

## A "site" for sore eyes

George L. Muntingh, Michelle Viljoen

Dept of Pharmacology and Clinical Pharmacy, School of Pharmacy, University of the Western Cape, Cape Town, South Africa

\*Corresponding author, email: [gmuntingh@uwc.ac.za](mailto:gmuntingh@uwc.ac.za)

### Abstract

It is known that not all red eyes are caused by infections. Furthermore, not all eye infections will react to antibiotic eye drops. Most cases of conjunctivitis are due to viral causes, do not require antibiotic eye drops and are usually self-limiting. Serious ophthalmic conditions such as infectious keratitis can lead to blindness; it is an emergency that requires specialist treatment. Also infectious endophthalmitis has become more frequent with the use of intravitreal injections. Intravitreal antibiotics are needed to try and prevent visual loss. To ensure therapeutic local exposure ophthalmic antibiotic solutions should be applied frequently into the eye.

**Keywords:** conjunctivitis, eye infection, keratitis, antibiotic

### Introduction

In primary healthcare, eye infections are a common presenting problem. 'Red eye', 'conjunctivitis' and 'corneal ulcer/keratitis' were among the top five problems most commonly referred to ophthalmology departments.<sup>1</sup>

To ensure a good visual outcome for the patient, the medical practitioner should make a prompt diagnosis and start appropriate interventions. Conjunctivitis typically does not threaten vision, but infections of the cornea or inside the eye are serious threats and require immediate referral to an ophthalmologist.

### Infectious conjunctivitis

Conjunctivitis is a common condition that causes dilation of the conjunctival blood vessels and resultant inflammation.

Both viral and bacterial conjunctivitis (Figure 1) present with a red eye and are highly contagious and perhaps not in keeping with William Shakespeare's infamous remark "*Take thou some new infection to thy eye, and the rank poison of the old will die.*"<sup>32</sup>

Assessment should include checking visual acuity and examination with a torch or slit lamp. Fluorescein drops should be instilled in the conjunctival sac and the eye viewed with the cobalt blue light of the slit lamp, or fundoscope, to rule out any signs of corneal ulceration or infection. A history of cold sores or shingles should be sought and the patient examined for cold sores or a vesicular rash in case the infection is due to *herpes simplex* or zoster virus.<sup>2</sup>

### Viral conjunctivitis

Viral conjunctivitis is the most common cause of infectious conjunctivitis. This infection is more common in adults than in children. Around 65–90% of cases are caused by adenovirus. Occasionally, *herpes simplex* or zoster virus is responsible. Patients can generally be advised that viral conjunctivitis is self-limiting and, as there are no specific treatments, for comfort they can use cold compresses, artificial tears or topical antihistamines.<sup>2,3</sup> Antibiotics are not needed, are costly and may increase antibiotic resistance. If there is evidence of *herpes simplex* or zoster virus then antivirals should be prescribed, such as aciclovir ointment or ganciclovir gel.

When viral conjunctivitis is severe or the patient experiences symptoms after its resolution, the patient should be referred to an ophthalmologist. This is to consider topical steroids and to exclude an immune 'post-viral' keratitis.

### Bacterial conjunctivitis

Although a less frequent cause of conjunctivitis, bacterial conjunctivitis is more common in children. The most common bacteria are *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Staphylococcus aureus*.<sup>4</sup>

When compared to placebo, the use of antibiotic eye drops is associated with improved rates of clinical and microbiological remission.<sup>4</sup> A broad-spectrum topical antibiotic is recommended. The medical practitioner can select the most convenient or least expensive option, as there is no clinical evidence suggesting the superiority of any particular antibiotic.<sup>3,4</sup>

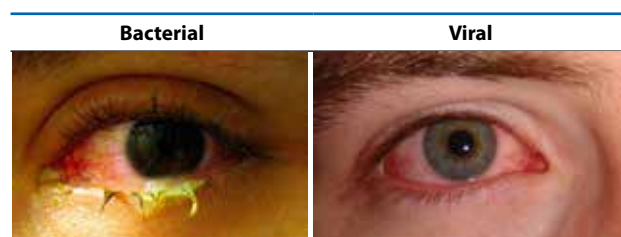
The initial treatment recommended by Therapeutic Guidelines: Antibiotic<sup>5</sup>:

- Chloramphenicol 0.5% eye drops, one to two drops every two hours for the first 24 hours, decreasing to six-hourly until the discharge resolves, for up to seven days
- Framycetin sulfate 0.5% eye drops, 1–2 drops every 1–2 hours for the first 24 hours, decreasing to eight-hourly until discharge resolves, for up to seven days.

It should be impressed on the patient that the frequency of eye drop installation should be adhered to as this will ensure and maintain a therapeutic concentration and therefore exposure to the antimicrobial in the eye.

Chloramphenicol 1% eye ointment may be used at bedtime. Gentamicin, tobramycin and quinolone eye drops are not recommended for empiric treatment. If the condition does not improve within five days, the patient should be immediately referred to an ophthalmologist.

