# Bacterial and viral infections of the eye

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**A patient with a red eye due to infection is likely to present to his or her GP. An accurate diagnosis and prompt and appropriate treatment can be sight saving.**

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The location of the outer eye on the surface of the body makes it vulnerable to infection by bacteria and viruses. The various defence mechanisms that combine to reduce this risk include an intact surface epithelium over the conjunctiva and cornea and the presence of eyelids that blink, spreading a tear film that facilitates adaptive and innate immune responses. Infection is likely in any age group if these protective mechanisms fail. Superficial corneal trauma predisposes to corneal infection, and contact lenses are a particular risk as they can be vectors for bacteria.

Bacterial conjunctivitis may accompany respiratory tract infections. Viral conjunctivitis is very contagious, and may also, but infrequently, accompany respiratory tract infections. Intraocular infection is uncommon, but viral retinitis may cause loss of vision in immunocompromised patients.

**IN SUMMARY**

- **Conjunctivitis is a common cause of a red eye. Suspect bacterial conjunctivitis in any patient with bilateral sticky red eyes. A persistent conjunctivitis with a watery discharge and pre-auricular lymphadenopathy is most likely to be caused by adenovirus and is very contagious.**
- **Bacterial conjunctivitis usually responds well to topical antibiotics.**
- **Bacterial keratitis threatens vision and must be excluded in any patient who presents with a red eye with a corneal opacity. Contact lens wearers are at particular risk.**
- **Herpes simplex can cause conjunctivitis, but disease recurrence causes a keratitis with typical dendritic corneal ulcers that stain with fluorescein. Keratitis is best treated with topical aciclovir.**
- **Herpes zoster ophthalmicus is likely to involve the eye when the rash appears on the nose or in the medial canthus.**
- **Eye involvement in herpes zoster ophthalmicus requires systemic therapy with aciclovir, famciclovir or valaciclovir.**

Figure 1. Acute bacterial conjunctivitis with typical conjunctival inflammation in the inferior fornix (conjunctival injection) and mucopurulent discharge.

Figure 2. Acute follicular conjunctivitis typical of infection with adenovirus or herpes simplex virus, affecting both superior and inferior tarsal conjunctiva. A preauricular lymph node may be palpable.

Figure 3. In herpes zoster ophthalmicus the presence of the rash in the medial canthus indicates that ocular complications may be expected. Follicular conjunctivitis and ulcerative blepharitis may be the first signs.

Conjunctivitis causes a red eye, but rarely threatens vision. Keratitis (corneal inflammation), however, can permanently affect sight, depending upon its proximity to the visual axis. Uveitis and acute angle closure glaucoma are also vision-threatening causes of a red eye, but are rare in the community and not often seen by GPs.

Consideration of the important clinical symptoms and signs, particularly the distribution of the outer eye inflammation (redness), helps in diagnosis (Table 1). In conjunctivitis, inflammation increases towards the fornices and inside the eyelids (conjunctival injection). Dilatation of the vessels immediately surrounding the cornea (ciliary injection) indicates corneal or intraocular inflammation.

## Diagnosis of conjunctivitis

### Bacterial conjunctivitis

A red eye with rapid onset of a sticky or mucopurulent discharge and conjunctival papillae indicates bacterial conjunctivitis (Figure 1). Any of the skin pathogens (such as *Staphylococcus*) or respiratory pathogens (such as *Streptococcus* and *Haemophilus influenzae*) may be the cause. In childhood particularly, bacterial conjunctivitis may accompany a respiratory tract infection. Conjunctivitis in elderly patients may be caused by Gram-negative bacteria (such as *Proteus* or *Enterobacter*), but this is rare and there is often a predisposing condition such as a dry eye or eyelid abnormalities, particularly ectropion.

