Should we be worried using steroids?

Tim Martin

Melbourne Museum- November 2019

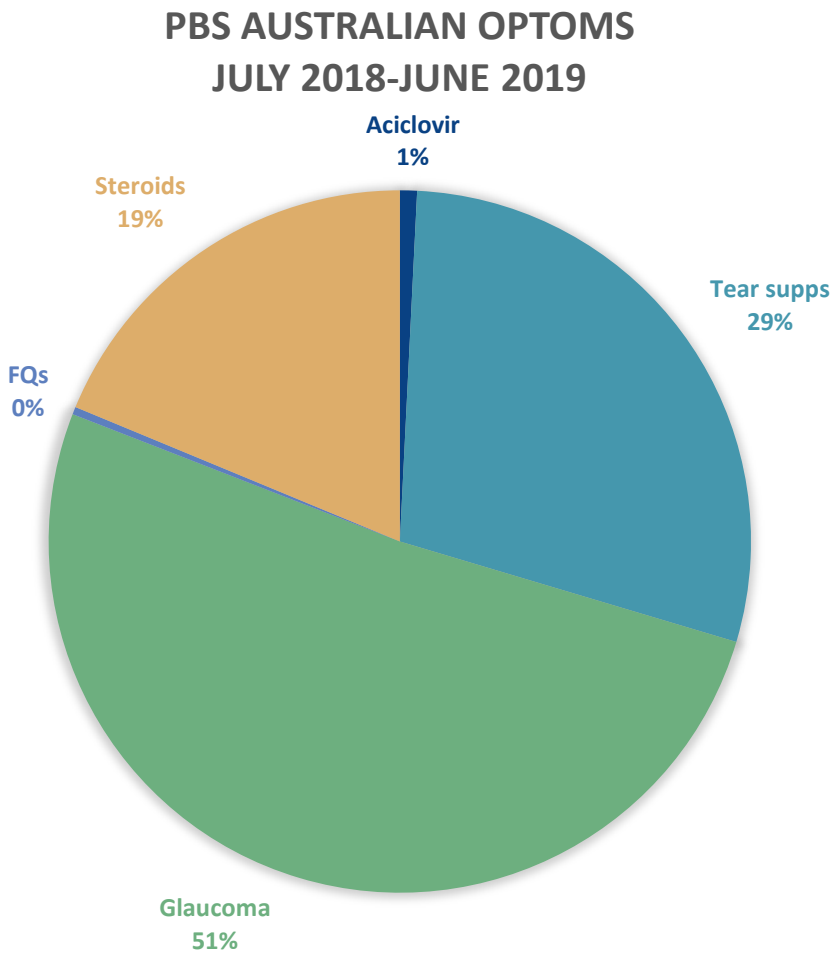
Learning Objectives:

At the end of the presentation, attendees should have a better understanding of:

1. The safety profile of topical steroids in pregnancy
2. Use of steroids in the context of viral conditions
3. The use of steroids in paediatric conditions

Which PBS listed eye drop is prescribed most frequently by Australian optometrists?

Distribution of PBS Optom Rx



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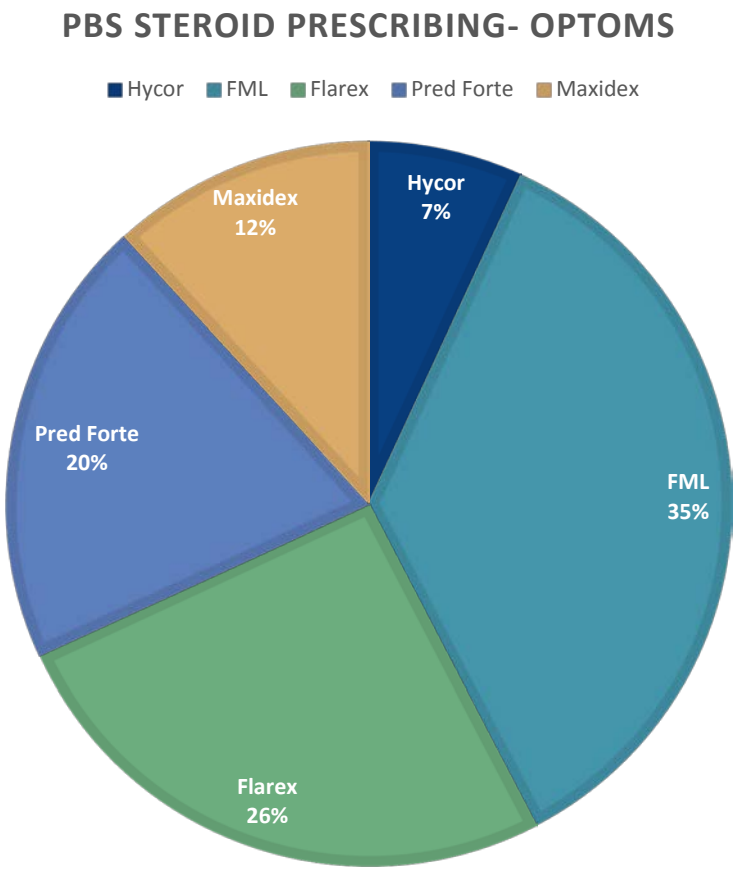
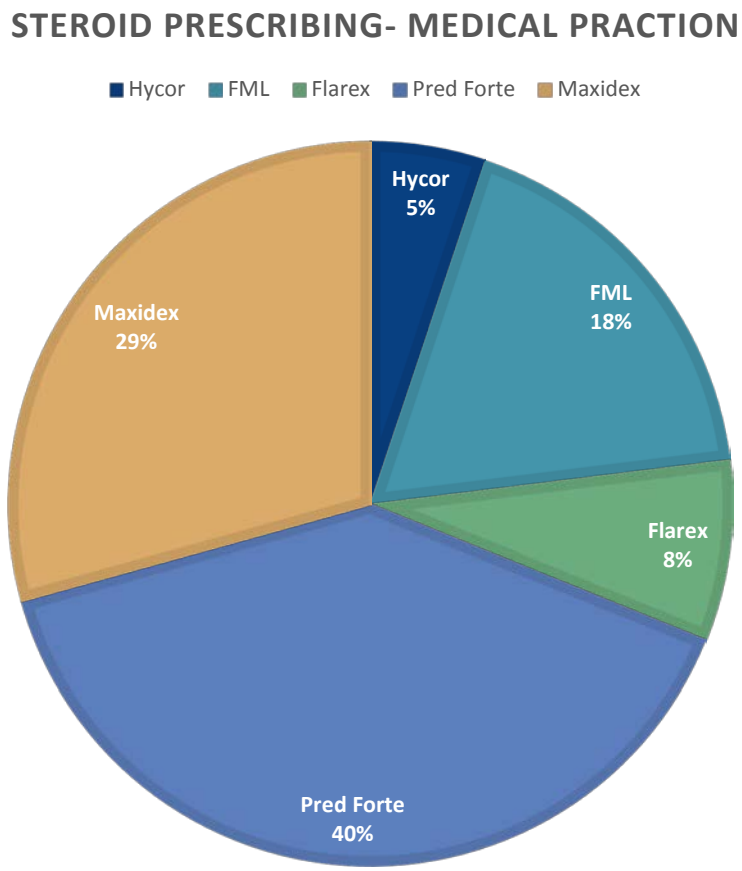
Steroid PBS Rx





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The worst news of 2019?

Optometry Australia

26 Feb. at 09:11 •

Attention optometrists: The Therapeutic Good Administration advises there is only limited supply of Flarex until 10 April and no Flucon until 15 March. More info: https://www.tga.gov.au/medicine-shortages-information-initiative

Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Drug and form	Potency[1]	Penetration[1]	Intraocular pressure rise
hydrocortisone ointment, 1%	low	++	++
fluorometholone suspension, 0.1%	mid	–	+++
prednisolone solution, 0.5%	mid	+	+++
prednisolone acetate suspension, 0.5%	high	+++	++++
fluorometholone acetate suspension, 0.1%	high	++	+++
dexamethasone suspension, 0.1%	high	++	++++
[1] with intact corneal epithelium			

Miss KL

January 2014 21 yo F

Last 4/7 R eye red, photophobic & blurry

R: 6/6^{2+} & L: 6/6

R G2.5+ perilimbal flush, KP in Arlt's triangle G2.5;

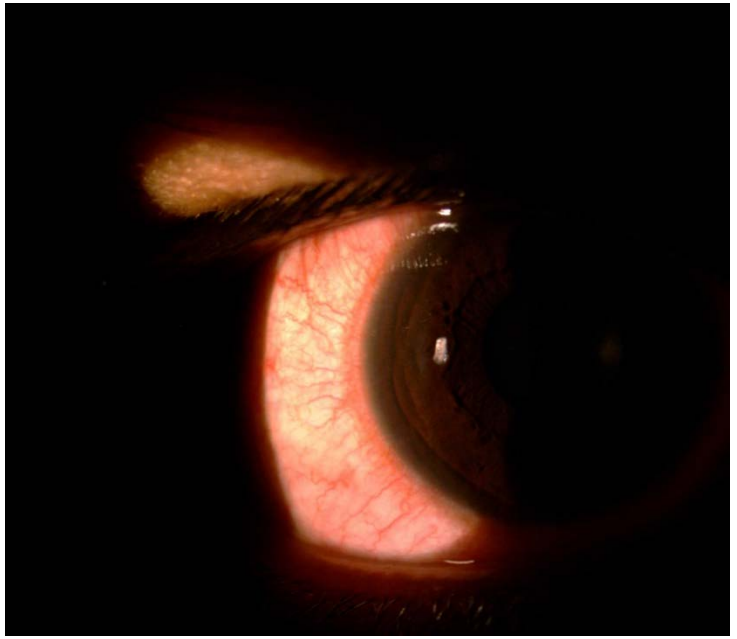
L quiet

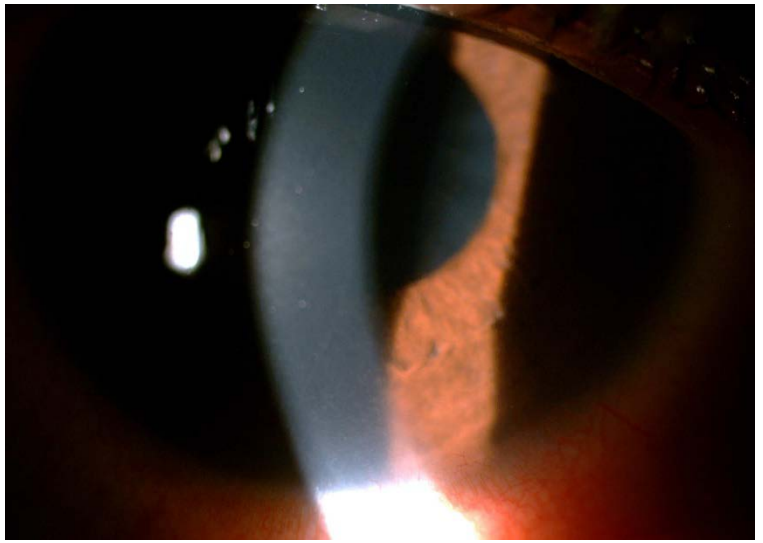
IOP 19 mmHg R=L (thicker CCT)

DFE: unremarkable

GH: mild asthma; targeted systemic history- nil

Mx: Pred Forte q1h w q15mins for 1/24 before bed, Atropine bid





Miss KL- January 2014

3 day review: Improving as expected, reduced Pred Forte to q2h

1-week review: R KP fading, conjunctiva & limbus quiet…
…but L KP & inferior-nasal ciliary flush

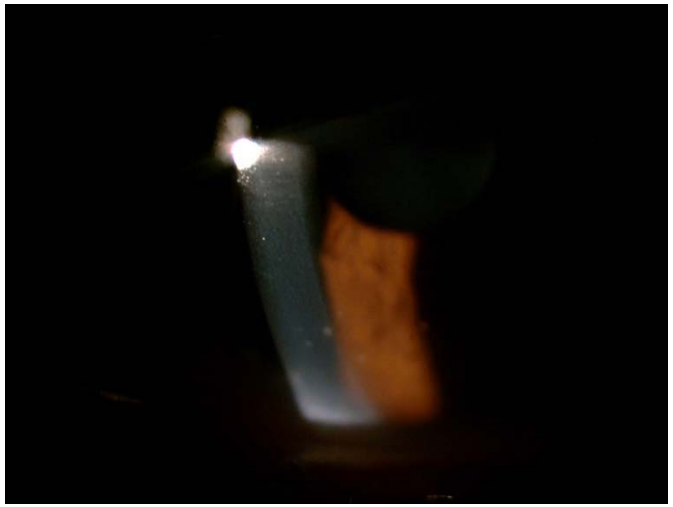
Treated both eyes but ordered systemic work-up w HLA-B27 & sarcoid considering bilateral disease- all negative

May 2014: Mild L sided AAU- resolved uneventfully

September 2014

R G1.5+ AAU

& IOP in low 20's



...but now 14 weeks pregnant!

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How would you manage uveitis in a pregnant lady?

Definitions of the Australian categories for prescribing medicines in pregnancy

Category B3

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Category C

Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

https://www.tga.gov.au/prescribing-medicines-pregnancy-database

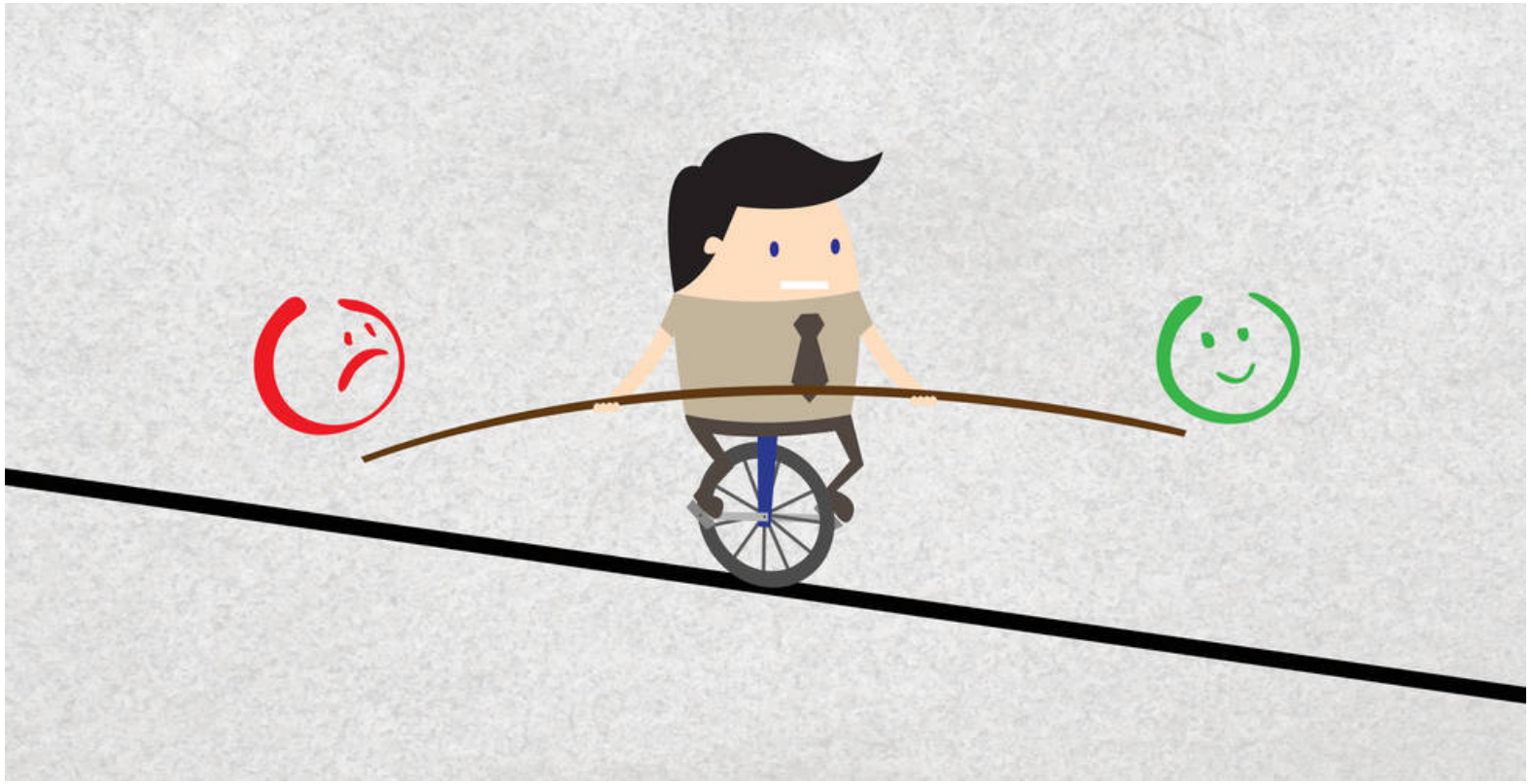
Steroids in pregnancy?

