



# Should we be worried using steroids?

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**Tim Martin**

BlueSky – A day in November 2019





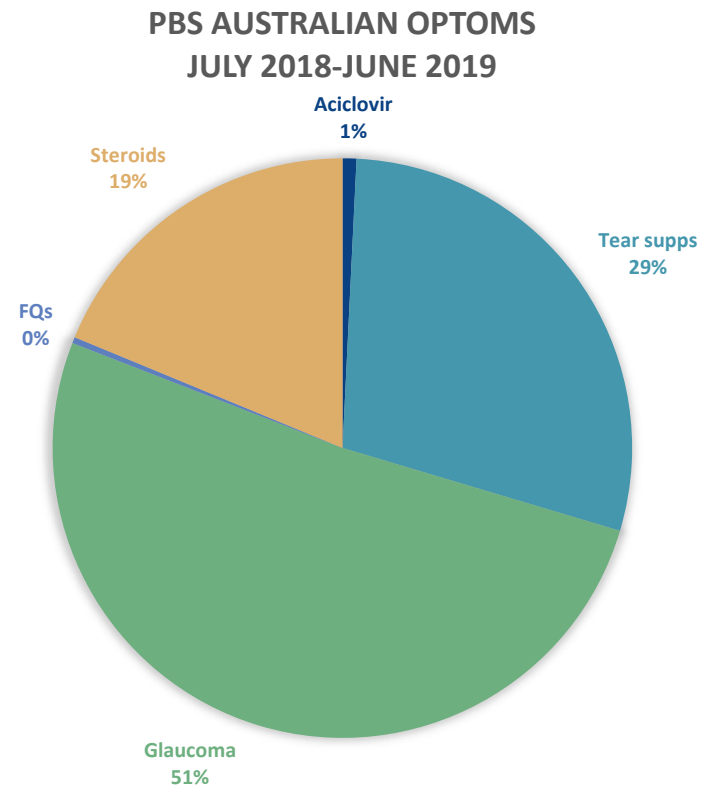
## Learning Objectives:

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



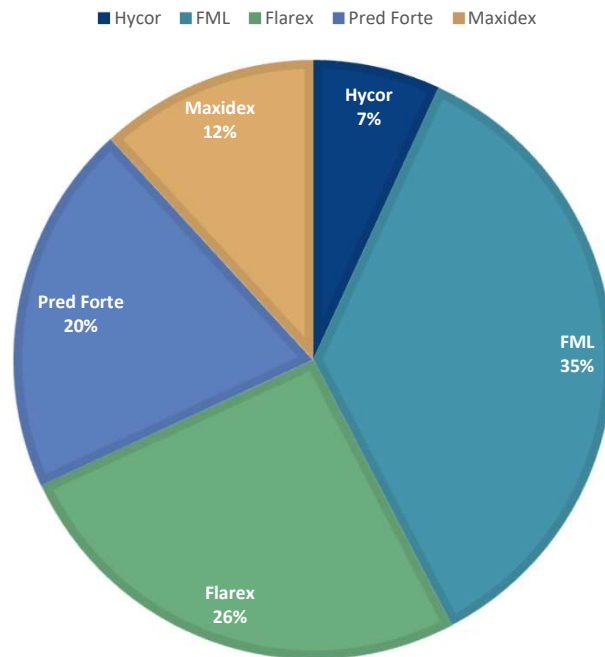
# Distribution of PBS Optom Rx



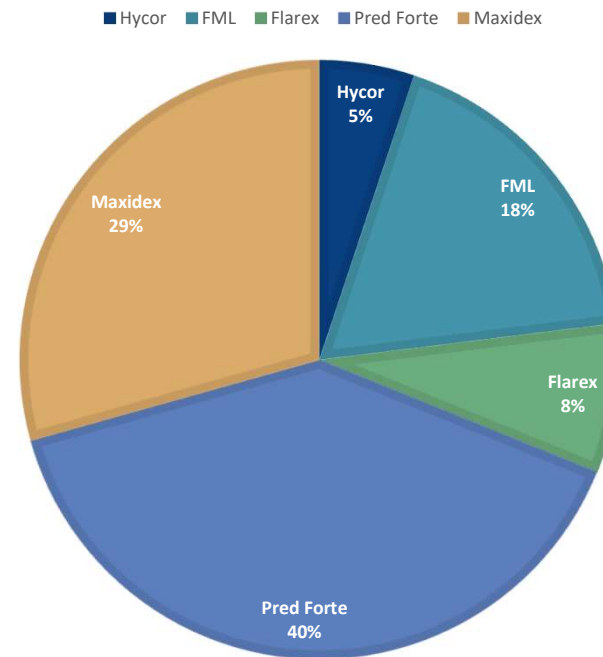


# Steroid PBS Rx

PBS STEROID PRESCRIBING- OPTOMS



PBS STEROID PRESCRIBING- MEDICAL PRACTITIONERS





# 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 <sup>1</sup> | Penetration <sup>1</sup> | 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                 | ++                       | ++++                      |
| <sup>1</sup> with intact corneal epithelium |                      |                          |                           |



**Miss KL**

**January 2014** 21 yo F

Last 4/7 R eye red, photophobic & blurry

R: 6/6<sup>2+</sup> & L: 6/6

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

L quiet

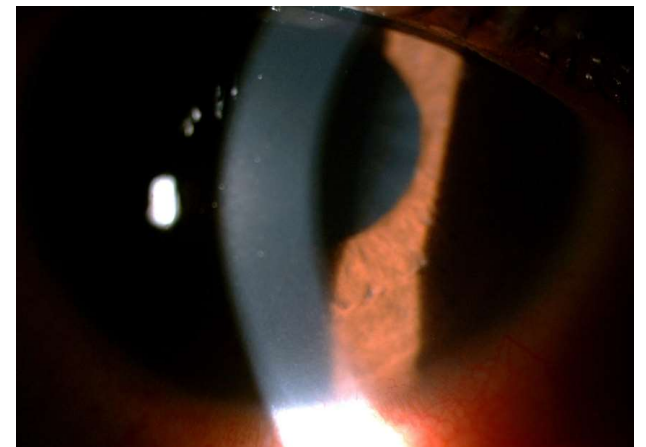
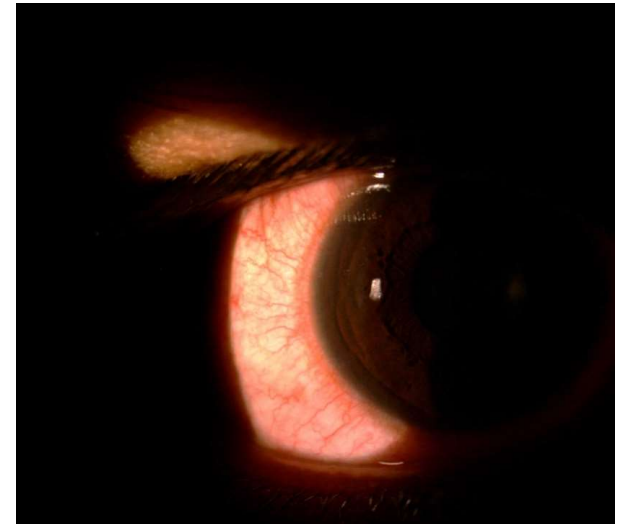
IOP 19 mmHg R=L (thicker CCT)

DFE: unremarkable

GH: mild asthma; targeted systemic history- nil

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

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## 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



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...but now 14 weeks pregnant!



