Infectious conjunctivitis

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Cases of conjunctivitis in routine optometric practice are commonplace. This article considers the clinical presentation of infectious conjunctivitis and its differential diagnosis. It discusses the non-pharmacological and pharmacological management options for practitioners, along with the implications for those with therapeutic speciality.

Course code: C-33682 | Deadline: November 15, 2013

Learning objectives
Understand how to elicit relevant symptomology in cases of conjunctivitis (Group 1.1.2)
Understand the importance of infection control when dealing with cases of conjunctivitis (Group 2.1.1)
Undertake appropriate examination to enable the differential diagnosis of conjunctivitis and advise patients accordingly (Group 6.1.7)

Learning objectives
Be able to explain to the patient about the implications of conjunctivitis (Group 1.2.4)
Understand the importance of infection control when dealing with cases of infectious disease (Group 2.1.1)
Be able to recognise the presentation of conjunctivitis cases (Group 8.1.1)

Learning objectives
Be aware of the non-pharmacological and pharmacological options for the management of conjunctivitis (Group 1.1.2)
Be able to consider the appropriate intervention measures for conjunctivitis (Group 2.1.6)
Be able to recognise severe cases of conjunctivitis that require onward referral (Group 4.1.2)

About the authors
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Introduction
Conjunctivitis, an inflammation of the conjunctiva, may be infective, allergic or irritant in nature. Infectious cases of conjunctivitis include bacterial and viral causes which may be acute, lasting no longer than three weeks, or chronic, lasting more than three weeks. It has been reported that infective conjunctivitis accounts for 35% of all eye-related cases in general practice, being more common in children and the elderly, with an incidence of 13-14 cases per 1,000 population per year. There appears to be no data relating to the prevalence within optometric practice, although clinical experience suggests that it is very common. This article will discuss the diagnosis and management of infective causes of conjunctivitis.

Bacterial conjunctivitis
The common causes of acute bacterial conjunctivitis include Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis. Predisposing risk factors for the development of bacterial conjunctivitis include superficial trauma to the ocular surface, contact lens wear, pre-existing viral conjunctivitis, blepharitis, diabetes, steroid use, other diseases compromising the immune system, and drugs that reduce ocular resistance to infection.

Symptoms of bacterial conjunctivitis include acute onset, discharge, discomfort, burning, grittiness and crusting of the eyelids, particularly in the morning – the eyelids may be stuck together in the morning and have to be bathed open (see Figure 1). The mucous discharge may also cause brief periods of blurred vision. Bacterial conjunctivitis may be unilateral, but can become bilateral, usually one to two days after the initial infection.

Signs include diffuse conjunctival injection, lid crusting, purulent or mucopurulent discharge, mild papillae on the palpebral conjunctiva, and less commonly, superficial punctate keratitis in the lower third of the cornea.

The differential diagnosis of bacterial conjunctivitis includes chlamydial and viral conjunctivitis, which shall be discussed in detail later, along with other forms, such as allergic and irritant conjunctivitis. Other, more serious causes of acute red eye, requiring urgent ophthalmological referral, must be excluded, including angle closure glaucoma, anterior uveitis, and keratitis (see Table 1).

Management of bacterial conjunctivitis is centred on self-care advice based upon expert opinion, as the infection usually resolves within one to two weeks without treatment. The patient should be advised:

- That the infection is self-limiting, resolves within one to two weeks and the risk of serious complications is low
- That topical antibiotics often make little difference, and are ineffective against viruses
- To cease contact lens wear if applicable
- Ocular comfort may be improved with the application of topical ocular lubricants (preservative-free)
- To clean away lid crusting and discharge from the closed eyes using sterile cotton wool (buds) soaked in cooled boiled water
- To clean their hands regularly (particularly after touching their eyes), avoid sharing towels and pillows to help prevent the spread of infection

Antibiotic treatment should be considered when the bacterial infection is severe (or likely to become severe). There is a lack of agreed definition on the different severities of infective conjunctivitis, but a severe infection may be considered as one that causes the patient considerable distress and discomfort, or that signs are judged to be severe based upon clinical examination and experience.