	MIMs	AMH
FML (Category B3)	There are no adequate well-controlled studies in pregnant women. Has been shown to be teratogenic, fetotoxic and embryocidal in rabbits when given in doses approximating the human dose and above. Safety of the use of topical steroids during pregnancy has not been established. Fluorometholone was ocularly applied to both eyes of pregnant rabbits on days 6 to 18 of gestation. A significant dose-related increase in foetal abnormalities and in foetal loss was observed. FML should be used with caution during pregnancy only if the potential benefit outweighs the potential risk to the foetus.	Safe
Flarex (Category B3)	Should be given to a pregnant woman only if clearly needed	"
Pred Forte (Category C)	In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. **These findings do not seem to be relevant to humans.** Reduced intrauterine growth and lower birth weight have been recorded in animals and humans after long-term or high dose treatment. Suppression of the adrenal cortex in the newborn baby may occur after long-term treatment. The short-term use of corticosteroids prior to delivery for the prevention of respiratory distress syndrome does not seem to pose a risk to the fetus or the newborn infant. There are no adequate and well controlled studies in pregnant women. Prednefrin Forte should be used during pregnancy **only if the potential benefit justifies the potential risk to the foetus.**	"
Maxidex (Category B3)	Reduced placental and birthweights have been recorded in both animals and humans after long-term treatment with corticosteroids. There are no adequate or well controlled studies in pregnant women. Currently available clinical data provide no conclusive evidence that corticosteroids caused an increased incidence of congenital abnormalities. Prolonged or repeated use during pregnancy was associated with an increased risk of intrauterine growth retardation, although this did not appear to be evident following short-term treatment. Topical corticosteroids should not be used extensively in pregnant women in large amounts or for prolonged periods of time. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism. Maxidex eye drops should not be used in pregnancy **unless the potential benefit to the mother outweighs the potential risk to the embryo or foetus**	"

Back to you

How do we determine if the benefit outweighs the risk?

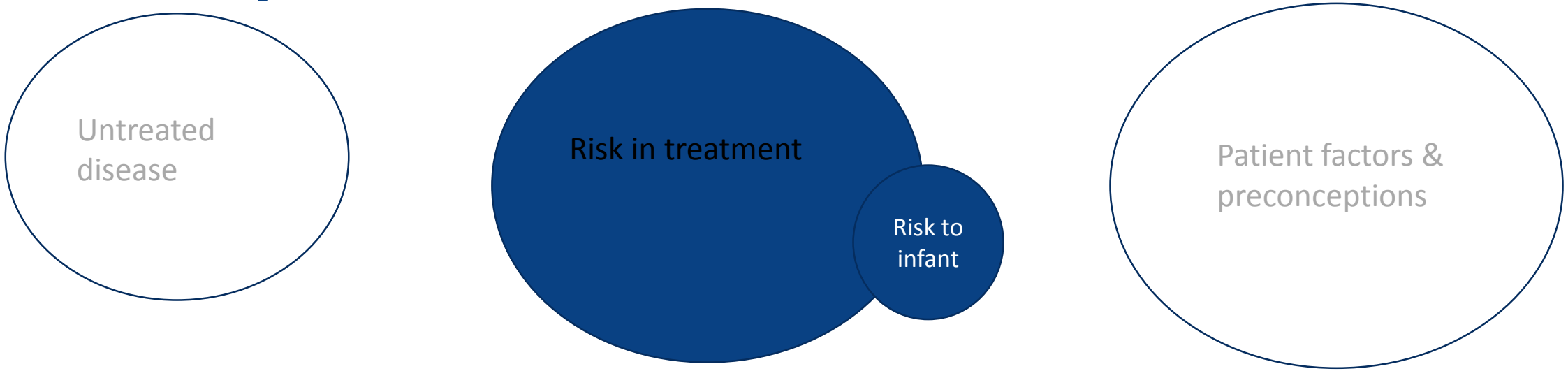
“only if the potential benefit justifies the potential risk to the foetus”



Risk analysis

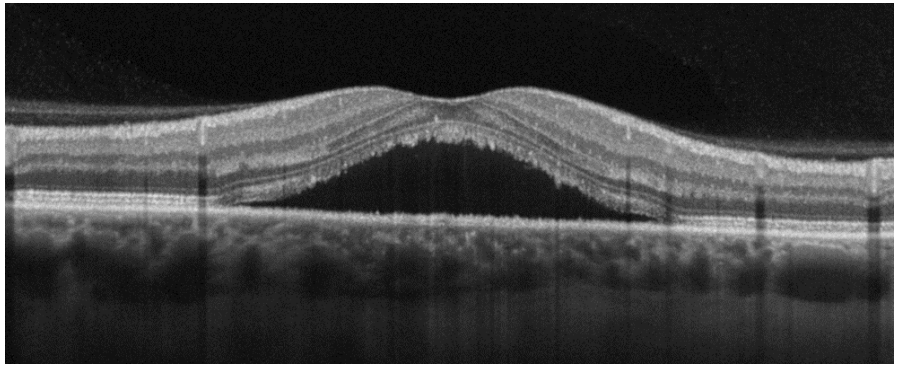
- IOP rise
- Cataract w recurrence
- Synechia formation
- Corneal odema
- Posterior spill-over
  - Vitritis
  - Macular oedema
  - Optic neurtitis

Risk analysis



Mother:

- IOP steroid response
- Cataract w chronic use
  - Activation of latent HSK/HZO
  - CSR



Infant:

???

Risk of cleft lip and palate- oral steroids

Inconsistent findings with **oral** steroids; no reported issues with topical

General incidence cleft lip AND palate ~ 1 in 2,000

Earlier meta-analysis 3.4-fold risk cleft palate in children who had used oral prednisone

The NBDPS is an ongoing multi-state population-based case-control study of birth defects

- 1997-2002 odds ratio 1.7
- 2003-2009 odds ratio 1.0
  - Summed 1.2 (0.9, 1.6)

Park-Wyllie, L., Mazzotta, P., Pastuszak, A., Moretti, M. E., Beique, L., Hunnisett, L., ... & Diav-Citrin, O. (2000). Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. *Teratology*, *62*(6), 385-392.

Skuladottir, H., Wilcox, A. J., Ma, C., Lammer, E. J., Rasmussen, S. A., Werler, M. M., ... Carmichael, S. L. (2014). Corticosteroid use and risk of orofacial clefts. *Birth defects research. Part A, Clinical and molecular teratology*, *100*(6), 499–506. doi:10.1002/bdra.23248

Steroids in pregnancy

Topical and periocular considered safe

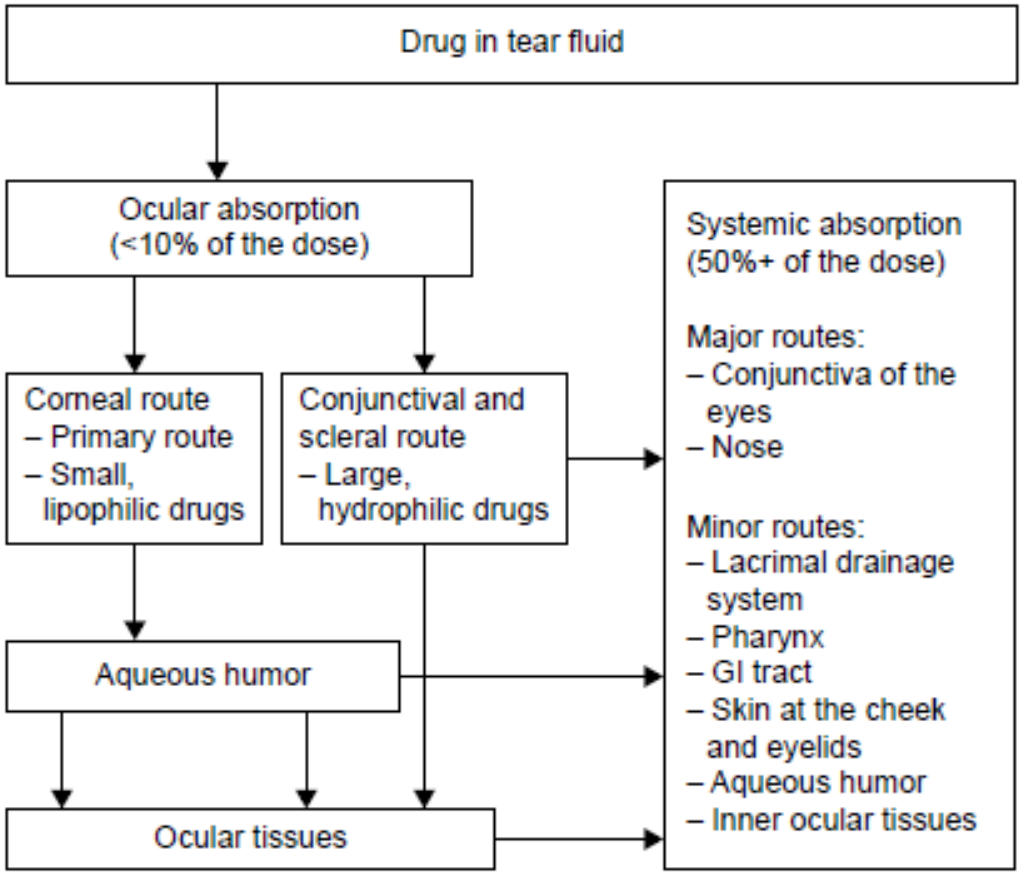
- Mild disease

Oral steroids

- Moderate to severe disease
  - Generally considered safe- lowest dose possible
  - Risk of cleft palate in oral use 1 month prior to conception- 1st trimester

Grotting, L. A., & Papaliodis, G. N. (2017). A Review of the Course and Treatment of Non-Infectious Uveitis during Pregnancy. In *Seminars in ophthalmology* (Vol. 32, No. 1, pp. 75-81). Taylor & Francis.

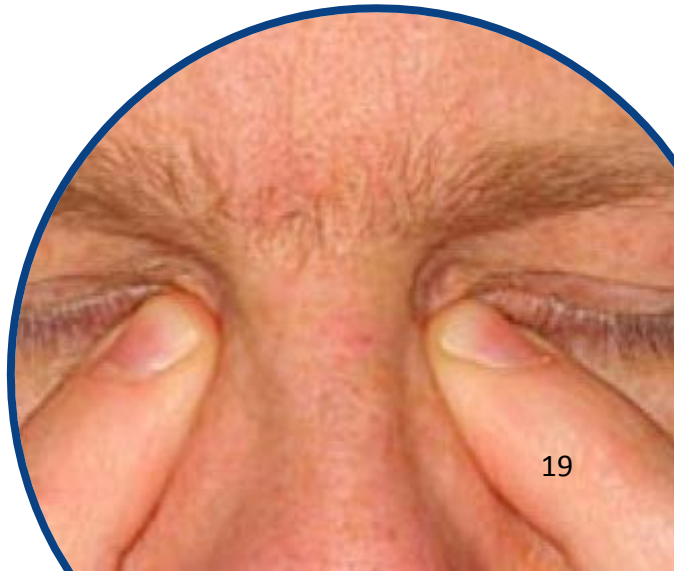
Pharmacokinetics of drops



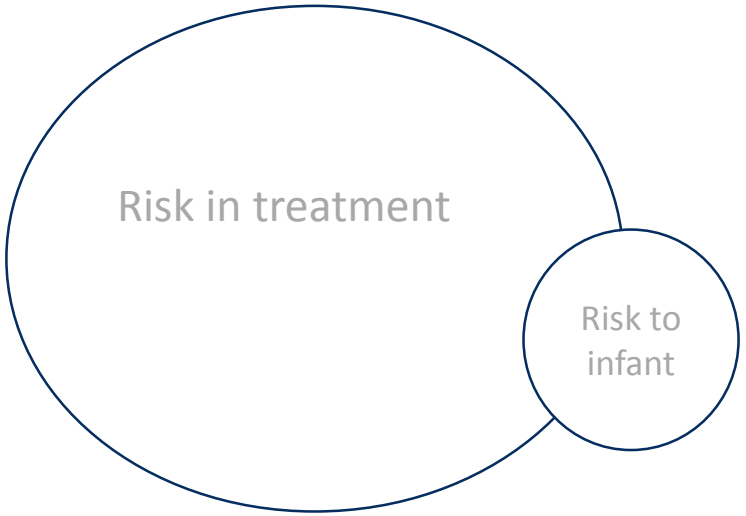
Farkouh, A., Frigo, P., & Czejka, M. (2016). Systemic side effects of eye drops: a pharmacokinetic perspective. *Clinical Ophthalmology (Auckland, NZ)*, *10*, 2433.