## **Q1: How would you manage uveitis in a pregnant lady?**

- A. No treatment- it will settle by itself
- B. Standard uveitis treatment: Pred. Forte hourly and Atropine
- C. Standard uveitis treatment and medication to lower IOP
- D. Refer- the ophthalmologist can decide



# 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.



# Steroids in pregnancy?

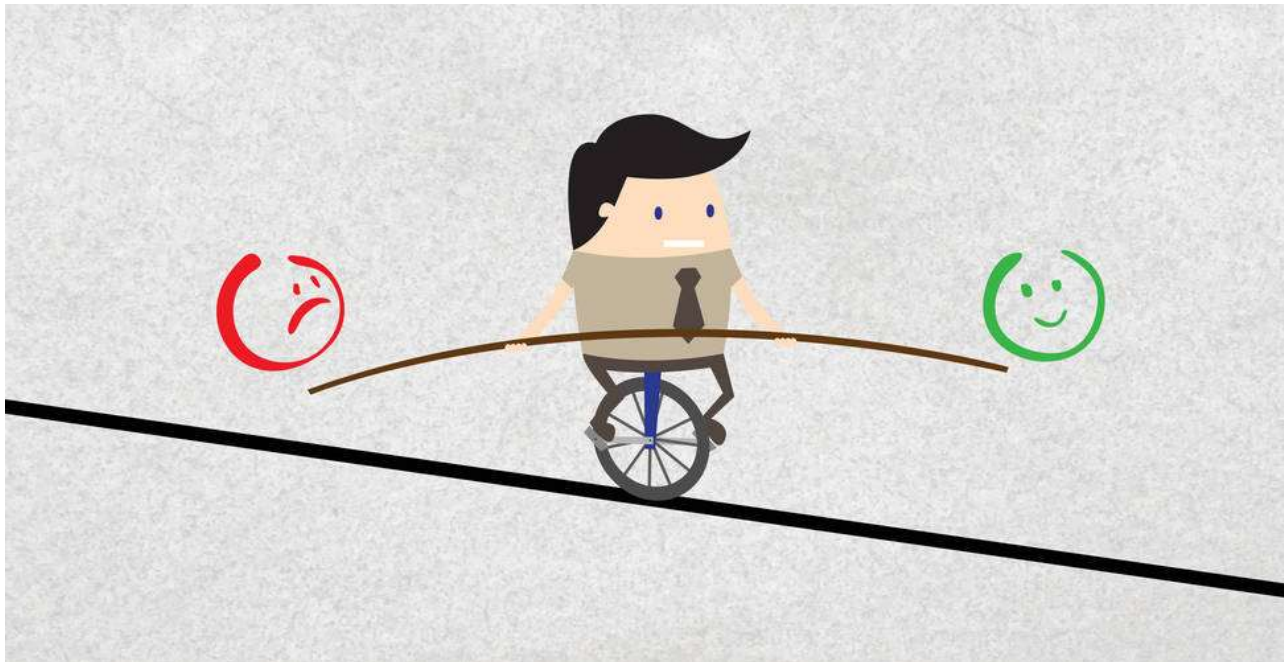
|                            | MIMs   | AMH  |
|----------------------------|--|------|
| FML<br>(Category B3)       | There are no adequate well-controlled studies in pregnant women. Has been shown to be teratogenic, fetotoxic and embryocidal in rabbits when given in doses approximating the human dose 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.<br>FML should be used with caution during pregnancy only if the potential benefit outweighs the potential risk to the foetus.  | Safe |
| Flarex<br>(Category B3)    | Should be given to a pregnant woman only if clearly needed   | “    |
| Pred Forte<br>(Category C) | In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. <b>These findings do not seem to be relevant to humans.</b> 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.<br>There are no adequate and well controlled studies in pregnant women. Prednefrin Forte should be used during pregnancy <b>only if the potential benefit justifies the potential risk to the foetus.</b>  | “    |
| Maxidex<br>(Category B3)   | Reduced placental and birthweights have been recorded in both animals and humans after long-term treatment with corticosteroids.<br>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.<br>Maxidex eye drops should not be used in pregnancy <b>unless the potential benefit to the mother outweighs the potential risk to the embryo or foetus</b> | “    |

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## 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



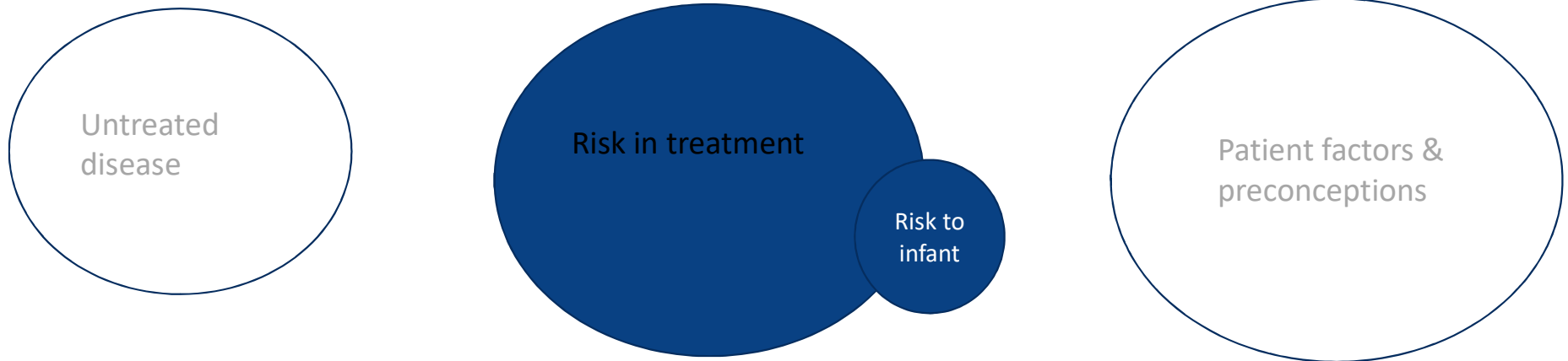
Untreated  
disease

Risk in treatment

Patient factors &  
preconceptions

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

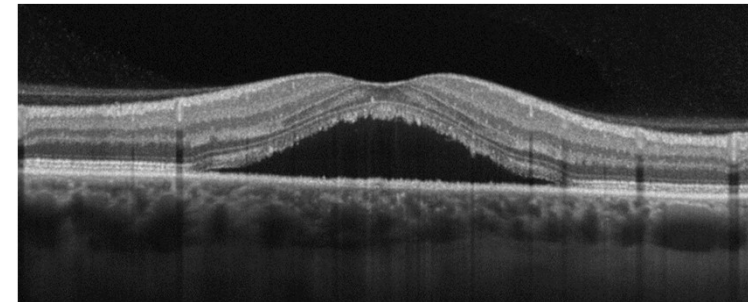
# Risk analysis



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.

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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

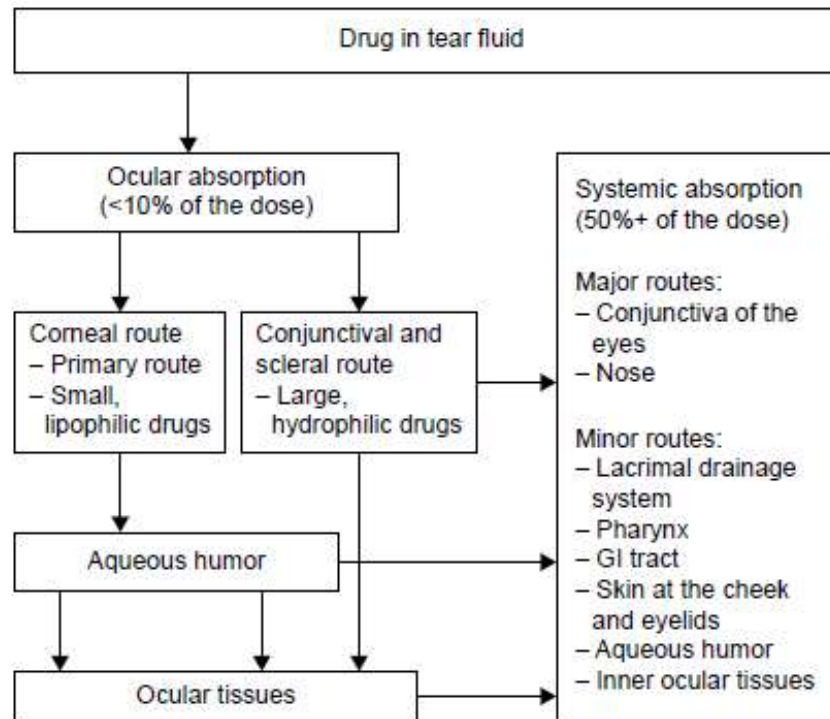
- Mild disease

Oral steroids

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

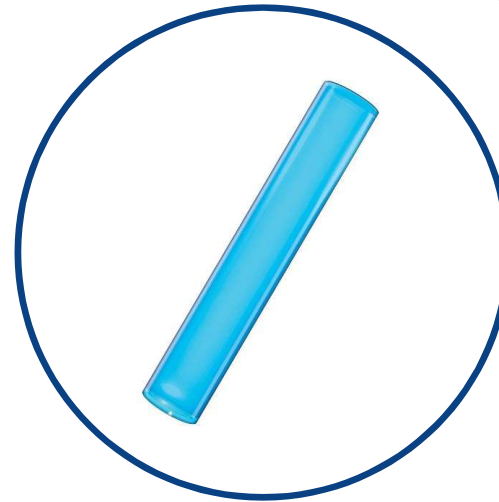


Farkouh, A., Frigo, P., & Czejka, M. (2016). Systemic side effects of eye drops: a pharmacokinetic perspective. *Clinical Ophthalmology (Auckland, NZ)*, 10, 2433.



