

# VERNAL KERATOCONJUNCTIVITIS

**N Freeman, MBChB, FC Ophth**

Department of Ophthalmology, Tygerberg Academic Hospital and University of Stellenbosch, South Africa

## ABSTRACT

Vernal keratoconjunctivitis (VKC) is a challenging chronic allergic conjunctivitis of childhood. As the name alludes, it includes corneal pathology and thus may threaten vision. This article discusses the epidemiology, summarises the immunopathogenesis and highlights the pertinent clinical features, using basic terminology and providing several clinical photographs. It also provides a user-friendly list of the medication currently available for the treatment of VKC and clearly states which cases should be referred to an ophthalmologist for treatment.

Vernal keratoconjunctivitis (VKC) has been singled out from the other allergic conjunctivitides (discussed in detail elsewhere in this issue) because the immunologist and paediatrician need to distinguish this condition, understand its effect on vision and refer to an ophthalmologist appropriately before sight is threatened.

VKC is a bilateral chronic recurrent allergic conjunctivitis of childhood, which occurs infrequently but is serious. Its onset is most common in the spring and summer months, hence the Greek name *vernal*, meaning 'occurring in spring'. Keratoconjunctivitis denotes the involvement of both the cornea (kerato) and the conjunctiva.

## EPIDEMIOLOGY

VKC has a predilection for warm dry climates such as South Africa.<sup>1</sup> Boys are more often affected than girls (greater than 2:1 ratio<sup>2</sup>) and the onset is usually after the age of 5 with remission in the late teens. It is very rarely seen in adults over 25 years of age.

The epidemiology of VKC suggests a hereditary predisposition and about 75%<sup>3</sup> of patients have an association with atopy. When present, the atopic clinical syndromes (eczema, asthma and rhinitis) do not necessarily coincide with the conjunctivitis. In some geographical areas the association with atopy seems to be less common.<sup>2</sup>

## IMMUNOPATHOGENESIS OF VKC

Included here is a brief summary of the immunopathogenesis of VKC, highlighting its differences from the other ocular allergic diseases.

VKC is a complex immunological disorder involving early- and late-phase allergic responses; both type I and type IV hypersensitivity reactions are implicated.<sup>4</sup> In VKC the cellular immune response leads to dysfunction in conjunctival biochemistry and histology. The cellular infiltration leads to conjunctival epithelial papillary

hypertrophy, followed by hyperplasia of the substantia propria and finally proliferation into giant papillae. These papillae tend to be located at the tarsal plate, at the limbus, or both. The mast-cell degranulation and histamine release leads to hyperaemia of the conjunctiva. Degranulation of the eosinophils causes release of cationic proteins that are toxic to the epithelium. The corneal epithelium develops erosions called punctate epithelial erosions (PEEs). If the inflammation remains unchecked, these erosions become confluent and are called macro-erosions. Debris adheres to Bowman's membrane (corneal epithelial basement membrane) in these macro-erosions, forming a vernal plaque. A ring scar results when this process heals.

Persistent rubbing and inflammation may lead to central thinning of the cornea, resulting in keratoconus. When the corneal epithelial stem cells located at the limbus are insulted, neovascularisation or conjunctivalisation of the peripheral cornea results.

## CLINICAL FEATURES

### Symptoms

The common possible presenting symptoms are similar to other ocular allergic diseases: intense itching (always present), eye rubbing, lacrimation, burning, photophobia and foreign body sensation. In order to distinguish VKC from the other allergic eye diseases it is important to examine the ocular surfaces for the clinical signs and forms.

### Signs and clinical forms

In mild cases the eyes may appear white and comfortable and there may be almost no signs on direct ophthalmoscopy. There may be a mucus discharge (Fig. 1) on the conjunctiva which tends to adhere to the superior tarsal conjunctiva. In established cases it may be possible for the general practitioner to discern the three clinical forms of the disease: **palpebral** (eyelids), **limbal** (border between cornea and sclera) and **mixed** (both limbal and palpebral signs). Anecdotally, the limbal signs are more prominent in dark-skinned races<sup>1</sup> and Caucasians tend to have more severe palpebral disease.



Fig. 1. Mucus discharge is often seen when averting the lids.

