

Greenlane Clini	cal Centre, Auc	kland, NZ
	2003	2025

	2005	2025
Ophthalmologists	19 P/T	50 P/T
Optometrists	1 P/T	9 P/T
Orthoptists	2 F/T	4 F/T
OPC / year	52,000	118,000
Acute consults / year	9,000	17,5000
Optom clinics	Retinal screening, paeds, CL	DRS, paeds, CLs, LV, Glaucoma, Corneal, Medical Retina, EEC, virtual Med Ret, Virtual Glaucoma

### Learning objectives:

- Present some cases of ophthalmic conditions that require oral medications to optimally treat
- Review the differential diagnoses of these conditions
- Review the current evidence for oral medication treatments
- Consider the contra-indications / considerations of use of the oral medications
- Discuss red flags when reviewing patients with these conditions
- Discuss the level of optometric management in these cases



### 1. Oral antibiotics • Since 2014, the vast majority of prescriptions (n = 2,568) were for antibiotics, which comprised 60 per cent of all oral medications prescribed. • The most prevalent of these was the macrolide antibiotic, azithromycin, which alone represented 39 per cent of all prescribed oral medications. • Other prescribed antibiotics included tetracyclines, such as doxycycline (18 per cent) and minocycline (1.0 per cent), and the penicillin-group antibiotic, amoxicillin (1.8 per cent). • From following up with individual practitioners, it is known that a small number of these antibiotics were prescribed for the management of infectious ocular conditions such as preseptal cellulitis and hordeolum, but the majority of azithromycin and tetracycline was prescribed for the management of meibomian gland dysfunction.









The presence of fragile epithelium indicates a higher risk of recurrence and that more intensive treatment is required to reduce this risk. In cases of RCES, the contralateral eye should be carefully assessed for the presence of a basement membrane dystrophy, such as MDF dystrophy.

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### Which oral antibiotic to use?

- doxycycline 100 mg PO mane x 6/52 (Per Os)
- azithromycin 250 mg tablets. PO. 2 tablets stat then 1 tablet mane x 3/7
- Both have been established as useful and effective treatments in the management of MGD (Foulks et al. 2013).
- One group recently compared pulsed oral Azithromycin (prescribed at 1g per week for 3 weeks) to oral doxycycline (prescribed at 100 mg BID for 6 weeks) for effectiveness and safety (Upaphong, Tangmonkongvoragul, and Phinyo 2023).
- The effectiveness of both drugs in the treatment of the MGD was equivalent within their predetermined level
- However, there was a significant difference in the rates of gastro-intestinal adverse events, being 4.4% in the azithromycin group compared to 15.9% in the doxycycline group (P = 0.03).
- Similar rates of gastro-intestinal adverse events (6% vs 24%, P < 0.005) were found in another study which utilised different dosing regimens (4g total in 30 days of doxycycline and 1.25 g total of azithromycin in 5 days) (De Benedetti and Vaiano 2019).
- Given the significant difference in adverse event rates of the two drugs, azithromycin should be preferred over doxycycline in the treatment of MGD. The shorter treatment duration and (often) less frequent dosing of azithromycin would also be expected to provide better compliance rates.

### Mechanism of action in MGD

- Doxycycline is a tetracycline antibiotic
- Azithromycin a macrolide antibiotic
- Both drugs work in MGD to lower the levels of pro-inflammatory exotoxin induced cytokines and metalloproteins (including IL-8, IL-1, MMP-1 and MMP-9) that are present in the meibomian gland and tear film in MGD.

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### Contra-indications to doxycycline include known hypersensitivity to any of the tetracycline class of antibiotics. As tetracyclines are deposited in growing bone and teeth (which can result in discolouration of teeth and rarely, dental hypoplasia), their use should be avoided in pregnant women and children under 12 years of age. Due to the 4-to-6-week course that is required to re-modulate the meibomian gland secretions, gastro-intestinal upset (nausea or diarrhoea) may be experienced due to alteration of the normal gut microbiome. Women may also develop thrush due to alteration of the vaginal microbiome by the antibiotic and rates of this side-effect are likely under-reported. Rare cases of benign intracranial hypertension have also been reported after taking tetracyclines. Take in the morning with a big glass of water, never last thing at night. May cause photo-sensitisation, avoid strong sunlight. There is no current high-level evidence that the higher dosage of 200 mg *mane* or 100 mg BD is more effective than lower doses but do come with a risk of higher rates of side-effects (Yousuf et al. 2023).





### Renal clearance rates

- Both oral medications should have the benefit to risk ratio assessed in patients with reduced renal clearance rates, such as in elderly or diabetic patients.
- Patients with renal clearance rates (eGFR of less than 50) should be discussed with a renal specialist as dosage titration may be indicated.
- (eGFR normally > 90, creatinine normally < 90)





## Why not just keep sending them to the hospital? Optometrists may be much more accessible for patients than hospital eye departments. May be in a better position to diagnose and manage ophthalmic conditions such as MGD-related cases of secondary evaporative dry eye and marginal keratitis. In this case, the patient was reviewed on 7 occasions in the Emergency Eye Clinic, requiring 7 days of leave from work, in addition to expenses related to each visit, such as transport and parking costs. Often patients require a support person who may also be required to take leave from their job. A locally based optometrist that can review these patients in a convenient time slot as needed may be a preferable alternative for such patients. Improves your skill set, challenges you and makes your job more interesting. Improves your relationship with other health care providers and demonstrates your scope of practice to them, creating referrals.





