Allergy in Kids and Teenagers

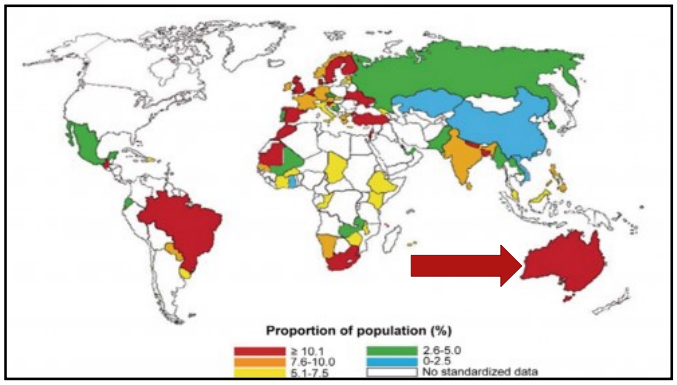
ELISSE HIGGINBOTHAM

1

Learning objectives

1. Understand the pathophysiology and interconnectedness of the atopic triad
2. Explore topical and systemic treatments for allergy suitable for children
3. Understand associated risks and other conditions related to allergy in children

2



3

Allergy in Australia

"Almost 20 per cent of the Australian population has an allergic disease, and it is predicted that by 2050, the number of patients affected by allergic diseases in Australia will increase by 70 per cent to 7.7 million (Australasian Society of Clinical Immunology and Allergy Limited 2013)"

"Australian children have the highest prevalence of food allergy in the world. A Melbourne-based study showed that 40–50 per cent of their population-based study participants experienced symptoms of an allergic disease in the first four years of their life (Peters 2017)"

"Centres with a particularly high prevalence of rhinoconjunctivitis in both age groups were Adelaide (15% in 6-7-year-olds. 23% in 13- 14-year-olds), Perth (15% and 23%)"
ISAAC 1997

Prescott 2013, 'A global survey of changing patterns of food allergy burden in children', World Allergy Organization Journal, vol. 6, no. 1.
Peters et al. 2017 'The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up', Journal of Allergy and Clinical Immunology, vol. 40, 1.

4

5

"You are allergic to strawberries, caffeine and bad air. You must avoid these substances and find a new planet to live on"

6

Causes of allergy

Inheritance?

Two parents	One parent	No family history of allergy
75%	50%	20%

Other

- Parental smoking
- Air pollution
- Environment
- Diet
- etc

7

MILD

Immediate signs or symptoms include:

- runny nose
- rubbing of the nose
- itchy nose
- Sneezing
- itchy, watery eyes
- congested nose
- snoring

LESS SO

Symptoms can affect day-to-day functioning:

- sleep disturbance
- daytime tiredness
- headaches
- poor concentration
- recurrent ear infections in children
- recurrent sinus infections in adults
- asthma can be more difficult to control.

8

Allergic eye disease impacts on Quality of Life (for kid and parent)

Original Investigation FREE

June 10, 2021

Association of Allergic Conjunctivitis With Health-Related Quality of Life in Children and Their Parents

Shi-yao Zhang, MD[1]; Jing Li, MD[1]; Ren Liu, MD[1]; et al

Author Affiliations | Article Information

JAMA Ophthalmol. 2021;139(8):830-837. doi:10.1001/jamaophthalmol.2021.1708

QOL was worse with AKC/VKC compared to SAC/PAC

Worse QOL was associated with more corneal staining

Impacts on emotional well being, school function and family dynamics

Comparable reduction in QOL compared with previous studies on paediatric glaucoma and cataract

9

The Atopic Triad and Atopic March

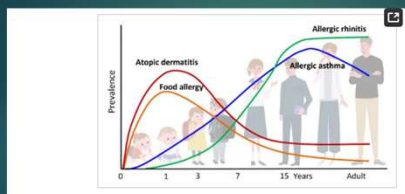


Figure 1. Atopic march. Atopic dermatitis (AD) generally develops first, followed by IgE-mediated food allergy (FA), allergic asthma (AA), and allergic rhinitis (AR). Development of FA, AA, and AR correlates with AD severity in infancy.

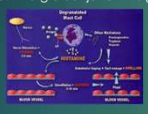
Around 40% of children with asthma have allergic conjunctivitis. Most patients with allergic conjunctivitis have concurrent rhinitis.