Correspondence: Dr N Freeman, Department of Ophthalmology, Tygerberg Academic Hospital and University of Stellenbosch, PO Box 19059, Tygerberg 7505. Tel 021-938-9380, fax 021-938-5511, e-mail drfree@sun.ac.za



Fig. 2(a)

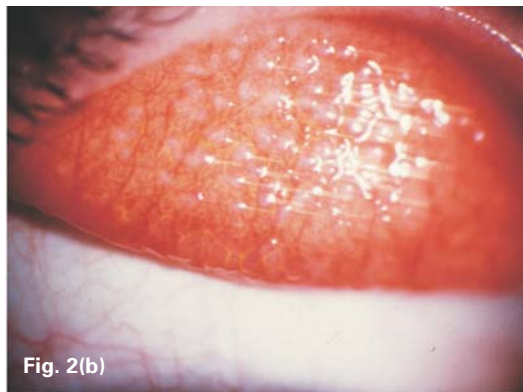


Fig. 2(b)

Fig. 2 (a) and (b). Papillae on the tarsal conjunctiva.



Fig. 3(a)



Fig. 3(b)

Fig. 3 (a) and (b). The upper lid may be avverted by applying gentle traction on the lashes and simultaneous pressure on the superior margin of the tarsal plate using a cotton bud.

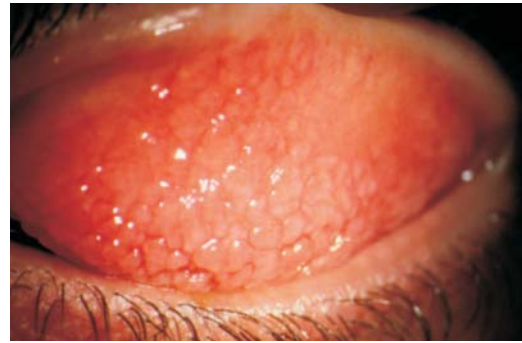


Fig. 4 (a) and (b). Cobblestone papillae on the superior tarsal plate.

The **palpebral** form has papillae of the superior conjunctiva over the tarsal plate of the upper lid (Fig. 2). These papillae may be seen by averting the eyelid. Aversion may be achieved by placing a cotton bud at the superior edge of the tarsal plate and applying gentle upwards traction on the superior lashes (Fig. 3). With time the papillae tend to become flattened on the corneal surface and begin to resemble cobblestones (Fig. 4). The conjunctiva over the inferior lid's tarsal plate is rarely affected.

In **limbal** VKC the papillae are more prominent at the limbus in the form of round gelatinous translucent nodules (Fig. 5). Small chalk-white deposits in the superficial conjunctiva known as Trantas dots may be seen straddling the limbus.

**Corneal complications** are common in more severe cases and may affect vision permanently. The corneal epithelium may have fine PEEs which are seen on staining with fluorescein and examining with a cobalt blue light. These are usually more prominent in the upper cornea but may extend to involve the entire cornea. In severe exacerbations, PEEs become confluent to form macro-erosions of the corneal epithelium. When these epithelial ulcers heal, they tend to form a ring scar (also called a vernal plaque) which remains in the subepithelium of the cornea. These may permanently affect vision when near the visual axis. The peripheral cornea may become vascularised and scarred (Fig. 6) in neglected and refractory cases. In dark-skinned children, pigment is also deposited on this limbal scarring.

There is a higher incidence of keratoconus (central corneal thinning and ectasia) in VKC patients.<sup>5</sup> Also, patients with VKC-associated keratoconus have a higher incidence of the complication of central corneal scarring.

Ptosis may also be seen in VKC patients. It is thought to be due to lid laxity caused by persistent rubbing and stretching of the levator muscle. The weight of the