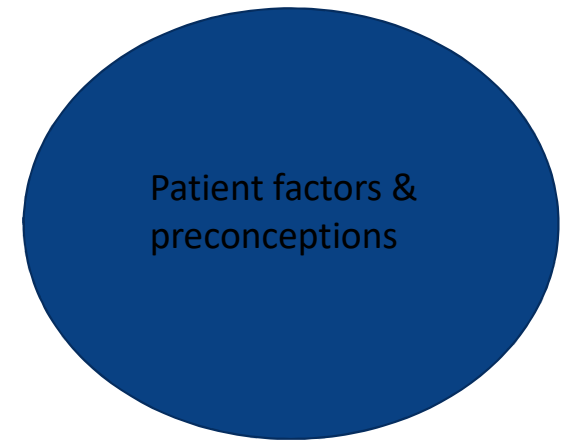
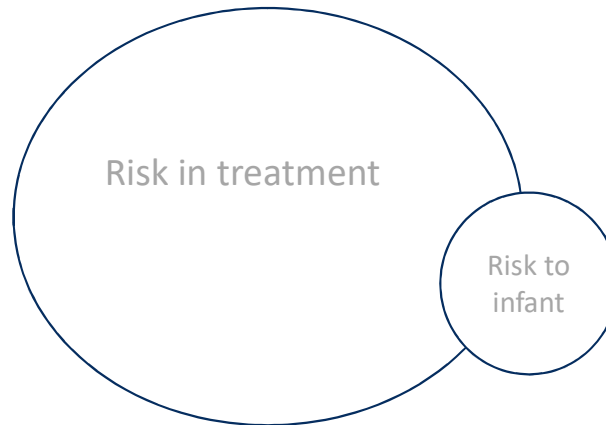
# Minimising systemic exposure

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

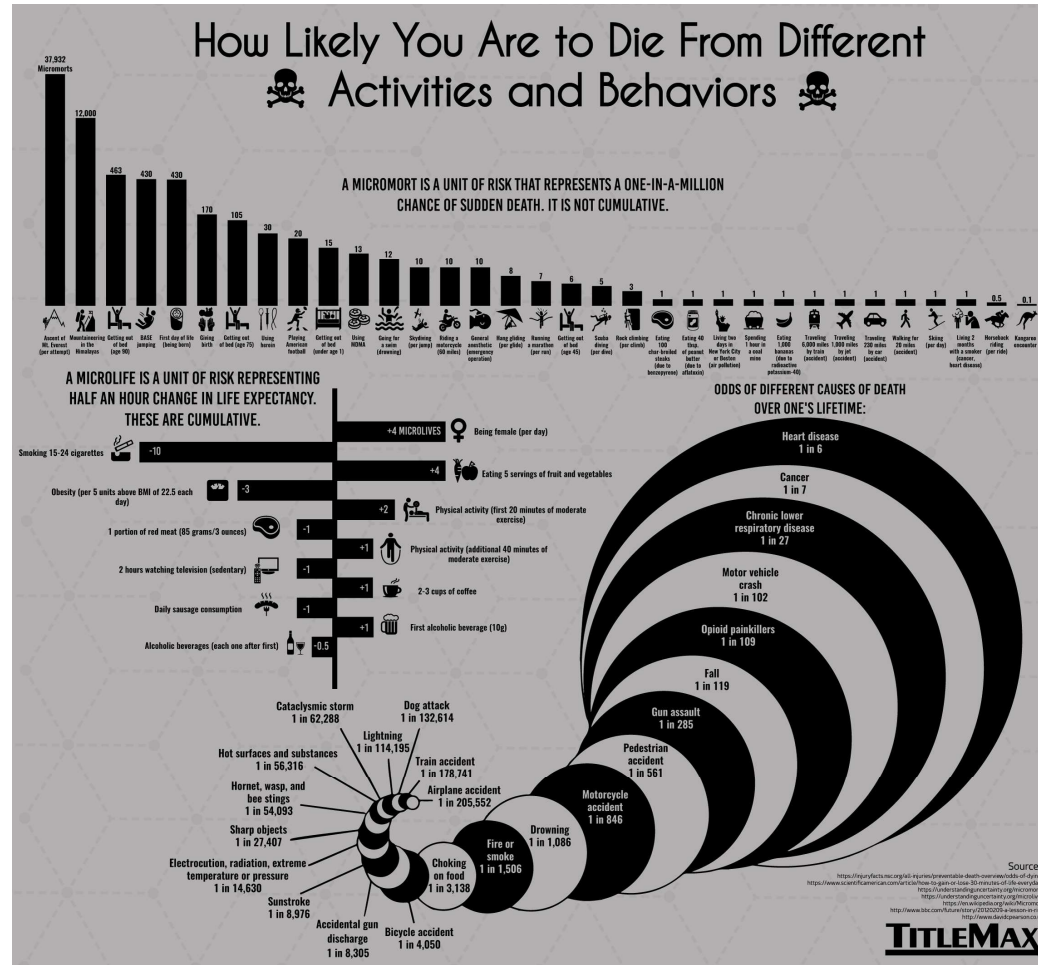




# Risk analysis



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



# Risk analysis

Untreated  
disease

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

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Risk in treatment

Risk to  
infant

Mother:

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

Infant:

?none

?cleft palate- none reported topical; some in oral

Patient factors &  
preconceptions

- 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





## Q2: During 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy, uveitis flare-ups occur...

- A. with more severity than in women who aren't pregnant
- B. with less severity than in women who aren't pregnant
- C. more often than in women who aren't pregnant
- D. **less often than in women who aren't pregnant**



## Discussion with another ophthalmologist

**2<sup>nd</sup> pregnancy** – 2<sup>nd</sup> 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 1<sup>st</sup> trimester vs prior to pregnancy

Reduced incidence flare ups 2<sup>nd</sup> & 3<sup>rd</sup> 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**

3<sup>rd</sup> pregnancy, 1<sup>st</sup> trimester

Not Pregnant



Pregnant

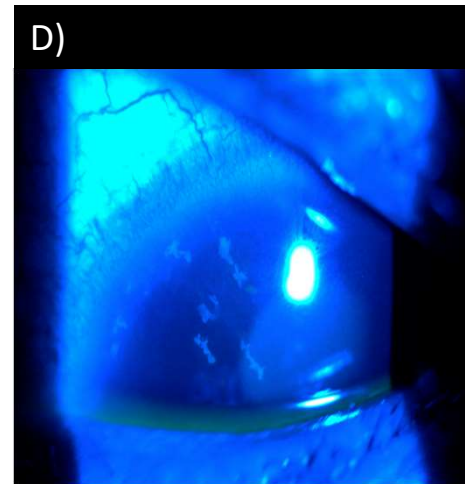
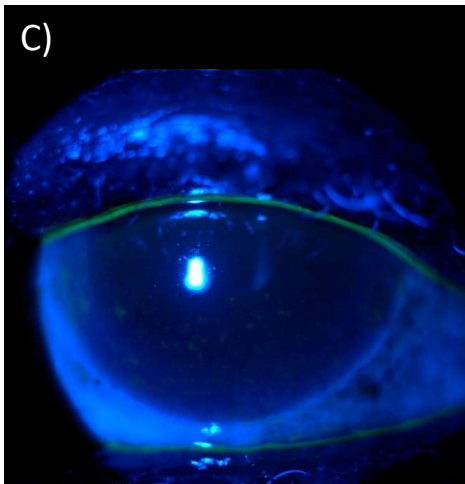
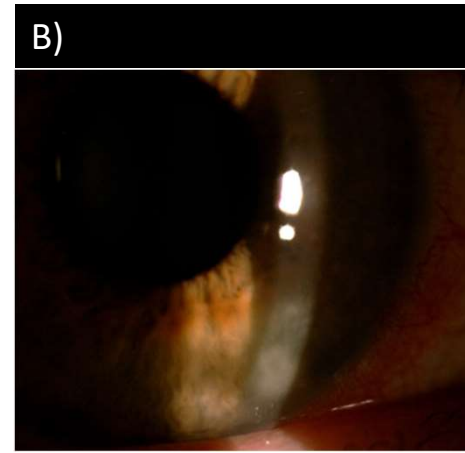
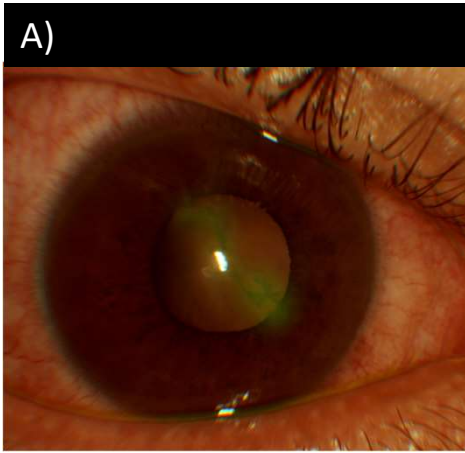




