

Oral Medication Guidelines – Lid swelling

Description

Eyelid swelling (oedema) is a non-specific feature of several ocular conditions, including orbital and pre-septal cellulitis, thyroid eye disease, ocular allergy, acute dacryocystitis and acute dacryoadenitis. It may occur in isolation or in combination with other ocular and/or systemic signs. Although not an exhaustive list, this document will outline some conditions of which lid swelling is a feature.

Significance

Causes of lid swelling range from the benign to the potentially sight – or life-threatening. It is important for the optometrist to differentiate between these conditions, treat when appropriate, and refer when required. Some lid swelling presentations will require immediate referral to an ophthalmologist for medical assessment and orbital imaging.

Ocular examination

Ocular examination in patients with lid swelling should include the following:

- comprehensive clinical history with attention to predisposing risk factors (e.g., recent sinus infection, trauma, history of hordeola/chalazia, etc.)
- gross examination of the lids and periorbital region
- visual acuity assessment
- ocular motility assessment
- examination to check for proptosis (exophthalmometry if available)
- pupil testing
- slit-lamp biomicroscopy of the anterior segment
- tonometry
- fundus examination.

Differential diagnoses

1. Ocular allergy (conjunctivitis or contact dermatitis)

Signs of ocular allergy can include mild to moderate lid oedema, often accompanied by chemosis. Ocular allergy can clinically resemble preseptal cellulitis due to the lid swelling and in some cases, differentiating between the two can be difficult (Bethel, 2000). Itching is the hallmark symptom of allergy. Additionally, patients with allergy may have bilateral

involvement, a history of allergic disease, and the absence of pyrexial (fever) symptoms. Optometric management of ocular allergy is covered in detail in the [ODOB's Oral medication guidelines](#) for allergic eye disease.

Ocular allergy rarely requires referral for further evaluation and treatment. Exceptions to this include vernal and atopic keratoconjunctivitis, due to their sight-threatening potential.

2. Acute dacryocystitis

Patients present with a rapid-onset, tender, red, swollen lid at the medial canthus, possibly with an associated abscess. In some cases, there may be significant swelling of the lacrimal sac. The conjunctiva may be injected. Acute dacryocystitis generally occurs secondary to obstruction of the nasolacrimal duct and is associated with preseptal cellulitis (see below) in some cases (Bowling, 2016). If infection is suspected, lacrimal probing and irrigation should not be performed (Penne & the Willis Eye Hospital, 2003).

Orbital cellulitis (see below) should be considered in severe cases (Penne & the Willis Eye Hospital, 2003). In the paediatric population, acute dacryocystitis can progress more rapidly, and if untreated may evolve into a lacrimal abscess, orbital cellulitis, or an orbital abscess (Ali, 2015).

Patients with acute dacryocystitis should be referred for ophthalmological assessment and management. Treatment includes oral antibiotics (for example, Amoxicillin + Clavulanic Acid (for more information on this antibiotic, please see below), and in some cases, IV antibiotic treatment is required (Ali, 2015; Bowling, 2016). Following the resolution of the acute infection, dacryocystorhinostomy is commonly required, and this may reduce the risk of recurrent infection (Bowling, 2016). Since the management of acute dacryocystitis is essentially surgical, the Board does not consider the prescribing of oral antibiotics to be appropriate by optometrists other than in exceptional co-management situations when access to ophthalmological care is compromised. In these circumstances a phone or e-consultation with an ophthalmologist is expected to take place to confirm the most likely diagnosis prior to the prescribing of oral antibiotics.

3. Acute dacryoadenitis

Acute dacryoadenitis, or swelling of the lacrimal gland, may be idiopathic or of infectious origin. Chronic dacryoadenitis can be associated with autoimmune disease or tumour. A thorough review of the causes and treatment of dacryoadenitis is beyond the scope of these guidelines and will be covered only briefly here.

In acute dacryoadenitis, affected patients report rapid onset discomfort in the upper temporal orbital region where the lacrimal gland is situated. On examination, swelling of the lateral superior eyelid gives rise to the characteristic S-shaped ptosis. There is associated eyelid

erythema and palpebral conjunctival injection, and chemosis may be present. The pre-auricular lymph nodes may be enlarged, and patients may have a fever (Bowling, 2016).