Antibiotic usage should also be considered where schools and childcare organisations require a child to be treated before allowing them to attend. However, evidence suggests that patients should delay the start of treatment by up to seven days to see if the infection resolves spontaneously, alongside self-care. An open label, randomised controlled trial found that, compared to immediate antibiotic treatment, delayed prescribing of chloramphenicol provided a similar severity and duration (mean 3.3 days versus 3.9 days) of symptoms and reduced the likelihood of re-attendance to the practitioner. The mean duration of symptoms in the non-treatment group was 4.8 days, supporting the advice that spontaneous resolution within one to two weeks is likely.

Very few clinical trials to investigate the efficacy of topical antibiotics for conjunctivitis have been conducted in primary care, where the majority of cases are likely to be encountered. In a double-blind, randomised placebo controlled study comparing the efficacy of fusidic acid to placebo in the treatment of infective conjunctivitis, although the bacterial eradication rate was greater in the treatment group, there was no statistically significant difference between cure rates in each group after seven days. Another study, comparing chloramphenicol to placebo in children with acute infective conjunctivitis, also found no statistically significant difference in cure rate between each group after seven days. Moreover, a meta-analysis of primary care studies has concurred with these findings. However, studies supporting the use of antibiotics in secondary care involving selected patients, such as polymixin-bacitracin, azithromycin, besifloxacin, moxifloxacin, ciprofloxacin and norfloxacin, produce a statistically significant and faster improvement in clinical resolution or bacterial eradication compared to placebo. Nevertheless, routine prescribing of antibiotics for acute infectious conjunctivitis in a primary care population may lead to increased antibiotic resistance, cause unnecessary side effects, and increase costs.

Antibiotics licensed for the treatment of conjunctivitis include:

- Erythromycin
- Clindamycin
- Azithromycin
- Ciprofloxacin
- Norfloxacin
- Fusidic acid

Figure 1 Bacterial conjunctivitis. Image courtesy of Tanalai at en.wikipedia
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Table 1 Differential diagnosis of bacterial conjunctivitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Allergic conjunctivitis</td>
<td>Usually bilateral, itching (pathognomonic), discomfort, burning, grittiness. History of atopy, seasonal or perennial variations</td>
<td>Diffuse conjunctival hyperaemia, chemosis, papillae on palpebral conjunctiva, mucous discharge, eyelid swelling (puffy eyes)</td>
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<tr>
<td>Irritant conjunctivitis</td>
<td>Caused by chemical toxicity and or delayed hypersensitivity response to topical drugs/preservatives/cosmetics – delayed onset after initial improvement of original condition. Irritation, pain, stinging, photophobia, blurred vision</td>
<td>Conjunctival hyperamia, eyelid swelling, diffuse punctate corneal and conjunctival staining. Occasionally corneal oedema, pseudodendrites, stromal infiltrates</td>
</tr>
<tr>
<td>Angle closure glaucoma</td>
<td>Sudden onset, usually unilateral, eyeball tenderness, pain, headache, reduced visual acuity</td>
<td>Marked limbal hyperaemia (ciliary injection), fixed dilated pupil, corneal oedema, shallow anterior chamber angle, elevated intraocular pressure (40-80mmHg). Sometimes anterior chamber flare and cells</td>
</tr>
<tr>
<td>Anterior uveitis</td>
<td>Sudden onset, usually unilateral (sometimes bilateral in chronic disease), eyeball tenderness, pain, headache, reduced visual acuity, photophobia</td>
<td>Watery discharge, marked ciliary injection, fixed, mid-dilated pupil, anterior chamber flare and cells, keratic precipitates, posterior synechiae. Sometimes raised intraocular pressure, corneal oedema, and poor pupil reactions</td>
</tr>
<tr>
<td>Keratitis (corneal inflammation)</td>
<td>Many forms of keratitis (including bacterial and viral causes), but usually unilateral, causing pain, photophobia and reduced visual acuity</td>
<td>Vary depending on the cause, but characterised by corneal lesions which may be epithelial, stromal, or both</td>
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of ocular infections in the UK that can be supplied by entry-level optometrists include chloramphenicol and fusidic acid. Chloramphenicol is a broad-spectrum bacteriostatic antimicrobial agent with action against most gram-positive and gram-negative bacteria, and is considered the first line antibiotic of choice for superficial ocular infections, such as bacterial conjunctivitis. The bacteriostatic mechanism of chloramphenicol is based upon preventing protein synthesis within the bacteria by interfering directly with substrate binding, rather than killing the bacteria – specifically, it binds to the 50s bacterial ribosomal subunit which inhibits peptidyl transferase from elongating protein chains, thus preventing peptide bond formation. Chloramphenicol is contraindicated in patients with blood dyscrasia (blood disorders affecting red blood cells or platelets) and those with a family history of blood dyscrasia, owing to a rare but serious side effect, aplastic anaemia, which may develop weeks or months after treatment has stopped. The greatest risk is found in those taking oral formulations, with the lowest risk observed in those using topical ocular therapy due to reduced systemic absorption. Pregnant and breastfeeding women should not be prescribed chloramphenicol owing to possible risk of grey baby syndrome with oral administration in the third trimester (newborns cannot metabolise chloramphenicol as their livers are not fully developed, such that the accumulation may cause hypotension and cyanosis) and risk of bone marrow toxicity, although the risk is low and has not been observed with topical ocular administration.

