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Continuing professional development

Conjunctivitis and chloramphenicol

At last there will be an effective over-the-counter treatment for acute bacterial eye infections. Chloramphenicol eye drops were licensed for OTC sale this week and OTC packs are to become available in the next few months. In this article, **Marvyn Elton** looks at what pharmacists can now do for people with conjunctivitis

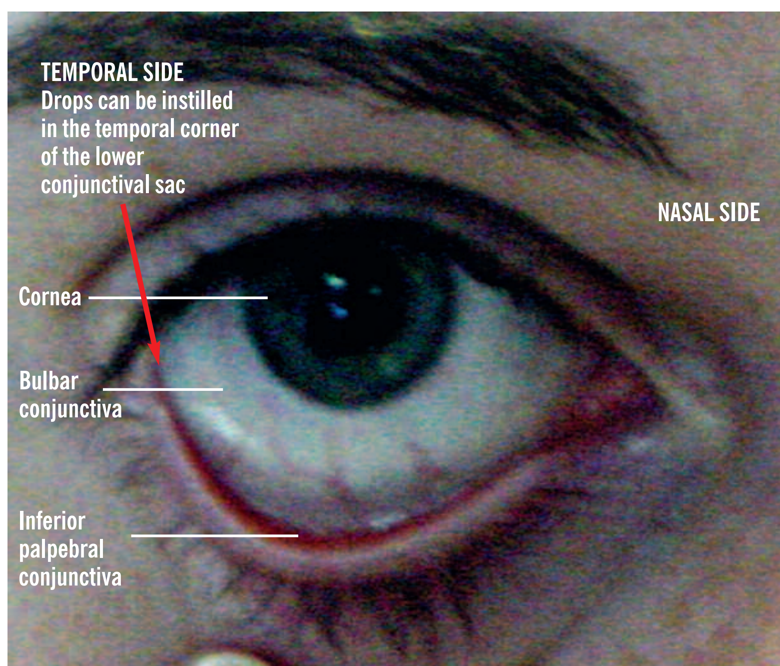
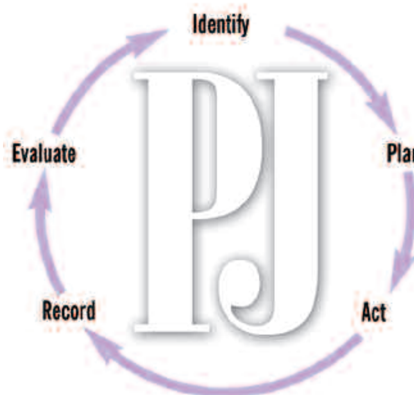


Figure 1: Structure of the conjunctiva



Identify knowledge gaps

1. What is the age restriction for OTC chloramphenicol?
2. What are the symptoms of bacterial conjunctivitis?
3. How safe are chloramphenicol drops?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "Appropriate management of common symptoms" (see appendix 4 of "Plan and record").

The conjunctiva is a highly vascularised mucous membrane. It covers the white of the eye (the sclera) and the inner surfaces of the eyelids (see Figure 1). The conjunctiva protects the sclera and decreases friction when we blink.

Conjunctivitis

Conjunctivitis means inflammation of the conjunctiva. There are four main types of conjunctivitis: bacterial, adenoviral, allergic and chlamydial. It is also possible for a foreign body on the conjunctiva to cause conjunctivitis. Conjunctivitis may be accompanied by soreness or discomfort, but the presence of pain is a sign that something else is wrong.

Bacterial conjunctivitis Bacterial conjunctivitis is more common in infants and children than in adults. In adults, 55 per cent of bacterial conjunctivitis is caused by *Staphylococcus aureus*, 20 per cent by *Streptococcus pneumoniae*, 10 per cent by *Moraxella* spp, 5 per cent by *Haemophilus influenzae* and 5 per cent by *Pseudomonas aeruginosa*. Staphylococcus and streptococcus are Gram positive bacteria, haemophilus and pseudomonas are Gram negative bacteria and moraxella is Gram variable. In infants and children, the most common bacteria causing conjunctivitis are *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Haemophilus influenzae*.

There are four main types of conjunctivitis: bacterial, adenoviral, allergic and chlamydial

In bacterial conjunctivitis, the eye is usually red because blood vessels dilate, and there is nearly always a yellow purulent discharge. So, a useful question to ask the patient (or child's parent) is: When you (or your child) woke up, were the eyelashes stuck together with a yellow discharge and did you have to wipe this away? If the answer is "yes", then the patient nearly always has a bacterial conjunctivitis.