### Oral antihistamines The second most commonly prescribed class (n = 352) Slightly surprising to me given how disappointingly ineffective oral antihistamines are for ocular allergies (IMHO). However, are really good for (allergic) lid dermatitis. 8.2 per cent of all the oral medications. cetirizine (6.7 per cent), loratadine (0.7 per cent), and chlorpheniramine (0.8 per cent). Both cetirizine and loratadine (2nd generation antihistamines) have a lower affinity for central nervous system H receptors (relative to 1st generation chlorpheniramine), thereby reducing the risk of the common side-effect of drowsiness. These antihistamines are available for purchase over the counter but may be cheaper if prescribed.



### Oral antihistamines cont. Antigen avoidance. Usual dosing: cetirizine 10mg PO mane or BD loratadine 10mg PO mane or BD chlorpheniramine: adults and children aged 12 years and older – 1 tablet every 4 to 6 hours. Do not take more than 6 tablets in 24 hours children aged under 12 years – doses are lower for children and babies, and they may take it less often than an adult. Do not give children < 6 years.</li> older adults who are frail – 1 tablet every 6 to 8 hours. Do not take more

 older adults who are frail – 1 tablet every 6 to 8 hours. Do not take more than 3 tablets in 24 hours.



### 3. Anti-virals

- Acyclovir (and since 2016, valaciclovir) comprised 7.4 per cent of oral medications (n = 320).
- Most common indication for these oral drugs is herpes zoster ophthalmicus
- Also been used in the treatment of herpes simplex keratitis (esp. with stromal or endothelial involvement)
- Also as an alternative or adjunct to topical acyclovir in treating epithelial HSK, for those unable to use or comply with the required frequency of application of the topical form.













### Choice of antiviral agent: Oral acyclovir +/- analgesia & NSAIDs (if appropriate) Well tolerated and is much more specific (approx 200)

- Well tolerated and is much more specific (approx. 200 x ) for targeting viral genetic material than mammalian (Patel and Sawant 2007).
- However, it does have limited bioavailability and also a short half-life, therefore requires frequent (5 times per day) dosing is required to achieve optimal anti-viral effect.
- Valaciclovir is a l-valyl ester of acyclovir, which converts to acyclovir after oral administration.
- This results in a 3 to 5 fold increase in bioavailability when compared with oral acyclovir in humans (Lin et al. 2001), meaning that a TDS dosing is able to achieve the same anti-viral therapeutic effect.
- This may result in better compliance and valaciclovir should now be considered over oral acyclovir in the treatment of cases of HZO.









### Herpes simplex blepharoconjunctivitis

• aciclovir 400 mg five times a day PO x 7 to 10 days

- valaciclovir:
- Adults—500 milligrams (mg) PO three times a day for seven days.
- Children—Titrate by body weight (get GP to prescribe)

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### 4. Analgesia

- Really just paracetamol (as we'll cover combined analgesia and antiinflammatories under NSAIDs)
- Paracetamol:
- Adults: 500 to 1000mg every four to six hours as necessary, with a maximum of 4000mg in any 24 hour period
- Children: 15 mg per kg, which can be given every four to six hours as required, with no more than four doses in 24 hours.
- Safe, can be bought OTC, but may be cheaper if prescribed
- Do not exceed maximum dosages as can be hepatotoxic
- Can also use Aspirin (325 mg to 650 mg every 4 to 6 hours) as needed to maximum dose of 3900 mg in 24 hours.
- (Just use paracetamol)

### 5. NSAIDs

• Represented approximately 3-5% of all oral medications prescribed by optometrists in NZ (2014 to 2019)

### Case: Anterior scleritis

- A 70-year-old male was seen in the Emergency Eye Clinic at Greenlane Clinical Centre
- He presented with left eye redness and pain which had been painful enough to awaken him from sleep x 3 days
- Serological screening had been previously conducted in 2018 (1<sup>st</sup> presentation of diagnosed scleritis) but was negative to all investigations.
- His general medical history was positive for hypertension, gout and hypercholesterolaemia.
- His vision (aided) was RE 6/9+ (no imp PH) LE 6/15+ (no imp PH).
- IOPs were RE 12 mmHg LE 14 mmHg.