However, it is also contraindicated in patients with previous episodes of myelosuppression (bone marrow suppression), those on myelotoxic (bone marrow suppressive) drugs (typically used in chemotherapy), or patients with a history of allergic reaction to chloramphenicol. Adverse events are minor, with transient stinging and burning sensation possible with topical ocular administration. The different preparations and dosage of chloramphenicol are shown in Table 2.

For instances where chloramphenicol is contraindicated, or for patients with a preference for twice-daily dosage, fusidic acid is a viable alternative with comparable efficacy. Fusidic acid is also a bacteriostatic antimicrobial, preventing protein synthesis by halting the
transformation of elongation factor G (which normally facilitates elongation of protein chains during translation of messenger RNA by the ribosome) from the ribosome. It is effective mainly on gram-positive bacteria, such as *Streptococcus* and *Staphylococcus* species. Transient side effects of fusidic acid include stinging, burning and blurring. As fusidic acid only requires twice-daily dosing, this can be beneficial in children and the elderly who may require help with applying the eye drops. Fusidic acid is available as a prescription only medicine in the form of 1% concentration gel (carbomer vehicle) called Fucithalmic (see Table 2).

Other topical antibiotics, suitable for the treatment of superficial ocular bacterial infections in the UK include: the quinolones ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin; the aminoglycosides, gentamicin and tobramycin; and the macrolide, azithromycin. These drugs are not considered first-line agents, but may be used in cases that are resistant to conventional treatment. However, these are only available to optometrists with additional supply (AS) and independent prescribing (IP) qualifications. Therefore, communication with the patient’s GP should be established for entry-level optometrists to co-manage the patient in such instances.

In cases where signs and symptoms last longer than three weeks, infective conjunctivitis is considered to be persistent or chronic. Management of these patients includes the continuation of self-care, described earlier, but should be examined again to refine or reassess the diagnosis. Importantly, conjunctival swabs should be taken for bacteria and chlamydia; therefore, the patient should be referred to an ophthalmologist for further investigation. While awaiting results, a broad-spectrum antibiotic should be prescribed (either initiate chloramphenicol eye drops where appropriate or select another antibiotic listed above if chloramphenicol treatment was ineffective). If bacterial cultures are positive, an antibiotic should be prescribed as directed by sensitivity results. If the patient’s symptoms last less than three weeks and a negative result is obtained, viral conjunctivitis was likely to have been the cause. If symptoms persist for more than three weeks, negative results do not preclude bacterial or chlamydial infection and, therefore, tests should be repeated.