Venereal infection with *Neisseria gonorrhoeae* may produce conjunctivitis when infected secretions contact the eye. Gonococcal conjunctivitis is usually seen in sexually active adults but may also occur three to five days postpartum in neonates whose mothers are infected. The infection should be suspected in any profusely purulent bilateral conjunctivitis and should be confirmed by Gram stain and culture of the discharge. Rarely the conjunctivitis associated with a venereal infection may be caused by *Neisseria meningitidis* infection.

### Viral conjunctivitis

Viral conjunctivitis produces a watery discharge, and there is frequently conjunctival and periorbital oedema and conjunctival follicles and, usually, preauricular lymphadenopathy (Figure 2). Various viruses have been implicated, including adenovirus and herpes simplex virus. Eyelid vesicles may be a transient feature of herpes simplex blepharoconjunctivitis and are an important clinical feature that distinguishes herpes simplex infection from other conjunctival viral infections such as adenovirus.

#### Herpes zoster ophthalmicus

Follicular conjunctivitis and ulcerative blepharitis may be the first signs of eye involvement in the acute phase of herpes zoster ophthalmicus (herpes zoster affecting the first division of the trigeminal or fifth cranial nerve, which supplies

**Table 1. Signs and symptoms of eye infections**

| Symptom or sign | Conjunctivitis | Keratitis | Uveitis | Acute angle closure glaucoma |
|---|---|---|---|---|
| Redness | Conjunctival injection | Ciliary injection | Ciliary injection | Ciliary injection |
| Pain | +/- | ++ | ++ | ++++ |
| Discharge | ++ | +/- | - | - |
| Visual acuity | Normal | ↓ | ↓ | ↓↓↓ |
| Pupil | Normal | Normal | Miotic | Mid-dilated and unreactive to light |

Figure 4. Acute bacterial keratitis should be suspected in any patient presenting with a red eye and a corneal opacity. Contact lens wearers are at particular risk of this condition.

Figure 5. In severe bacterial keratitis a central corneal opacity is easily visible on examination with a bright light. In this patient, the additional white linear opacity visible behind the inferior cornea indicates sterile pus in the anterior chamber.

Figure 6. Acute bacterial keratitis in a contact lens wearer is frequently caused by infection with *Pseudomonas*. In this established infection there is a hypopyon and the cornea has extensive ulceration with thinning and abscess formation.

sensation to the skin of the forehead, side of the nose and the eye). Eye involvement should be expected when the skin rash affects the side of the nose or the medial canthus (Hutchinson's sign); this indicates involvement of the nasociliary branch in the varicella–zoster virus infection. Pain and sensory changes in the forehead or scalp may precede the characteristic rash that begins with erythematous spots that rapidly form papules and vesicles over the forehead – these skin lesions start to form crusts within a week (Figure 3). The blepharoconjunctivitis usually resolves within 10 days and early on may mask an underlying episcleritis.

### Chlamydial conjunctivitis and trachoma

In urban communities chlamydia is contracted as a sexually transmitted disease. Ocular infection presents as a persistent follicular conjunctivitis, which resembles adenoviral infection with conjunctival follicles, preauricular lymphadenopathy and a watery, sometimes mucoid discharge. The conjunctival inflammation fails to resolve spontaneously within a month. The diagnosis should be confirmed using polymerase chain reaction (PCR) or immunofluorescence microscopy to detect chlamydial DNA or antigen in scrapings of conjunctival epithelial cells.

Endemic *Chlamydia trachomatis* infection causes trachoma, a chronic blinding eye infection that is still prevalent in Aboriginal communities. Recurrent chlamydial infection in children causes follicular conjunctivitis which may develop in adulthood into cicatrizing conjunctivitis, where eyelid distortion with in-turning lashes (trichiasis), tear film disturbance and corneal opacification can cause blindness.