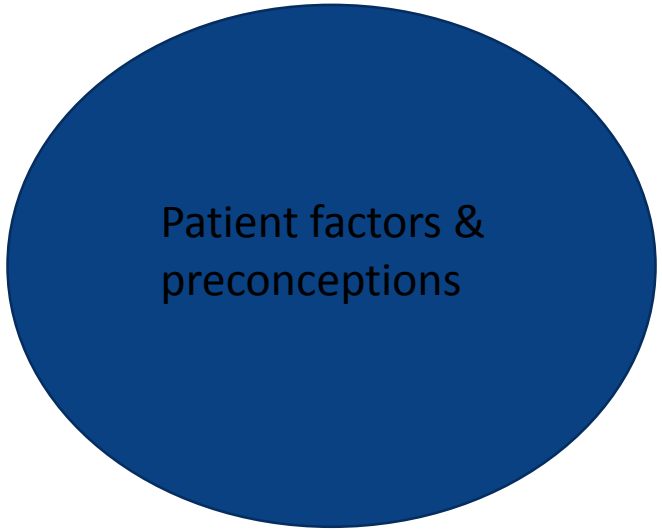
Minimising systemic exposure

- Digital punctal occlusion
- Semi-permanent or “permanent” punctal plugs

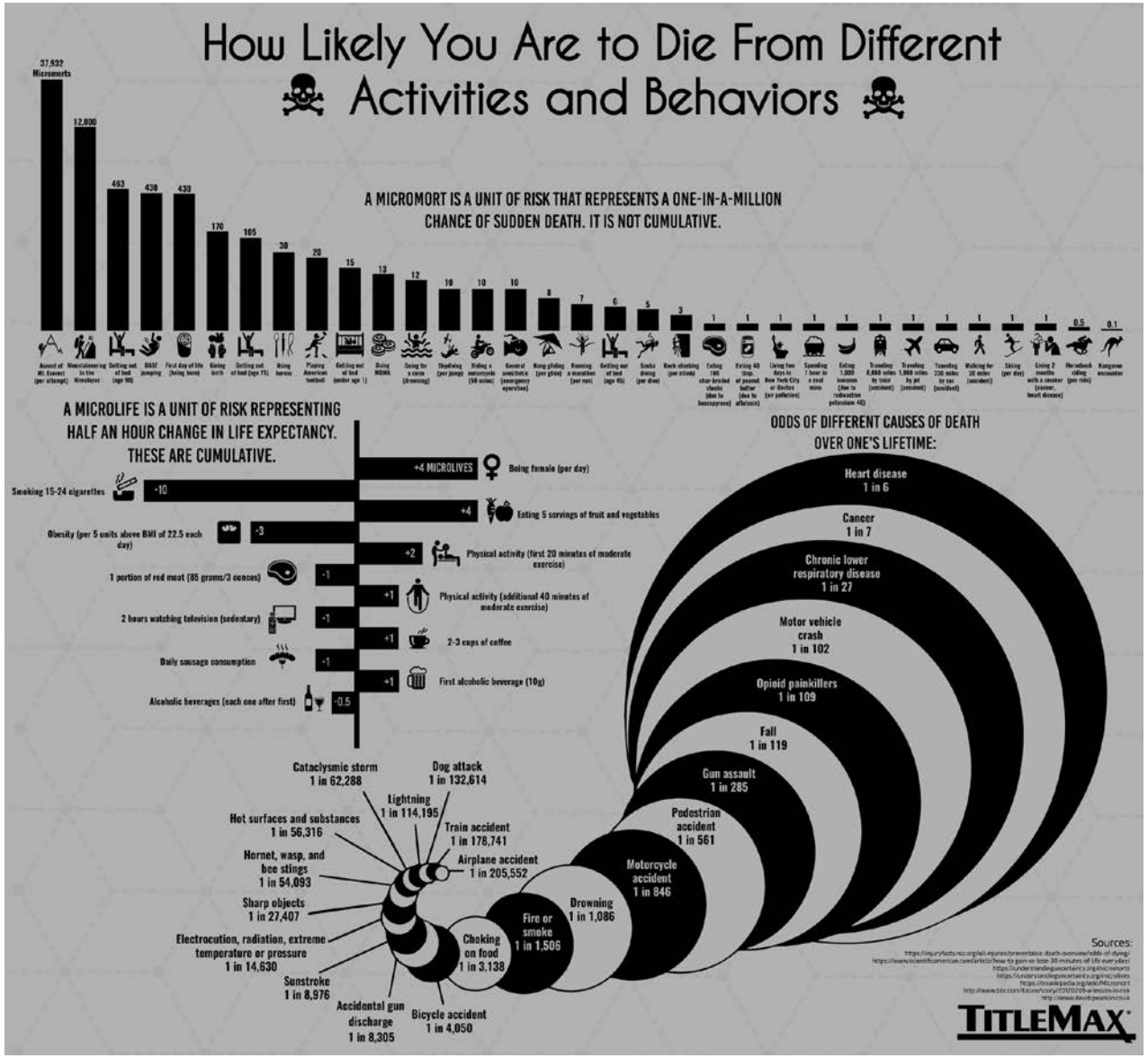


Risk analysis





- Personal decision
- Humans are inherently poor at assessing risk?

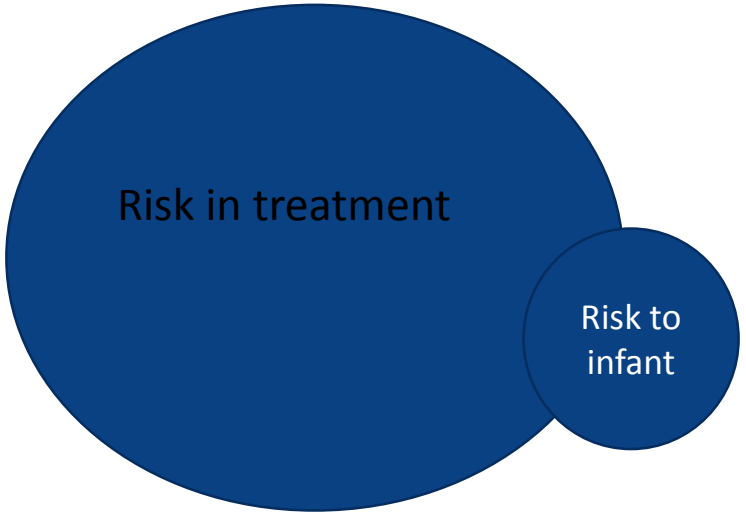


Which activity carries the highest risk of death?

https://www.visualcapitalist.com/crunching-the-numbers-on-mortality/likelihood-of-death/

Risk analysis

- IOP rise
- Cataract w recurrence
- Synechia formation
- Corneal oedema
- Posterior spill-over
  - Vitritis
  - Macular oedema
  - Optic neurtitis



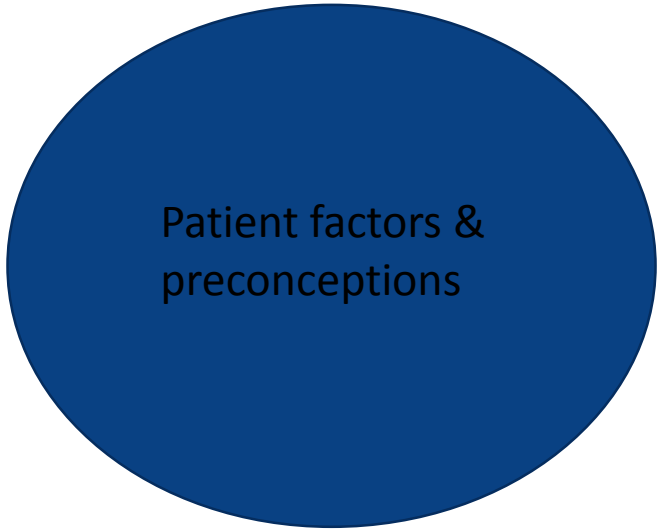
Mother:

- IOP steroid response
- Cataract w chronic use
  - Activation of latent HSK/HZO
  - CSR

Infant:

?none

?cleft palate- none reported topical; some in oral



- Personal decision
- Humans are inherently poor at assessing risk?

Ophthal management advice for Miss KL

Frequent Pred. Forte eye drops w closure of lids & punctal occlusion

No IOP lowering drops at that time

Patient was happy with this advice

Uveitis resolved & healthy baby

Discussion with another ophthalmologist

2nd pregnancy – 2nd trimester, unilateral AAU again: we treated with Pred Forte

Me: “Are we going to have to do this every pregnancy? Should we be doing anything differently?”

Ophthal: “It will get better when she is **properly** pregnant”

What we know about uveitis & pregnancy?

Similar likelihood of episodes in 1st trimester vs prior to pregnancy

Reduced incidence flare ups 2nd & 3rd trimester

No change to severity

Possible flare-up/relapse in 3-6/12 after delivery

- Maybe less risk of this in idiopathic uveitis vs VKH or Bechet's
- Lactation- some inflammatory conditions get worse- unclear in uveitis?

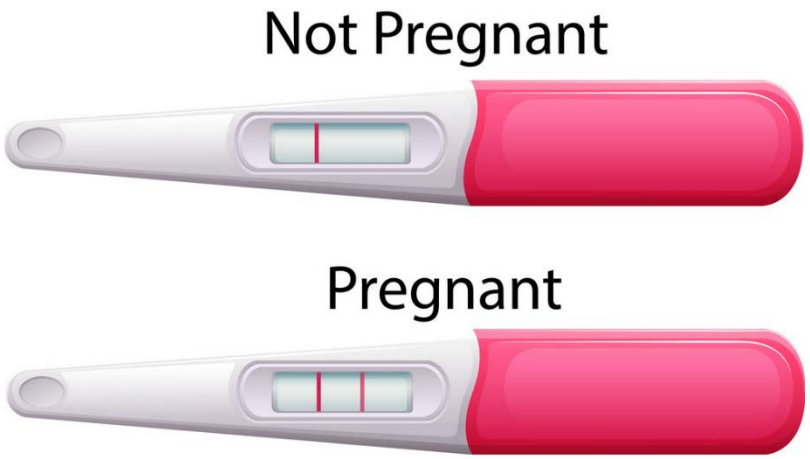
Chiam, N. P., & Lim, L. L. (2014). Uveitis and gender: the course of uveitis in pregnancy. *Journal of ophthalmology*, *2014*.

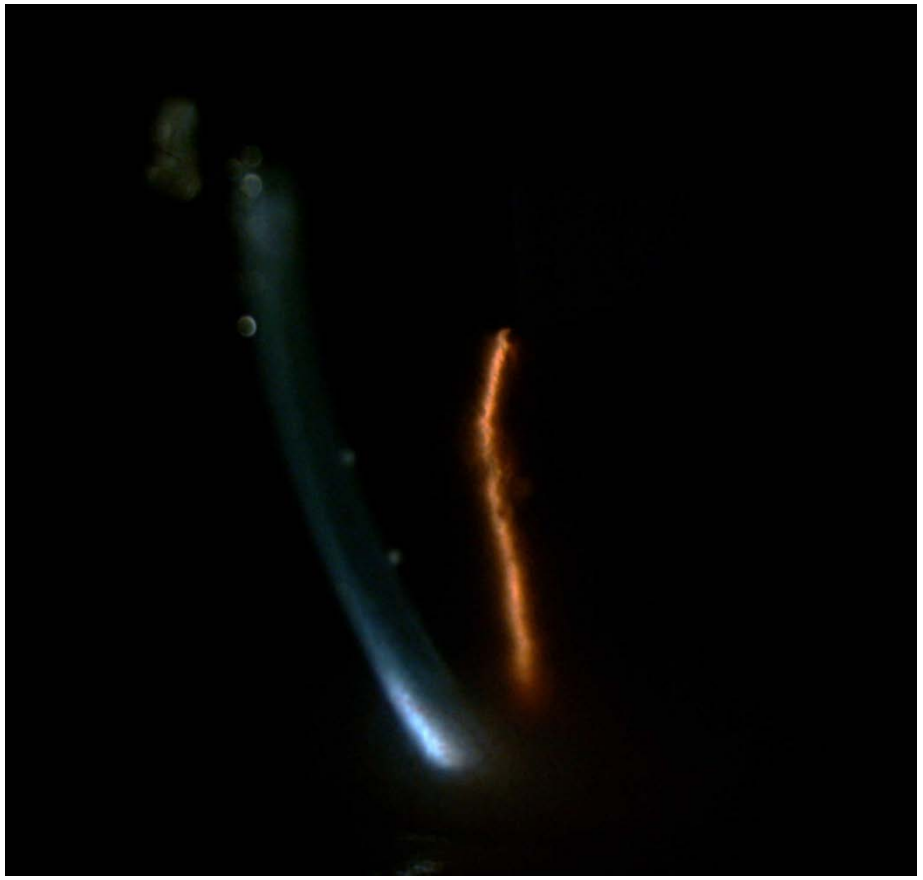
Rabiah, P. K., & Vitale, A. T. (2003). Noninfectious uveitis and pregnancy. *American journal of ophthalmology*, *136*(1), 91-98.

Miss KL

June 2019

3rd pregnancy, 1st trimester



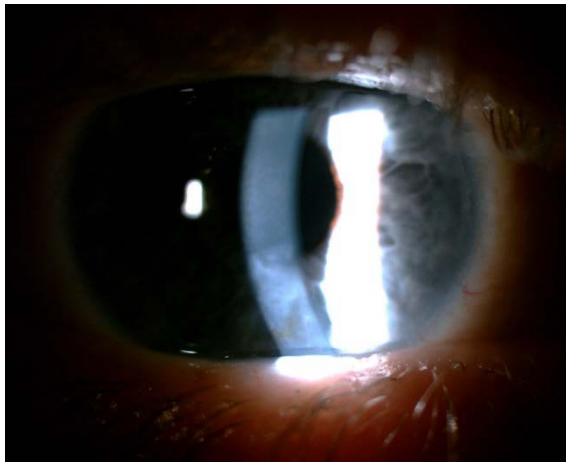


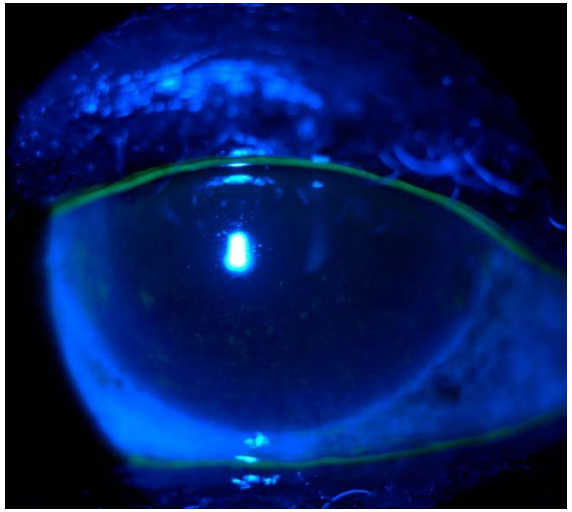
Topical steroids in pregnancy- summary

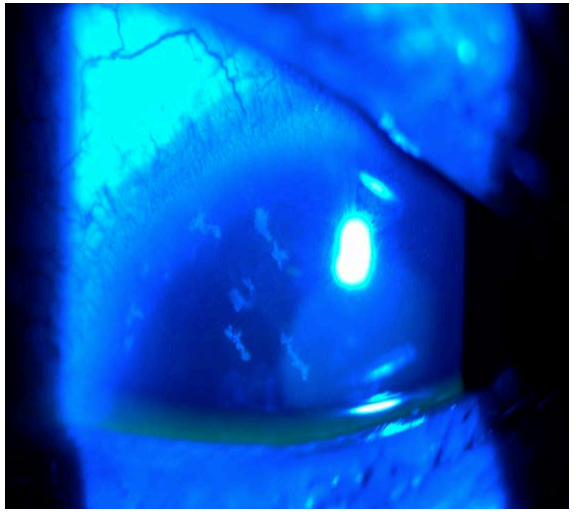
- There is conflicting recommendations regarding use of topical steroids in pregnancy
  - No definitive studies & probably never will be
  - *Probably* safe with topical but warrants patient consenting & educated decision
  - consider punctal occlusion

- Uveitis still occurs in pregnancy with same severity, but less frequently in 2nd & 3rd trimesters

Which of the following is the most common initial presentation of HZO?