**Chlamydial conjunctivitis**

Chlamydial conjunctivitis, also known as adult inclusion conjunctivitis, is caused by the bacterial microorganism *Chlamydia trachomatis* and typically affects young, sexually active adults with genital chlamydial infection. The genital infection may be asymptomatic, but one in 300 develop chlamydial conjunctivitis. Signs and symptoms may be unilateral or bilateral, and cases often present as persistent conjunctivitis (two or more weeks duration) or those unresponsive to previous topical antibiotic therapy. Signs include eyelid oedema, which may be accompanied with ptosis, mucopurulent discharge, conjunctival oedema and injection, large follicles in upper and/or lower fornix, corneal epitheliopathy (usually superior), corneal subepithelial and or marginal infiltrates, and superior pannus formation. Other signs may include pre-auricular lymph node swelling and limbal and/or bulbar conjunctival follicles.

The differential diagnosis of chlamydial conjunctivitis includes other causes of conjunctivitis and acute red eye as described earlier. Patients with suspected chlamydial conjunctivitis and those presenting with persistent conjunctivitis, unresponsive to antibiotic therapy, should be advised of self-care measures and referred urgently to an ophthalmologist for management. Conjunctival swabs should be taken to determine the causative microorganism and if a positive chlamydia culture is obtained, the patient should also be tested at a genitourinary clinic to exclude any other sexually transmitted disease. Management involves systemic oral antibiotic therapy to treat the underlying infection using tetracyclines such as doxycycline or macrolides such as azithromycin and erythromycin.

**Neonatal conjunctivitis**

Due to a lack of immunity and local lymphoid tissue, the neonatal eye is particularly vulnerable to infection, which may spread and cause life-threatening complications. The most common cause of neonatal conjunctivitis (ophthalmia neonatorum) is chlamydia (6.9 cases per 100,000 live births) and can result in a rapidly progressing, severe eye infection that is associated with pneumonia. Less commonly, gonorrhoea may also cause neonatal conjunctivitis (3.7 cases per 100,000 live births). In both cases, infection is passed to the infant from the mother in the birth canal as result of sexually transmitted disease. Occurring within the first 30 days of life, signs are often

<table>
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<tr>
<th>Medication</th>
<th>Formulation</th>
<th>Dosage</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>Chloramphenicol (POM)</td>
<td>0.5% eye drops 5mL (Chloromycetin, Mercuri) or 10mL (non-proprietary); also available in single use preservative free form (Minims, Bausch &amp; Lomb)</td>
<td>One drop every two to four hours, reduce frequency as infection improves to ‘four times’ daily, continue 48 hours after resolution</td>
<td>Personal or family history of blood dyscrasia, myelosuppression, concurrent use of myelotoxic drugs, history of allergic or toxic reaction to chloramphenicol or its excipients</td>
</tr>
<tr>
<td></td>
<td>1% eye ointment 4 g (non-proprietary)</td>
<td>Apply three to four times a day. If eye drops also prescribed, apply only at night</td>
<td>As above</td>
</tr>
<tr>
<td>Fusidic acid (POM)</td>
<td>1% eye gel 5g (Fucithalmic, LEO)</td>
<td>Apply two times a day, continue 48 hours after resolution</td>
<td>History of allergic or toxic response to fusidic acid or its excipients</td>
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Table 2 Topical formulations of chloramphenicol and fusidic acid available for the treatment of ocular bacterial infections in the UK
bilateral and include eyelid swelling, profuse mucopurulent discharge, conjunctival injection and oedema, corneal epitheliopathy, and can result in corneal ulceration or even perforation (particularly in gonorrhoeal infection), if not treated promptly.46 In chlamydial infection, follicles are absent in neonates (unlike in adults) as lymphoid tissue has not yet fully developed.46 Less common causes of neonatal conjunctivitis include viruses and other bacteria. Although infants less than 28 days old are unlikely to be observed in optometric practice, those with signs suggestive of conjunctivitis of any type must be referred urgently for management by an ophthalmologist due to sight and life threatening potential.46,48,49 Management is guided by bacterial culture, staining results, and laboratory tests: systemic penicillin or a cephalosporin is used for gonorrhoeal infection; systemic aciclovir for herpes (virus) infection.46,47,49 Systematic erythromycin for chlamydial infection; and systemic aciclovir for herpes (virus) infection.46,47,49

