS FOR FUNGAL KERATITIS

- Ocular trauma
- Contact lenses
- Long term use of topical corticosteroids and antibiotics
- Systemic disease especially diabetes and immunocompromised patients
- Pre-existing eye surface infections

LABORATORY DIAGNOSIS

- Tissue sampling (corneal scraping using a surgical blade or platinum spatula) for microscopy and culture. Excessive scraping should be avoided as scarring may occur.
- In contact lens wearers, the lens(es), containers and lens solution may also be used for sampling.
- Tissue swabbing is usually inadequate because of the predilection of fungi to penetrate into deeper layers of the cornea.

TREATMENT OF FUNGAL KERATITIS

Fungal keratitis requires urgent ophthalmological referral and prompt initiation of topical and/or oral antifungal therapy (ideally after obtaining cultures). All cases require topical therapy with systemic or intraocular therapy added in immunosuppressed patients, those with deeper infections and where there is a poor response to topical therapy.

TREATMENT: FUNGAL KERATITIS

Natamycin (5%) eye drops are the treatment of choice. One drop 1–2 hourly for three to four days, then one drop 3–4 hourly for 14–21 days or until resolution of keratitis. Gradual dose reduction at 4–7 day intervals may be beneficial.

Voriconazole 1% drops hourly for 2 weeks can also be used; however, natamycin has better visual acuity outcomes and a lower rate of perforation.

Amphotericin B 0.15% eye drops can be used for yeast infections if natamycin is not available. One drop every hour for the first 48 hours and then a slow reduction in frequency based on the clinical response.

FUNGAL KERATITIS WITH DEEP INFILTRATES

Voriconazole 400 mg PO twice daily for 2 doses, then 200 mg twice daily, increasing if required to 300 mg twice daily; combine this with topical therapy.

Instrastromal injection of voriconazole is an alternative to oral voriconazole and achieves high tissue concentrations but the risk of perforation is higher. This is combined with topical therapy.

SURGICAL INTERVENTION

This is currently an option for patients with disease that is refractory to medical treatment to control deep and severe fungal infections. It is usually done within four weeks of presentation in order to limit progression of the infection to other areas of the eye which results in a poorer prognosis.

NON-TUBERCULOUS MYCOBACTERIAL (NTM) KERATITIS

Patients with NTM keratitis often have a history of trauma with corneal foreign bodies or ocular surgery. The patients usually complain of decreased vision, photophobia and a variable degree of pain. Referral to an ophthalmologist is required for the diagnosis and management of a patient with suspected NTM keratitis. The definite identification of the causative organism requires corneal scraping to obtain material for microscopy and culture. For cases of keratitis after LASIK, the flap should be lifted, and cultures from the interface should be performed.

CAUSES

Mycobacterium chelonae-abscessus, *Mycobacterium fortuitum* and slow-growing mycobacteria.

RISK FACTORS FOR NON-TUBERCULOUS MYCOBACTERIAL (NTM) KERATITIS

- History of trauma with penetration of the corneal epithelium and corneal foreign bodies
- Ocular surgery (especially post LASIK surgery) and suture removal
- Contact lens wearers
- Topical steroid use, especially in corneal transplant recipients

TREATMENT: NON-TUBERCULOUS MYCOBACTERIAL KERATITIS

As the antibiotic susceptibility of NTM isolates varies among different species, laboratory susceptibility testing of each individual strain is essential for antibiotic selection.

Triple topical therapy with gatifloxacin 1 drop 4 times daily or moxifloxacin 1 drop 4 times daily **AND** amikacin (50 mg/mL) **AND** clarithromycin (10 mg/mL) or azithromycin (2 mg/mL).

Systemic antibiotics such as clarithromycin 500 mg PO 12 hourly **AND** doxycycline 100 mg PO 12 hourly may also be used for recalcitrant cases.

Avoid topical steroid therapy because it may reduce the local immune defence and contribute to the development or progression of NTM keratitis.

There are no clear guidelines for the duration of therapy. The average duration of treatment ranges from weeks to months.

Surgery is often required where there is progression of disease or no response to antibiotics.

PROTOZOAN KERATITIS

Acanthamoeba keratitis is a rare parasitic corneal infection usually associated with trauma or soft contact lens use. It is both difficult to diagnose and to treat and requires urgent specialist management by an ophthalmologist.