## Topical steroids in pregnancy- summary

- 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 2<sup>nd</sup> & 3<sup>rd</sup> trimesters

**Q3: Which of the following is the most common initial presentation of HZO?**

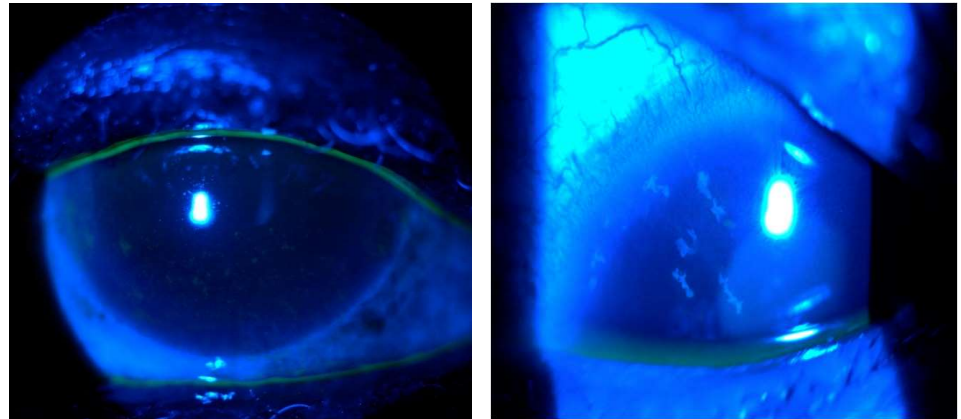


# Corneal complications with HZO

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.



**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

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Mr GS

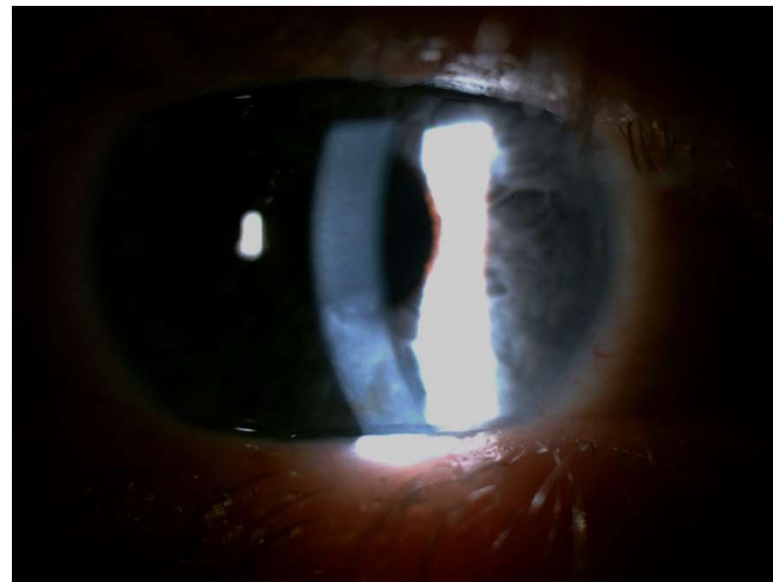
V w SVD R) 6/12 & L) 6/7.5

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

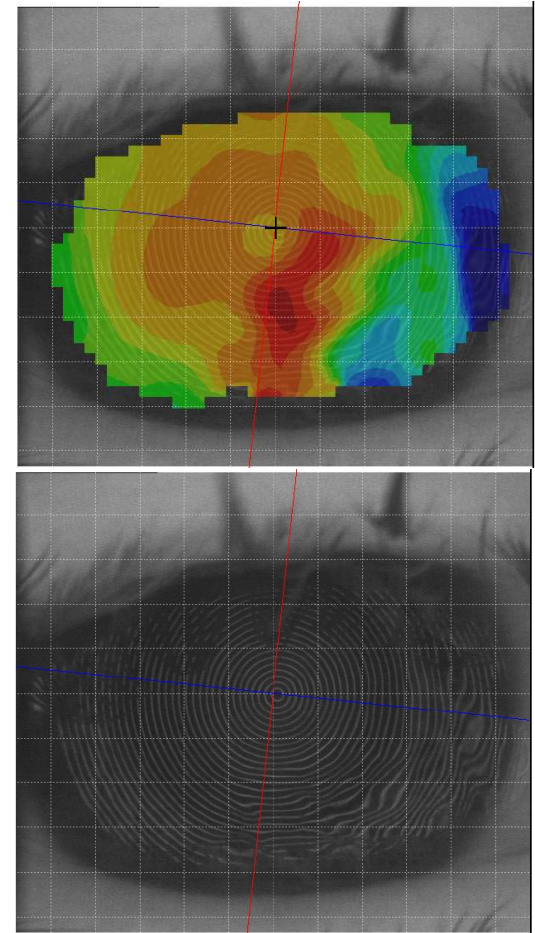
Mx: Pred Forte qid & Acivision tid for prophylaxis

2/7 review- feeling much better

2/12 later: after SLOW taper haze improved

VA R: 6/15<sup>2</sup>- & L: 6/6<sup>2+</sup> with myopic shift in R

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Mr GS

Flare up 2/12 later

Same management & again slow taper

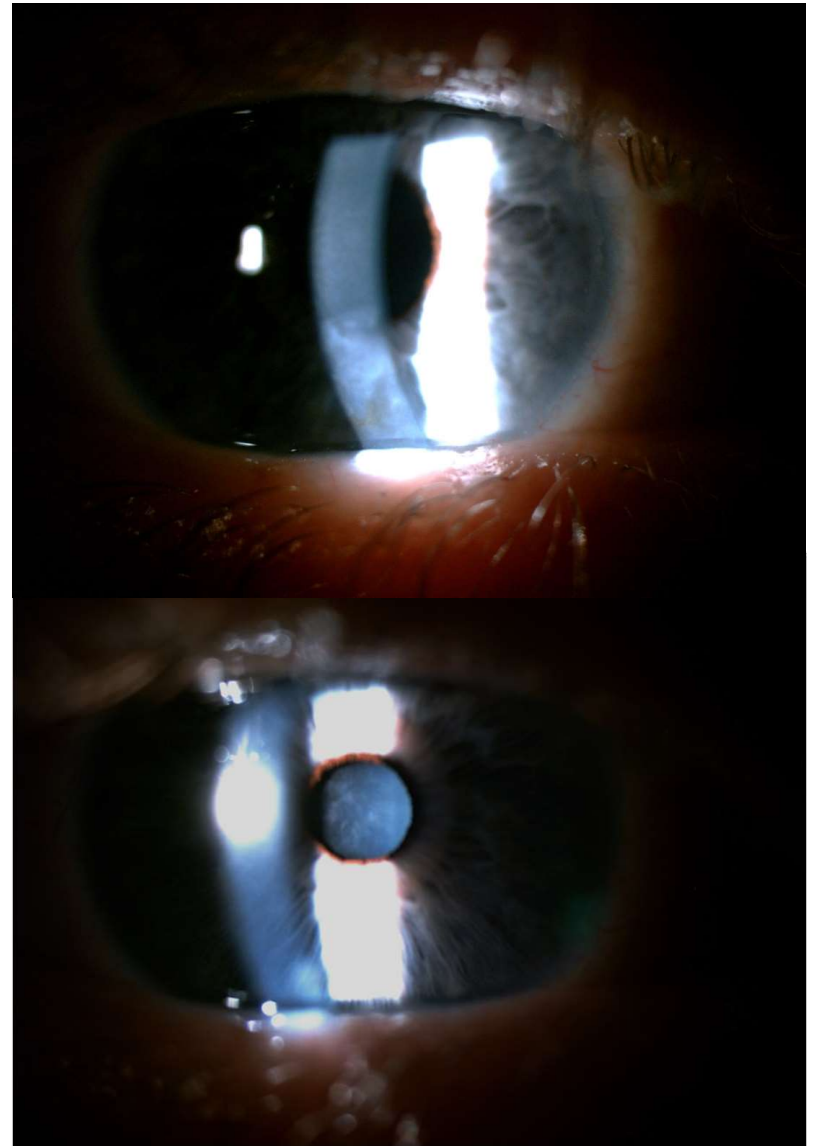
IOP slowly crept up in R to high teens,  
then 26mmHg