Acute dacryoadenitis is frequently idiopathic and can be unilateral or bilateral. Approximately 50% of these patients will have signs of dry eye. Idiopathic dacryoadenitis is not well-understood, although there is evidence of an innate immune response. Patients with suspected idiopathic dacryoadenitis should be referred for ophthalmological assessment. The disease tends to respond to high dose oral corticosteroid treatment, although there is a high recurrence rate (Mombaerts, 2015). Acute-onset infectious dacryoadenitis is commonly caused by viral organisms, including Epstein-Barr virus (most likely), adenovirus, herpes zoster, herpes simplex, rhinovirus or cytomegalovirus (Mombaerts, 2015). Disease resolution occurs over four to six weeks. The benefits of treatment with oral antiviral or anti-inflammatory medication have not been well-established (Mombaerts, 2015).

Less frequently, acute dacryoadenitis can be caused by bacterial organisms, with *staphylococcus aureus* the most common bacterial cause. Dacryoadenitis can develop from an adjacent skin infection, from cellulitis secondary to sinusitis or via haematogenous spread (Mombaerts, 2015). In these cases, there is lacrimal gland swelling and purulent conjunctival discharge. Patients require referral for treatment with broad spectrum systemic, including intravenous (IV) antibiotics. They may also undergo surgical drainage if there is an associated abscess (Mombaerts, 2015).

4. Preseptal cellulitis

Preseptal cellulitis is an infection of the subcutaneous tissues anterior to the orbital septum. The orbital septum is a thin fibrous structure, part of the anterior connective tissue framework, and functions to contain the orbital fat (Lee & Yen, 2011) Preseptal cellulitis does not involve the globe or the orbit; the orbital septum functions, for the most part, as a barrier to the spread of infection from the eyelid into the orbit (Liu *et.al.*, 2006).

Preseptal cellulitis is typically caused by *staphylococcus aureus* or *streptococcus pyogenes* infection, following skin trauma (e.g., insect bites or lacerations), spread from focal ocular or periocular infection (e.g., acute hordeolum, dacryocystitis, conjunctivitis, sinusitis) or spread via the blood from a remote infection (Bowling, 2016; Sanfilippo & Troutbeck, 2003). In children, *haemophilus influenzae* is a common causative organism (although the incidence has declined since the introduction of the Hib vaccine), and patients may report a concurrent upper respiratory tract infection (Lee & Yen, 2011; Lessner & Stern, 1992; Wawless & Martin, 1986). Fungal aetiology needs to be considered in immunocompromised patients. Preseptal cellulitis can occur at any age, but it is most-commonly encountered in children, and is responsible for approximately 2/1,000 paediatric emergency department presentations (Brugha & Abrahamson, 2012; Goldman *et.al.*, 2008; Liu *et.al.*, 2006).

Symptoms of preseptal cellulitis include (Bowling, 2016; Liu *et.al.*, 2006):

- swollen, firm, warm, tender red eyelid (this can be severe), almost always unilateral
- fever
- watery eyes.

Signs of preseptal cellulitis include (Sagir *et.al.*, 2018; Wawless & Martin, 1986):

- hyperaemic swelling of eyelid and periorbital area due to impeded venous flow
- conjunctival injection
- chemosis has been reported in preseptal cellulitis but is not a common finding.

It is imperative to assess visual acuity, ocular motility, colour vision and pupil responses in suspected preseptal cellulitis to aid in the exclusion of possible orbital cellulitis, which is an ophthalmic emergency. It is important to note that in preseptal cellulitis, visual acuity is preserved, ocular motility is normal, pupil reactions are intact, and proptosis is absent. In some cases, a CT scan of the orbit and sinuses may be undertaken to exclude orbital cellulitis (Sanfilippo & Troutbeck, 2003). Although less serious than some other orbital infections, preseptal cellulitis can be associated with severe complications, including abscess formation, meningitis, and cavernous sinus thrombosis. Preseptal cellulitis can progress rapidly to orbital cellulitis. Both pre-septal and orbital cellulitis are more frequently encountered in the paediatric population (Lee & Yen, 2011). In children with prolonged eyelid oedema, secondary amblyopia can occur in the affected eye, so these patients need to be closely monitored (Lee & Yen, 2011).