Early diagnosis is essential. The infection can be difficult to treat due to the resilient nature of the cyst form. Diagnosis is made on the basis of the clinical picture and isolation of organisms from corneal culture or detection of trophozoites and/or cysts on histopathology. However, a negative culture does not rule out Acanthamoeba infection. Confocal microscopy and PCR assays to detect Acanthamoeba DNA may also assist with the diagnosis.

TREATMENT: ACANTHAMOEBA KERATITIS

- Topical 0.02% chlorhexidine or polyhexamethylene biguanide (PHMB, 0.02%) should be empirically given to treat both the trophozoites and cysts.
- Treatment with either chlorhexidine or PHMB is often combined with propamidine isethionate (Brolene®) or hexamidine (Desmodine®).
- Give eye drops every hour for 48 hours, then every hour while awake for 72 hours, then one drop every 2 hours while awake for 3–4 weeks. Taper slowly based on clinical response. The duration of therapy may last six months to a year.
- Pain control can be helped by topical cycloplegic solutions and oral nonsteroidal medications and immunosuppressive agents should be considered if there is an associated scleritis. The use of corticosteroids to control inflammation is controversial.
- Surgery may be required to restore visual acuity.

VIRAL KERATITIS

- Viral keratitis is a serious and sight-threatening infection and is a common cause of keratitis, especially in developed countries. Urgent referral to an ophthalmologist is essential for management.
- Causes include: herpes simplex virus (types 1 and 2) and varicella zoster virus.
- Herpetic epithelial keratitis may occur unilaterally or bilaterally and may be accompanied by a blepharoconjunctivitis, involving lesions of the lid and a follicular response of the conjunctiva.
- The diagnosis of HSV is often made clinically, however, laboratory diagnosis can be made by means of a PCR on corneal scrapings.

TREATMENT

Since most cases of HSV epithelial keratitis resolve spontaneously within three weeks, the rationale for treatment is to minimise stromal damage and scarring. Gentle epithelial debridement may be performed to remove any infectious virus that may induce stromal keratitis. Treatment should be carried out under the supervision of an ophthalmologist.

TREATMENT: VIRAL KERATITIS

HERPES SIMPLEX VIRUS

Trifluridine eye drops, one drop every 1–2 hours up to 9 drops per day until re-epithelialisation, then one drop 4 hourly up to 5 times daily for a total course of up to 21 days.

OR

Acyclovir 3% ointment 5 times daily (with 4 hourly intervals). Continue treatment for at least 3 days after healing.

OR

Ganciclovir 0.15% gel one drop 5 times daily (with 4 hourly intervals) until the corneal ulcer heals and then 1 drop 3 times daily for 7 days.

OR

Vidarabine ointment: Use 5 times per day for up to 21 days

Acyclovir 400 mg PO three times daily – can be given to patients unable to tolerate topical medications, to patients that are severely affected or immunocompromised patients.

Secondary prophylaxis with acyclovir 400 mg PO 12 hourly for 1 year can reduce recurrences.

A cycloplegic agent may be added to any of the above regimens for comfort from ciliary spasm.

VARICELLA ZOSTER VIRUS

Famciclovir 500 mg PO 8 hourly for 10 days

OR

Valacyclovir 1 g PO 8 hourly for 10 days

OR

Acyclovir 800 mg PO five times daily for 10 days

Acute pain control is achieved by local care and oral analgesics.

LACRIMAL APPARATUS

CANALICULITIS

Canaliculitis is caused by infection of the lacrimal apparatus. This infection will cause small stones which are concretions consisting of sulphur granules and these concretions will form pockets in which the infection will not be subject to the antimicrobial property of the tear film.

CAUSES

- Common: Staphylococci, Streptococci, *Actinomyces* spp
- Rare: *Arachnia*, *Fusobacterium*, *Nocardia* spp., *Candida* spp.
- After using intracanalic plugs: *Mycobacterium chelonae* has been reported

TREATMENT: CANALICULITIS

Apply hot packs to the punctal area four times a day.

Referral to an ophthalmologist for removal of granules and local irrigation with an antibiotic solution.

Topical antibiotic (moxifloxacin, fortified cefazolin 50 mg/mL) with or without canalicular irrigation with fortified cefazolin solution.

Surgical therapy may be required.