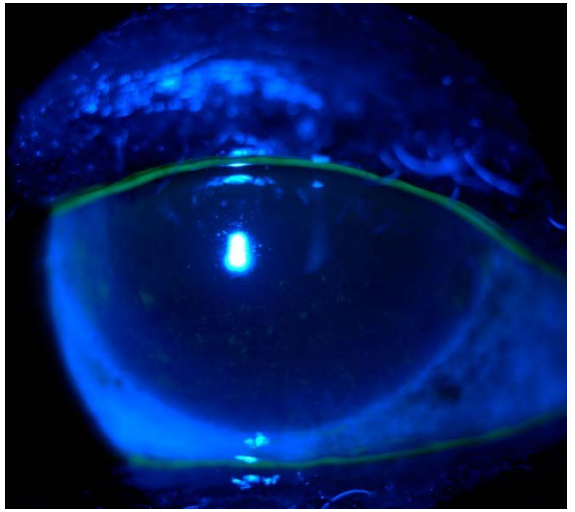


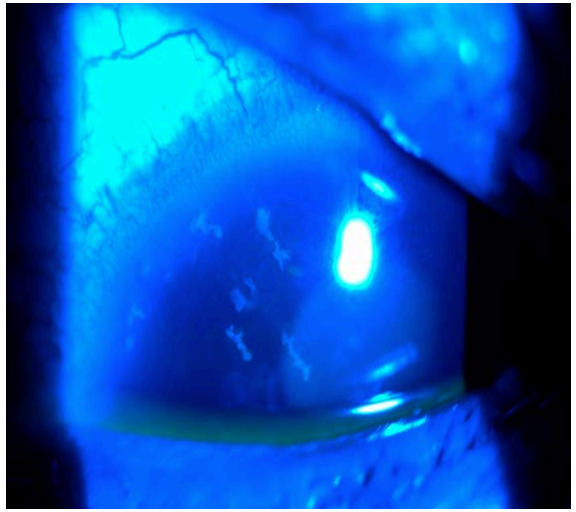
Corneal complications with HZO

Of 94 patients with acute herpes zoster ophthalmicus who were seen during a six-year period, 61 had corneal involvement.

The corneal complications in the order of chronological clinical occurrence were:

- **punctate epithelial keratitis in 51%,**
- **early pseudodendrites in 51%,**
- anterior stromal infiltrates in 41%,
- sclerokeratitis in 1%,
- kerato-uveitis/endothelitis in 34%,
- serpiginous ulceration in 7%,
- delayed corneal mucous plaques in 13%,
- disciform keratitis in 10%,
- neurotrophic keratitis in 25%,
- and exposure keratitis in 11%.





Some of the **earlier lesions seemed to result from viral infection**, whereas **later lesions** resulted from limbal vasculitis, an immunologic mechanism to soluble viral antigen, a delayed hypersensitivity reaction, or damage to nerves and tissues. An elucidation of the lesions awaits better viral and immunologic detection techniques and further histopathologic study. Modern topical and systemic antiviral therapy, corticosteroids, and surgery have a role in treatment.

Liesegang, T. J. (1985). Corneal complications from herpes zoster ophthalmicus. *Ophthalmology*, *92*(3), 316-324.

Mr GS

December 2014

39 yo M

PC: Photophobia 6pm last night, blurred couple days prior to that

POH: Over last 10 years multiple HSK flare ups, 1.5 years since last episode, 2 years prior to that, every 6 months prior to that

GH: Anxious as wife having chemo./radiation for breast cancer & stressed at work

-ve Mx

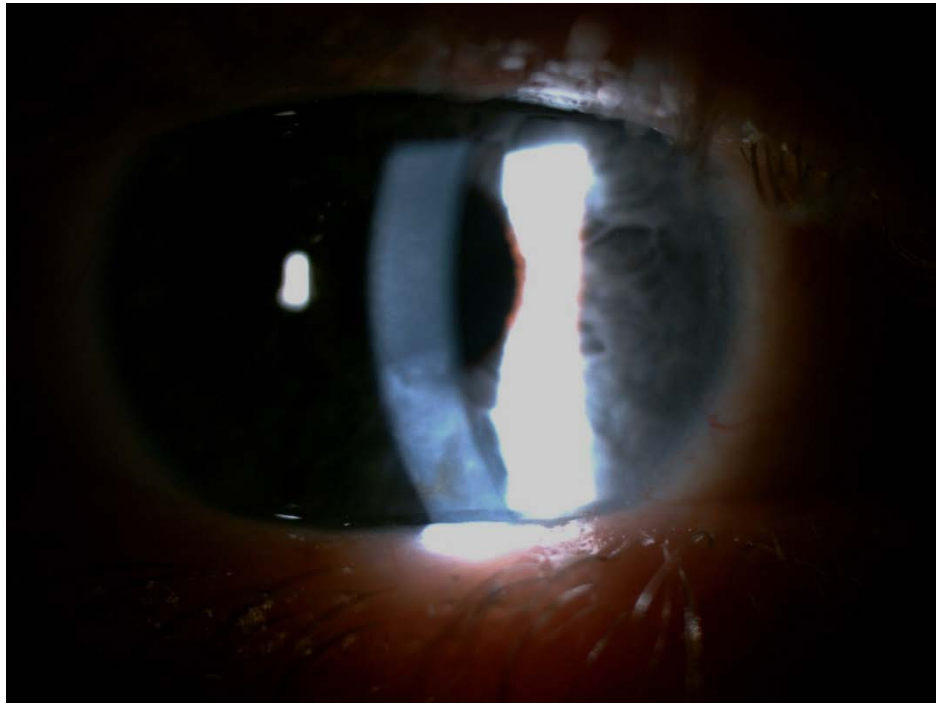
Mr GS

V w SVD R) 6/12 & L) 6/7.5
PH R) 6/9.5 & L) 6/6-

R) inferior nasal large old anterior stromal HSK scar ~3-4mm Surrounding haze w focal white terminal scars within, **no overlying stain**
faint G1+ cell under area of scar

L) 3 trace pigmented KP on central endo, cornea clear, AC quiet, no stain

IOP 14mmHg R=L



Mr GS

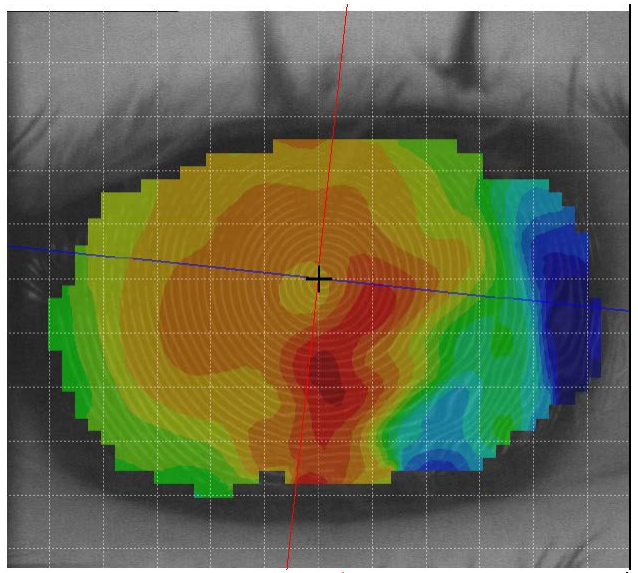
Dx: Mild/early reactivation of R HSK kerato-uveitis

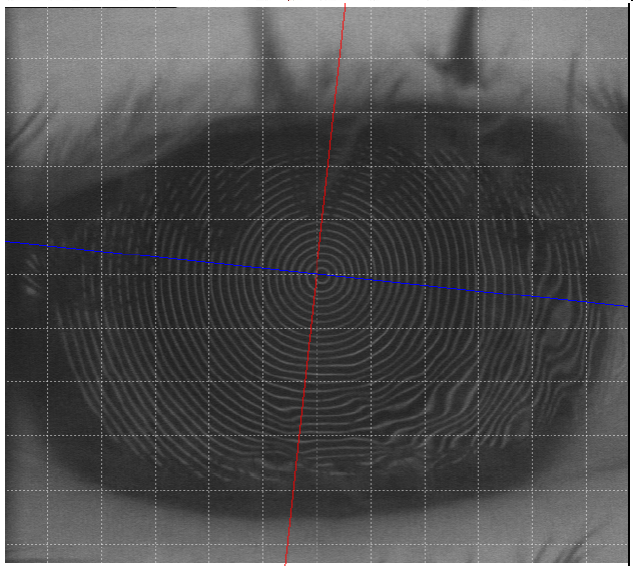
Mx: Pred Forte qid & Acivision tid for prophylaxis

2/7 review- feeling much better

2/12 later: after SLOW taper haze improved

VA R: $6/15^{2-}$ & L: $6/6^{2+}$ with myopic shift in R





Mr GS

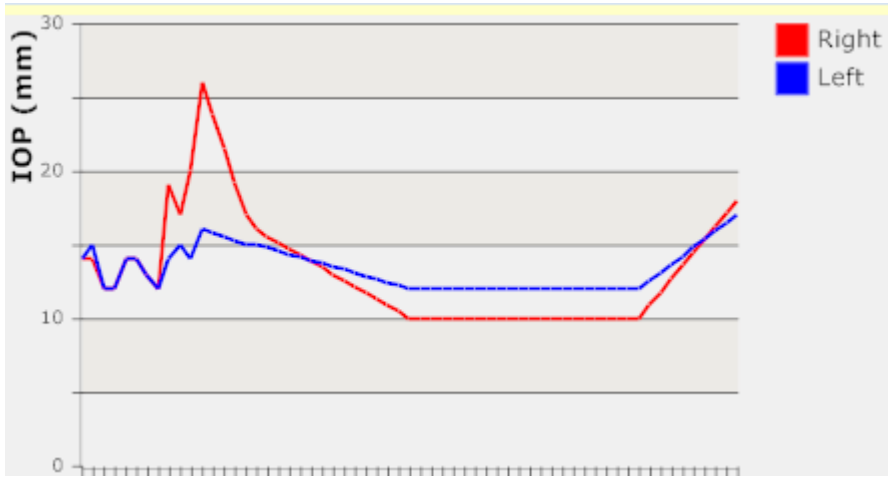
Flare up 2/12 later

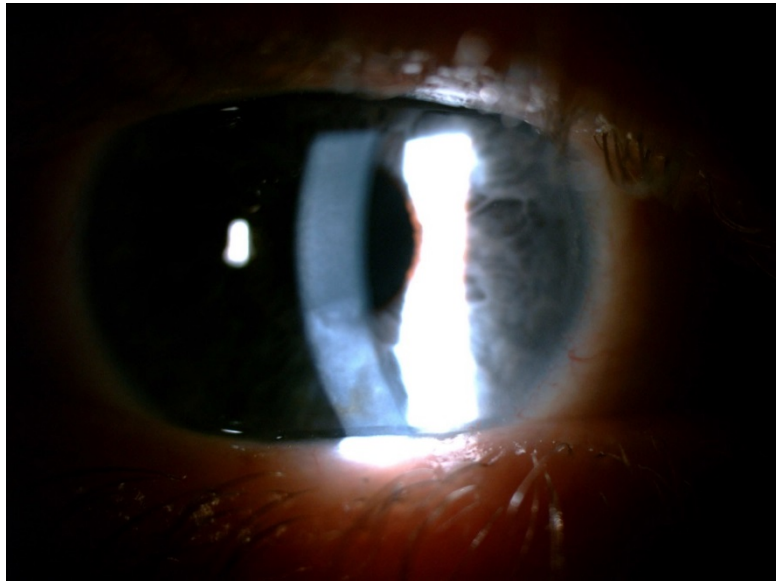
Same management & again slow taper

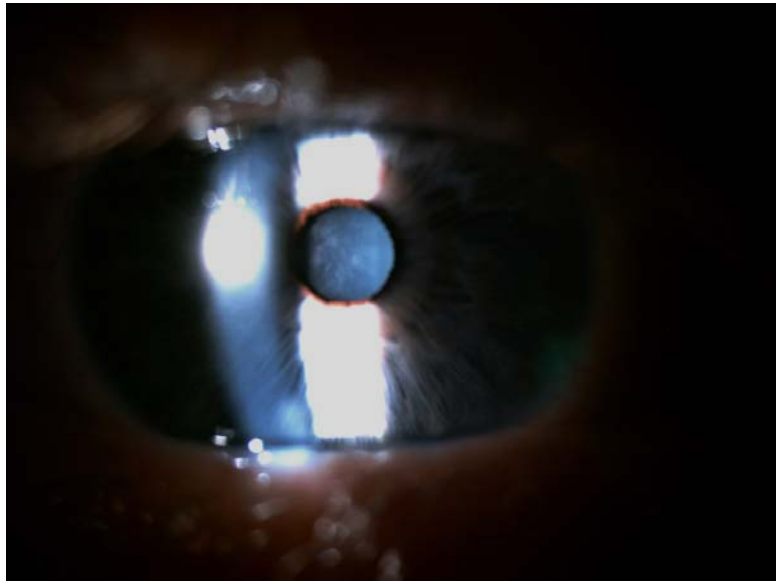
IOP slowly crept up in R to high teens, then 26mmHg

VA ↑↓ ~ 6/24

Developed R PSC & cortical cataract







Tim Martin 2019

Would they be better off with oral antivirals?

HEDS1 & HEDS2

National Eye Institute's Herpetic Eye Disease Study (HEDS) in 1999 gave authoritative results for the oral treatment and prevention of ocular herpes simplex. HEDS I showed that topical prednisone was helpful in treating patients with stromal keratitis. It also demonstrated that there is no benefit to adding oral acyclovir in stromal keratitis if the patient is already taking topical steroids and antivirals.