Dupuis 2020
doi: 10.1186/s13223-020-0403-9

Tsuge M, Ikeda M, Matsumoto N, Yorifuji T, Tsukahara H. Current Insights into Atopic March. *Children*. 2021; 8(11):1067. https://doi.org/10.3390/children8111067

10

Allergic responses, early and late

	Seasonal	Perennial
Early	SAC: Allergic conjunctivitis (type 1) 	PAC: Allergic Conjunctivitis (type 1) 
Late	Vernal and Atopic keratoconjunctivitis (Type 1+4) VKC and AKC  Eyerounds.org	

11

Seasonal SAC VKC

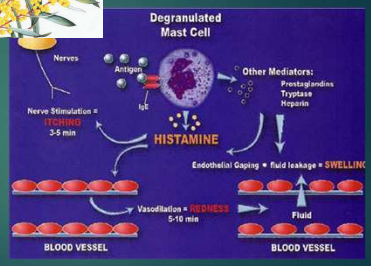
Perennial PAC AKC

EARLY _____ LATE
ACUTE----------CHRONIC
Type 1 HS _____ Type 1+4

Not vision threatening ------ VISION THREATENING

12

Seasonal Allergic Conjunctivitis (SAC)

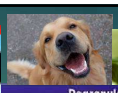


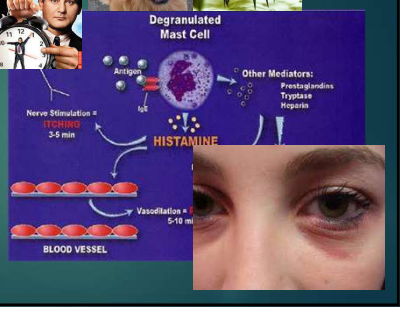
Release of:
- Histamine
- Prostaglandins
- Leukotrienes
- Eosinophilic chemotactic factor

Signs:
- Conj hyperemia (some chemosis)
- Itching
- Watering

13

Perennial Allergic Conjunctivitis (PAC)





Release of:
- Histamine
- Prostaglandins
- Leukotrienes
- Eosinophlic chemotactic factor

Signs:
- Bulbar conj hyperemia and chemosis
- Palpebral papillae and follicles
- Itching
- Watering
- "Allergic Shiners"

14

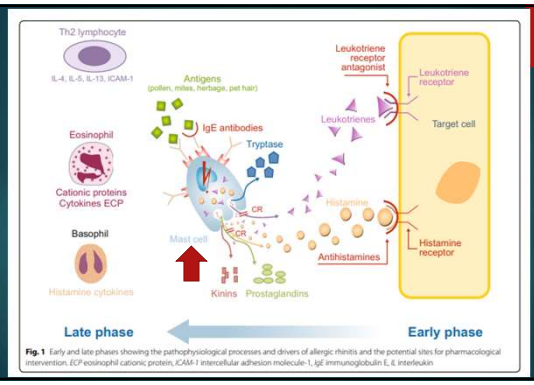
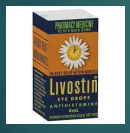


Fig. 1 Early and late phases showing the pathophysiological processes and drivers of allergic rhinitis and the potential sites for pharmacological intervention. *ECP* eosinophil cationic protein, *ICAM-1* intercellular adhesion molecule-1, *IgE* immunoglobulin E, *IL* interleukin

15

Topical solutions

1. Settle the itch
- Antihistamines



Examples of drops in this class (others available)

2. Settle the problem
- Antihistamines + mast cell stabilisers

16

Systemic solutions

Oral anti-histamine medication ok in most brands from age 2 up
- PROS: fixes most symptoms inc itchy nose and ears, as well as eyes
- Potentially more familiar than drops, often easy to get @ pharmacy
- Well tolerated
- CONS: Takes longer to act and need higher dose for same effect

Nasal spray
- jury out on impact of steroids, possibly amplified effect in children
- an option especially if excessive dry eye with oral

Other options → anti-allergy injections/under the tongue immunotherapy
- Cost ~$100+/month, may be months or years.