DACRYOCYSTITIS

- Acute dacryocystitis consists of inflammation of the lacrimal sac, typically caused by infection. When pressure is applied to the inflamed tear duct, purulent material may be expressed through the lacrimal punctum. Patients may present with conjunctivitis and preseptal cellulitis. The infection can extend beyond the septum, and causes orbital cellulitis, but this is rare.
- Chronic dacryocystitis is more common than acute dacryocystitis and there are several stages of presentation:
  - Catarrhal: there is intermittent conjunctival hyperaemia and epiphora, with mucoid discharge that is normally sterile.
  - Lacrimal sac mucocele: stagnant tears collect and there is dilation of the lacrimal sac, with mucoid content.
  - Chronic suppurative: epiphora and chronic conjunctivitis are observed, with erythema of the lacrimal sac. There is reflux of purulent material with pressure, and microorganisms are often isolated.

CAUSES

Streptococcus pneumoniae, Staphylococus aureus, Haemophilus influenzae, Streptococcus pyogenes, Staphylococcus epidermidis, Enterobacteriaceae, *Pseudomonas aeruginosa* (rare).

LABORATORY DIAGNOSIS

Exudate from punctum must be collected for Gram stain and culture. Culture is necessary to guide antibiotic therapy.

TREATMENT: ACUTE DACRYOCYSTITIS

EMPIRIC TREATMENT OF MILD INFECTION LIMITED TO THE LACRIMAL SAC AND LID

- Apply heat and massage
- Cephalexin 500 mg PO 6 hourly for 7–10 days
- Amoxicillin-clavulanate 1000 mg PO 12 hourly for 7–10 days
- Cotrimoxazole (TMP-SMX) 2 double strength tablets PO 10–12 hourly for 7–10 days
- Surgery may be required

EMPIRIC TREATMENT OF ACUTE INFECTION WITH SIGNS AND SYMPTOMS OF ORBITAL CELLULITIS

Vancomycin 15–20 mg/kg IV 8–12 hourly (to achieve serum trough concentrations of 15–20 μg/ml)

AND

Ceftriaxone 2 g IV every 24 hours *OR* cefotaxime 2 g IV 6 hourly *OR* piperacillin-tazobactam 4.5 g IV 8 hourly

If penicillin and/or cephalosporin allergic, then give levofloxacin 750 mg IV/PO every 24 hours with the vancomycin.

Surgery may be required.

TREATMENT: CHRONIC DACRYOCYSTITIS

Treat conservatively with lacrimal sac massage and lacrimal irrigation.

Surgery is reserved for cases refractory to conservative treatment.

ENDOPHTHALMITIS

Endophthalmitis refers to bacterial or fungal infection within the eye, including involvement of the vitreous and/or aqueous humor. Most cases of endophthalmitis are exogenous, a result of inoculation of organisms via trauma, eye surgery, or as an extension of keratitis. In such cases, the aqueous humor may be seeded first before extension into the vitreous. The remaining cases are endogenous, resulting from haematogenous bacteraemic or fungaemic seeding of the eye.

Prior to therapy, culture a needle aspirate of both vitreous and aqueous humor. Adjust antibiotics after isolation of the pathogen and determination of antimicrobial susceptibility.

ACUTE POSTOPERATIVE ENDOPHTHALMITIS

This is the most common form of endophthalmitis and is almost always due to bacteria. It occurs within six weeks of cataract surgery or other ocular procedures such as penetrating keratoplasty, scleral buckling, secondary intra-ocular lens implantation, glaucoma drainage device implantation and pars plana vitrectomy. Preoperative antisepsis steps are key to preventing endophalmitis and povidone-iodine or chlorhexidine is mandatory to reduce ocular surface colony counts as much as possible prior to cataract surgery. In addition, intracameral cefuroxime is frequently used post cataract surgery to reduce the likelihood of developing endophthalmitis.

CAUSES

Coagulase-negative staphylococci, *Staphylococcus aureus*, Streptococci, *Enterococcus* spp. and Gram-negative bacilli.

TREATMENT: ACUTE POSTOPERATIVE ENDOPHTHALMITIS

This is a medical emergency – immediate ophthalmologic consultation is needed. Intravitreal antibiotics must be given and a vitrectomy performed in severe cases. The role of systemic antibiotics is not known, however, is usually given with severe cases.