HEDS II demonstrated results that are more relevant to the primary care optometrist. This study showed that oral acyclovir in a prophylactic dosage of 400mg b.i.d. reduced the rate of recurrence of any form of ocular herpes in the following year by 41%. Further, HEDS II showed a 50% reduction in the recurrence of severe forms of ocular herpes, such as disciform keratitis, if acyclovir is taken for a year as described.

http://www.revoptom.com/continuing_education/tabviewtest/lessonid/106745/

Mr GS

Consideration of oral prophylaxis

- Valtrex 500mg daily
- Taper Pred Forte from qid, reducing weekly then switch to Flarex qd due to history of IOP response

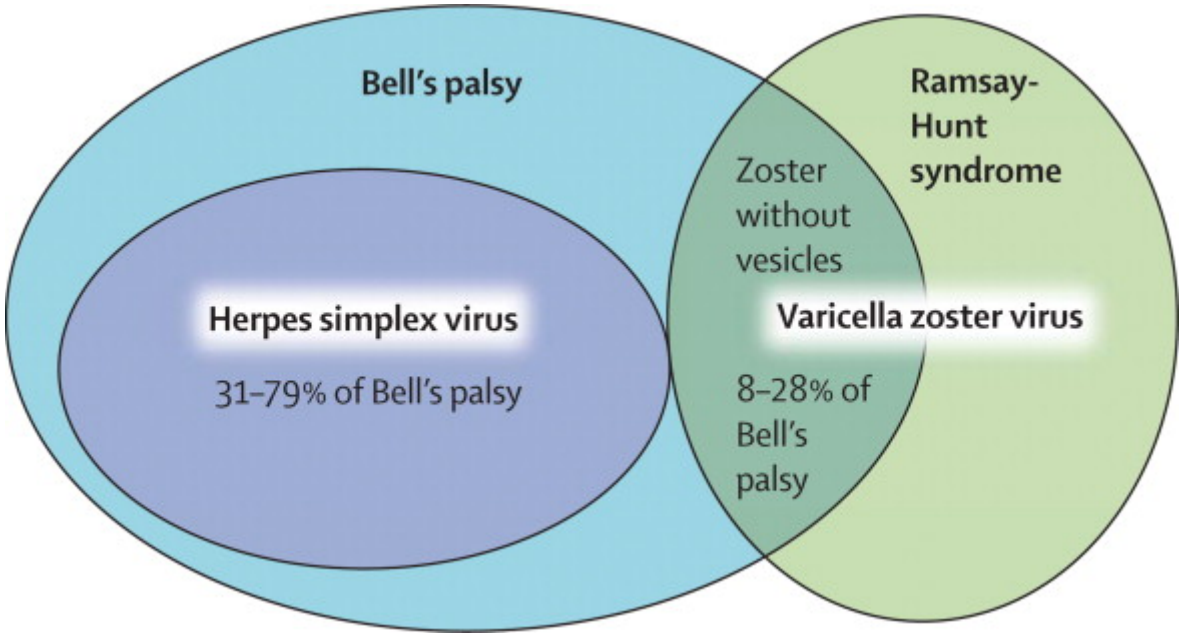
- Once stable four months later R cataract surgery
- VA R: $6/6^{+}$ & L: $6/4.8^{+}$

Mr GS

Continued Valtrex 500mg & FML daily

Good run for 2 years with no active HSK

Did have an episode of Bell's Palsy early 2019- resolved as expected



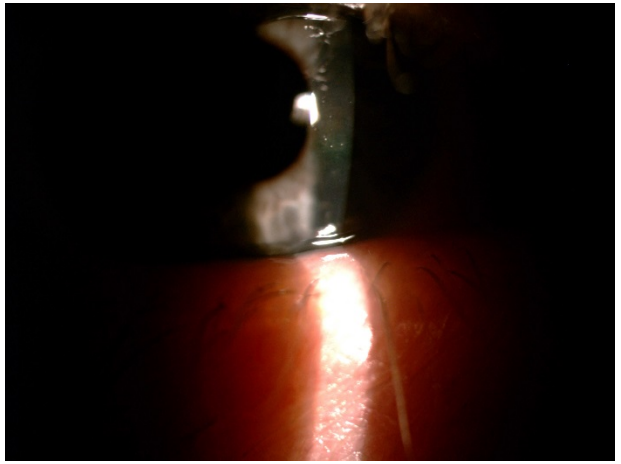
Hato, N., Murakami, S., & Gyo, K. (2008). Steroid and antiviral treatment for Bell's palsy. *The Lancet*, *371*(9627), 1818-1820.

Mr GS

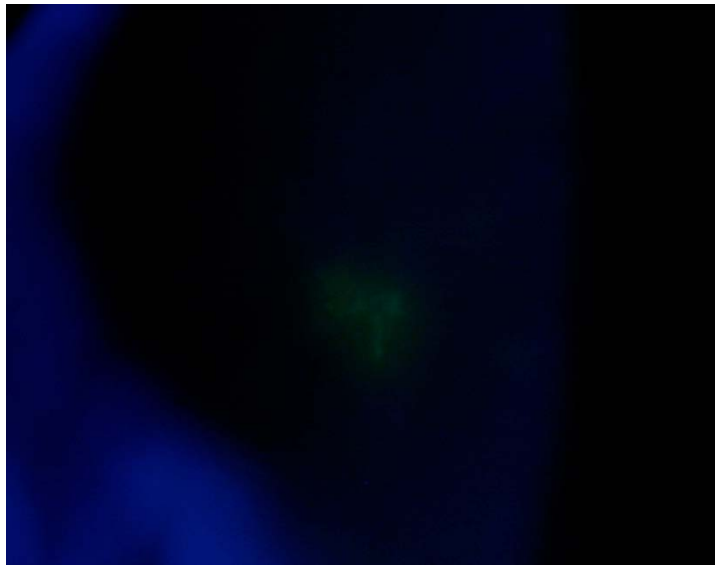
PC: R red eye & watery eye, reduced vision, gritty sensation. Started since Saturday (more so Sunday). Had cold on and off over the past 2 weeks.

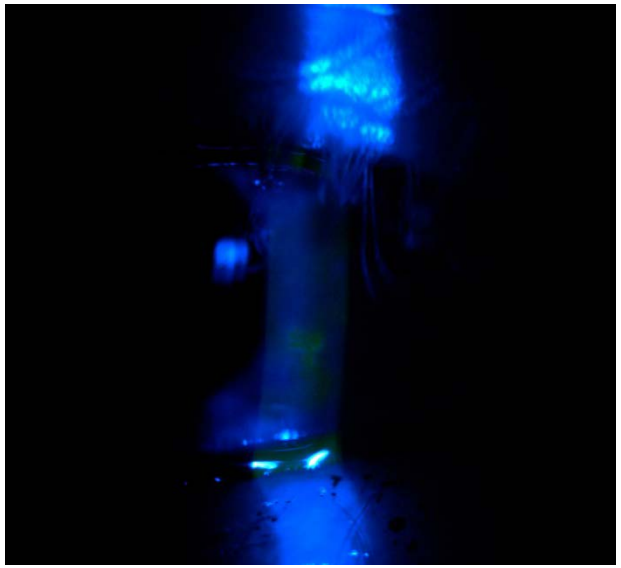
A month ago had started using Flarex once a day, because of FML being unavailable, used it for 3 weeks, now back to FML

Increased Valtrex to tid yesterday (ie 1,500mg daily) & seems to be better



VA 6/4.8^{2-}R=L





Oral Dosing for Herpes Simplex (superficial eye disease)

- Aciclovir (Zovirax) 400mg PO five times a day
- Valaciclovir (Valtrex) 500mg PO three times a day
- Famciclovir (Famvir) 250mg PO three times a day

For day for seven to ten days (21 days?)

Although HSV epithelial keratitis is self-limited in most cases, the rationale for aggressive antiviral therapy is to prevent corneal nerve damage and potential future immunologic disease.

Double the dose for HZO- watch out for ZED's study

Welder JD, Kitzmann AS, Wagoner, MD. Herpes Simplex Keratitis. EyeRounds.org. December 31, 2012

Recommended management of Herpetic Keratitis

As per the previous slide plus

- Appropriate steroid therapy followed by a slow taper*
- Antiviral coverage commensurate with the steroid therapy
- Long-term antiviral prophylaxis (1 year or greater)

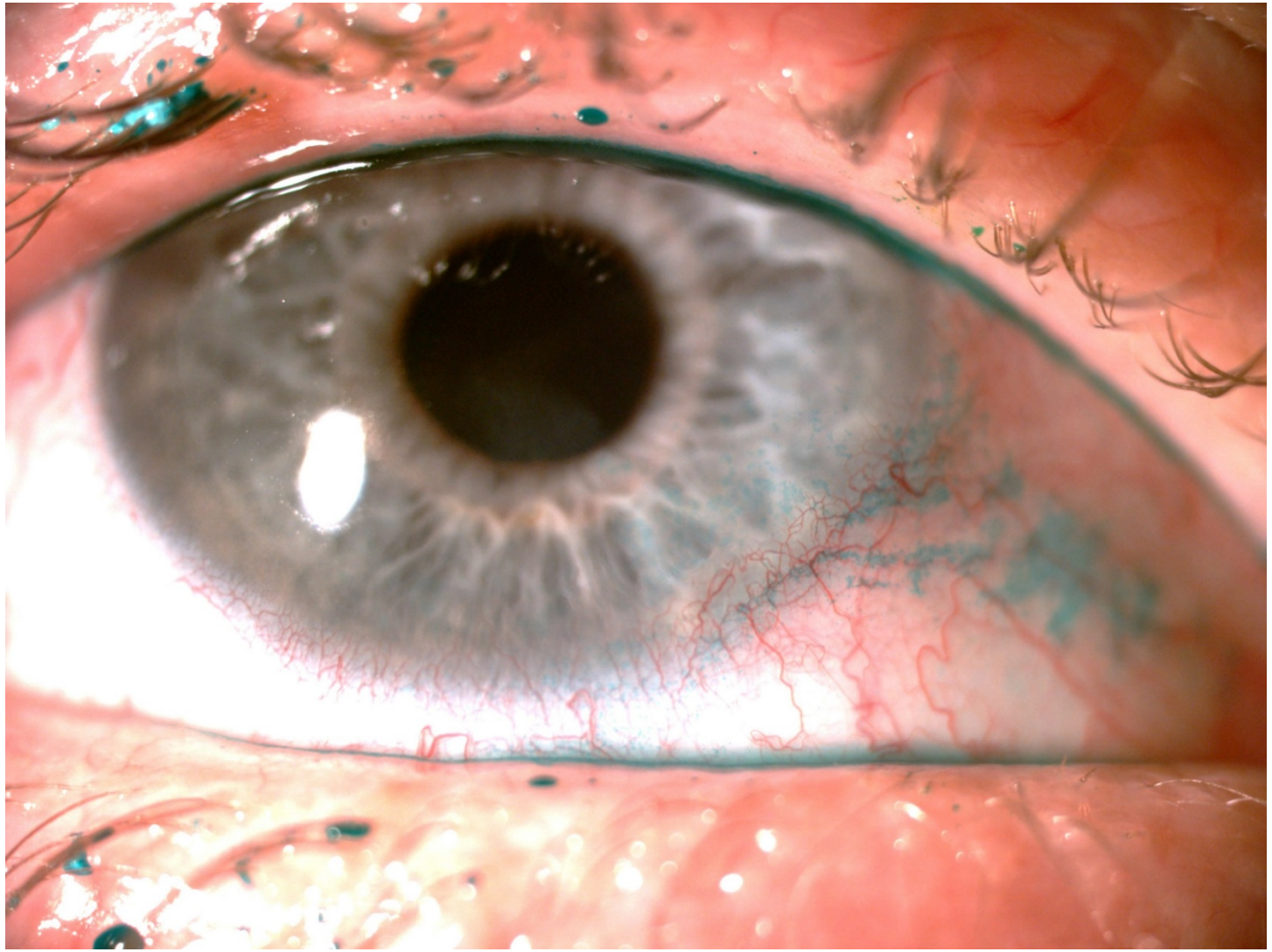
*Slow taper is often down to every other day or even once weekly