Bacterial conjunctivitis is usually self-limiting — it takes seven to 10 days to resolve. However, most patients (or parents) will want immediate treatment and an antibiotic preparation could be prescribed or sold. The patient should be told to take care not to touch the infected eye and then touch the unaffected eye because this could transfer the infection. Eye make up could also be contaminated and should be replaced.

Adenoviral conjunctivitis Adenoviral conjunctivitis is more common in adults than in children. Adenoviruses are also implicated in causing the common cold (rhinoviruses are the main cause). Ten of the 31 serotypes of adenovirus have been implicated in causing conjunctivitis, with types 8 and 19 being the most frequent cause.[1]

Panel 1: Chloramphenicol eye drops

Who to refer If a patient comes into the pharmacy with a red eye, the pharmacist can ask the appropriate questions to determine if conjunctivitis is present and, if so, which type. If a bacterial or adenoviral cause is suspected, then chloramphenicol eye drops can be recommended. If the symptoms do not improve within two days, the patient should be referred to an optometrist or doctor. The Royal Pharmaceutical Society's Practice Guidance on OTC chloramphenicol eye drops lists other circumstances in which the patient should be referred. These include:

- Copious purulent discharge that reaccumulates after being wiped away
- Affected vision or pain in the eye
- Patients with glaucoma or dry eye syndrome or who have had eye surgery or laser treatment in the past six months

Contact lens wearers are prone to eye infections. Those with conjunctivitis should be referred to a optometrist of GP. In some cases, the practitioner may advise the patient to return to the pharmacy to purchase chloramphenicol. Contact lenses should not be worn during an eye infection (because bacteria can survive on lenses and reinfect the eye) or if eye drops are used. Soft lenses should not be worn for 24 hours after the course of chloramphenicol drops is complete.

Efficacy Chloramphenicol eye drops were introduced in 1948. Chloramphenicol is a broad spectrum antibiotic, active against Gram positive and Gram negative bacteria. It is bacteriostatic and prevents bacteria from reproducing by selectively inhibiting protein synthesis by bacterial ribosomes.

Chloramphenicol eye drops will be effective against nearly all cases of acute bacterial conjunctivitis in adults and children who present in the pharmacy. It is the gold standard against which new antibiotic eye drops are compared. There are few reports of bacterial resistance and the OTC sale of chloramphenicol eye drops from pharmacies is unlikely to promote resistance — studies still indicate high susceptibility rates despite decades of use.

Chloramphenicol eye drops are not, however, active against chlamydia or *Pseudomonas aeruginosa*. *P aeruginosa* is the worst type of bacterium to infect the eye. It is a common cause of a bacterial corneal ulcer in people who wear soft contact lenses. The eye will commonly be painful. If untreated, the infection can cause the eye to fill with pus within 24 to 48 hours; a condition called endophthalmitis. The eye can be blinded permanently. If the infection spreads, in some cases death can occur. *P aeruginosa* is treated with aminoglycoside antibiotics (eg, gentamicin eye drops are instilled hourly and sometimes gentamicin is used systemically) and requires hospital admission.

Dosage Although GPs commonly prescribe chloramphenicol eye drops for adults, children and infants at a dose of one drop four times a day, the drops can be used more frequently. The dosage for the OTC product is one drop every two hours for the first 48 hours, then one drop every four hours for a further three days. Patients can be advised that doses can be missed in order to sleep fully.

Storage As all pharmacists are aware, in a pharmacy, chloramphenicol eye drops must be stored upright in a refrigerator, set between 2 and 8C. It is best practice to keep the eye drops in the refrigerator during use, but this may be impractical for patients instilling the drops every two hours. The drops are stable for four months at a temperature not exceeding 25C.

Once opened, the refrigerated shelf-life is 28 days. However, the usual course of treatment OTC is five days and OTC products will be labelled "discard after five days".