As preseptal cellulitis can, in some cases, progress to orbital cellulitis, with potential sight- and life-threatening complications, management is not normally undertaken by optometrists in New Zealand, particularly in the case of children, and patients should be referred for ophthalmological assessment and treatment. The exception to this, is in cases with limited access to ophthalmological care. If the patient would need to travel a significant distance to a hospital, the optometrist can, after phone or e-consultation with an ophthalmologist to confirm the most likely diagnosis, initiate appropriate oral antibiotic management in a co-management situation. Because of the risk of serious complications, patients should be monitored regularly for improvement. The optometrist should also liaise closely with the patient's general practitioner.

Medical management of preseptal cellulitis is focused on aggressive antibiotic therapy, with either oral or intravenous agents. It is also important to consider underlying pre-disposing factors such as sinusitis (Lessner & Stern, 1992). There is conflicting opinion on antibiotic regimens for the treatment of preseptal cellulitis (Goldman *et.al.*, 2008): There are no randomised controlled studies that have investigated the optimal antibiotic treatment regimen, and treatment is normally empirical, to cover the common causative organisms (and Gram's stain and culture results) (Lee & Yen, 2011). Local trends in antimicrobial resistance need to be considered.

If the preseptal cellulitis is mild, treatment can normally be undertaken on an outpatient basis with a broad-spectrum antibiotic (Bowling, 2016) Treatment duration is typically 7 to 10 days but is guided by symptom resolution (Lee & Yen, 2011).

In Aotearoa New Zealand, treatment can be with one of several antibiotic agents. The combination agent Augmentin (amoxicillin 500 mg and clavulanic acid 125 mg), is taken 2 – 3 times per day (for 7 to 10 days) for the treatment of preseptal cellulitis. Amoxicillin is a penicillin antibiotic with broad spectrum activity (although it is more effective against Gram-positive than Gram-negative micro-organisms) (Chaudhry *et.al.*, 2007) Clavulanic acid is a β -lactamase inhibitor. It is not effective as an antibiotic when used alone but is used to overcome antibiotic resistance in bacteria that secrete β -lactamase (Kaur *et.al.*, 2011). Patients are expected to show improvement the day following the first dose (Sanfilippo & Troutbeck, 2003).

Adverse effects resulting from the use of Augmentin can include diarrhoea (very common), hepatitis, nausea, vomiting, hypersensitivity reactions, Stevens Johnson syndrome and cholestatic jaundice (more common in patients aged over 65 years). The use of Augmentin is contraindicated in patients with penicillin hypersensitivity and those with drug-associated jaundice or hepatic dysfunction. The risk of acute liver toxicity is greater in patients taking combination therapy (amoxicillin + clavulanic acid) than in patients taking amoxicillin alone.

Amoxicillin can interact with several other medications. For a full list, review the New Zealand Formulary (New Zealand Formulary, 2018). Of note, the coagulation status of patients taking warfarin and either amoxicillin or Augmentin should be monitored due to increased risk of bleeding. Additionally, the incidence of skin rashes is higher in patients who are also taking allopurinol (for gout/kidney disease) and patients taking both medications should be warned of this, although no other action needs to be taken (New Zealand Formulary, 2018). Patients taking Augmentin should be informed about the importance of maintaining adequate hydration, due to the risk of gastrointestinal upset. The World Health Organisation recommends that patients requiring the oral typhoid vaccine should discontinue the antibiotic three days before receiving the live oral vaccine, and re-start three days after, as augmentin can reduce the immune response to the vaccine.

Augmentin is pregnancy category B1 on MIMS Gateway (Bethel, 2000). The safety of Augmentin has not been evaluated, although no harmful effects on the human foetus have been observed, and animal studies have not shown evidence of an increased occurrence of foetal damage.

Another oral antibiotic that can be used in the treatment of preseptal cellulitis is flucloxacillin 500 mg every 6 hours for approximately 7 days. Flucloxacillin is a penicillin antibiotic. Penicillins bind to proteins to interrupt biosynthesis of cell walls, resulting in cell lysis and death.

Common flucloxacillin-associated adverse effects include nausea, vomiting and diarrhoea. Less common adverse effects include rash, urticaria (hives) or purpura (blood spots on the skin).

There are a number of other very rare potential adverse effects reported on NZ Formulary. Flucloxacillin should not be used in patients with penicillin hypersensitivity or those with hepatic disorders associated with the drug.

As with other antibiotics, flucloxacillin can interact with several other medications. For a full list, refer to the NZ Formulary. The recommendations for patients taking flucloxacillin and receiving the oral typhoid vaccine are the same as those given above for augmentin.