Mr GS

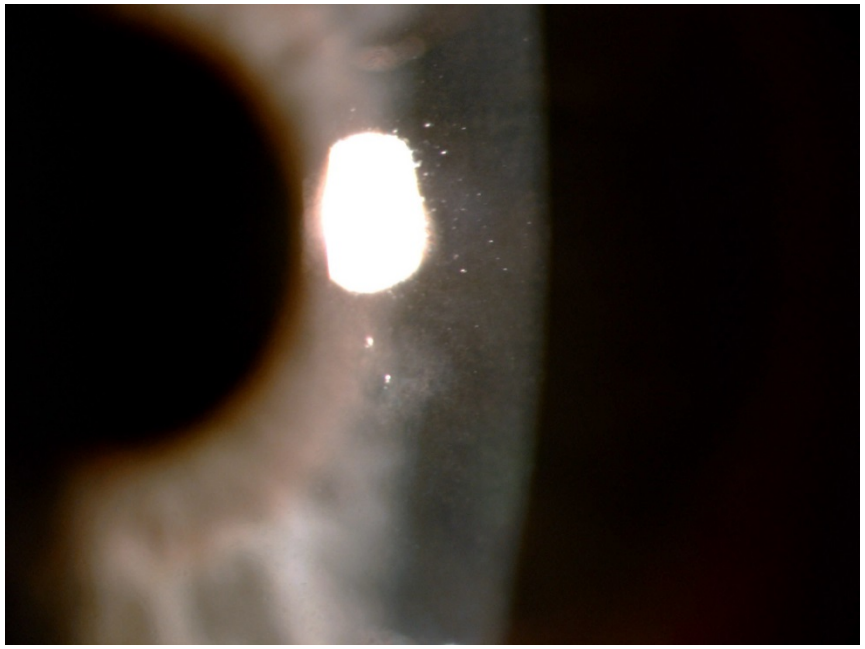
3/7 later

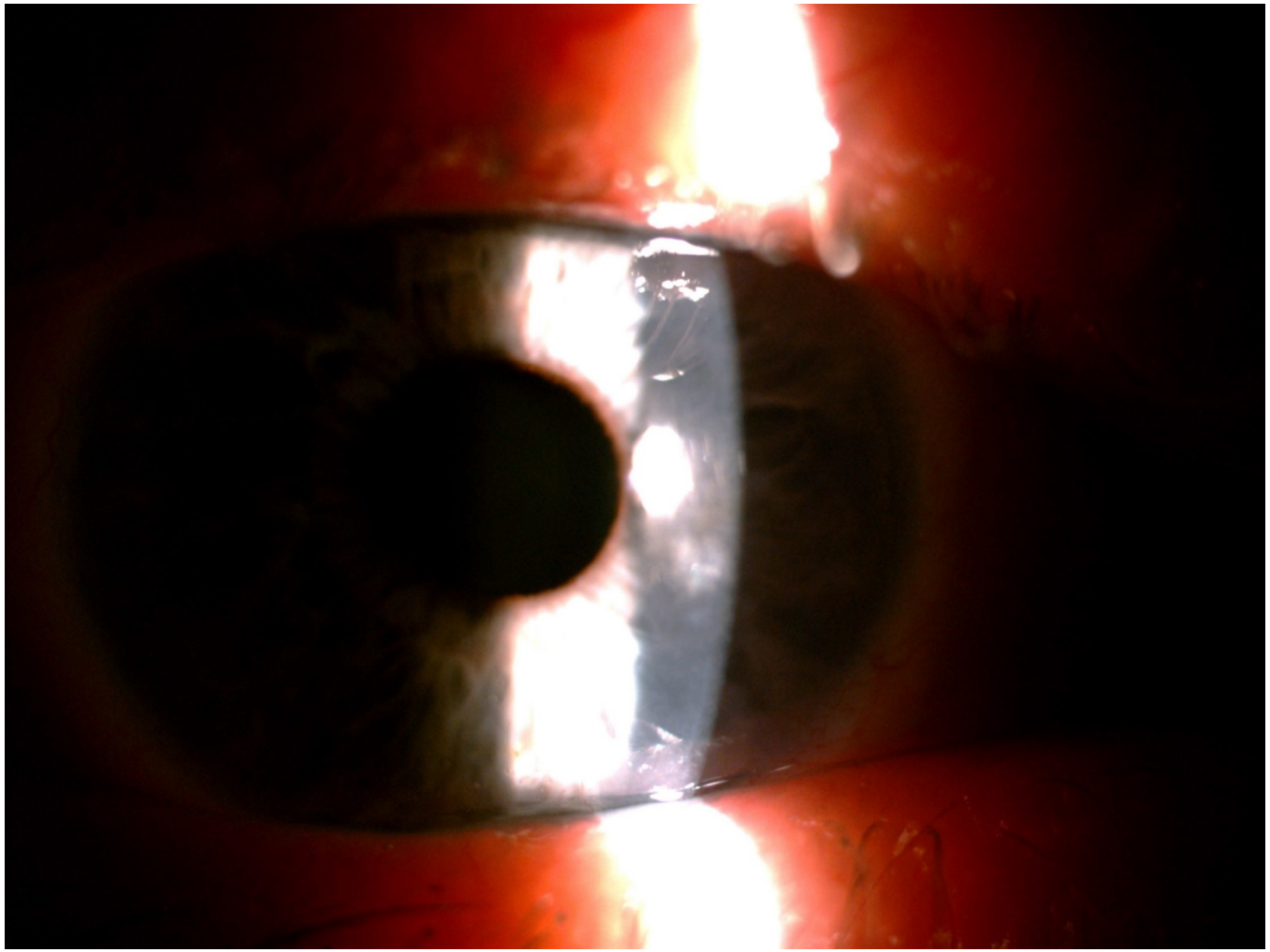
No dendritric staining

Reduce Aciclovir ung to tid,
continue w Valtrex
1,500mg daily & review

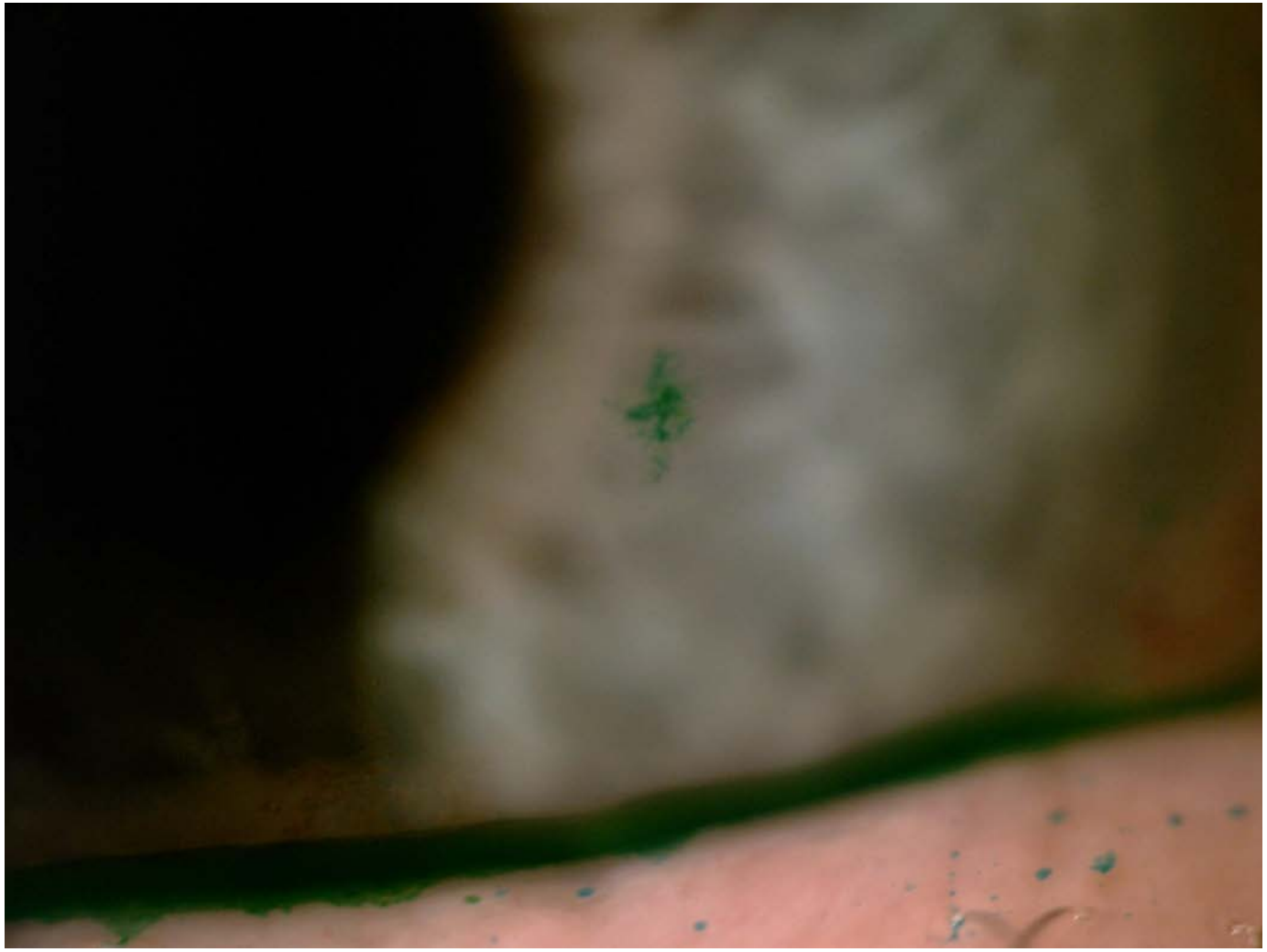


4 weeks



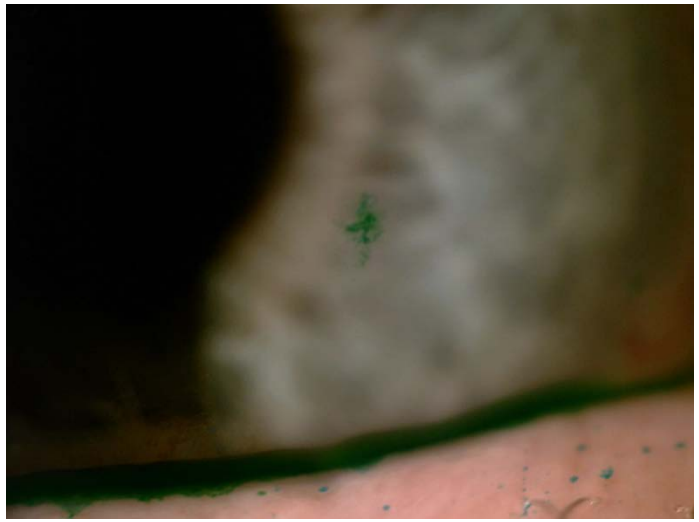


4 weeks



What would you do now?

- Resume topical acyclovir?
- Increase dosage of oral Valtrex?
- Try a different oral antiviral in case there is resistance?
- Increase use of steroids?



Corneal ophthal advice

Clinically I note a tiny residual epithelial defect and surrounding stromal inflammation. This would not be expected to be active viral replication and is more likely inflammatory.

- oc. Chlorsig TDS for a week (to prevent bacterial infection, but mainly to lubricate significantly to allow healing)
- g. Maxidex QID 1 week, TDS 1 week, BD 1 week, D 1 week, then back to FML once daily
- g. Cellufresh to continue frequently
- valaciclovir to continue same dose

Note that if another active episode occurs, oral valaciclovir 500 mg TDS for 5–7 days should be enough, so the toxicity of topical aciclovir should be unnecessary. Along the same lines, we should switch to unpreserved topical steroids if healing does not occur reasonably quickly.

Herpetic conditions & steroids- summary

- Make sure you have adequate antiviral cover
  - This may be oral or topical
- Recognise when process is active infection (usually early epithelial disease) vs inflammatory (stromal , disciform, uveitis)
- If multiple recurrent episodes, then consider oral prophylaxis (long-term)
- May need long-term steroid maintenance with FML or Flarex every day or every other day

Mast RB

Early 2018

L eye very red following swimming

4.5 yo boy: Existing patient- just started kinder

POH: Partially accommodative L ST with mild L amblyopia

GH: High functioning ASD

Prone to asthma & eczema

Penicillin allergy

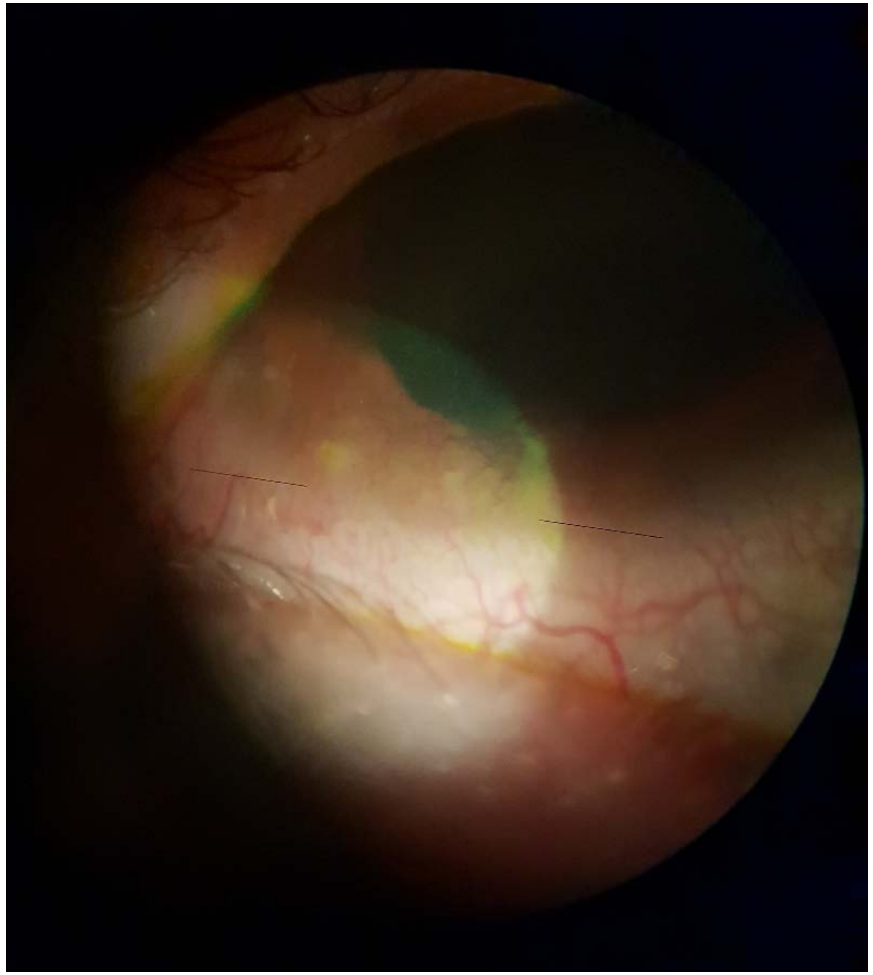
Aberrant immune system

- Regular GI & URTI infections
- Being investigated by paediatric rheumatologist

Mast RB

S/L:

- L inferior nasal corneal vascularisation with raised epithelium & follicles at adjacent limbus
- Lower lid internal hordeolum
- Evert: superior tarsal conjunctiva quiet

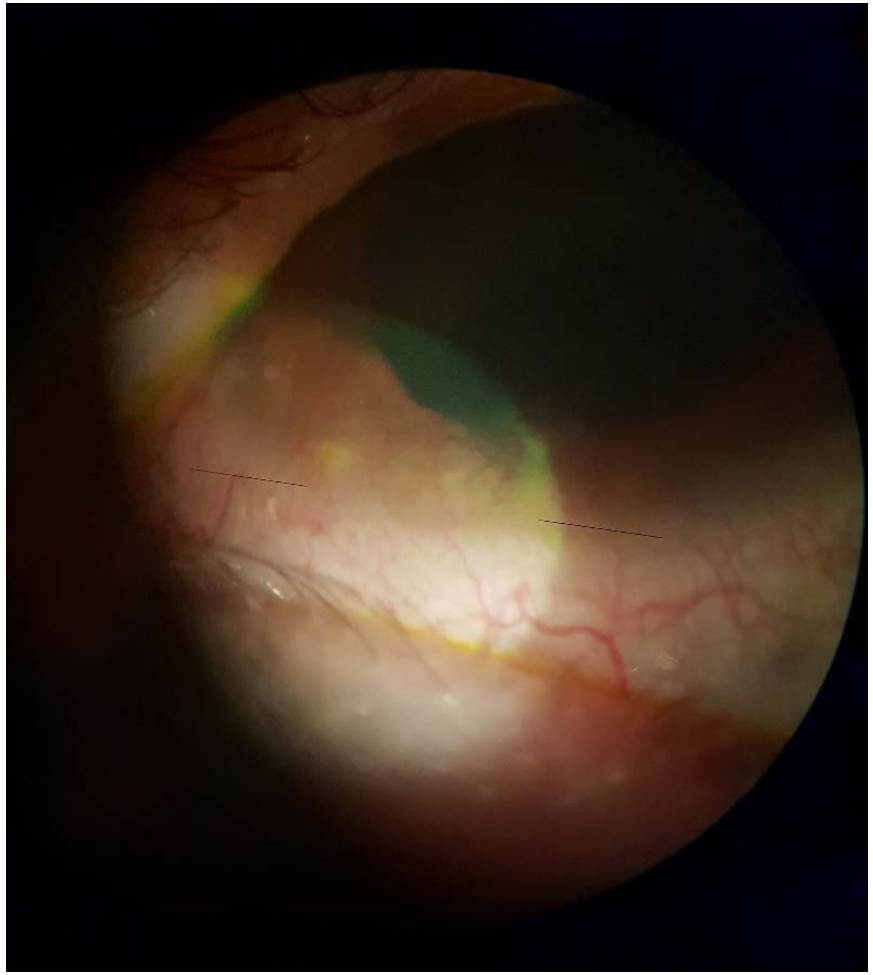


How would this be best managed?