## Diagnosis of keratitis

### Bacterial keratitis

Corneal infection or keratitis should be suspected when there is a corneal opacity or fluorescein staining of the cornea in a red eye (Figure 4). Bacterial corneal infections are uncommon in our community, but should be excluded in contact lens wearers presenting with a red eye. The cornea surrounding the opacity may be generally hazy and a collection of pus within the anterior chamber (a hypopyon) may be seen at the lower margin of the cornea as a white to yellow line in the most severe cases (Figure 5). The infection typically is confined to the cornea but often spreads rapidly throughout it. Gram-negative bacteria such as *Pseudomonas aeruginosa* are likely pathogens in contact lens wearers (Figure 6).

*Corynebacterium*, skin flora such as staphylococci, and Gram-negative bacteria such as *Moraxella* and *Klebsiella* may cause corneal abscesses in elderly or immunocompromised patients.

All corneal infections can rapidly deteriorate to involve most of the cornea within a short time. Early diagnostic suspicion of bacterial keratitis and urgent referral to an ophthalmologist is indicated.

### Viral keratitis

Viral keratitis (herpes simplex or herpes zoster) causes corneal ulceration without abscess formation. Although patients may complain of pain, the severity of the pain is significantly less than would be expected from a corneal epithelial defect of similar size resulting from trauma.

#### Herpes simplex keratitis

Infection of the cornea with herpes simplex virus presents as dendritic ulceration and indicates recurrent disease in a patient who carries the herpes simplex virus (Figure 7). The cornea should be stained with topical fluorescein: when the eye is examined with a blue light, areas of corneal epithelial cell loss fluoresce bright green, displaying the typical branching pattern. Rose Bengal is an alternative stain. This condition must be excluded in any patient who presents with a red eye. Often there will be a triggering event, such as concurrent illness, sunburn or other stress.

Deeper corneal inflammation caused by herpes simplex virus infection is frequently chronic and complex and may

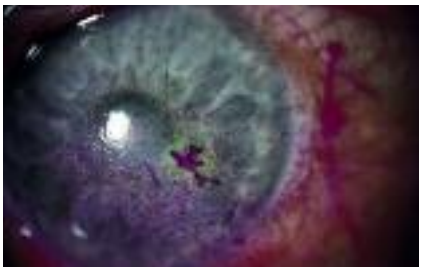

Figure 7. Herpes simplex corneal infection. The dendritic ulcers stain easily with topical Rose Bengal (as here), and also with topical fluorescein.

Figure 8. Corneal herpes simplex infection showing disciform keratitis. The endothelium is involved, causing localised corneal oedema with stromal opacity and thickening, together with epithelial microcystic changes.

Figure 9. Herpes simplex can produce a complex appearance in patients who have had a number of recurrences of the keratitis. Co-existing epithelial ulceration and stromal inflammation result from viral infection.

Figure 10. Fluorescein-stained corneal epithelial ulceration in herpes zoster ophthalmicus. The lesions often appear raised rather than ulcerating, although they have the same linear branching appearance as herpes simplex corneal ulceration.

Figure 11. Herpes zoster ophthalmicus can cause permanent loss of corneal sensation. In this patient, the corneal epithelium appears dry and there are multiple tiny areas of epithelial cell loss, together with corneal opacification and an early ulcer.

cause localised oedema with stromal opacity and thickening (disciform keratitis) or deep corneal inflammation with surface ulceration (Figures 8 and 9). The patient may recall a previous episode and usually presents with a corneal opacity that may be accompanied by an ulcer. The eye is red with the pattern of ciliary injection. An ophthalmological consultation is needed to confirm this diagnosis and take responsibility for the management.

### Herpes zoster ophthalmicus

Corneal ulceration in herpes zoster ophthalmicus has a variety of forms. In the acute phase of the infection, during the conjunctivitis, a superficial punctate epithelial keratitis may be detected as a granular pattern when the cornea is stained with fluorescein. Confluence of these lesions with the addition of mucus from the tear film may result in dendritic figures or stellate lesions that stain moderately with fluorescein (Figure 10). These lesions usually resolve spontaneously.