VA  $\uparrow\downarrow$  ~ 6/24

Developed R PSC & cortical cataract



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**Q4: Would this patient be better managed with oral antivirals?**

- A. Yes**
- B. No**



## HEDS<sub>1</sub> & HEDS<sub>2</sub>

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/](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<sup>+</sup> & L: 6/4.8<sup>+</sup>

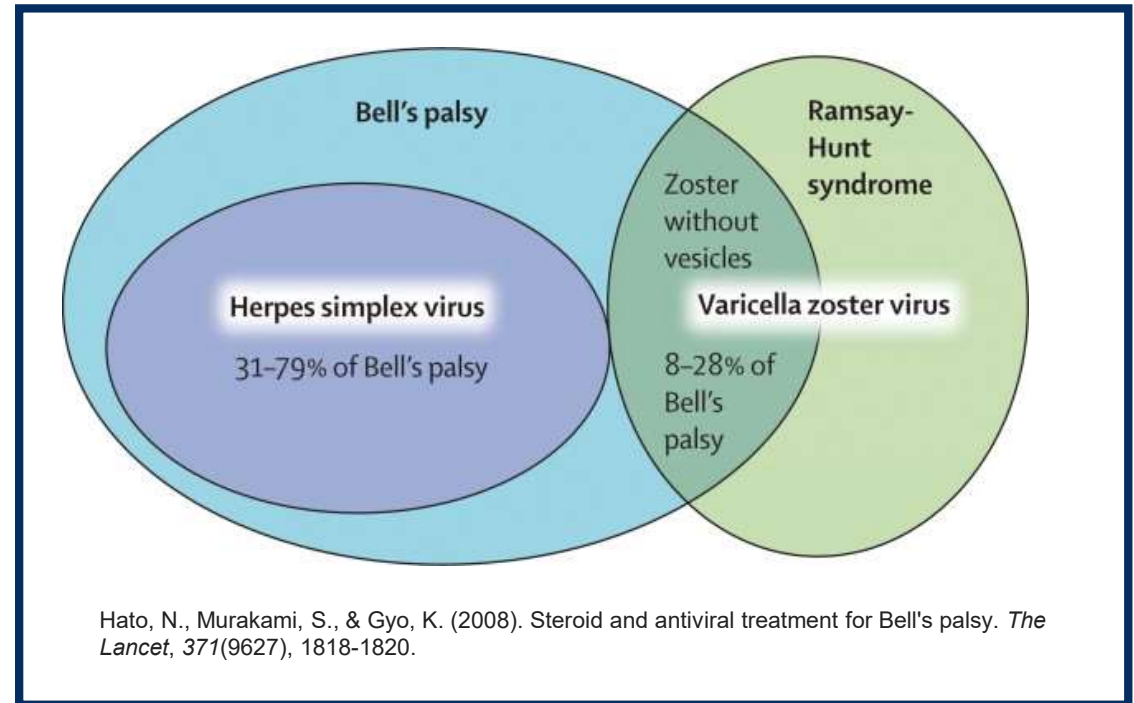


Mr GS

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





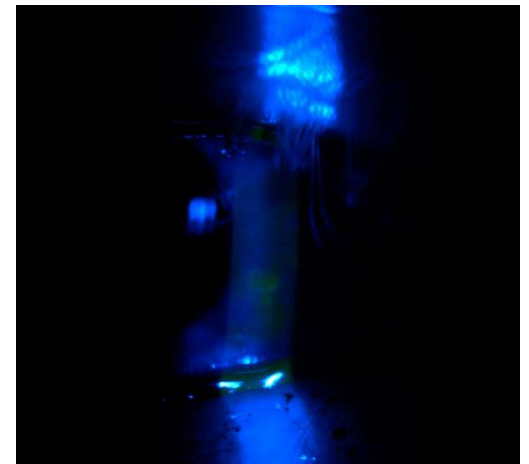
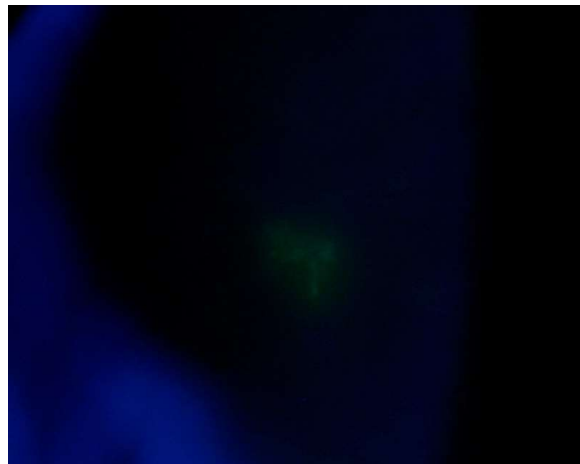
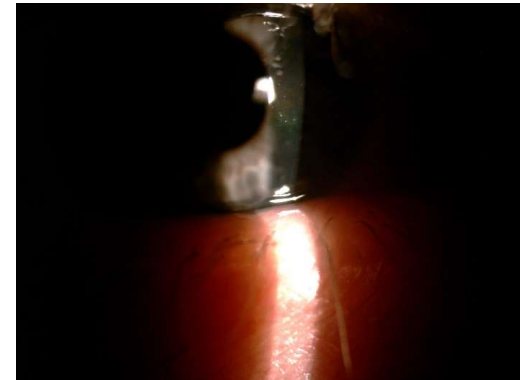
**Mr GS**

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<sup>2</sup>-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