### Common NSAIDs and dosings

- Non-selective NSAIDs:
- diclofenac (Voltaren) 50mg q8-12h (max 150 mg / day)
- ibuprofen (Brufen) 400mg q4-6h or 600-800 mg q6-8h (max 3200 mg acute or 2400 mg chronic)
- aspirin 325 1000 mg q4-6h (max 4000 mg)
- (but to get significant anti-inflammatory effect risks toxicity)
- COX-2 selective:
- celecoxib 200 mg mane or 100 mg q12h (max 400 mg / day)
- (reduced GI upset risk, but still exists)



### Case: Anterior scleritis

- Given ibuprofen 400 mg PO TDS x 5 days
- Also omeprazole 20 mg PO mane
- Good response and resolution
- A note on the investigations:
- Approximately 50% of patients diagnosed with clinically determined scleritis will have no identifiable associated cause, approximately 30%–40% have an systemic autoimmune condition confirmed when immunological assessment is undertaken, most frequently granulomatosis with polyangiitis (formerly termed Wegener's granulomatosis) or rheumatoid arthritis (Sims 2012).

# Treatment of scleritis (anterior or posterior) Systemic medications that may be utilised to treat scleritis include: (initially) non-biologic agents (such as oral steroids, oral NSAIDs) biologic immunomodulators if the clinical response is insufficient or if cases become refractory. These include anti-tumor necrosis factor alpha and anti-CD20 agents (by sub-specialist ophthalmologists). Ocular and systemic morbidity is ultimately reduced by the timely (diagnosis and) treatment with sufficient sort and long term immunosuppression.





### 6. Steroids

- Rarely prescribed by optoms in NZ (max 2% of oral med scripts)
- Almost invariably within a hospital setting













### 7. PPIs

- Omeprazole, a proton pump inhibitor (PPI), was prescribed 63 times, comprising 1.5 per cent of the total prescribed medications.
- Seemingly unusual prescription for an optometrist?
- PPIs inhibit the production of acid in the stomach and in two-thirds of cases these were prescribed alongside anti-inflammatories, such as oral prednisolone (n = 45), to offset gastro-oesophageal side-effects, such as peptic ulcers that might arise from oral steroid and non-steroidal anti-inflammatory medication use.
- The source of prescriptions for this medication tended to be limited to
  optometrists working in collaborative relationships with ophthalmologists
  in a public hospital or private ophthalmology clinic setting, prescribed for
  patients on existing oral anti-inflammatory therapy.

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### PPIs

- Omeprazole PO 20 mg mane
- Use as gastric cover even for short or pulsed oral steroid and NSAID prescribing.

### 8. Diamox

 Acetazolamide, a reversible carbonic anhydrase inhibitor used mainly in glaucoma treatment, comprised 2.7 per cent of oral prescriptions (n = 115).



### Case: AACG cont.

- On examination, she showed 3+ diffuse conjunctival injection RE and had a white conjunctiva in the LE.
- The right eye showed diffuse corneal oedema with microbullae, whilst the LE cornea was clear.
- Van Herrick assessment showed narrow anterior chambers of both eyes.
- 1 drop of Alcaine (proxymetacaine 0.5%) were instilled in each eye and then 2 drops of glycerol BP 100% were instilled in the RE to better visualize the R anterior chamber during gonioscopy and the posterior of the eye.
- Gonioscopy showed a completely closed angle in the RE with no peripheral anterior synechiae (PAS). The left anterior chamber was closed superiorly and temporally, slitonly nasally and open to the posterior trabecular meshwork inferiorly.
- Both crystalline lenses showed nuclear sclerosis +++.
- Undilated views of the optic nerve heads showed 0.3 cupping with no disc swelling.





### Case: AACG cont.

- The next day her vision had further improved to RE 6/15 (pinhole 6/12) and LE 6/9+. IOPs were RE 15 mmHg LE 10 mmHg. As her angles were still narrow despite the LPIs, she continued her topical medications until she underwent successful RE cataract extraction 3 weeks later in her RE and 2 months later in her LE.
- At the final follow up, her vision was 6/7.5 unaided in each eye.
- Gonioscopy showed deep and quiescent anterior chambers with no PAS.
- 0.3 cupping in each eye with normal retinal nerve fibre layer thicknesses in each eye on the OCT scans.
- She was therefore discharged back to her optometrist for annual diabetic retinopathy checks.







### 9. Odds and ends

- Intravitreals (Avastin, Lucentis, Eylea, triamcinolone)
- Sodium fluorescein 250 mg IV stat for FFA
- Indocyanine Green 25 mg IV stat for ICGA
- Anti-Protozoals (co-trimoxazole)
- Metformin?
- Lorazepam?
- Blood tests
- Pregnancy tests

### Summary / final clinical pearls:

- Like mycophagology, get to know a few really well that you are comfortable with and stick to these.
- Scope is determined by (Registration Board), experience, inter-professional relationships and geographic isolation.
- Despite the range of medications prescribed, the ODOB in NZ has not been alerted to any out-of-scope prescribing of oral medications.
- Further, there have not been any adverse incidents specifically relating to the issuing of therapeutic prescriptions by optometrists in New Zealand reported to the Accident Compensation Corporation or Health and Disability Commission.
- This suggests that despite their ability to manage a broader range of ocular conditions, the optometry profession, as a whole, is practising appropriately and appears still to be referring and/or co-managing (rather than independently managing cases) requiring more complex therapeutic management.