17

Topical therapy for allergic eye disease		Age	Dose
Antihistamine	Levocabastine (*Livostin®, Zyrtec®*)	>6 y old	bd-qid
Combined antihistamine + vasoconstrictor	Antazoline + Naphazoline (*Albalon-A®*) Antazoline + Xylometazoline (*Otrivine Antistin®*) Pheniramine + Naphazoline (*Naphcon-A®, Visine-Allergy®*)	Adult >12	Q6-12h
Mast cell stabiliser	Na Cromoglycate (*Opticrom®, Cromo-Fresh®*) Lodoxamide (*Lomide®*)	>6 y old >4 y old	4-6x day Qid
Combined antihistamine + mast cell stabiliser	Azelastine (*Eyezep®*) Olopatidine (*Patanol®*) Ketotifen (*Zaditen®*)	>4 y old >3 y old >3 y old	bd
NSAID	Ketorolac (*Acular®*) Diclofenac (*Voltaren Ophthalmic®*)	>3 y old Adult	qid
Steroid	Fluorometholone (*FML®, Flarex®*) Prednisolone (*0.5% Minims, Prednefrin Forte®*) Dexamethasone (*Maxidex®*) Hydrocortisone (*Hycor®*)	>2y old	bd-qid 2-6xday
Ciclosporin	Compounded ciclosporin – various concentrations Ciclosporin 0.09% (*Cequa®*) *OFF LABEL Ciclosporin 0.1% (*Ikervis®*) *OFF LABEL	~>4y old	qd-bd

18

Topical therapy for allergic eye disease

Antihistamine	Levocabastine (*Livostin®, Zyrtec®*)	Potential side effects/issues:
Combined antihistamine + vasoconstrictor	Antazoline + Naphazoline (*Albalon-A®*) Antazoline + Xylometazoline (*Otrivine Antistin®*) Pheniramine + Naphazoline (*Naphcon-A®, Visine-Allergy®*)	Rebound redness
Mast cell stabiliser	Na Cromoglycate (*Opticrom®, Cromo-Fresh®*) Lodoxamide (*Lomide®*)	Takes 2-4 weeks to kick in
Combined antihistamine + mast cell stabiliser	Olopatidine (*Patanol®*) Ketotifen (*Zaditen®*)	-----
NSAID	Ketorolac (*Acular®*) Diclofenac (*Voltaren Ophthalmic®*)	Not very effective
Steroid	Fluorometholone (*FML®, Flarex®*) Prednisolone (*0.5% Minims, Prednefrin Forte®*) Dexamethasone (*Maxidex®*) Hydrocortisone (*Hycor®*)	Risk of IOP spike and/or cataract development
Ciclosporin	Compounded ciclosporin – various concentrations Ciclosporin 0.09% (*Cequa®*) *OFF LABEL Ciclosporin 0.1% (*Ikervis®*) *OFF LABEL	Hard to get hold of

19

Topical therapy for allergic eye disease

Antihistamine	Levocabastine (*Livostin®, Zyrtec®*)
Combined antihistamine + vasoconstrictor	Antazoline + Naphazoline (*Albalon-A®*) Antazoline + Xylometazoline (*Otrivine Antistin®*) Pheniramine + Naphazoline (*Naphcon-A®, Visine-Allergy®*)
Mast cell stabiliser	Na Cromoglycate (*Opticrom®, Cromo-Fresh®*) Lodoxamide (*Lomide®*)
Combined antihistamine + mast cell stabiliser	Olopatidine (*Patanol®*) Ketotifen (*Zaditen®*)
NSAID	Ketorolac (*Acular®*) Diclofenac (*Voltaren Ophthalmic®*)
Steroid	Fluorometholone (*FML®, Flarex®*) Prednisolone (*0.5% Minims, Prednefrin Forte®*) Dexamethasone (*Maxidex®*) Hydrocortisone (*Hycor®*)
Ciclosporin	Compounded ciclosporin – various concentrations Ciclosporin 0.09% (*Cequa®*) *OFF LABEL Ciclosporin 0.1% (*Ikervis®*) *OFF LABEL

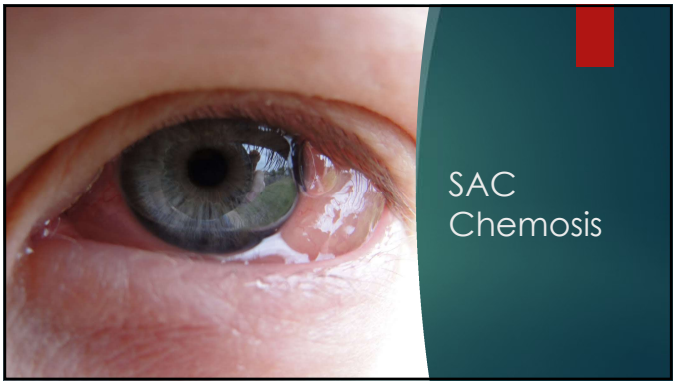
PICK ME!
PICK ME!