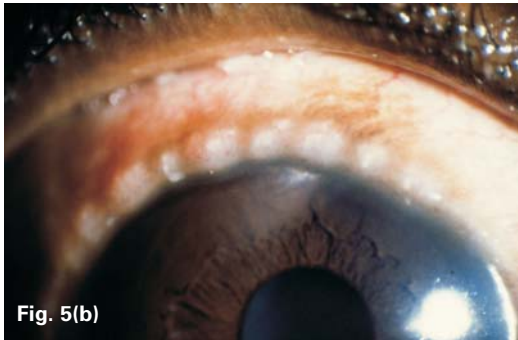
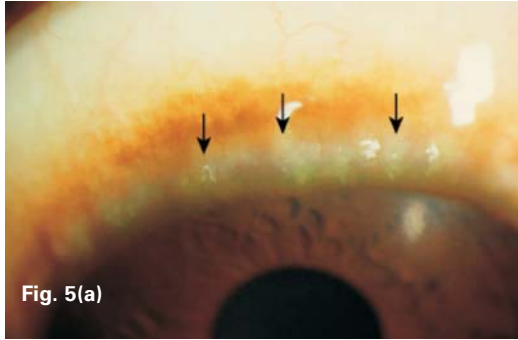


Fig. 5(a) and (b). Papillae at the limbus (black arrows) are seen as gelatinous translucent nodules. Trantas dots are seen as small white concretions.

thickened conjunctival tissue may also lead to mechanical ptosis.

## DIAGNOSTIC APPROACHES

The clinical features listed above are usually adequate to confirm the diagnosis. A family history of atopy is often but not always present. The paediatrician or immunologist should look for papillae on the superior tarsal conjunctiva and thickening of the limbal tissues, and perform fluorescein staining of the cornea.

Most ophthalmologists in South Africa use clinical signs alone to make the diagnosis of VKC. Conjunctival cytology and conjunctival biopsy are not often used, but can assist in confirming an uncertain diagnosis. The pathologist needs to be experienced in the interpretation of conjunctival cytology because it is difficult to distinguish between VKC and other allergic disorders of the eye histologically. Unfortunately it is not always possible to find an experienced pathologist locally. Serum IgE and skin-prick tests are of no value in VKC.<sup>6</sup>

When diagnosis is in question, and especially when vision is affected, prompt referral to an ophthalmologist is appropriate.

## MANAGEMENT

Management should be aimed firstly at eliminating, where possible, the potential causative or exacerbating allergens such as pets and smoke. Dry-eye-associated symptoms can also be addressed by reducing exposure to air conditioning and wearing protective wrap-around sunglasses in dry, hot and windy conditions. Adequate lubrication in the form of drops improves symptoms of dry eye.

Medical treatment is aimed at improvement of symptoms, reducing complications and to an extent modu-

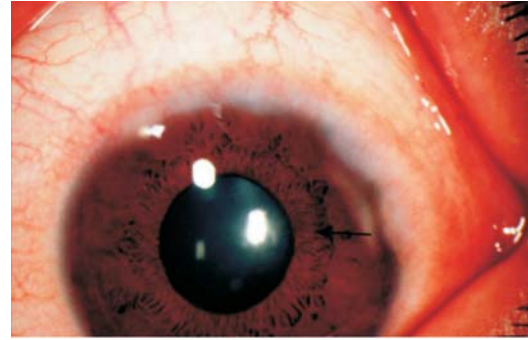


Fig. 6. Vascularisation and scarring of the peripheral cornea.

lating the immune response until the immunological process spontaneously goes into remission. Medical treatment involves the use of a combination of mast-cell stabilisers, topical and systemic antihistamines, topical steroids and cyclosporin drops, sub tarsal injections of steroids and very occasionally systemic steroids.

VKC can have severe breakthrough exacerbations on treatment and, as in other atopic-related diseases, these cases need to be treated promptly and aggressively.

For the reader's convenience, a complete list of the medications available in South Africa and used in the treatment of VKC is given below with some pertinent points. The medications listed under severe disease should be prescribed (and monitored for complications) by ophthalmologists only.

### Mild disease

VKC is classified as mild if there is no corneal staining and normal vision. A single agent or a combination of these agents may be used, depending on response after at least a month of use.

### Mast-cell stabilisers

- Sodium cromoglycates (Stop-allergy; Genop) (Cromabak; Genop)(Cromohexal; Hexal)
- Lodoxamide (Alomide; Alcon)

These may be given 1-4 x daily depending on symptoms. Patients and parents need to be informed that this medication takes at least 10 days to become effective.

### Topical antihistamines

- Levocabastine (Livostin; ED Janssen-Cilag)
- Emedastine (Emadine; Alcon)

These reduce symptoms, but do little to reduce the severity of VKC.