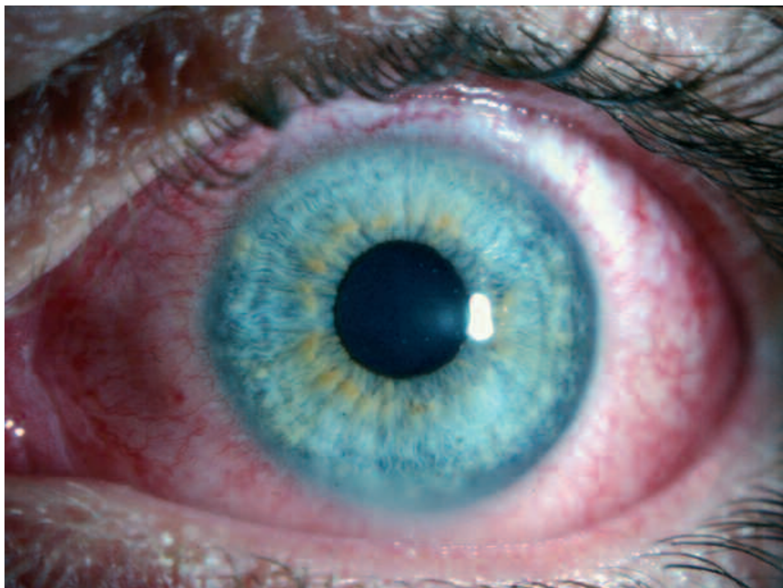
Safety It is, theoretically, possible for topical chloramphenicol to be absorbed systemically via conjunctival blood vessels. Chloramphenicol penetrates the cornea to enter the aqueous fluid and this drains from the eye via the canal of Schlemm. This canal runs around the eyeball between the cornea (the transparent front of the eye) and the sclera. Most of the aqueous fluid passes from the canal of Schlemm into aqueous veins, which drain into the conjunctival veins. In addition, a proportion of the eye drop can drain from the eye via the nasolacrimal duct into the nasopharynx (users can sometimes taste the eye drop after it has been instilled) and then into the gastrointestinal tract.

The OTC product should not be recommended to pregnant or breast feeding women or for children under two years.

Adenoviral conjunctivitis usually presents as a red eye with watery discharge and a gritty feeling. The eyelid may also be swollen. Photophobia is possible and in such cases, the patient should be referred to a GP. Symptoms of a cold can be present. To distinguish a bacterial conjunctivitis from an adenoviral conjunctivitis, the patient can be asked: Was there a yellow discharge or a watery discharge? If there is a watery discharge, the patient can be asked if he has a cold or has had a cold recently.

Adenoviral conjunctivitis will usually resolve spontaneously within two weeks and no treatment is necessary. Chloramphenicol does, however, have some anti-adenoviral activity. Over-the-counter chloramphenicol eye drops are indicated for treating acute bacterial conjunctivitis, but it is acceptable to recommend OTC chloramphenicol for adenoviral conjunctivitis.

Again, the patient should be advised to take care not to transfer the infection to an unaffected eye. In addition, care should be taken not to transfer the infection to other people (eg, hand towels should not be shared).



Marvyn Elton

Conjunctivitis presents as a red eye

Allergic conjunctivitis Allergic conjunctivitis is common in spring and summer. If it occurs in the hay fever season, it is called sea-

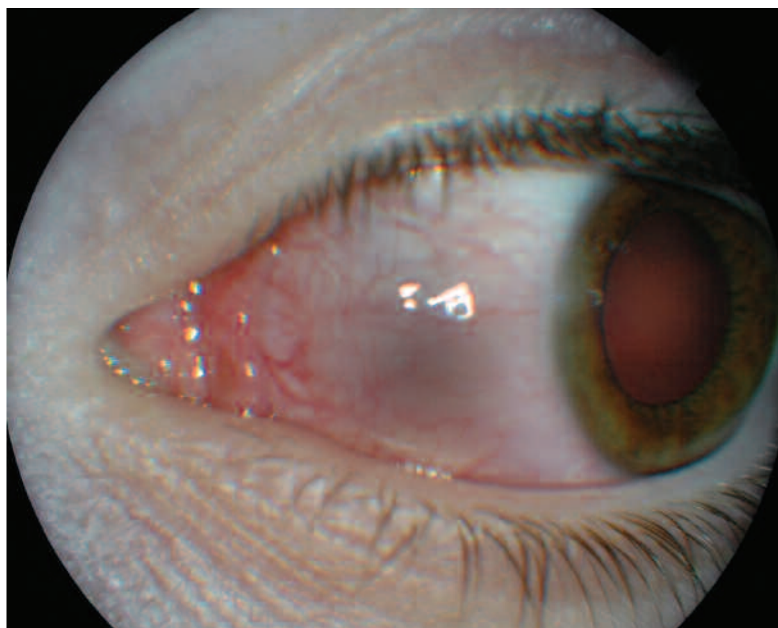
sonal allergic conjunctivitis (hay fever eyes) and if it occurs all year round, it is called perennial allergic conjunctivitis. Perennial allergic conjunctivitis is commonly caused by animal dander and the patient can be asked if he or she has been in contact with animals. Other causes of allergy include the use of eye drops containing benzalkonium chloride.