Intravitreal antibiotics: Vancomycin 1 mg **AND** ceftazidime 2.25 mg. This can be repeated in 2–3 days based on clinical response.

Systemic antibiotics: Moxifloxacin 400 mg PO daily for 10 days

Note: The intraocular lens implant does not need to be removed.

CHRONIC PSEUDOPHAKIC ENDOPHTHALMITIS

Chronic pseudophakic endophthalmitis is a rare complication of cataract surgery. "Pseudophakic" refers to the intraocular lens. It is a rare complication, presenting as a chronic low-grade infection.

CAUSES

Propionibacterium acnes, coagulase-negative staphylococci and diphtheroids.

TREATMENT: CHRONIC PSEUDOPHAKIC ENDOPHTHALMITIS

Treatment requires at least vitrectomy and intravitreal vancomycin 1 mg. Systemic antibiotics are not indicated.

Total capsulectomy and removal or exchange of intraocular lens is usually performed as well as this is associated with a high cure rate.

POST-TRAUMATIC ENDOPHTHALMITIS

Occurs after penetrating trauma to the globe of the eye.

RISK FACTORS	CAUSES
Retained intraocular foreign body	*Bacillus cereus*
Disruption of the lens	Coagulase-negative staphylococci
Corneal wound	Streptococci
Retinal break or detachment	Gram-negative bacilli
Delay in primary repair (beyond 12–24)	*Candida* spp.
	Aspergillus spp.

TREATMENT: POST-TRAUMATIC ENDOPHTHALMITIS

Post-traumatic endophthalmitis is a fulminant disease and requires aggressive treatment by an ophthalmologist with a combination of vitrectomy and intravitreal antibiotics. Systemic antibiotics are usually only given with severe infection though of unproven value.

Intravitreal antibiotics: Vancomycin 1 mg **AND** ceftazidime 2.25 mg. This can be repeated in 2–3 days based on clinical response.

Systemic antibiotics: Ceftazidime 2 g IV 8 hourly **AND** vancomycin 15–20 mg/kg IV 8–12 hourly.

POST-INTRAVITREAL INJECTION ENDOPHTHALMITIS

Regular injections of antivascular endothelial growth factor medications into the vitreous are often used to treat wet macular degeneration. In addition, corticosteroids are often injected intravitreally for a variety of reasons. Each injection carries a risk of endophthalmitis similar to that of cataract surgery and in certain centres post-injection endophthalmitis is seen more frequently than post-cataract surgery endophthalmitis.

CAUSES

Viridans streptococci and coagulase-negative staphylococci.

TREATMENT: POST-INTRAVITREAL INJECTION ENDOPHTHALMITIS

This may be managed by intravitreal antibiotics alone. For persistent cases, a vitrectomy may be required.

Intravitreal antibiotics: Vancomycin 1 mg **AND** ceftazidime 2.25 mg. This can be repeated in 2–3 days based on clinical response and adjusted to culture and sensitivity results.

BLEB-RELATED ENDOPHTHALMITIS

A filtering bleb is used to treat severe glaucoma that has failed medical management. It is a surgically created defect in the sclera which allows excess aqueous humor to leak out of the anterior chamber and be absorbed into the systemic circulation. A bleb may become infected (blebitis) and the bacteria may enter the eye, resulting in endophthalmitis. The onset of endophthalmitis is usually abrupt and occurs months to years following surgery.

CAUSES

Streptococci (*S. viridans* or *S. pneumoniae*), *Haemophilus influenzae, Moraxella catarrhalis*, *S. aureus* and *S. epidermidis.*

The outcome of bleb-related endophthalmitis in many patients is typically poor and aggressive treatment including vitrectomy is advised.

TREATMENT: BLEB-RELATED ENDOPHTHALMITIS

A combination of intravitreal and systemic antibiotics should be given.

Intravitreal antibiotics: Vancomycin 1 mg **AND** ceftazidime 2.25 mg

Systemic antibiotics: Moxifloxacin 400 mg PO daily for 7–10 days

ENDOGENOUS BACTERIAL ENDOPHTHALMITIS

Endogenous (hematogenous) bacterial endophthalmitis is rare, occurring in only two to 15% of all cases of endophthalmitis and results from bacterial seeding to the eye during bacteraemia. Sources of bacteraemia include endocarditis, urinary tract infections, abdominal abscesses, meningitis, indwelling catheters, procedures such as endoscopy that cause transient bacteraemia, and intravenous drug use. This is usually associated with the presence of risk factors, although rarely it can develop in the absence of concomitant risk factors. Risk factors include diabetes mellitus, malignancies, immunosuppression and end-stage renal or liver disease.