Flucloxacillin is given as pregnancy category B1 on the associated Medsafe datasheet. As with other penicillins, it is generally considered to be safe in pregnancy. There is limited information on the human use of flucloxacillin during pregnancy. In animal studies there have been no teratogenic effects observed.

For patients allergic to penicillins, cefalexin can be used to treat preseptal cellulitis. Cefalexin is a cephalosporin antibiotic that interrupts cell wall biosynthesis resulting in cell lysis and bacterial death. Dosing for cefalexin is 500 mg every 6 hours for up to 7 days.

Cefalexin is contraindicated in patients with cephalosporin hypersensitivity, and prescribers should lower dose in patients with significant renal impairment. The most common adverse effects of cefalexin are gastrointestinal upset (nausea, vomiting, diarrhoea, abdominal discomfort) and headache. Cases of Stevens-Johnson syndrome have been reported. Less frequently reported adverse effects are available on the NZ Formulary.

The recommendations for patients taking cefalexin and receiving the oral typhoid vaccine are the same as those given above for Augmentin and flucloxacillin. On the Medsafe data sheet for Cefalexin (accessed 2021), this medication is classified as pregnancy category A (by the Australian Drug Evaluation Committee), indicating that the drug is considered safe in pregnancy. However, as with any medication used during pregnancy, the benefits should be considered to outweigh potential risks.

Patients with immune compromise (for example, individuals undergoing chemotherapy treatment for cancer) may require hospitalisation for treatment of preseptal cellulitis, with one study reporting a mean hospital stay of 5 days (range 0 to 11 days) for 21 immune-compromised patients with preseptal cellulitis (Sagir *et.al.*, 2018). Other patients likely to require hospitalisation for treatment include children and patients with severe infection or systemic toxicity (Lee & Yen, 2011).

Patients with severe infection, or those who fail to respond to oral treatment, may require the use of IV antibiotics. IV antibiotic treatment can include penicillins, cephalosporins, fluoroquinolones, aminoglycosides or other antibiotic agents (Liu, *et.al.*, 2006).

The Starship Children's Hospital Clinical Guidelines (Starship Childrens Hospital, 2018) recommend IV antibiotics for most children with preseptal cellulitis (the exception being mild cases of confirmed pre-septal cellulitis). The antibiotics most used are:

- Amoxicillin + clavulanic acid 30 mg/kg every 8 hours
- Cefuroxime 30 mg/kg, every 8 hours.

Once there is symptomatic improvement, the patient commences a week-long course of oral antibiotic therapy with either:

- Amoxicillin + clavulanic acid (30 mg/kg with maximum 625 mg total/dose), three times per day
- Cephalexin 20 mg/kg twice a day (maximum 500 mg/dose).

The Board considers the management of paediatric preseptal cellulitis to be outside the scope of optometrists, other than in exceptional co-management situations. Children with suspected preseptal cellulitis should be referred urgently for paediatric ophthalmological care.

Surgical management is not generally required for patients with preseptal cellulitis, with the exceptions being cases with an associated foreign body, or eyelid abscess requiring drainage and debridement (Lee & Yen, 2011).

5. Orbital cellulitis

Orbital cellulitis is a relatively uncommon (less common than preseptal cellulitis (Chaudhry *et.al.*, 2008), potentially sight and life-threatening infection of the soft tissues posterior to the orbital septum. Although it can occur at any age, it is most frequently encountered in children (peak incidence in the 0-to-15-year age group) (Chaudhry *et.al.*, 2007). Common causative organisms include *streptococcus pneumoniae*, *staphylococcus aureus*, *streptococcus pyogenes* and *haemophilus influenzae* (Bowling, 2016). The infection typically originates in the paranasal sinuses but can also be the result of spread from preseptal cellulitis, dacryocystitis, skin or dental infections, and trauma (Chaudhry *et.al.*, 2007).

Symptoms of orbital cellulitis include:

- progressive painful swelling around the eye, with exacerbation of pain on eye movement
- reduced vision
- double vision
- history of sinus infection or recent upper respiratory tract infection.

Signs of orbital cellulitis include:

- periorcular and conjunctival injection and oedema
- proptosis
- ophthalmoplegia
- reduced visual acuity
- impaired colour vision
- relative afferent pupillary defect
- choroidal folds and optic disc swelling.