20

AntiH + Mast Cell Stabiliser

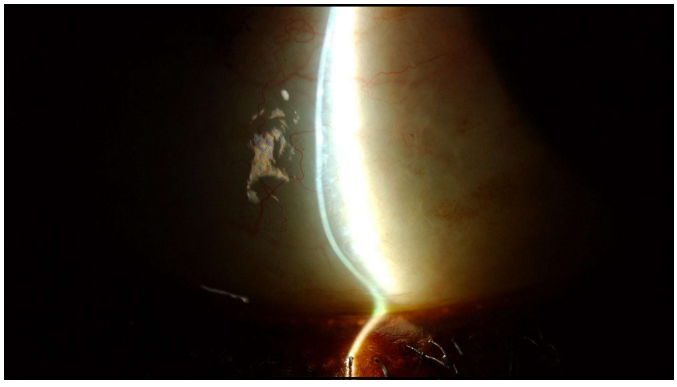
Ketotifen	Olopatadine
Available in unit dose	Doesn't sting as much
Available without prescription	Requires prescription
Possibly less effective/less quick?	More effective *
Cost cheaper? ($17-21)	More expensive ($18-40)

21

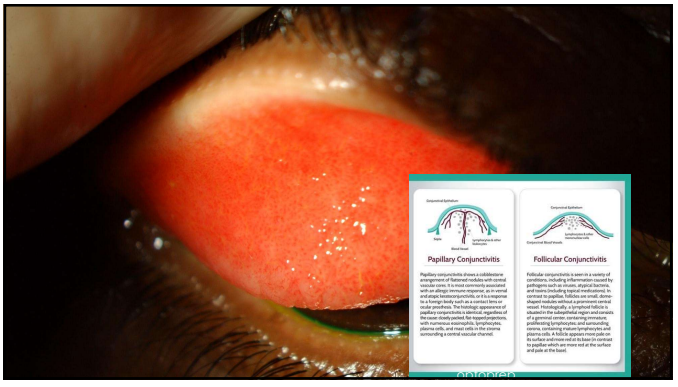


SAC Chemosis

22



23



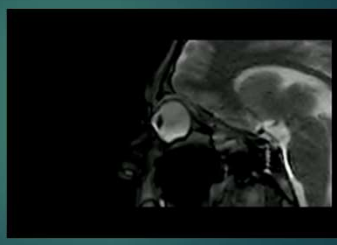
24

Beware keratoconus – NO RUBBING!

Consider if:

- Rx cyl is increasing
- Ret reflex unreliable
- VA not as good as expected
- Corneal changes (eg thinning)
- Changes to topography

More common in atopy, and starts to develop in this age group.



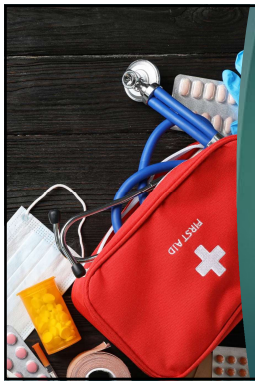
25

But it's not working…..

- They are using the drops
- They are using the drops properly
- They are using the drops, and they are in date and haven't been left in the sun for a week..
- There is definitely nothing else going on (always reconsider your diagnosis)…

What now?