CAUSES

Streptococci (*S. pneumoniae*, *S. milleri* group, group A and B streptococci), *Staphylococcus aureus*, *Klebsiella pneumoniae* or other Gram-negative organisms, *Neisseria meningitidis, Bacillus cereus* (heroin use).

TREATMENT

The treatment of endogenous bacterial endophthalmitis includes a combination of intravitreal and systemic antibiotics. The duration of systemic antibiotics should be determined by the need to treat the underlying source of bacteraemia (e.g. six weeks in many cases of endocarditis).

Pars plana vitrectomy plus intravitreal antibiotic injection is indicated in most cases, rather than intravitreal antibiotic injection alone, because of the virulent nature of most of the pathogens involved.

TREATMENT: ENDOGENOUS BACTERIAL ENDOPHTHALMITIS

Both intravitreal and systemic antibiotics should be given.

INTRAVITREAL ANTIBIOTICS

Vancomycin 1 mg

AND

Ceftazidime 2.25 mg. Repeated doses may be indicated based on clinical response.

SYSTEMIC ANTIBIOTICS

Cefotaxime 2 g IV 4 hourly OR ceftriaxone 2 g IV daily

AND

Vancomycin 1 g IV 12 hourly

Vancomycin levels should be monitored and the dose adjusted to maintain a serum trough level between 15 and 20 mg/L.

CANDIDA ENDOPHTHALMITIS

The source of *Candida* endophthalmitis can be endogenous or exogenous.

ENDOGENOUS CANDIDA ENDOPHTHALMITIS	EXOGENOUS CANDIDA ENDOPHTHALMITIS
• Follows candidaemia with hematogenous seeding of the eye • Often presents first as chorioretinitis with minimal vitritis, then later progresses to produce vitreous and sometimes aqueous infection • Chorioretinitis accounts for 85% of ocular disease while endophthalmitis occurs only in 15% • Most often asymptomatic and ophthalmology consultation recommended	• The exogenous form follows trauma, eye surgery, or progression of fungal keratitis (corneal infection) • Fungi are directly inoculated into the aqueous and/or vitreous fluid

CAUSES

Candida albicans and *Candida* spp.

TREATMENT OF ENDOGENOUS CANDIDA ENDOPHTHALMITIS

Patients who have only chorioretinitis can be treated with a systemic antifungal agent alone. For patients whose lesions threaten the macula or exhibit mild to moderate vitritis, use intravitreal injections of antifungal agents in combination with systemic antifungal therapy in order to attain

immediate high concentrations of the agent in the posterior compartment of the eye. For patients who have moderate to heavy vitritis, vitrectomy and intravitreal injection of antifungal agents together with systemic therapy is almost always necessary.

Intravitreal injections of amphotericin B or voriconazole may need to be repeated 48 hours or more after the initial injection if there is no clinical improvement. Duration of treatment should be at least for four to six weeks with the final duration dependent on resolution of the lesions as determined by repeated ophthalmolgical examinations.

TREATMENT: ENDOGENOUS CANDIDA ENDOPHTHALMITIS

SYSTEMIC ANTIFUNGAL TREATMENT

Fluconazole 800 mg (12 mg/kg) IV loading dose FOLLOWED BY fluconazole 6–12 mg/kg (400–800 mg) IVI or PO daily if the isolate is shown to be susceptible

OR

Voriconazole 400 mg (6 mg/kg) IV 12 hourly for two doses, then 300 mg (4 mg/kg) IVI or PO 12 hourly

OR

Amphotericin B 0.7–1 mg/kg IV daily **AND** flucytosine 25 mg/kg PO 6 hourly, if isolates are non-susceptible to fluconazole/voriconazole

OR

Liposomal amphotericin B 5 mg/kg IV daily **AND** flucytosine 25 mg/kg PO 6 hourly if isolates are non-susceptible to fluconazole/voriconazole

INTRAVITREAL ANTIFUNGAL TREATMENT

Amphotericin B 5–10 mcg in 0.1 mL sterile water

OR

Voriconazole 100 mcg in 0.1 mL sterile water or normal saline

TREATMENT OF EXOGENOUS CANDIDA ENDOPHTHALMITIS

In patients with exogenous *Candida* endophthalmitis with vitritis, both systemic antifungal therapy and intravitreal therapy is required as per the recommendations for endogenous endophthalmitis. A vitrectomy is required when the vitreous is heavily involved.