Later in the course of the infection a deeper stromal keratitis causes two types of corneal opacities that do not stain with fluorescein: nummular ('coin-like') keratitis and disciform keratitis. The discrete multiple lesions within the stroma of nummular keratitis usually appear after about two weeks. Disciform keratitis appears later, but usually within three months of onset of the rash. Although this keratitis can affect any part of the cornea it is often found centrally, causing localised corneal oedema that appears as a hazy circumscribed area of corneal thickening with intact epithelium that does not stain with fluorescein. Slit lamp examination may reveal a coexisting iritis and endothelial inflammatory cell deposits or keratic precipitates.

Sensory loss in herpes zoster ophthalmicus can permanently affect the eyelids, conjunctiva and cornea. Long-term loss of corneal sensation can render the cornea susceptible to ulceration (a neurotrophic keratitis) at any subsequent time – the patient will not experience pain as a clue to the presence of the condition (Figure 11). The corneal epithelium appears cloudy and small areas of epithelial loss may become confluent, forming large oval ulcers with non-healing opaque margins. Ophthalmological consultation is needed to confirm such diagnoses.

## Diagnosis of intraocular infections

### Bacterial endophthalmitis

Intraocular bacterial infection or endophthalmitis is rare but may complicate any penetrating ocular trauma, including intraocular surgery (Figure 12). The diagnosis should always be considered in any patient with a full thickness globe laceration who subsequently develops a very red painful eye. Such infections are accompanied by intense inflammation and significantly reduced visual acuity. Anterior chamber and vitreous inflammation prevents a view of the retina on ophthalmoscopy (there is a poor or absent red reflex), and there is frequently an anterior chamber hypopyon. Prompt ophthalmological referral is required.

### Intraocular complications of viral infection

Herpes simplex may cause a unilateral uveitis (Figure 13). In the acute phase of infection the clinical features resemble any idiopathic uveitis with flare and cells in the anterior chamber. Although affected patients will have serological evidence of past infection with herpes simplex virus, serum IgG positive against herpes simplex virus types 1 or 2 is not diagnostic, as past exposure is prevalent. Acute retinal necrosis in AIDS patients may be caused by infection of the retina with herpes simplex virus.

Herpes zoster may cause an acute or chronic uveitis, secondary open angle glaucoma, cataract, retinitis and, uncommonly, optic neuritis. In immunocompromised patients, the varicella–zoster virus can produce progressive multifocal chorioretinitis that rapidly results in profound visual loss.

Figure 12. Bacterial endophthalmitis. Here a penetrating eye injury resulted in a corneal laceration that was repaired with interrupted nylon sutures. Postoperatively severe eye pain, inflammation and significantly reduced vision developed. Slit lamp examination shows anterior chamber inflammation obscuring iris detail. The red reflex is absent.

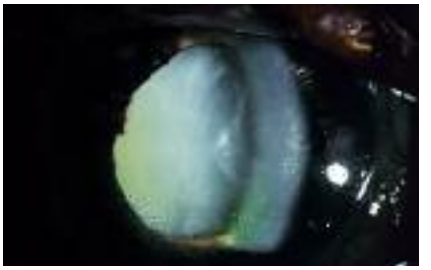

Figure 13. Uveitis caused by herpes zoster ophthalmicus is readily diagnosed by finding keratic precipitates on the posterior corneal surface at slit lamp examination. In this patient there are extensive iris adhesions to the anterior lens capsule (posterior synechiae).

## Management of conjunctivitis

Conjunctivitis may be managed in general practice.

### Bacterial conjunctivitis

Suspected bacterial conjuctivitis need not be routinely swabbed. If it fails to improve with topical antibiotics another cause of conjunctivitis should be suspected and referral to an ophthalmologist considered.