## 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)

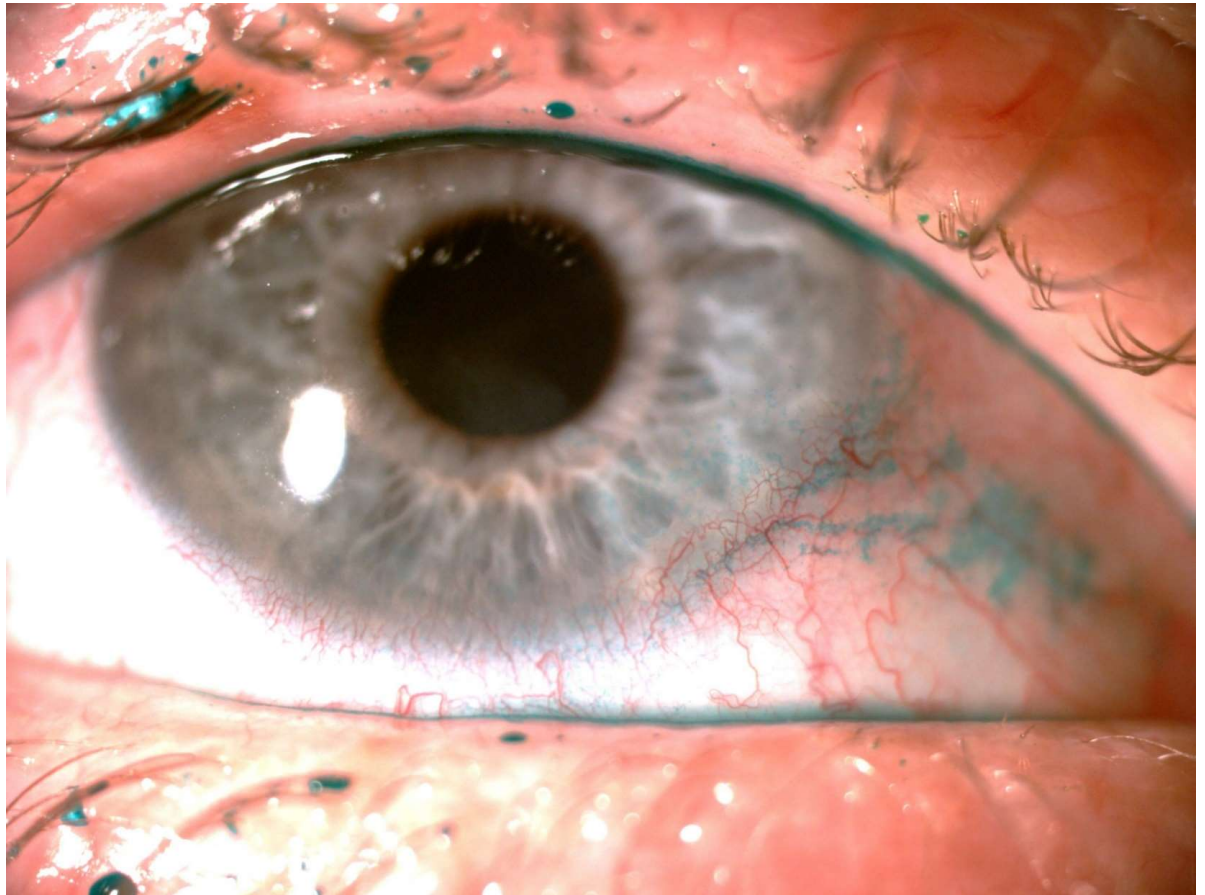
\*Slow taper is often down to every other day or even once weekly

3/7 later

No dendritic staining

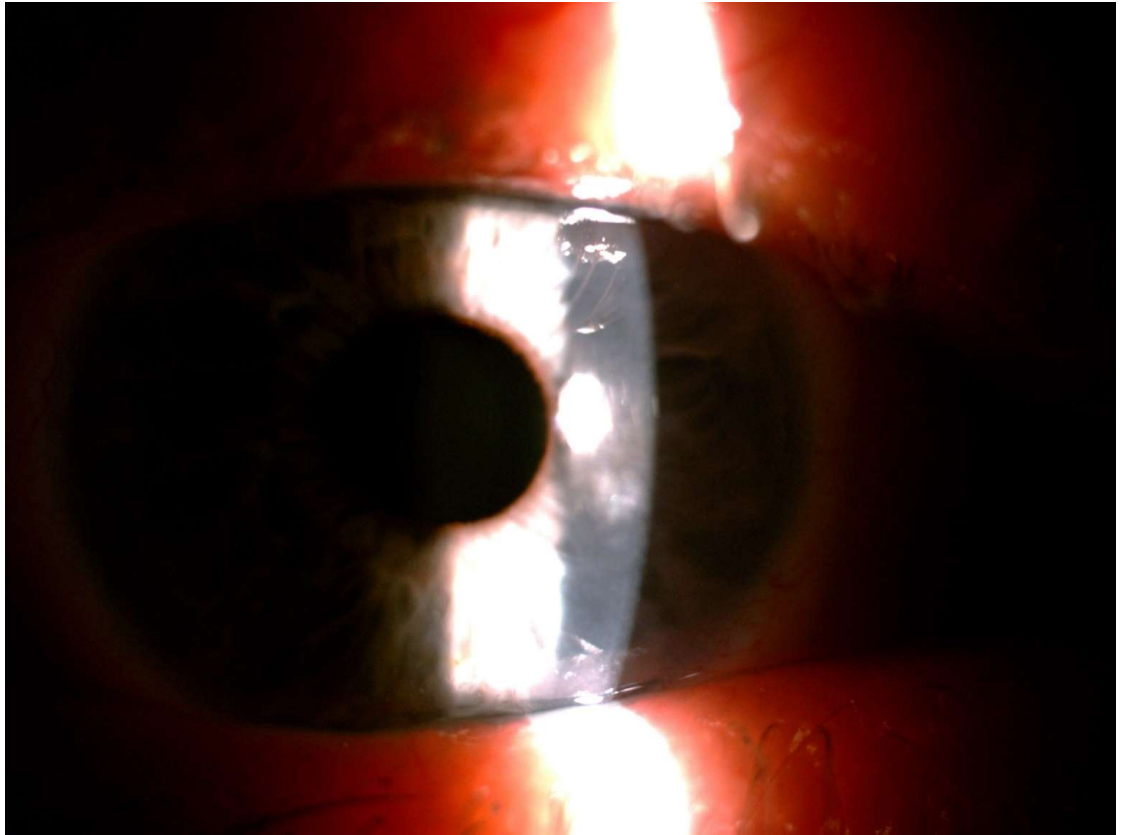
Reduce Aciclovir ung to tid,  
continue w Valtrex  
1,500mg daily & review

*Tim Martin 2019*





**4 weeks**



*Tim Martin 2019*



**4 weeks**



*Tim Martin 2019*



## Q5: What would you do now?

- A. Resume topical aciclovir
- B. Increase dosage of oral Valtrex
- C. Try a different oral antiviral in case there is resistance
- D. 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

*Tim Martin 2019*

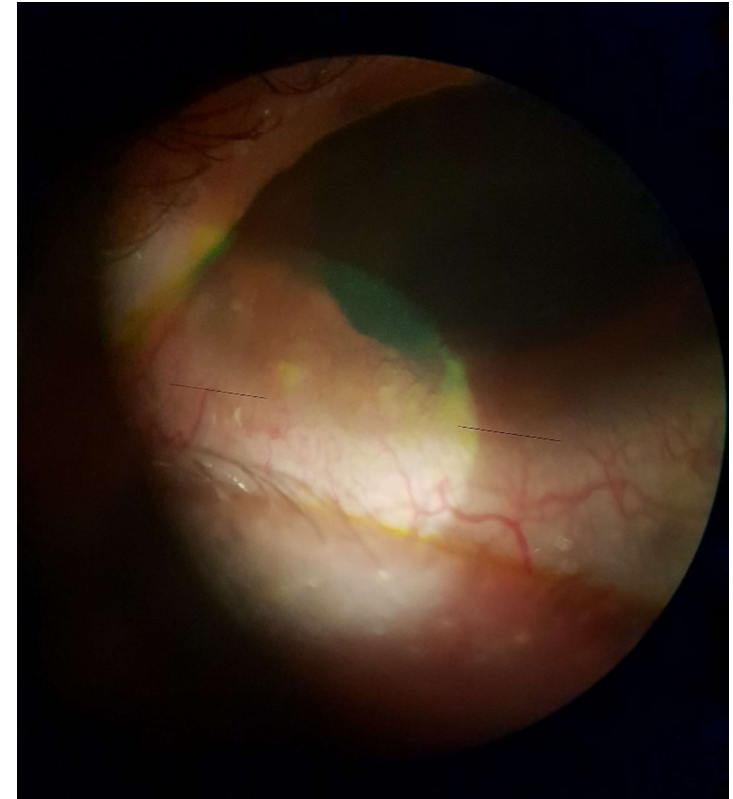




## Mast RB

S/L:

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





## Q6: How would you manage this condition?

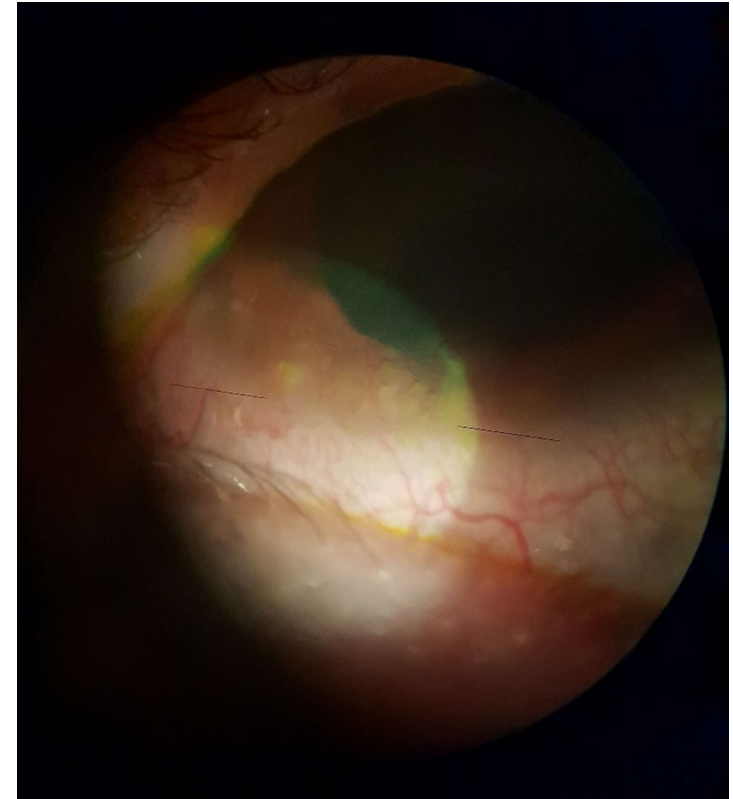
- A. Chlorsig *qid*
- B. **Chlorsig *qid* & Flarex *qid***
- C. Ciloxan *q1h*
- D. Ciloxan *qid* & FML *qid*



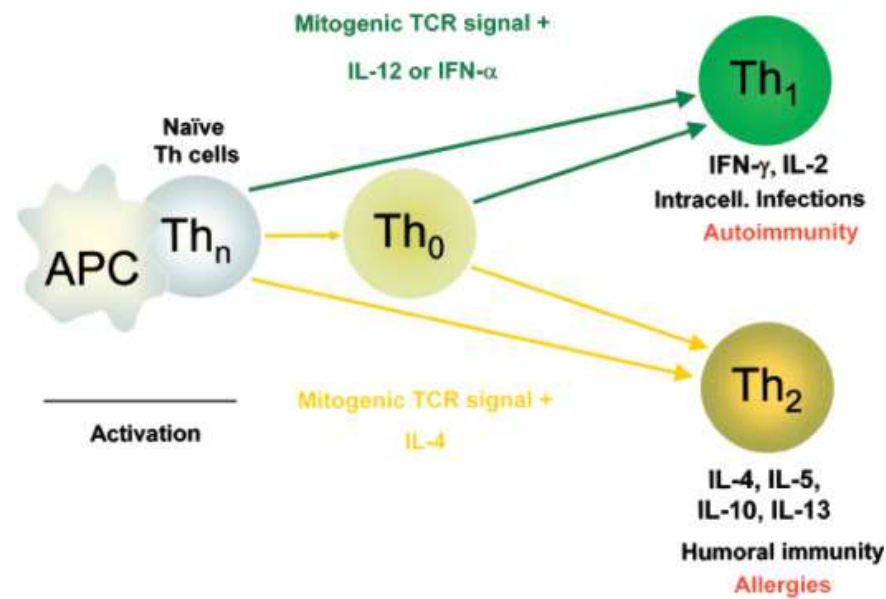
## Mast RB

### Management:

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



# How does the paediatric immune response differ?

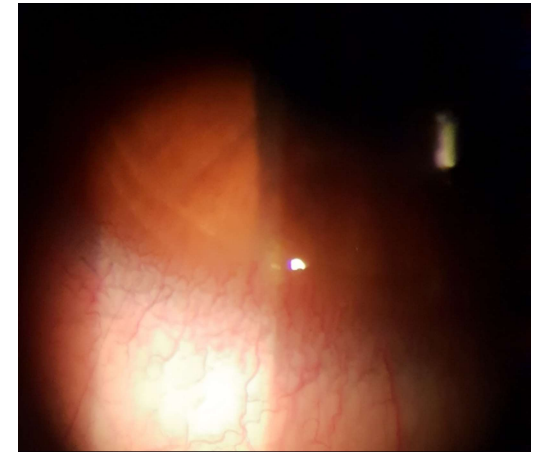


Biedermann, T., Röcken, M., & Carballido, J. M. (2004, January). Th1 And Th2 lymphocyte development and regulation of Th cell-mediated immune responses of the skin. In *Journal of Investigative Dermatology Symposium Proceedings* (Vol. 9, No. 1, pp. 5-14). Elsevier.

# 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





## Q7: Compared with adults, the risks of using steroids in paediatric cases are...?

- A. the same
- B. higher regarding risk of cataract formation
- C. **higher regarding risk of intraocular pressure rise**
- D. Higher regarding risk of cataracts and intraocular pressure rise

# Steroids in childhood

|            | MIMs  |
|------------|---|
| FML        | Safety and effectiveness have not been demonstrated in children under 2 years of age.   |
| 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 <b>risk of corticosteroid induced ocular hypertension may be greater in children and may occur earlier than in adults</b> . 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, <b>increased susceptibility to raised IOP and cataract formation have been described in the literature</b> .   |

# Higher risk IOP rise in children

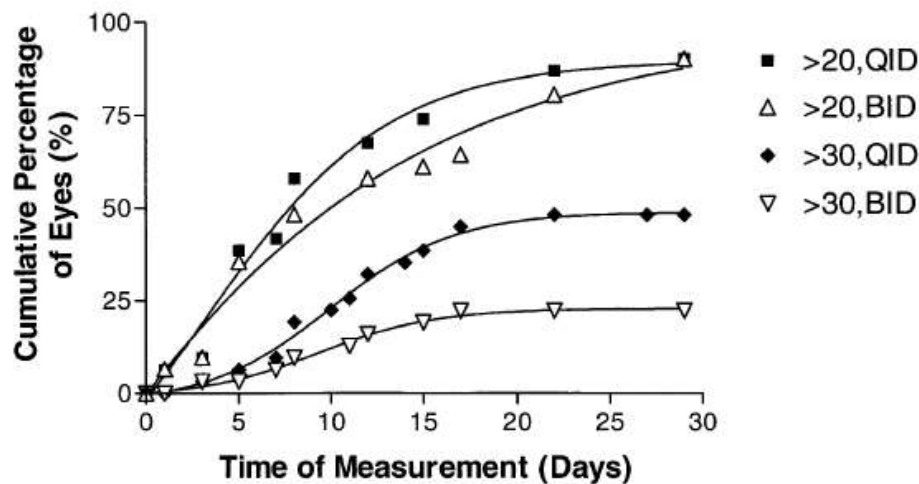


Figure 1. Cumulative percentage of eyes with intraocular pressure measurements more than 20 mmHg and 30 mmHg in both twice daily and four times daily groups.

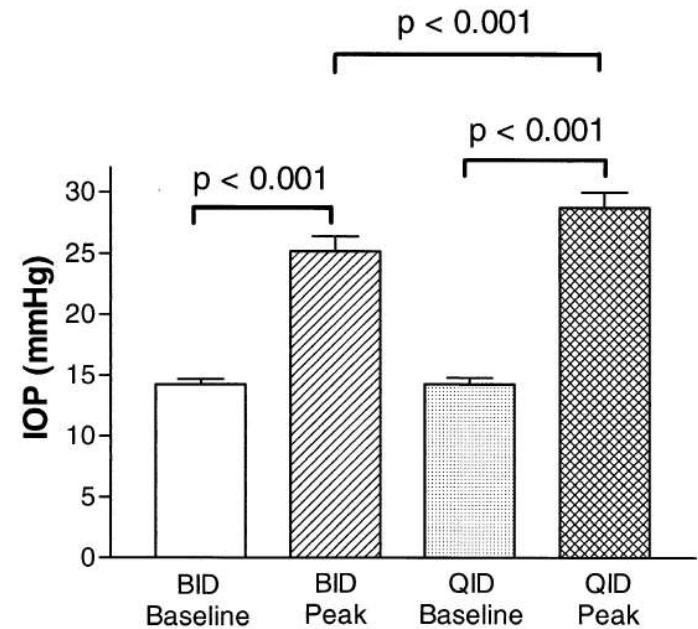


Figure 2. The difference between peak intraocular pressure (IOP) measurements of twice daily and four times daily groups as well as their respective preoperative IOP measurements.