Usually, both eyes are affected, but if only one eye is affected, this would not rule out allergic conjunctivitis. There will be what is commonly called a "spring pink" eye rather than a red eye. An itchy eye is a typical indicator, so the patient can be asked if he or she has itchy eye(s). There will be a watery discharge and sometimes there may be a ballooning out of the conjunctiva (chemosis). The eyelid can be swollen.

Patients should be advised to try to avoid the allergen. For example, if the allergic conjunctivitis is caused by grass, the patient should avoid grassy areas. Sodium cromoglicate (a mast cell stabiliser) 2 per cent or antihistamine (eg, antazoline or azelastine) eye drops can be used. Sodium cromoglicate can be used prophylactically, if necessary, throughout the hay fever season. Antazoline sulphate 0.5 per cent can be used in children over five years and azelastine 0.05 per cent eye drops can be sold for use in children over 12 years.

Chlamydial conjunctivitis Chlamydial conjunctivitis is less common than the other three types of conjunctivitis. Chlamydia are mycoplasms — midway between a virus and a bacterium. Unlike bacteria, they do not have a cell wall. Chlamydial infections are more common in younger adults than older ones. If chlamydial conjunctivitis is present, a systemic infection will also usually be present.

Neonatal conjunctivitis is a conjunctival inflammation that occurs during the first month of life and chlamydia is the most common cause. There is approximately a 50 per cent risk of a baby acquiring the infection during birth if the mother has an active chlamydial infection. Chlamydial conjunctivitis should be suspected in any infant younger than 30 days with conjunctivitis. Presentation is typically between five and 14 days after birth.



Marvyn Elton

Chemosis (ballooning out of the conjunctiva) may be seen in allergic and chlamydial conjunctivitis

The eye drops should be used at a dose of one drop every two hours for 48 hours, then one drop every four hours

In chlamydial conjunctivitis the eye will be red and, often, the redness is a darker shade compared with bacterial, adenoviral or allergic conjunctivitis. Discharge can vary from watery to mucopurulent in adults and neonates. The eyelid may be swollen and chemosis may be present. Treatment of chlamydial conjunctivitis in neonates is with erythromycin suspension four times a day for two weeks. Treatment in adults is with erythromycin, doxycycline or tetracycline for about six weeks.

If there is a misdiagnosis and chloramphenicol eye drops are used, the eye will not improve. A chlamydial cause must be ruled out because an untreated chlamydial conjunctivitis can cause conjunctival and corneal scarring, which can affect vision.

Panel 2: How to administer eye drops

Instilling one drop four times a day sounds straightforward, but self-administration of eye drops can be tricky. Problems commonly encountered include difficulty aiming the bottle, shaky hands and reflex blinking. There is a risk of either squeezing out too many drops or the drop missing the eye and running down the cheek. If possible, therefore, it is probably best for patients to ask someone else to do it for them.

The patient should tilt his or her head back slightly. The lower eye lid should be pulled down gently and a drop instilled in the temporal corner (the corner of the eye farthest from the nose) of the lower conjunctival sac (see Figure 1, p725). The patient should look towards his or her nose so that he or she cannot see the drop descending. If the drop runs down the face, another drop should be instilled.

If the patient has no one to help and is likely to have difficulty with administration, aids for instilling eye drops, such as Autodrop (Owen Mumford) and Opticare (Cameron Graham Associates) are available. Autodrop claims to:

- Hold the eye open to prevent blinking
- Direct the gaze through a pinhole and away from descending drops
- Ensure accurate placement of drops and less wastage

One aid, Opticare Arthro has extended arms and is designed especially for people with arthritic hands. Opticare and Opticare Arthro are both prescribable on an NHS FP10 prescription.

It is good practice for the person instilling the eye drops to wash and dry his or her hands before and after administration.

Chloramphenicol eye drops

In England, in 2003, one and a half million chloramphenicol eye drop prescription items were dispensed (including single use packs, eg, Minims).[2] Although the eye drops can now be sold over the counter, chloramphenicol ointment remains a prescription-only medicine. The ointment stays in contact with the eye for longer than drops but can blur vision.

Panel 1 gives more information about the drops, including the OTC dose, storage and safety. Rare safety issues include aplastic anaemia and grey baby syndrome.