26



Allergy 2.0

What to do when the usual stuff isn't working

27

Incidence of ALLERGY to drops

- Allergy to eye drops ~4% in the literature
- Benzalkonium chloride (BAK) is used in approximately 70% of ophthalmic formulations
- BAK toxicity causes ocular surface disease including goblet cell loss, conjunctival sub-epithelial inflammation and fibrosis; reduced QOL in BAK preserved meds
- **If in doubt… go preservative free**

28

Drops that are without preservative

29

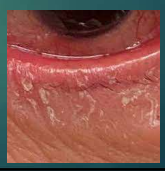
Think LATE disease

VERNAL KERATOCONJUNTIVITIS (VKC)

- More common in children
- More common in hot and dry climates
- More common in boys
- Onset often <age 10

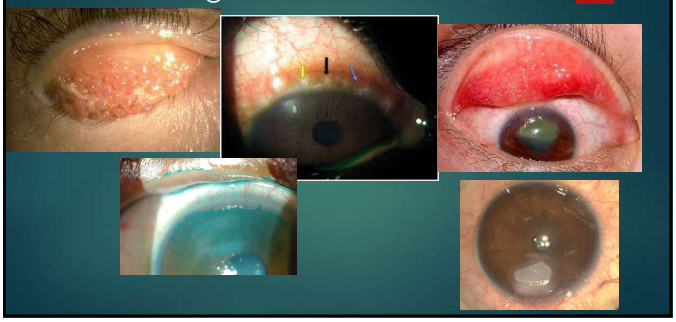
ATOPIC KERATOCONJUNCTIVITIS (AKC)

- History of atopy (esp dermatitis > rhinitis)
- Lids almost always involved
- Age usually late teens→50+



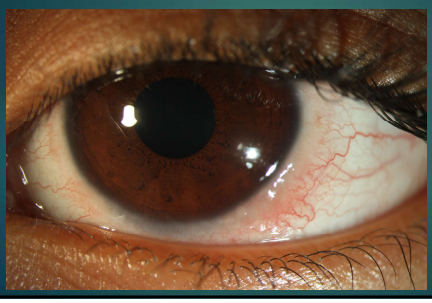
30

Common signs of late disease



31

Another case



32

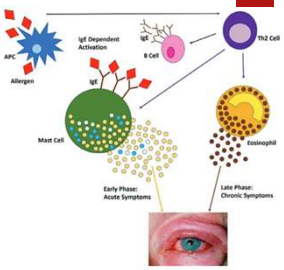
Management of VKC

- Type 1 + Type 4 = activation of eosinophils
- → Antihistamines and MC stabilisers ineffective
- → Bring on the steroids
- → Treat early and aggressively if corneal involvement (PredForte q1h if sight threatening; consider Flarex if more peripheral/limbal)

33

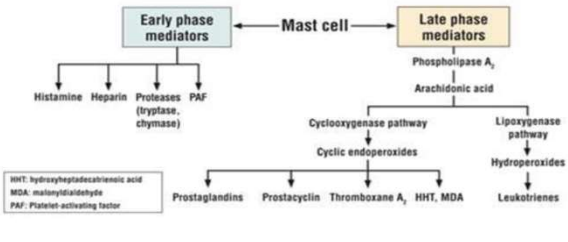
Why do steroids work better?

- No longer only type 1 hypersensitivity – now type IV
- As eosinophils activated, cytotoxic chemicals including EBM metalloproteases released
- Need something that interferes with cyclooxegenase and lipoxygenase pathways,



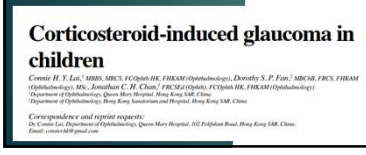
Trivedi CXO: 2021, 104:3; 334-349.

34



35

Watch out for IOP spikes



Corticosteroid-induced glaucoma in children

- Can happen earlier in children (even a day after starting the steroid)
- Using FML reduces the risk by around 50% - but it is not zero
- Refer for ocular hypertension management if iops >21 on 2 occasions or >30 on one.
- Majority resolve with time, some do not.