In cases of exogenous *Candida* endophthalmitis in which the aqueous is the major site of intraocular infection (e.g. from contiguous spread of fungal keratitis) systemic therapy is required as per endogenous fungal endophthalmitis, in addition to intracameral and topical therapy.

TREATMENT: EXOGENOUS CANDIDA ENDOPHTHALMITIS

SYSTEMIC AND INTRAVITREAL ANTIFUNGAL TREATMENT

As per endogenous endophthalmitis

INTRACAMERAL AND TOPICAL ANTIFUNGAL TREATMENT

Intracameral injection of voriconazole 50 mcg in 0.05 mL of sterile water **AND** topical voriconazole eye drops (1%) hourly

OR

Intracameral amphotericin B 5 mcg in 0.05 mL sterile water **AND** topical amphotericin B eye drops 0.15% in sterile water hourly

ENDOPHTHALMITIS DUE TO MOULDS

Endophthalmitis due to moulds is uncommon in temperate climates but is common in warm tropical regions. *Fusarium* and *Aspergillus* spp. account for most cases of mould endophthalmitis and these can occur as a result of endogenous (haematogenous) spread or be exogenous in origin. Loss of vision is a common consequence of mould endophthalmitis.

A sample of vitreous and/or aqueous fluid should be obtained for microscopy and culture prior to antifungal treatment. Patients with mould endophthalmitis require aggressive treatment with a combination of modalities that include surgery to remove any foreign bodies, vitrectomy in most cases, and intraocular and systemic antifungal therapy.

TREATMENT: MOULD ENDOPHTHALMITIS

All patients require systemic therapy together with intraocular injections and surgery if indicated.

SYSTEMIC THERAPY FOR MOULD ENDOPHTHALMITIS

IF MOULD IS VORICONAZOLE SUSCEPTIBLE

Voriconazole 6 mg/kg IV every 12 hours for two doses, THEN 4 mg/kg IV every 12 hours for patients with severe disease. Oral therapy, using 200 mg twice daily on an empty stomach, can be used following an initial response to the IV formulation. In less severe cases, oral voriconazole can be used as initial therapy; the oral loading dose is 400 mg twice daily for two doses, FOLLOWED BY 200 mg twice daily. Dose adjustment is based on serum voriconazole levels, if available.

IF MOULD IS VORICONAZOLE RESISTANT

Liposomal amphotericin B 5 mg/kg IV once daily OR amphotericin B deoxycolate 1 mg/kg IV once daily.

The duration of systemic antifungal therapy for mould endophthalmitis depends upon the clinical response determined by serial ophthalmic examinations and whether the infection was exogenous or endogenous. If exogenous, therapy is usually continued for at least one month (and sometimes several months) after resolution of all signs of active intraocular infection. For endogenous endophthalmitis, the duration of therapy is determined by the type, extent, and response to therapy of the systemic fungal infection being treated. Treatment is typically for several months.

EXOGENOUS MOULD OPHTHALMITIS, ANTERIOR CHAMBER ONLY

Systemic therapy*

AND

Intracameral injection of voriconazole 50 mcg in 0.05 mL of sterile water **AND** topical voriconazole eye drops (1%) hourly

OR

Systemic therapy*

AND

Intracameral amphotericin B 5 mcg in 0.05 mL sterile water **AND** topical amphotericin B eye drops 0.15% in sterile water hourly

A corneal transplant is indicated if the aqueous involvement is due to an extension of keratomycosis.

EXOGENOUS OR ENDOGENOUS MOULD OPHTHALMITIS WITH VITREOUS INVOLVEMENT

Systemic therapy*

AND

Intravitreal amphotericin B 5–10 mcg in 0.1 mL sterile water OR voriconazole (if isolate susceptible) 100 mcg in 0.1 mL sterile water or normal saline. Repeated intravitreal infections may be required depending on the clinical response.