**Figure 1:** Conjunctivitis



Note discharge in the medial canthus ([http://medbox.iab.me/modules/en-wikem/wiki/File\\_Conjunctivitis.html](http://medbox.iab.me/modules/en-wikem/wiki/File_Conjunctivitis.html))

([http://medbox.iab.me/modules/en-wikem/wiki/File\\_Conjunctivitis.html](http://medbox.iab.me/modules/en-wikem/wiki/File_Conjunctivitis.html))

### Gonococcal conjunctivitis

*Neisseria gonorrhoeae* causing conjunctivitis is relatively uncommon but should be considered in neonates and sexually active young adults. If suspected, the medical practitioner should take conjunctival swabs for Gram staining and special culture for *Neisseria* species.<sup>6</sup> Patients should be referred immediately to an ophthalmologist. Antibiotic therapy is the recommended treatment and ceftriaxone is the drug of choice.<sup>3</sup> Additionally, patients should lavage the infected eye with saline and add therapy to cover for *Chlamydia*.<sup>2</sup>

### Chlamydial conjunctivitis

Most cases of Chlamydial conjunctivitis are unilateral and have concurrent genital infection. Symptoms usually include conjunctival hyperemia, mucopurulent discharge and lymphoid follicle formation.<sup>6</sup> Patients with symptoms should be referred immediately to an ophthalmologist. Oral antibiotics, such as azithromycin or doxycycline, are effective treatments.<sup>7</sup>

### Infectious keratitis

Infection of the cornea (or microbial keratitis) is an ophthalmic emergency requiring immediate attention as it can progress rapidly. It is a significant cause of corneal blindness<sup>8</sup> and is one of the most common causes of visual impairment in working age adults.<sup>9</sup> In the USA, nearly 30 000 cases of microbial keratitis are reported annually.<sup>10</sup>

If infectious keratitis is suspected, the medical practitioner should take a history to look for risk factors such as contact lenses, corneal abrasions, physical and chemical trauma, refractive surgery, diabetes, immunosuppressive diseases and topical steroids.<sup>10,11</sup> The type of infecting organism varies according to the climate and geographical region and the patient's risk factors.

### Bacterial keratitis

Bacterial infection is the most common cause of infectious keratitis. Common causal bacteria include *S. aureus*, coagulase-negative staphylococci, *S. pneumoniae* and *Pseudomonas aeruginosa*.<sup>10,11</sup>

*P. aeruginosa* is the most common microorganism implicated in bacterial keratitis among contact lens wearers. Less commonly, fungi or acanthamoeba can be responsible (Figure 2).<sup>12</sup> Fungi should be suspected when there is trauma particularly with vegetative matter and is more common in rural environments. Increase suspicion for acanthamoeba, if a patient has been swimming or in a spa while wearing contact lenses.



**Figure 2:** Acanthamoeba Keratitis

Specific antifungal or anti-acanthamoebal therapy is needed and treatment may last some months and can include regimens of various topical preparations, e.g. Neomycin-Polymyxin, B-Gramicidin, polyhexamethylene biguanide (PHMB), chlorhexadine, and voriconazole. Some practitioners recommend oral ketoconazole.<sup>13-15</sup>

The signs and symptoms of bacterial keratitis (Figure 3) can include pain, photophobia, blurred vision, corneal opacity or pus inside eye, or contact lens wearers with red eye or increasing pain. These should be referred promptly to an ophthalmologist for a slit lamp examination and corneal scraping.<sup>16</sup>

The mainstay of treatment is topical antibiotics and options include monotherapy with fluoroquinolones (ciprofloxacin 0.3% or ofloxacin 0.3% 1–2 drops hourly for 48 hours, then every 4 hours until healed) or some authors prefer fortified aminoglycoside/cephalosporin combinations (fortified cefalotin



**Figure 3:** Eye with non-ulcerative sterile keratitis

(<https://commons.wikimedia.org/wiki/File:Clare-314.jpg>)

5% plus gentamicin 0.9% 1–2 drops hourly for 48 hours, then reduce frequency according to treatment response).<sup>5</sup> These regimens have similar effectiveness but fluoroquinolones reduce the risk of chemical conjunctivitis and ocular discomfort. Compared to ofloxacin, ciprofloxacin increases the risk of white corneal precipitates.<sup>17</sup> Occasionally, corneal grafting may be needed to eradicate the organism or repair damage.

In primary healthcare, chloramphenicol is the most common first-line antibiotic prescribed for red eye. It is a bacteriostatic, broad-spectrum antibiotic but devoid of activity against *P. aeruginosa*.<sup>18</sup> Therefore, primary healthcare providers should not prescribe chloramphenicol when microbial keratitis is suspected as this delays appropriate treatment, with the risk of the patient losing vision or the eye.<sup>18,19</sup>

### Herpes simplex keratitis

Keratitis caused by herpes simplex virus is an important cause of infectious blindness in developed countries. The global incidence of herpes simplex keratitis was calculated at approximately 1.5 million with 40 000 new cases of severe monocular visual impairment or blindness per year.<sup>20</sup> Herpes simplex keratitis can be classified as epithelial, stromal, endothelial or mixed, depending on which layer of the cornea is involved. It may also be considered as primary or recurrent depending on whether it is the patient's first episode. If suspected, the practitioner should ask about a history of cold sores or previous viral keratitis as this can be the first clue to the diagnosis. The clinical features of herpes simplex virus keratitis can be identified on slit lamp examination.<sup>21,22</sup>