Simple sticky eye in the absence of conjunctival inflammation does not require urgent referral – the purulent discharge observed is often the result of poor drainage from the eye as the nasolacrimal ducts may not be fully formed (congenital nasolacrimal duct obstruction), in which case there maybe spontaneous resolution within the first 12 months.50-53

Viral conjunctivitis
Viral conjunctivitis is the most common form of acute infective conjunctivitis, typically caused by adenovirus, of which there are over 30 serotypes, and is highly contagious.54-56 Predisposing risk factors include recent history of cold or upper respiratory tract infection, low hygiene standards, contact with infected individuals in crowded environments, and transmission of virus from hands or contact instruments (for example a tonometer prism).57,58

Symptoms include acute onset, often bilateral, with discomfort, burning, grittiness and the eyelids may be stuck together in the morning. Signs may include watery discharge, diffuse conjunctival hyperaemia, follicles on the palpebral conjunctiva, and pre-auricular lymphadenopathy (tenderness and swelling).54,58 Less common signs include pin-point (petechial) sub-conjunctival haemorrhages, and, in severe cases, pseudomembrane formation, representing coagulated exudate that is loosely adhered to the palpebral conjunctiva.54 Corneal involvement may be observed in some cases, where diffuse punctate epithelial lesions are present within the first two weeks, followed by sub-epithelial lesions which can persist for several months.54,61 Again, differential diagnosis includes other forms of conjunctivitis and acute red eye (see Table 1). Given that viral conjunctivitis is highly contagious, hands should be washed carefully (and examination gloves worn if available) before and after examination of the eyes, with non-contact instruments used where possible. Viral conjunctivitis is a self-limiting condition, which usually resolves within a few weeks. As discussed earlier, studies have shown that most cases of infective conjunctivitis (both bacterial and viral) resolve within seven days, even without treatment.13,14 Further, current topical anti-viral agents are ineffective against adenovirus, with antibacterial agents also having no effect.15 Thus, patients should be advised of self-care advice – the use of cold compresses and cooled artificial tears may also provide symptomatic relief.16 Patients should be monitored to check for the development of corneal lesions (keratitis) and pseudomembrane formation, in which case they should be referred urgently for ophthalmological assessment. Here, conjunctival swabs may be taken to identify the causative virus and rule out other infective causes of conjunctivitis, and in some cases, topical steroids may be prescribed.59,60 Pseudomembranes can be removed by debriding them from the palpebral conjunctiva using a sterile, wet cotton bud or forceps, after instillation of topical anaesthetic.60

Conclusion
Infectious conjunctivitis is relatively common, but is usually a self-limiting condition in which the patient should be advised to use artificial tears and lid hygiene measures. If the condition lasts for more than two weeks, pharmaceutical treatment is warranted. Viral cases are highly contagious so patient and practitioner hygiene is imperative. Patients with suspected chlamydial conjunctivitis, neonatal conjunctivitis and those presenting with persistent conjunctivitis, unresponsive to antibiotic therapy, should be referred urgently to an ophthalmologist for management.