AND

A vitrectomy is required

RETINITIS

ACUTE RETINAL NECROSIS

Acute retinal necrosis (ARN) is an uncommon condition that can affect both immunocompetent and immunocompromised patients of any age. It is a severe, sight-threatening disease which can progress rapidly with retinal necrosis, retinal detachment and blindness. Urgent specialist management by an ophthalmologist is required.

The most common cause is varicella zoster virus, followed by herpes simplex virus. Rarely CMV and EBV have been reported as causative agents. Typically features of ARN include posterior uveitis, with or without anterior uveitis, and retinitis. Bilateral ARN can occur in up to 70% of untreated patients. A laboratory diagnosis needs to be made rapidly by means of PCR on eye fluid. Treatment should not be delayed while waiting for laboratory results.

Treatment consists of initial systemic treatment for at least six weeks with or without intravitreal injection. The initial treatment is often followed by chronic suppressive treatment for six months.

Intravitreal injection of foscarnet of ganciclovir can be considered, in addition to systemic treatment, if:

- the retinitis threatens or involves the optic nerve or macula
- severe occlusive vasculitis is present
- there is serous detachment involving the posterior pole

Intravitreal treatment should never be given without systemic treatment to protect the other eye.

Steroids may be considered in immunocompetent patients, but only after stabilisation of the retinitis with antiviral therapy for at least 24–48 hours. Steroids must not be given to immunocompromised patients. Complications of steroid use include severe exacerbation of ARN with vitreous haemorrhage and retinal detachment.

TREATMENT: ACUTE RETINAL NECROSIS

IMMUNOCOMPETENT PATIENTS

INITIAL TREATMENT

Acyclovir 10–15 mg/kg IV 8 hourly for 7–10 days

OR

Valacyclovir 2 g PO 6-8 hourly for 7–10 days (total dose of 6–8 g per day)

FOLLOWED BY

Acyclovir 800 mg PO 5 times per day to complete 6 weeks treatment

OR

Valacyclovir 1 g PO 8 hourly to complete 6 weeks treatment

Consider: intravitreal foscarnet 2.4 mg/0.1 mL OR ganciclovir 2–5 mg/0.1 mL; 1–2 doses in the first 1–3 days of treatment

Consider: Prednisone 0.5–1 mg/kg PO after at least 24–48 hours of antiviral therapy with gradual tapering

CHRONIC SUPPRESSIVE TREATMENT

Valacyclovir 1 g PO daily for 6 months

IMMUNOCOMPROMISED PATIENTS

INITIAL TREATMENT

Acyclovir 10–15 mg/kg IV 8 hourly for 10–14 days

FOLLOWED BY

Acyclovir 800 mg PO 5 times per day to complete 6 weeks treatment

OR

Valacyclovir 1 g PO 8 hourly to complete 6 weeks treatment

Consider: intravitreal foscarnet 2.4 mg/0.1 mL OR ganciclovir 2–5 mg/0.1 mL; 1–2 doses in the first 1–3 days of treatment

No corticosteroids must be given

CHRONIC SUPPRESSIVE TREATMENT

Valacyclovir 1 g PO daily for 6 months

PROGRESSIVE OUTER RETINAL NECROSIS

Progressive outer retinal necrosis (PORN) is a rapidly progressing necrotising herpetic retinopathy with features distinct from those of acute retinal necrosis. PORN is caused by reactivation of either varicella zoster or herpes simplex virus and is a disease of immunocompromised patients, typically in HIV-infected patients with CD4 counts of less than a 100 cells/μl.

PORN does not respond as well to antiviral treatment compared to ARN, which is why more aggressive treatment with ganciclovir and/or foscarnet is recommended. Corticosteroid treatment is generally not given because minimal inflammation is seen. Following the initial treatment, chronic suppressive antiviral treatment should be given until the immune system reconstitutes on antiretroviral therapy, in order to prevent recurrences in the affected eye and to protect the other eye. Despite aggressive treatment outcomes are generally poor with significant morbidity and mortality.