Epithelial herpes simplex keratitis typically manifests as a dendritic ulcer. To visualise the ulcer, fluorescein staining and a cobalt blue light are needed (Figure 4).<sup>21</sup> Preferred treatment is aciclovir ointment five times daily for 14 days.<sup>23–25</sup>

Stromal herpes simplex keratitis presents with haze or opacity of the stroma, with or without ulceration, scarring or vascularisation. Endothelial keratitis is characterised by keratic precipitates on the endothelium and corneal oedema.<sup>23</sup> Management of stromal and endothelial keratitis involves referral to an ophthalmologist for oral antivirals (aciclovir or valaciclovir), topical steroids and follow-up until the episode has resolved.<sup>25</sup>



**Figure 4:** Herpes simplex virus dendritic ulcer

(<https://emedicine.medscape.com/article/1194268-treatment>)

### Infectious endophthalmitis

Endophthalmitis is an inflammation of the interior of the eye (Figure 5) and is also an ocular emergency, requiring urgent referral to an ophthalmologist to prevent permanent loss of vision. Endophthalmitis is an uncommon diagnosis but can have devastating visual outcomes. Endophthalmitis may be endogenous or exogenous. Exogenous endophthalmitis is



**Figure 5:** Endophthalmitis

Conjunctival hyperemia with hypopyon in the anterior chamber

(<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/415216>)

caused by introduction of pathogens through mechanisms such as ocular surgery, open-globe trauma, and intravitreal injections. Endogenous endophthalmitis occurs as a result of hematogenous spread of bacteria or fungi into the eye.<sup>26</sup>

Infectious cause is the most common and various bacteria and fungi have been isolated as the cause of the endophthalmitis. The most common microorganisms involved are coagulase-negative staphylococci, *S. aureus*, streptococci and Gram-negative bacilli, Viruses: *Herpes simplex*, Fungi: *Candida* spp., Parasites: *Toxoplasma gondii*. A minor procedure is needed to obtain samples of vitreous and aqueous humour to isolate the organism. Other causes include penetrating trauma, allergic reaction, and retained intraocular foreign bodies.<sup>26</sup>

Urgent treatment is needed with intravitreal antibiotics such as ceftazidime or vancomycin injected by an ophthalmologist. In some cases vitrectomy may be beneficial to avoid loss of vision.<sup>5,27</sup> If there is a delay in administering intravitreal treatment, give single doses of:

- Oral ciprofloxacin 750 mg (child: 20 mg/kg up to 750 mg) plus intravenous vancomycin (adult and child 15 mg/kg), or
- Gentamicin (adult and child 5 mg/kg) intravenous plus intravenous cefazolin 2 g (child: 50 mg/kg up to 2 g).<sup>5</sup>

### Adverse effects of topical antibiotics

Typically bacterial infections are treated with antibiotic drops of which some may cause systemic adverse effects. Underestimated is the fact that the volume of the drop produced by commercial dispensers (25–50  $\mu$ L) exceeds the capacity of the conjunctival sac (10  $\mu$ L), therefore a relative large volume of the liquid drains out of the eye. This liquid may be systemically absorbed through different pathways including conjunctiva, nose, lacrimal drainage, pharynx, gastrointestinal tract, aqueous humour, lids, cheeks and inner ocular tissues. However, the risk of systemic absorption is low since the corneal epithelium and conjunctival epithelium act as natural barriers limiting absorption of ocular drug resulting in a bioavailability of 5–10%.<sup>28</sup> Some adverse effects can include skin irritation, itching or rash with sulfonamide, sulfacetamide and neomycin.<sup>28</sup> Fluoroquinolones can cause local

irritation, stinging, chemosis, conjunctival hyperaemia, corneal precipitations and alteration of taste.<sup>29</sup>

A minimal dose and concentration of the antibiotic must be used in pregnancy to limit systemic absorption. Patients must be advised of punctal occlusion, nasolacrimal pressure and wiping extra liquid to prevent systemic absorption.<sup>30</sup> Medical practitioners should always refer to the ABCD pregnancy category before prescribing antibiotics to pregnant women. Antibiotics such as chloramphenicol, tobramycin, fluoroquinolones and topical antivirals, e.g. aciclovir, are considered safe to use during pregnancy.<sup>31</sup>

## Conclusion

Patients with eye infections typically present with pain, blurred vision and a red eye. Conjunctivitis is the most common eye infection to present to primary healthcare providers and rarely threatens vision. Corneal infection (keratitis) and endophthalmitis although less common pose a serious risk to vision. If the patient has a history of blurred vision, pain, photophobia, corneal opacity or hypopyon, specialist assessment is urgently called for.

Primary healthcare providers should avoid prescribing topical antibiotics for an eye infection unless the patient has bacterial conjunctivitis. Viral conjunctivitis is common and self-limiting. Urgent referral to an ophthalmologist for microbiological samples and treatment is needed for infectious keratitis and endophthalmitis.

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