Aplastic anaemia There have been concerns about topical chloramphenicol and bone marrow depression (aplastic anaemia). These concerns first emerged with the publication of a paper by Rosenthal and Blackman in 1965. In

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Read the Royal Pharmaceutical Society's practice guidance on OTC chloramphenicol eye drops and formulate questions that you can ask to decide if a patient needs to be referred to a GP. The guidance is available on the practice section of the Society's website (www.rpsgb.org/practice) and laminated copies of the guidance will be issued with *The Journal* next week.
2. Cascade the training for OTC chloramphenicol eye drops to your staff.
3. Discuss the POM to P switch of chloramphenicol eye drops with your local optometrist.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

1982, Fraunfelder *et al* published a report concerning a 73-year-old woman who died of aplastic anaemia following a one-month course of chloramphenicol eye drops prescribed after cataract surgery.[3] In fact, this patient was also taking eight other drugs including triamterene and phenacetin (an analgesic), which are also associated with blood dyscrasias. After this publication, prescriptions for topical chloramphenicol in the US fell by 90 per cent in two years, probably due to fears of litigation. In the US, fucithalmic is the first choice for acute infective conjunctivitis.

In 1995, Doona and Walsh, two geriatricians from Dublin, had a letter published in the *BMJ* directly implicating topical chloramphenicol in aplastic anaemia. They advised that British doctors should follow the example in the US and restrict their use of topical chloramphenicol.[4]

The association between systemic chloramphenicol and aplastic anaemia is well founded and thus it is recommended that systemic use of the drug should be reserved for life-threatening infections and that blood counts should be monitored during systemic therapy. However, to date, no one has demonstrated detectable levels of the drug systemically in patients treated with chloramphenicol eye drops. For example, in 1979, Trope *et al* observed five children under the age of nine years. Topical chloramphenicol was administered every two hours to both eyes for five to seven days and systemic absorption was not demonstrated by two sensitive assays.

Although it is highly unlikely that chloramphenicol eye drops can cause aplastic anaemia, the OTC product should not be recommended to patients with a personal or family history of bone marrow depression.

Grey baby syndrome In infants under 30 days old, systemic chloramphenicol can cause an acute failure of blood circulation, known as grey baby syndrome. The lack of clinically significant systemic absorption of the eye drops makes grey baby syndrome highly unlikely with the OTC product, but it should not be recommended for children under two years of age.

Problems instilling eye drops include difficulty aiming the bottle, shaky hands and reflex blinking

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Working with other health care professionals

Three terms are often used when talking about health care professionals who deal with eye health: ophthamologist, optometrist and dispensing optician.

Ophthalmologists Ophthalmologists are medically qualified doctors who specialise in eye conditions. Often they are members of the Royal College of Ophthalmologists. Fellows or members may use the following post nominals: FRCOphth, MRCOphth and DRCOphth. Orthoptists usually work in hospitals with ophthalmologists. They are concerned with diagnosing and treating abnormal ocular motility (eg, arising from injury) and problems relating to vision such as strabismus (squint).

Optometrists Optometrists (also known as an ophthalmic opticians) are qualified to test and examine eyes. They can play a role in diagnosing various conditions, such as glaucoma and diabetes. Generally, optometrists will have read a degree in optometry or equivalent (known as PQE part 1), completed a preregistration year and passed a professional qualifying examination (PQE part 2). Some ophthalmic opticians are members (MCOptom) or fellows (FCOptom) of the College of Optometrists. Registered ophthalmic opticians are exempt from the general rules of the Medicines Act 1968, in that they may sell or supply some medicines provided it is in the course of their professional practice and it is an emergency (although emergency is not defined). These medicines include 0.5 per cent chloramphenicol eye drops and 1 per cent chloramphenicol ointment. A full list is available in "Medicines, ethics and practice". Pharmacists may supply these medicines to registered ophthalmic opticians or patients under their care on presentation of a signed order.

Dispensing optician A dispensing optician fits spectacles and sometimes contact lenses, but does not perform eye tests. There are several routes to becoming a dispensing optician, including taking a two-year full-time course. Dispensing opticians may be designated fellow of the British Dispensing Opticians (FBDO) or the British Optical Association (FBOA).

Dispensing opticians and ophthalmic opticians practising in the UK are regulated by the General Optical Council. All opticians must be registered with the General Optical Council before they may practise in the UK. The register can be accessed at www.optical.org. Optometrists are identified by a registration number that starts with "01-", and dispensing opticians a number that starts with "D-". Unlike pharmacists registered with the Royal Pharmaceutical Society, registered opticians do not use a post nominal to indicate that they are registered with the General Optical Council.