TREATMENT: PROGRESSIVE OUTER RETINAL NECROSIS

INITIAL TREATMENT

Ganciclovir 5 mg/kg IV 12 hourly for 2–3 weeks

AND

Intravitreal foscarnet 1.2 mg/0.05 mL OR ganciclovir 2 mg/0.05 mL 2–3 times weekly for 2 weeks

OR

Foscarnet 90 mg/kg IV 12 hourly for 2 weeks

AND

Intravitreal foscarnet 1.2 mg/0.05 mL OR ganciclovir 2 mg/0.05 mL 2–3 times weekly for 2 weeks

FOLLOWED BY

Valganciclovir 900 mg PO 12 hourly until healing occurs

Total duration is not well defined and depends on the patient's response to treatment.

Optimise ART treatment in HIV-infected patients

CHRONIC SUPPRESSIVE TREATMENT

Valacyclovir 1 g PO daily for 3–6 months

CYTOMEGALOVIRUS RETINITIS

CMV retinitis is the most common serious ocular complication seen in HIV-infected persons with CD4 counts below 100 cells/mm^3. It is caused by reactivation of latent CMV infection. It is typically seen in patients not taking antiretroviral therapy (ART) but may be seen as a new retinitis after starting ART as a CMV immune recovery retinitis.

A laboratory diagnosis needs to be made rapidly by means of PCR on eye fluid.

TREATMENT: CMV RETINITIS

IMMEDIATE SIGHT THREATENING LESIONS (E.G. WITH MACULAR INVOLVEMENT)

Intravitreal injection of either ganciclovir (2 mg/injection) for 1–4 doses over a period of 7–10 days to provide higher intraocular levels of the drug

AND

Ganciclovir 5 mg/kg IV 12 hourly OR valganciclovir 900 mg PO 12 hourly for 14–21 days

The initial treatment should be followed by valganciclovir 900 mg PO daily as chronic suppressive therapy.

PERIPHERAL LESIONS, NON-SIGHT-THREATENING

Valganciclovir 900 mg PO 12 hourly with food for first 14–21 days of induction therapy, followed by 900 mg PO daily as chronic suppressive therapy.

NOTE

With impaired renal function antiviral doses needs to be adjusted according to creatinine clearance. Patients who are not on ART need to start ART 7–14 days after CMV therapy is initiated. Valganciclovir chronic suppressive therapy should be continued until the CD4 count remains above 100 cells/mm^3 for 6 months.

ORBITAL CELLULITIS

Orbital cellulitis is an infection involving the contents of the orbit (fat and ocular muscles) and not the globe. It needs to be distinguished from preseptal cellulitis (sometimes called periorbital cellulitis) which is generally a mild condition that rarely leads to serious complications, whereas orbital cellulitis may cause loss of vision and even loss of life. Orbital cellulitis is often a consequence of bacterial sinusitis, however, it may be a complication of other local infections, ocular trauma or surgery. It is more common in young children than older children and adults.

The diagnosis of orbital cellulitis is typically made on clinical grounds and can be confirmed by computed tomography (CT) scanning. Blood cultures should be collected from patients with suspected orbital cellulitis before the administration of antibiotics, despite a low yield. If surgery is performed, the material obtained should be sent for microscopy and culture to direct specific therapy.

CAUSES

Staphylococcus aureus, Streptococcus pneumoniae, other streptococci e.g. *S. pyogenes, Haemophilus influenzae, Moraxella catarrhalis*, anaerobes and Gram-negative bacilli (post-trauma).

TREATMENT: ORBITAL CELLULITIS

Vancomycin 15–20 mg/kg IV 8 hourly (target trough serum concentrations of 15–20 μg/mL)

AND

Ceftriaxone 2 g IV given daily

AND

Metronidazole 1 g IV 12 hourly

Alternatively piperacillin-tazobactam 4.5 g IV 8 hourly may be used together with vancomycin IV

NOTE

For penicillin/cephalosporin allergic patients, substitute with levofloxacin 750 mg IV daily and metronidazole. Daptomycin 6mg/kg IV daily can be used in place of vancomycin.

There have been no controlled trials to define the optimal duration of antimicrobial therapy in orbital cellulitis or when to switch from intravenous to oral treatment. For patients with uncomplicated orbital cellulitis (without abscess or other complications) whose infection responds well, it is reasonable to switch to oral therapy to complete a total duration of 2–3 weeks antibiotics therapy.

Oral therapy should be based on culture and sensitivity results. Where no culture results are available use clindamycin 300 mg 8 hourly alone or in combination with amoxicillin-clavulante 875 mg 12 hourly.