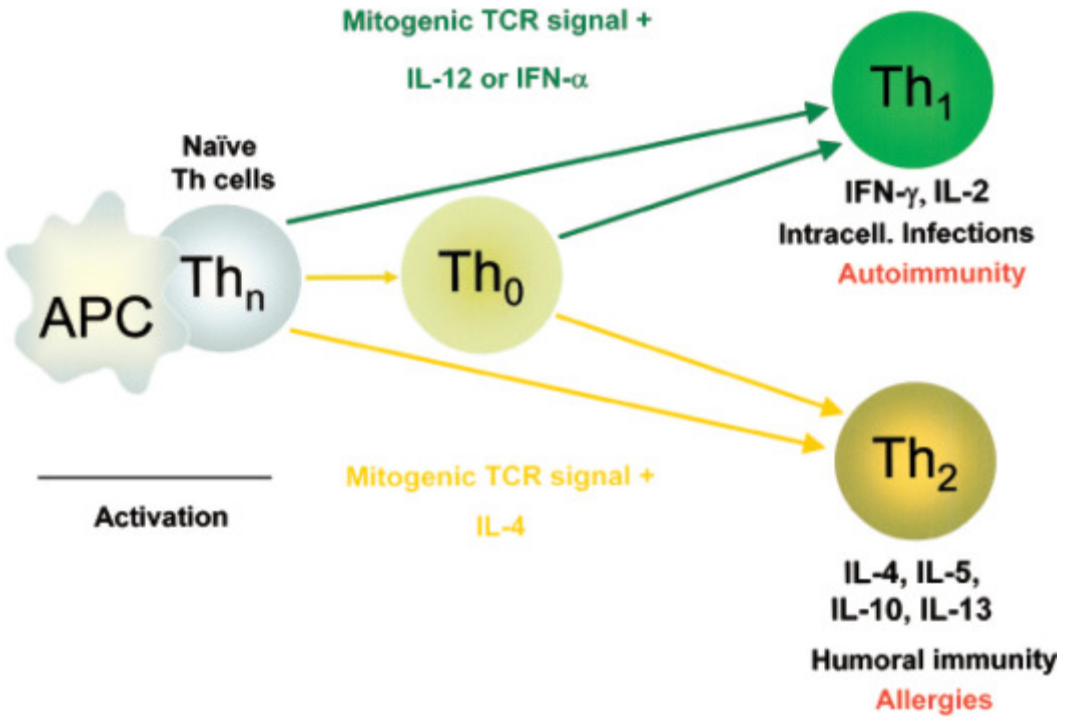
Mast RB

Management:

- Flarex & Chlorsig qid
- Warm compress for internal hordeolum
- Once settled- lid hygiene for maintenance



How does the paediatric immune response differ?



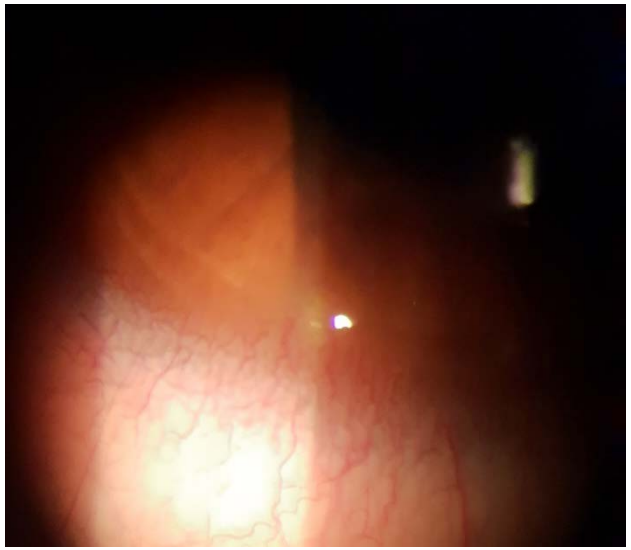
Biedermann, T., Röcken, M., & Carballido, J. M. (2004, January). Th1 And Th2 lymphocyte development and regulation of Th cell–mediated immune responses of the skin. In *Journal of Investigative Dermatology Symposium Proceedings* (Vol. 9, No. 1, pp. 5-14). Elsevier.

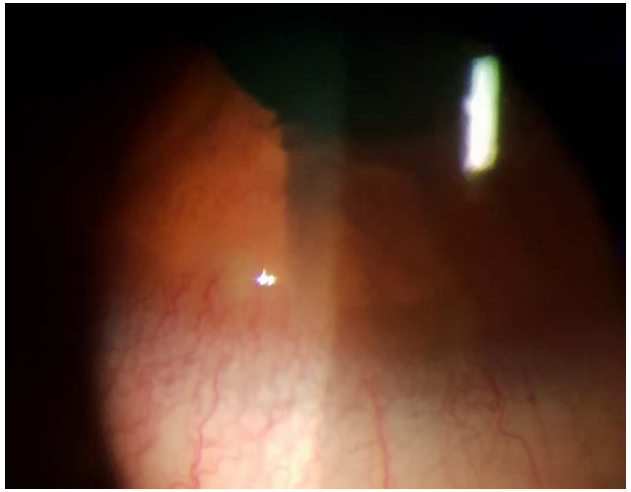
How does the paediatric immune response differ?

Phlyctenular KC

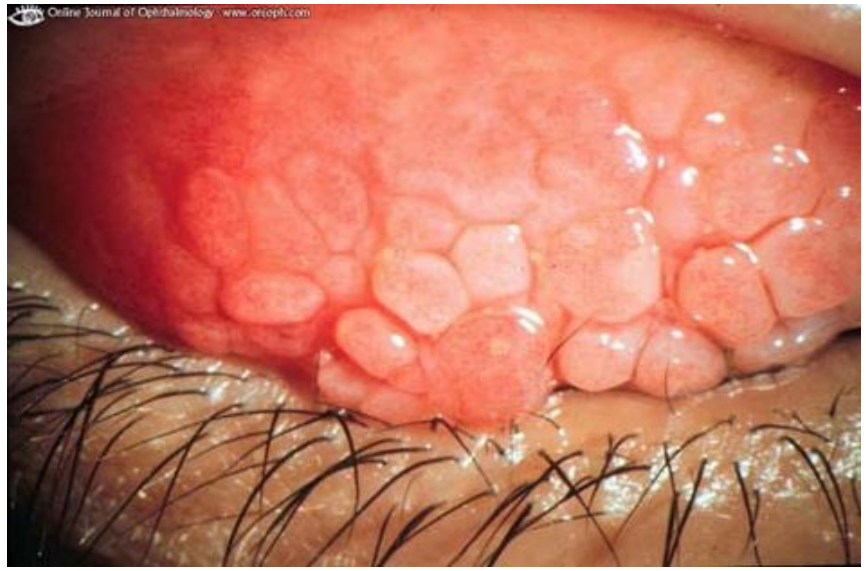
- Occurs primarily in 6-16 year old age group
- Females > males
- Historically- related to TB, still the case in developing countries
- Now most common w Staph. Exotoxins
  - May be associated w ocular rosacea
  - Also Chlamydia, HSV & Strep. Viridians

- Originally thought to be IgE/allergy mediated
- Limbal Langerhans cells/ Helper T Cells- suggest delayed hypersensitivity reaction





How does the paediatric immune response differ?



VKC

- Childhood & resolves during puberty
- Males > females

Can be palpebral, limbal or mixed forms

Hallmark finding of cobblestone papillae

- Some may have limbal, tarsal or mixed presentation
- Cobblestone **may not be present until later disease**

Limbal finding of Trantas dots & limbal nodules (eosinophils & dead epithelial cells)

Risk of shield ulcers & corneal scarring

Steroids in childhood

	MIMs	AMH
FML	Safety and effectiveness have not been demonstrated in children under 2 years of age.	Safe
Flarex	Safety and effectiveness in children have not been established. It is advisable that the intraocular pressure be checked frequently. This is especially important in paediatric patients, as the **risk of corticosteroid induced ocular hypertension may be greater in children** and **may occur earlier than in adults**. Flarex is not approved for use in paediatric patient	"
Pred Forte	Safety and effectiveness have not been demonstrated with Prednefrin Forte eye drops in paediatric patients. Prednefrin Forte eye drops is not recommended to be used in paediatric patients.	"
Maxidex	The safety and effectiveness of Maxidex eye drops in paediatric patients have not been established. However**, increased susceptibility to raised IOP and cataract formation have been described in the literature.**	"

Higher risk IOP rise in children

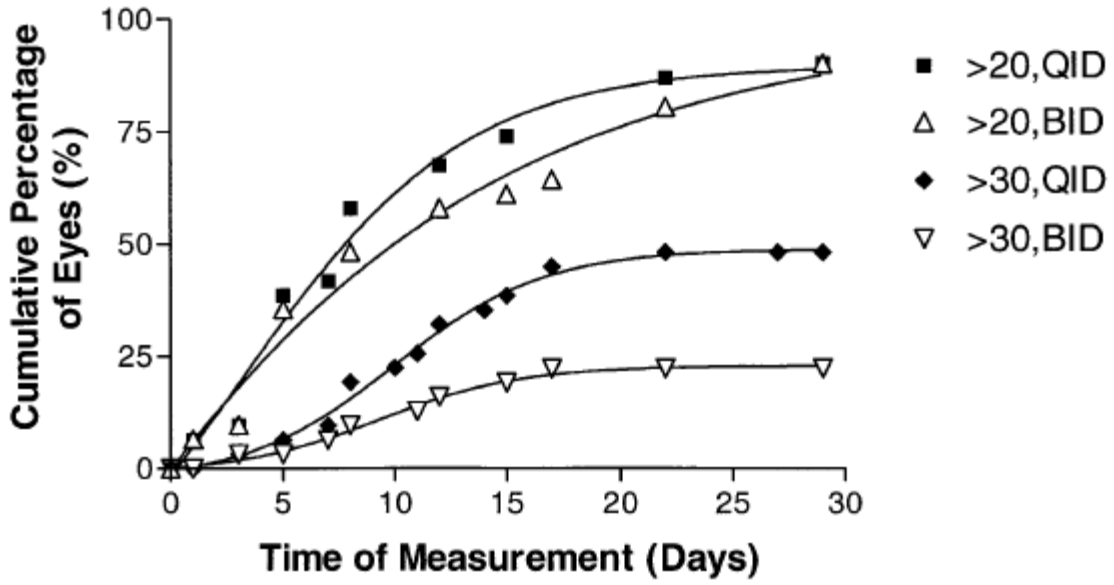


Figure 1. Cumulative percentage of eyes with intraocular pressure measurements more than 20 mmHg and 30 mmHg in both twice daily and four times daily groups.

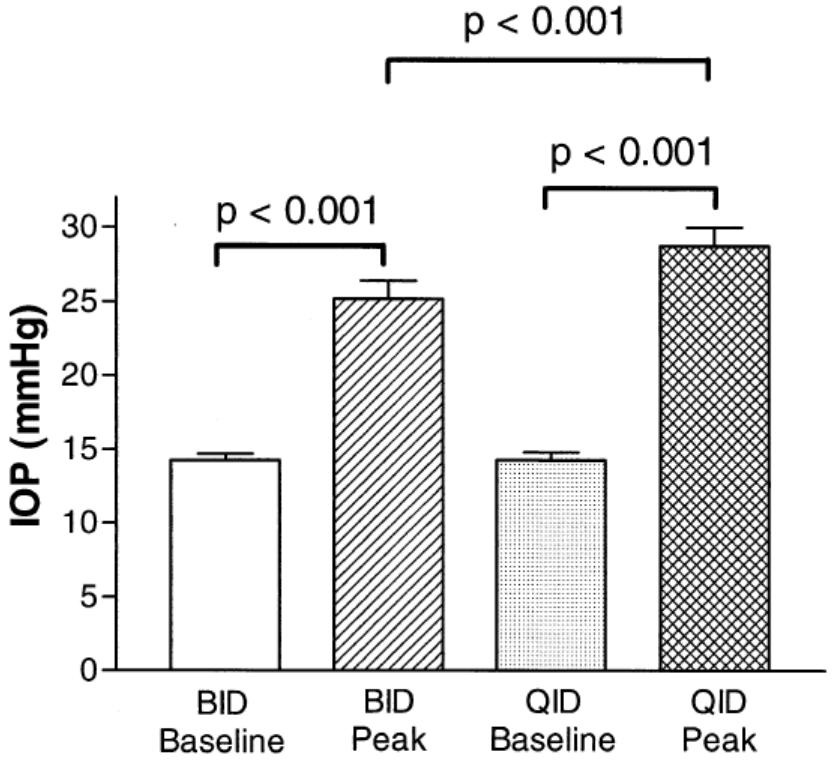


Figure 2. The difference between peak intraocular pressure (IOP) measurements of twice daily and four times daily groups as well as their respective preoperative IOP measurements.

Ng JS, Fan DS, Young AL, et al. Ocular hypertensive response to topical dexamethasone in children: a dose-dependent phenomenon. Ophthalmology 2000;107:2097e100

OHT with Maxidex

Table 1. Ocular Hypertensive Response to Topical 0.1% Dexamethasone in Different Studies

	Armaly[20]	Biedner et al[21]	Kwok et al[14]	Present Study	
Age (yrs)					
Mean	Adult	9.7	6.1	5.8	
Range	(16–40)	(4–19)	(3–10)	(2–10)	
Frequency of administration (time/day)	3	4	6	4	2
Duration of administration (wks)	4	6	4	4	4
Sample size	80	44	16	31	31
Low responder (change in IOP <6 mmHg)	53 (66%)	39 (89%)	1 (6%)	3 (10%)	5 (16%)
Intermediate responder (change in IOP 6–15 mmHg)	23 (29%)	4 (9%)	6 (38%)	13 (42%)	18 (58%)
High responder (change in IOP > 15 mmHg)	4 (5%)	1 (2%)	9 (56%)	15 (48%)	8 (26%)

IOP = intraocular pressure.

Ng JS, Fan DS, Young AL, et al. Ocular hypertensive response to topical dexamethasone in children: a dose-dependent phenomenon. Ophthalmology 2000;107:2097e100

Armaly, M. F. (1965). Statistical attributes of the steroid hypertensive response in the clinically normal eye: I. The demonstration of three levels of response. *Investigative Ophthalmology & Visual Science*, *4*(2), 187-197.

Biedner, B. Z., David, R. O. B. E. R. T., Grudsky, A. L. E. X. A. N. D. E. R., & Sachs, U. R. I. E. L. (1980). Intraocular pressure response to corticosteroids in children. *British Journal of Ophthalmology*, *64*(6), 430-431.