The bacteria that commonly cause conjunctivitis are generally sensitive to

antibacterial eye drops, although these are not truly broad spectrum. Chloramphenicol (Chloromycetin Eye Preparations, Chlorsig, Minims Chloramphenicol) has a useful spectrum of action against Gram-positive bacteria and some Gram-negative bacteria such as *Haemophilus influenzae* and *Proteus*. Ciprofloxacin (CiloQuin, Ciloxan) and ofloxacin (Ocuflox) are active against all the common bacteria with the exception of some streptococci. Gentamicin sulfate (Genoptic, Minims Gentamicin Sulfate), neomycin sulfate (Minims Neomycin), neomycin sulfate with polymyxin B sulfate (Neosporin Ophthalmic), framycetin sulfate (Soframycin Eye) and tobramycin (Tobrex Ophthalmic) provide broad activity against Gram-negative bacteria, but are less likely to adequately treat streptococcal infection.

Clinical assessment of the most likely infecting organism and consideration of any known allergies should direct the choice of agent. Antibacterial eye drops should be administered every two hours for the first 48 hours and then four times daily for up to five days, until the inflammation has resolved. If the inflammation fails to resolve after a week the diagnosis must be reviewed.

Acute bacterial conjunctivitis caused by *N. gonorrhoeae* or *N. meningitidis* needs systemic antibiotic therapy. Parenteral cephalosporins are usually given, but the choice of antibiotic should be guided by the known sensitivities of gonococcal isolates from that community.

Topical chloramphenicol and an oral cephalosporin (such as cefaclor [Ceclor Cefkor, Keflor] are indicated for the relapsing *H. influenzae* conjunctivitis that may be caused by persistence of this organism in the sinuses or nasopharynx.

### Viral conjunctivitis

Specific drug therapy is not indicated for adenoviral conjunctivitis. Topical antibiotics are not necessary because secondary bacterial conjunctivitis is unlikely. Symptomatic relief with cold compresses may be beneficial. Patients should be advised that the conjunctivitis remains infectious until the watery discharge and inflammation resolves, which may take up to two weeks. They should wash their hands thoroughly after wiping their eyes and avoid sharing household items such as towels.

Herpes simplex blepharoconjunctivitis should be treated with topical aciclovir ointment (Zovirax Ophthalmic Ointment) five times a day for 10 days.

In the acute phase of herpes zoster ophthalmicus, topical antibiotics such as chloramphenicol may protect against a secondary bacterial conjunctivitis. Treatment is indicated during the initial blepharoconjunctivitis, when there is a severe mucopurulent conjunctivitis or when the eyelid vesicles are crusting.

### Chlamydial conjunctivitis and trachoma

Chlamydial conjunctivitis and trachoma can be effectively treated with oral azithromycin (Zithromax)1 g for adults and 20 mg/kg (up to 1 g) for children over 6 kg once a week for three weeks. (For neonates and children under 6 kg use erythromycin 10 mg/kg orally, six-hourly for three weeks).

The World Health Organization has recommended this treatment be given annually to all children and young adults with active trachoma in endemic areas. However, elimination of trachoma as a blinding eye disease requires provision of adequate water supplies, sewerage and a public health program that monitors prevalence of the infection and encourages personal hygiene, particularly face washing. To this end, the WHO has developed the SAFE strategy, which lists the measures necessary to control trachoma blindness:

- S is surgery for trichiasis
- A is antibiotic (azithromycin) for treatment of active trachoma in families
- F is facial cleanliness
- E is environmental improvement including water supply and sanitation.

## Management of keratitis

### Bacterial keratitis

Acute bacterial keratitis is a vision-threatening condition and is best managed by an ophthalmologist. Diagnosis of the causative organism, determination of the antibiotic sensitivities and administration of appropriate topical antibiotics every 30 to 60 minutes facilitate management. Treatment of a severe or central corneal abscess in hospital is preferable, as eye drops can be given, if necessary, very frequently throughout 24 hours and specific therapy can be guided by the antibiotic sensitivities of the bacteria and the daily clinical progress. Topical fluoroquinolones have a broad spectrum of activity against many Gram-negative and Gram-positive bacteria and may be chosen as single agent therapy.