### Combination mast-cell stabiliser + antihistamine

- Olopatadine (Patanol; Alcon)

### Non-steroidals

- Oral aspirin has been shown to be effective in VKC, but children need to be older than 16 years.
- Non-steroidal drops are of no use in VKC and should be avoided in children for this condition.

## Steroids

- Fluoromethalone (FML; Allergan) (Flucon; Alcon)

Administered 1-4 x daily

The clinician must be aware of the possibility of precipitating glaucoma and must refer the patient to an ophthalmologist if more than one course of steroid is used.

## Severe disease

VKC is classified as severe if there is any corneal involvement, or if large papillae are present that are not responding to treatment. The additional treatments used in severe disease are listed below, but should be administered and monitored for complications by an ophthalmologist.

## Steroids

- Dexamethasone 0.1% (Spersadex; Adcock Ingram)
- Prednisolone forte 1% (Predforte; Allergan)

These can be used 2-12 x daily.

These drugs cause secondary glaucoma and cataracts; they should only be used for acute exacerbations.

Depot steroid injections in the upper conjunctival fornix are reserved for severe cases.

## Cyclosporin A

This potent steroid-sparing immune modulator is not available commercially in topical form in several countries, including South Africa. It is prepared by some academic hospital pharmacies in drop form. It is used in severe VKC cases by ophthalmologists.

Like that of many allergic diseases, the treatment of VKC is to date often unsatisfactory because the goal of treatment is symptom relief and complication reduction until the condition finally goes into its natural course of remission. The clinician needs to remind the parent and patient of this concept during the management of this challenging chronic disease.

The worldwide increased interest in advancing ocular treatment,<sup>7</sup> as well as an increase<sup>8</sup> in allergic diseases internationally, should lead to the development of additional therapies, which are much needed in the management of severe VKC.

## CONCLUSION

VKC has ocular signs that are distinctive from other ocular allergic disorders. These need to be recognised by the non-ophthalmologist, so that appropriate treatment and referral are instigated promptly. All severe cases of VKC and mild VKC which does not respond to initial treatment need to be referred to an ophthalmologist, as should any patient in whom decreased vision is detected. VKC is a debilitating disease because of the severe discomfort, but more importantly it is a potentially sight-threatening disorder.

## Declaration of conflict of interest

The author has no conflict of interest.

## REFERENCES

1. Dahan E, Appel R. Vernal conjunctivitis in black children and its responses to therapy. *Br J Ophthalmol* 1983; **67**: 688.
2. Neumann E, Gutman MJ, Blumenkrantz N, Michaelson IC. A review of four hundred cases of vernal conjunctivitis. *Am J Ophthalmol* 1959; **47**: 166.
3. Kanski J. *Clinical Ophthalmology*, 5th ed. Oxford: Butterworth-Heinemann, 2003.
4. Katelaris CH. Ocular allergy: implications for the clinical immunologist. *Ann Allergy Asthma Immunol* 2003; **90**: suppl 3, 23.
5. Totan Y, Yepsen IF. Incidence of keratoconus in subjects with vernal keratoconjunctivitis: a videokeratographic study. *Ophthalmology* 2001; **108**: 824-827.
6. Dartjohm KG, Wilkins M. External eye diseases and the oculocutaneous disorders. In: Taylor D, Hoyt GS, eds. *Pediatric Ophthalmology and Strabismus*, 3rd ed. Philadelphia: Elsevier Saunders, 2005.
7. Bielory L. Update on ocular allergy treatment. *Expert Opin Pharmacother* 2002; **3**: 541-553.
8. Davies RJ, Rusznak C, Devalia JL. Why is allergy increasing? Environmental factors. *Clin Exp Allergy* 1998; **28**: suppl 6, 8-14.

## FIGURE CREDITS

Figs 1, 2a & 3. N Freeman.

Figs 2b, 4b & 5b. Reproduced from Kanski JJ. *Clinical Ophthalmology*, vol 2. Slide set vol 2, External eye disease. Oxford: Butterworth-Heinemann, 1996.

Figs 4a, 5a & 6. Reproduced from Dartjohm KG, Wilkins M. External eye diseases and the oculocutaneous disorders. In: Taylor D, Hoyt G S, eds. *Pediatric Ophthalmology and Strabismus*, 3rd ed. Philadelphia: Elsevier Saunders, 2005.