36

VKC

Onset usually before age 10, lasts 2 – 10 years
- Chronic, bilateral
- Background of atopy

- Seasonal exacerbations (summer) or perennial symptoms
- Usually self limiting, but about 5% continue

SYMPTOMS
- Severe itch and photophobia
- FB sensation / thick mucus / blepharospasm

AKC

- Onset in 2nd – 5th decade (range 7 – 76 years)
- Chronic, bilateral
- Part of generalised atopic disease (atopic dermatitis / eczema)
- Perennial symptoms +/- seasonal exacerbations

SYMPTOMS
- Severe itch
- Watering / mucus discharge / redness
- Blurred vision / photophobia / pain

37

VKC

SIGNS
- Papillary conjunctivitis
  - Cobblestone papillae
  - Limbitis: gelatinous papillae
  - Horner-Trantas dots
- Superficial punctate keratitis

- Shield ulcer
  - Fibrin and mucus plaque deposition, leading to macroerosions and ulceration

AKC

SIGNS
- Periocular skin changes
  - Scaly, flaky dermatitis with lichenified, thickened skin
  - Ectropion and lagophthamos
- Destruction of lid margin
- Papillary / follicular conjunctivitis
  - Lower lid involved more than upper lid (vs VKC)
  - Subepithelial fibrosis
- Keratopathy
  - Punctate keratitis / neovascularisation / scar / MK

38

Management (post referral)

VKC

Aggressive early treatment
- Continue Patanol or Zaditen bd
- Topical steroid q1h, then taper

Possibly:
- Topical ciclosporin?
- Subtarsal triamcinolone injection
- Systemic immune suppression

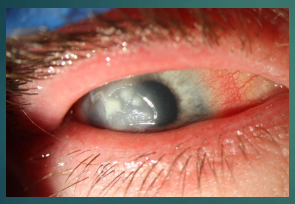
AKC

Aggressive early treatment
- Continue Patanol or Zaditen BD
- Topical steroid q1h then taper with clinical response (Prednefrin Forte or Maxidex)

Possibly:
- Topical cyclosporin (tacrolimus)
- Systemic immune suppression in severe cases

39

CORNEAL INVOLVEMENT = "KC"



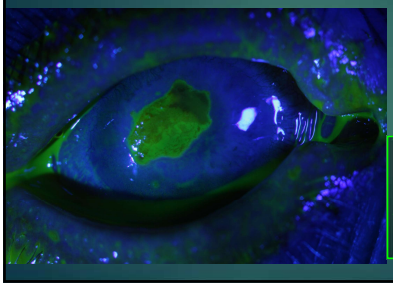
Shield ulcer

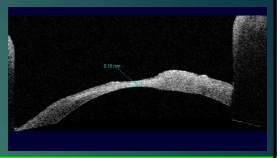
REFER ASAP

Treatment:
Intensive topical steroids
Debridement of ulcer in theatre + subtarsal triamcinolone
Antibiotic cover

40

VKC Case





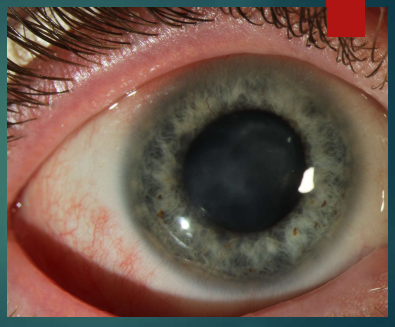
The battle: treating VKC and infection
- Inflammation → treat with steroid
- Steroid → predisposition to infection

Systemic treatment required:
- Oral prednisolone
- Oral methotrexate

41

3 years later

VA 6/18
due to central scarring



42

Take home messages

1. Manage SAC and PAC with combination antihistamine/mast cell stabilisers (OK to use longer term and more effective)
2. Add oral antihistamines if additional symptoms
3. If limbitis, add steroid
4. Consider steroids with reduced steroid response (Fluoromethalone) if peripheral – children are faster and less predictable steroid responders
5. If corneal involvement, refer EARLY for aggressive treatment – these are chronic disease and will not settle with AH/MCS alone (AKC and VKC)
6. Age of interest and atopic profile overlap with keratoconus – watch for it

43

Thanks and references

- With thanks to Dr Georgia Cleary for information and images

Useful papers and links

- ASCIA https://www.allergy.org.au/
- Tsuge M, et al. 2021 'Current Insights into Atopic March', Children, 8, 11, pp1067. https://doi.org/10.3390/children8111067
- Zhang SY, Li J, Liu R, Lao HY, Fan Z, Jin L, Liang L, Liu Y. Association of Allergic Conjunctivitis With Health-Related Quality of Life in Children and Their Parents. JAMA Ophthalmol. 2021 Aug 1;139(8):830-837. doi: 10.1001/jamaophthalmol.2021.1708. PMID: 34110380; PMCID: PMC8193548.

44