Maxidex vs FML in children

Table 3. Comparison of Clinical Characteristics among Patients on Dexamethasone and Fluoromethalone

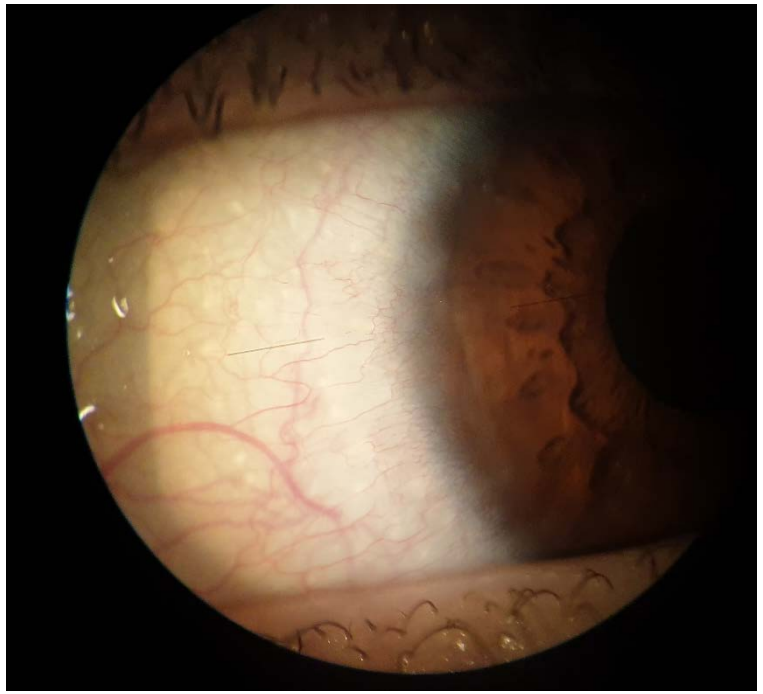
Variable	Dexamethasone	Fluoromethalone	Paired *t* Test (*P*)
Spherical equivalent (D)			
Mean ± SD	+0.23 ± 1.07	+0.38 ± 1.28	0.314
Range	(−2.75)–(1.75)	(−2.75)–(+3.00)	
Preoperative IOP (mmHg)			
Mean ± SD	[illegible]	[illegible]	0.527
Range	11.30–20.70	9.00–19.30	
Maximal IOP change (mmHg)			
Mean ± SD	15.48 ± 8.71	5.83 ± 4.96	0.001*
Range	(−2.60)–(+31.00)	(+1.00)–(+17.00)	
Peak IOP (mmHg)			
Mean ± SD	30.66 ± 8.35	20.66 ± 6.03	0.001*
Range	13.00–48.00	11.30–36.30	
Time to peak IOP (days)			
Mean ± SD	15.56 ± 8.29	14.94 ± 11.04	0.880
Range	3.00–31.00	1.00–35.00	

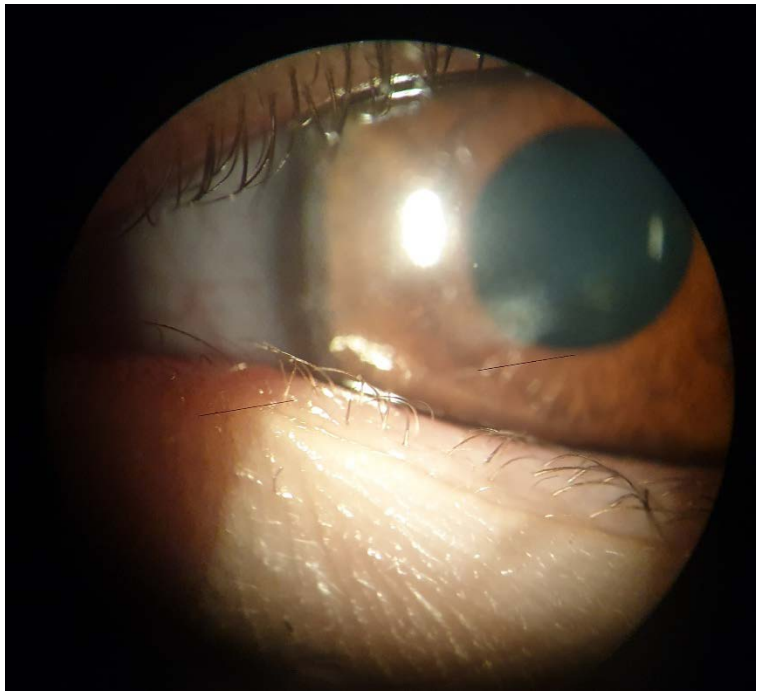
SD = standard deviation; D = diopter; IOP = intraocular pressure.

* Statistically significant at 95% confidence interval.

Kwok AK, Lam DS, Ng JS, et al. Ocular hypertensive response to topical steroids in children. Ophthalmology 1997;104:2112e16.

Mast RB





Phone a friend time

Likelihood of chronic issues & steroid dependence

- Risk of PSC & IOP rise

- Referral to corneal ophthal for opinion (to keep dad on board) & commence steroid sparing agents

Phone a friend time

Management advice:

- **Maxidex**- higher dose first two weeks then taper over three months
- Cyclosporin A 0.05% weekly replacement bottles

Schedule 4 Prescription Only Medicine		
Anti-infectives	**Anti-inflammatories**	**Decongestants/ anti-allergics**
Aciclovir Azithromycin Bacitracin Cephazolin Ciprofloxacin Framycetin Ganciclovir Gentamicin Gramicidin Neomycin Ofloxacin Polymyxin Tetracycline Tobramycin	Cyclosporin Dexamethasone Diclofenac Fluorometholone Flurbiprofen Hydrocortisone Ketorolac Loteprednol Prednisolone	Olopatadine

Spadavecchia, L., Fanelli, P., Tesse, R., Brunetti, L., Cardinale, F., Bellizzi, M., ... & Armenio, L. (2006). Efficacy of 1.25% and 1% topical cyclosporine in the treatment of severe vernal keratoconjunctivitis in childhood. *Pediatric allergy and immunology*, *17*(7), 527-532.

Yücel, O. E., & Ulus, N. D. (2016). Efficacy and safety of topical cyclosporine A 0.05% in vernal keratoconjunctivitis. *Singapore medical journal*, *57*(9), 507.

Non-steroidal options

Cyclosporin A

- Initial studies looked at 2% with improvement in first 2-4 weeks
- 0.05% qid- Takes longer (about 3 months)
- Better for longer term use?

Tacrolimus 0.1% bid

- Can't be prescribed by optometrists

Require compounding

- Appropriate concentration?
- Quality control
- Cost
- Long-term treatment

Oral doxycycline

- Helpful especially if ocular rosacea component
- Not in children <8 years
  - Dental enamel

Spadavecchia, L., Fanelli, P., Tesse, R., Brunetti, L., Cardinale, F., Bellizzi, M., ... & Armenio, L. (2006). Efficacy of 1.25% and 1% topical cyclosporine in the treatment of severe vernal keratoconjunctivitis in childhood. *Pediatric allergy and immunology*, *17*(7), 527-532.

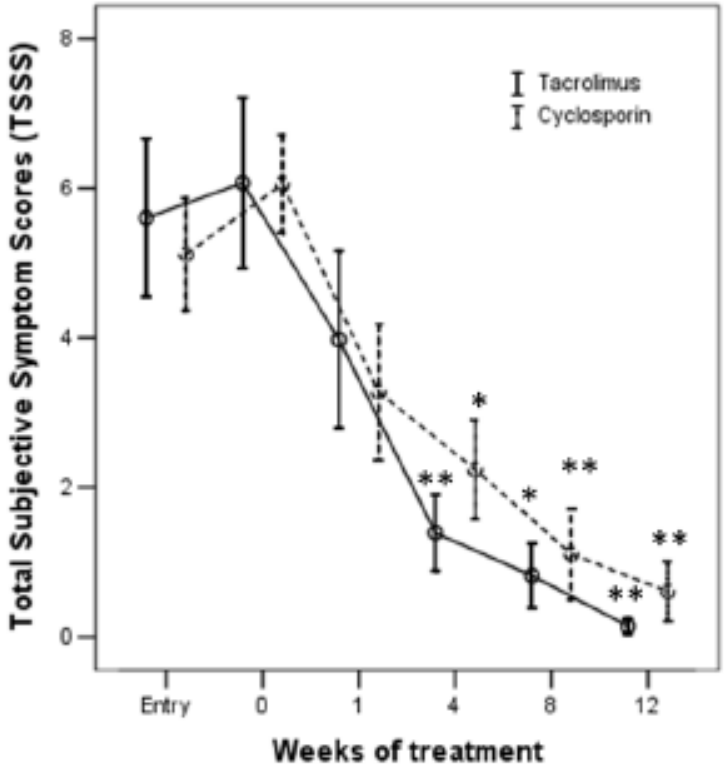
Yücel, O. E., & Ulus, N. D. (2016). Efficacy and safety of topical cyclosporine A 0.05% in vernal keratoconjunctivitis. *Singapore medical journal*, *57*(9), 507.

Double masked comparison of 0.1% Tacrolimus ointment vs 2% Cyclosporine eye drops

Followed improvement in symptom scores with VKC

Statistically no difference between Cyclosporin & Tacrolimus

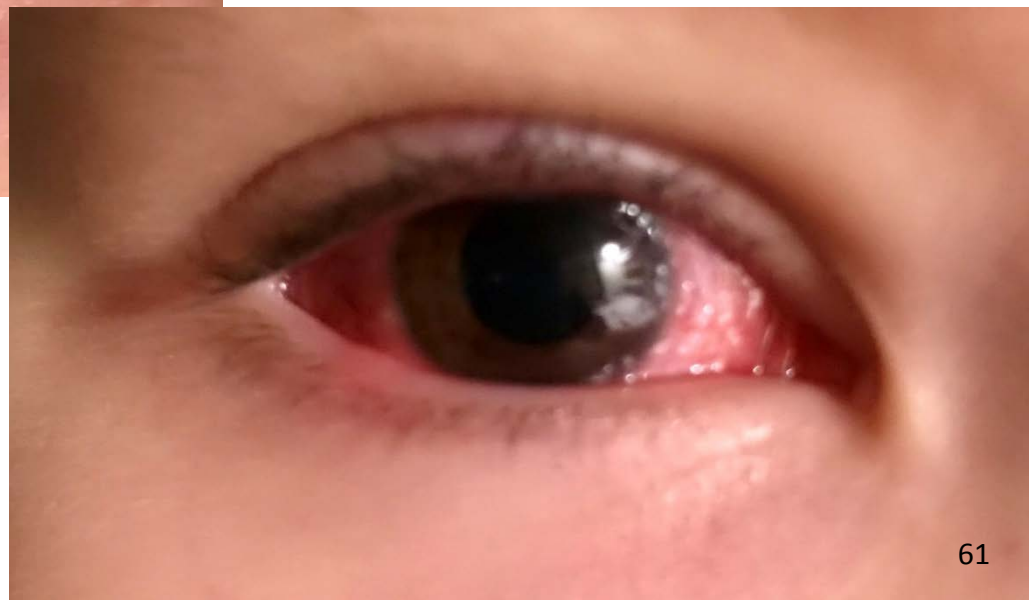
Continued improvement over three months



Vichyanond, P., & Kosrirukvongs, P. (2013). Use of cyclosporine A and tacrolimus in treatment of vernal keratoconjunctivitis. *Current allergy and asthma reports*, *13*(3), 308-314.

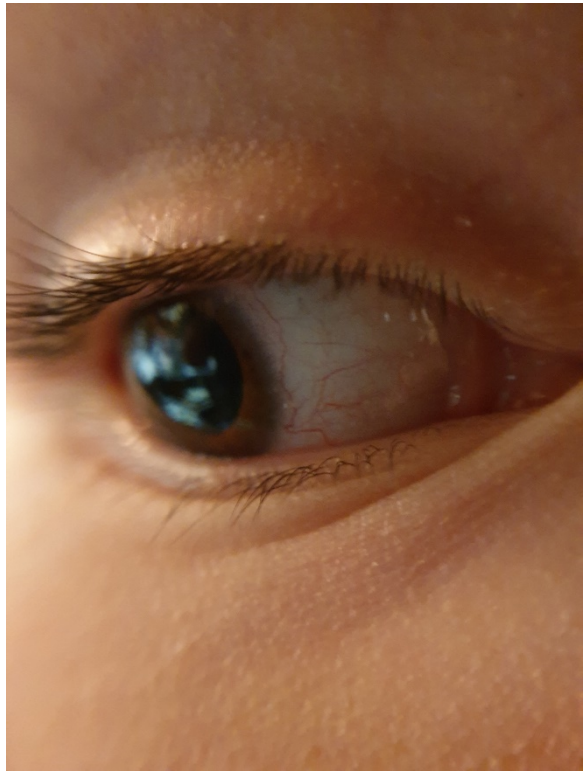
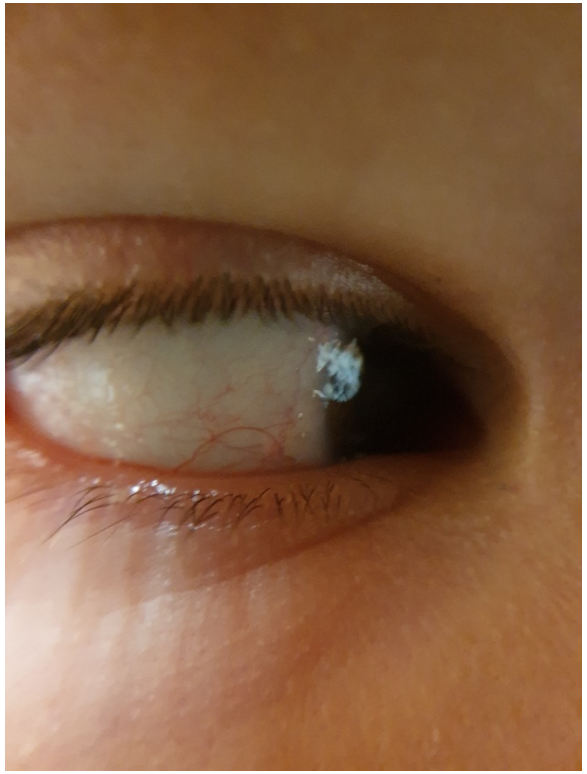
Labcharoenwongs, P., Jirapongsananuruk, O., Visitsunthorn, N., Kosrirukvongs, P., Saengin, P., & Vichyanond, P. (2012). A double-masked comparison of 0.1% tacrolimus ointment and 2% cyclosporine eye drops in the treatment of vernal keratoconjunctivitis in children. *Asian Pacific journal of allergy and immunology*, *30*(3), 177.

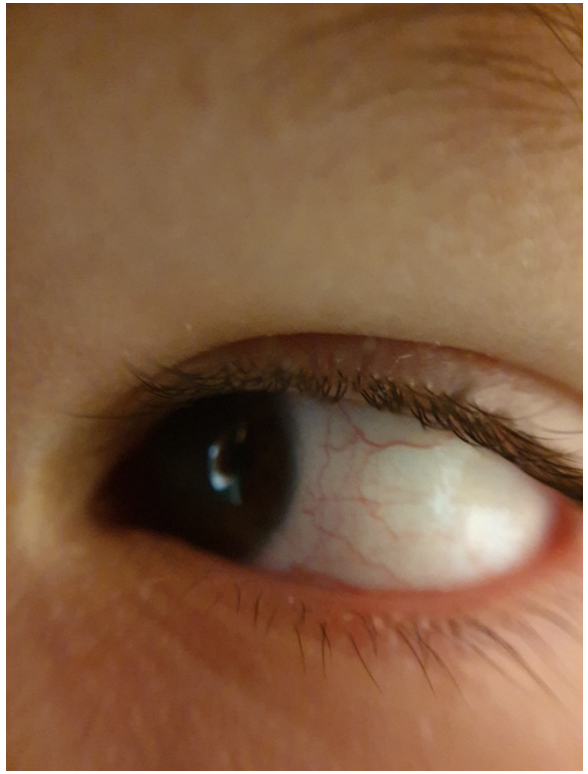
Sunday night!



Tim Martin 2019

October



Paediatric steroids- summary

- Red eye conditions less common than adults but when they do occur often:
  - allergy or delayed hypersensitivity mediated
  - Recurrent

- Use of steroids in paediatric does seem to carry a higher risk and early IOP response than adults
- Treat underlying condition but if steroid dependent then consider steroid-sparing agents
  - These carry extra cost and require long-term use

Summary

Differentiate infective vs inflammatory processes

Use steroids the way they should be- hard enough to control condition & taper

- Maybe we need to rethink our position on Maxidex?
- Probably more harm in undertreating condition for longer

Steroid IOP responses do occur (& more in paediatrics)

- Anyone is a steroid responder with enough time/dosage?

Don’t forget steroid sparing options

- But expensive & harder to source

THE UNIVERSITY OF MELBOURNE

Thank you

Thanks for listening

Tim Martin

Melbourne Museum- November 2019