It is important for the optometrist to differentiate between preseptal and orbital cellulitis. It is imperative to assess visual acuity, colour vision, pupil responses as these may be impaired in orbital cellulitis due to optic neuropathy. Proptosis is common in orbital cellulitis, but it is important to discriminate between true proptosis and lid swelling. Sight threatening complications can include optic neuropathy, exposure keratopathy, endophthalmitis and central vascular occlusion. Life threatening sequelae of orbital cellulitis include encephal meningitis, cavernous sinus thrombosis, sepsis, and intracranial abscess formation (Bowling, 2016).

Orbital cellulitis is an ophthalmic emergency, requiring immediate assessment (including orbital imaging) and treatment. Patients with orbital cellulitis are admitted to hospital for IV antibiotics, with supplementary oral antibiotic treatment for anaerobic microbes. After improvement on IV antibiotic treatment, the patient receives an oral antibiotic course. Optic nerve function is closely monitored during treatment. Surgery is performed if there is an orbital abscess, lack of response to antibiotics or severe optic nerve compression (Bowling, 2016).

6. Thyroid eye disease (Graves' ophthalmopathy)

Thyroid eye disease is also known as thyroid-associated orbitopathy and Graves' ophthalmopathy. Although Graves' ophthalmopathy most frequently occurs in patients with Graves' hyperthyroidism, it can also occur in euthyroid individuals, or hypothyroid patients with a history of Hashimoto's thyroiditis (Wiersinga & Bartalena, 2002). It is estimated that the incidence of Graves' disease (not ophthalmopathy specifically) is approximately 13.9 per 100,000 in the United States, with women more frequently affected (Jacobsen *et.al.*, 1997). Almost half of patients with Graves' hyperthyroidism will report symptoms of Graves' ophthalmopathy (Bahn, 2010).

Systemic signs and symptoms of hyperthyroidism include weight loss, heat intolerance, palpitations, and palmar erythema. In the initial congestive stage, patients can present with painful, red eyes, and associated lid and periorbital swelling (Bowling, 2016).

Symptoms of Graves' ophthalmopathy include (Penne & the Willis Eye Hospital, 2003):

- swollen eyelids
- double vision
- red eye
- reduced vision.

Signs of Graves' ophthalmopathy include (Penne & the Willis Eye Hospital, 2003):

- periorbital oedema
- chemosis
- proptosis
- lid retraction
- lid lag on down gaze

- corneal exposure staining (due to proptosis and lid retraction)
- ocular motility restriction
- relative afferent pupillary defect
- optic neuropathy
- impaired colour vision
- visual field defects
- in Graves' ophthalmopathy, there is enlargement of the extraocular muscles. This can be visualised with CT imaging. The inferior rectus is most frequently involved, followed by the medial rectus.

It is essential for the optometrist to rule out optic nerve involvement in patients with Graves' ophthalmopathy. Corneal exposure may also be sight threatening in some patients. Approximately 3 to 5% of patients with Graves' ophthalmopathy have severe disease, with painful inflammation and sight-threatening compressive optic neuropathy or corneal exposure (Wiersinga & Bartalena, 2002). Patients are more likely to develop severe disease if they have a history of smoking cigarettes (Bahn, 2010).

Patients with suspected Graves' ophthalmopathy need to be referred for medical management (if not already diagnosed). If there are sight-threatening complications of the disease, this warrants urgent ophthalmological referral for management.

Treatment of Graves' ophthalmopathy depends on disease severity. In many cases a multi-disciplinary team will be required, including endocrinologists, general practitioners, ophthalmologists, and optometrists. In mild cases lubricant drops can be used for corneal exposure, and cold compresses for lid oedema. During sleep, the head can be elevated to reduce periorbital oedema. Eyelid taping can help to alleviate mild exposure keratopathy. In moderate to severe disease, the mainstay of treatment is systemic corticosteroids (for example, IV followed by a course of oral treatment). If the disease does not respond to corticosteroid treatment, decompression of the orbital wall can be considered to increase the volume of the orbit. Once the active inflammatory phase has remitted, surgery for strabismus or eyelid retraction can be considered (Penne & the Willis eye Hospital, 2003).

Informed consent

When prescribing medication, as with all healthcare interventions, the optometrist is responsible for ensuring that the patient has been advised of the possible risks and benefits associated with the proposed prescription medication, in order that the patient can make an informed decision and provide consent to the treatment plan.

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