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 <sup>20</sup> | Biedner et al <sup>21</sup> | Kwok et al <sup>14</sup> | 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             |
| Duration of administration (wks)                 | 4                    | 6                           | 4                        | 4             |
| Sample size                                      | 80                   | 44                          | 16                       | 31            |
| Low responder (change in IOP <6 mmHg)            | 53 (66%)             | 39 (89%)                    | 1 (6%)                   | 3 (10%)       |
| Intermediate responder (change in IOP 6–15 mmHg) | 23 (29%)             | 4 (9%)                      | 6 (38%)                  | 13 (42%)      |
| High responder (change in IOP > 15 mmHg)         | 4 (5%)               | 1 (2%)                      | 9 (56%)                  | 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

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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

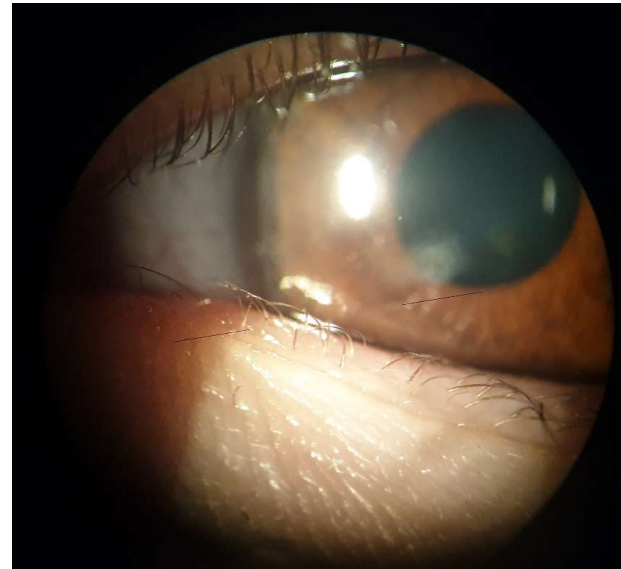
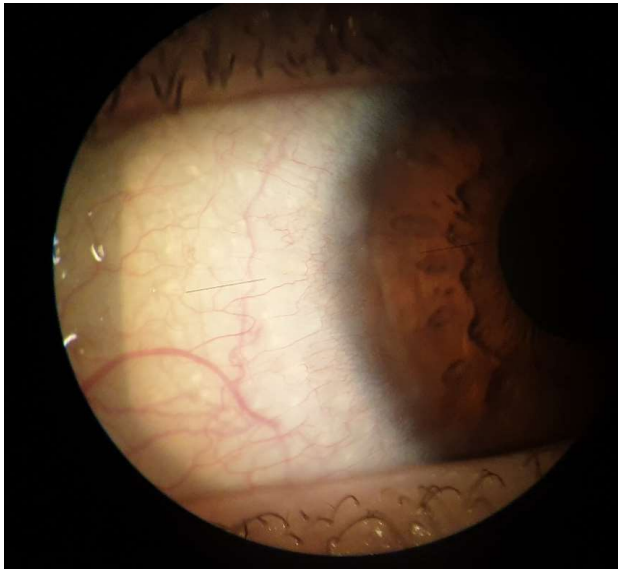
| Variable                  | Dexamethasone    | Fluoromethalone   | Paired <i>t</i> Test ( <i>P</i> ) |
|---------------------------|------------------|-------------------|-----------------------------------|
| Spherical equivalent (D)  |                  |                   |                                   |
| Mean $\pm$ SD             | +0.23 $\pm$ 1.07 | +0.38 $\pm$ 1.28  | 0.314                             |
| Range                     | (-2.75)-(+1.75)  | (-2.75)-(+3.00)   |                                   |
| Preoperative IOP (mmHg)   |                  |                   |                                   |
| Mean $\pm$ SD             | 15.18 $\pm$ 2.89 | 14.83 $\pm$ 2.25  | 0.527                             |
| Range                     | 11.30-20.70      | 9.00-19.30        |                                   |
| Maximal IOP change (mmHg) |                  |                   |                                   |
| Mean $\pm$ SD             | 15.48 $\pm$ 8.71 | 5.83 $\pm$ 4.96   | 0.001*                            |
| Range                     | (-2.60)-(+31.00) | (+1.00)-(+17.00)  |                                   |
| Peak IOP (mmHg)           |                  |                   |                                   |
| Mean $\pm$ SD             | 30.66 $\pm$ 8.35 | 20.66 $\pm$ 6.03  | 0.001*                            |
| Range                     | 13.00-48.00      | 11.30-36.30       |                                   |
| Time to peak IOP (days)   |                  |                   |                                   |
| Mean $\pm$ SD             | 15.56 $\pm$ 8.29 | 14.94 $\pm$ 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 on steroid sparing agents



## Q8: Which of the following can Australian optometrists prescribe for a paediatric patient?

- A. Steroid medications
- B. Steroids and Cyclosporin A**
- C. Steroids, Cyclosporin A & Tacrolimus
- D. Steroids, Cyclosporin A, Tacrolimus and oral doxycycline



# 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/<br>anti-allergics |
| Aciclovir<br>Azithromycin<br>Bacitracin<br>Cephazolin<br>Ciprofloxacin<br>Framycetin<br>Ganciclovir<br>Gentamicin<br>Gramicidin<br>Neomycin<br>Ofloxacin<br>Polymyxin<br>Tetracycline<br>Tobramycin | Cyclosporin<br>Dexamethasone<br>Diclofenac<br>Fluorometholone<br>Flurbiprofen<br>Hydrocortisone<br>Ketorolac<br>Loteprednol<br>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.

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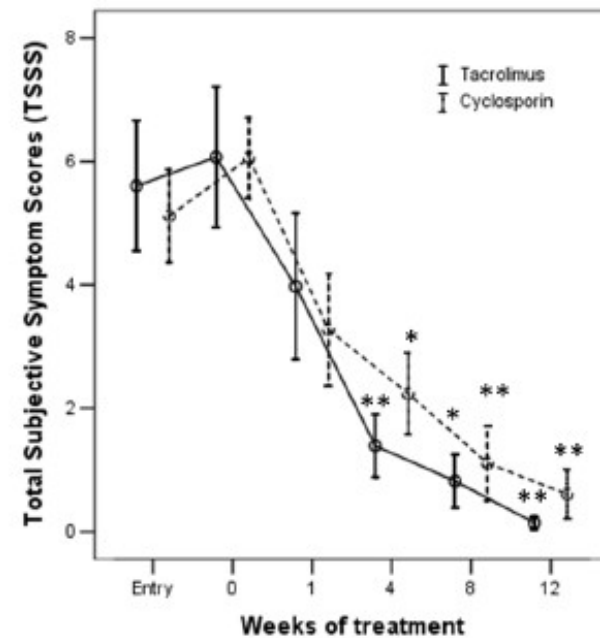


# Double masked comparison of 0.1% Tacrolimus ointment vs 2% Cyclosporine eye drops

Followed improvement in symptom scores with VKC

Statistically no difference between Cyclosporin & Tacrolimus

Continued improvement over three months



Vichyanond, P., & Kosirukvongs, 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., Kosirukvongs, 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!**

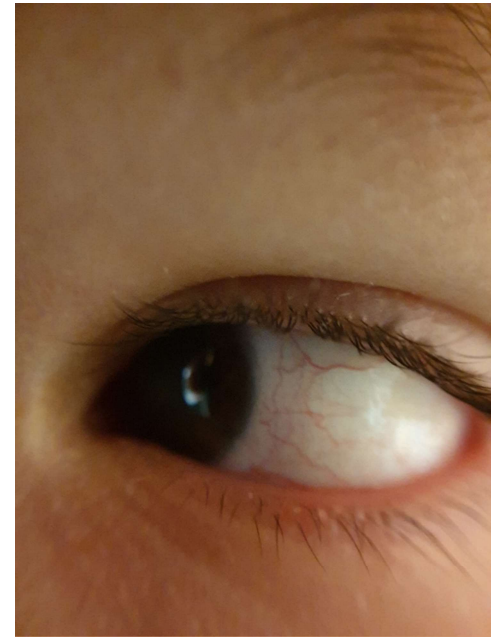


*Tim Martin 2019*





October



Tim Martin 2019



## 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



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# Thank you

Thanks for listening,  
and thanks to my family

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**Tim Martin**

BlueSky – A day in November 2019