In severe keratitis the ophthalmologist may prefer initially to treat with topical fortified antibiotics in combination, e.g. a cephalosporin with an aminoglycoside. (Fortified antibiotics are topical antibiotics modified to increase the available antibiotic. These eyedrops are frequently manufactured in the hospital pharmacy from parenteral preparations.) Such therapy has the best chance of efficacy, particularly during the first 48 hours of treatment, until the antibiotic sensitivities of the microbial infection are known.

### Viral keratitis

#### Herpes simplex keratitis

Dendritic ulcers due to herpes simplex are best managed by removal of the infected corneal epithelium using a sterile cotton bud, after application of topical anaesthetic. Topical ocular antibacterial and antiviral preparations in ointment form, such as chloramphenicol (Chloromycetin Eye Preparations, Chlorsig) every three hours and aciclovir five times a day, should be given until the epithelial defect has healed. Aciclovir should then be continued for a further 10 days. Geographic ulcers (wide and deeper herpes simplex ulcers, i.e. expanded linear ulcers) are

best managed with topical aciclovir five times a day until the epithelium has healed and three times a day for an additional week. Referral to an ophthalmologist is indicated if the ulcer fails to improve during treatment.

Herpetic keratitis will frequently heal with a scar that can compromise visual acuity if the infection was in or near the visual axis. In children less than 5 years old this may cause amblyopia. Ophthalmological assessment is necessary so a supervised program of patching of the unaffected eye can be carried out to maximise vision in the affected eye.

Oral aciclovir is no more efficacious in the management of dendritic ulceration than topical therapy. Currently topical therapy is more economical and is preferred. However, in patients who are immunosuppressed and have suffered recurrent herpes simplex keratitis, prophylactic oral aciclovir could be considered. A dosage of 800 mg a day in two divided doses has been shown to significantly decrease recurrences of both epithelial and stromal keratitis.[1]

### Herpes zoster ophthalmicus

Systemic therapy with oral aciclovir, famciclovir (Famvir) or valaciclovir (Valtrex) is advisable in herpes zoster ophthalmicus.[2] Ideally, treatment should commence within three days of the onset of the rash and continue for seven days.

The keratitis, uveitis and secondary glaucoma that may occur are all amenable to topical corticosteroids such as prednisolone phosphate 0.5% (Predsol Eye/Ear drops [Eye], Minims Prednisolone) and dexamethasone 0.1% (Maxidex). Slit lamp examination is mandatory to assess the response, and an ophthalmologist should monitor therapy. Other measures such as partial tarsorrhaphy may be needed to protect the cornea in cases of neurotrophic keratitis. Specific therapy for glaucoma may also become necessary.

Late complications of herpes zoster ophthalmicus include cataract and corneal scarring; surgery may improve visual acuity in these cases.

## Management of intraocular bacterial and viral infections

If an intraocular infection is suspected as the cause of a red eye, the patient should be referred promptly to an ophthalmologist. Bacterial endophthalmitis is treated with intraocular antibiotics. Viral infections causing acute retinal necrosis are managed with systemic antiviral therapy.[3]

## Conclusion

It is most important to establish a diagnosis in any case of a red eye. Conjunctivitis usually carries with it a good prognosis for vision. Early diagnosis and prompt referral to an ophthalmologist can save the eyesight in patients with bacterial keratitis, and this condition should always be specifically sought in any contact lens wearer who presents with a red eye.

A recurrent red eye should alert GPs to the possibility of herpes simplex keratitis. In patients who have had herpes zoster ophthalmicus, late complications can be difficult to diagnose, particularly those associated with reduced corneal sensation. Slit lamp examination is advisable. MT

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