

Allergic Ocular Disease

A Review of Pathophysiology and Clinical Presentations

**Leonard Bielory¹, Paul E. Goodman²,
and Elliott M. Fisher^{*3}**

¹Immuno-ophthalmology,
University of Medicine and Dentistry of New Jersey,
New Jersey Medical School, 90 Bergen Street,
Newark, NJ 07103-2499

²Department of Internal Medicine,
Thomas Jefferson Medical Center,
Philadelphia, PA

³Department of Cornea, External Disease, and Refractive Surgery,
University of Medicine and Dentistry of New Jersey,
New Jersey Medical School, 90 Bergen Street,
Newark, NJ 07103-2499

Introduction

The eye is a common target of inflammatory responses induced by local and systemic hypersensitivity reactions. Certain inflammatory ocular conditions resulting from immune responses are easily recognizable because of the direct visibility of conjunctival blood vessels. When such ocular reactions occur, they are often seen first by the clinical allergist/immunologist who is in a position to correlate ocular and systemic findings. Therapy can be directed at treating underlying disease in addition to local eye symptoms. To assist the clinician in better understanding allergic ocular disease, important elements of ocular anatomy and cellular components are discussed. The clinical features and pathophysiology of various immune-related ophthalmologic entities such as allergic conjunctivitis (AC), atopic keratoconjunctivitis

*Author to whom all correspondence and reprint requests should be addressed.

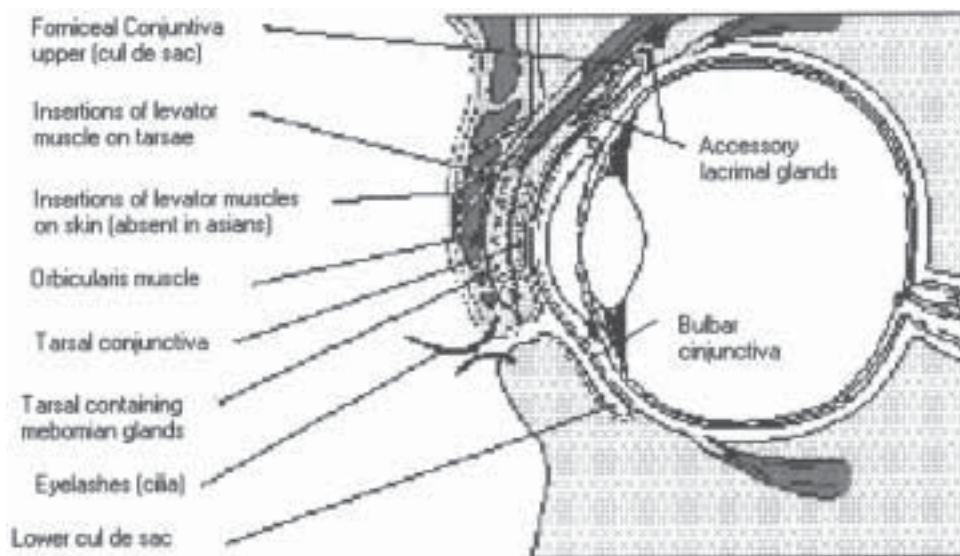


Fig. 1. Ocular and external adnexal anatomy.

(AKC), vernal keratoconjunctivitis (VKC), and giant papillary conjunctivitis (GPC) are reviewed.

Anatomy, Histology, and Immune Function of Ocular Tissues

Conjunctiva

The conjunctiva is the most immunologically active tissue of the external eye. It has been shown to undergo lymphoid hyperplasia in response to a stimulant (1). This vascular mucous membrane extends from the periphery of the cornea at the limbus to the lid margin of the eyelid. The conjunctiva is divided into three portions: bulbar, palpebral, and forniceal. The bulbar conjunctiva covers the anterior portion of the sclera, the palpebral conjunctiva lines the inner surface of the eyelids, and the forniceal conjunctiva covers the conjunctival sac bounded by the bulbar and palpebral conjunctiva (Fig. 1).

Histologically, the conjunctiva is divided into the epithelial layer and substantia propria. The epithelial layer is comprised of stratified columnar cells stacked 2–5 cells in thickness, whereas the lamina propria is composed of loose connective tissue. The substantia propria is further classified into a superficial glandular layer and a loose, deep fibrous layer. This anatomic arrangement allows for large amounts of fluids to accumulate, as seen in periorbital angioedema.

Two layers of lymphatic vessels collect lymph from the superficial and deep regions of the substantia propria. Lymphatic fluid from the temporal portion of the eye drains into the preauricular nodes; fluid from the nasal portion of the conjunctiva collects in the submental nodes. Lymph follicles are primarily found in the forniceal conjunctiva.

Mast cells and other inflammatory cells are normally found in the substantia propria, just below the epithelial junction. Initial reports of conjunctival mast cell populations were based on the differential physiological response to compound 48/80 that causes connective tissue mast cells to degranulate, but not mucosal mast cells. In the rat animal model, the response to a single application of 48/80 suggests that the conjunctival mast cells primarily belong to the connective tissue type of mast cells (2).

Mononuclear cell (MNC) populations of the normal human conjunctiva are primarily located in the epithelium and include Langerhans' cells ($CD1+$; 85 ± 16 cells/mm²) and $CD3+$ lymphocytes (189 ± 27 cells/mm²) with a $CD4+/CD8+$ ratio of 0.75 (3). The Langerhans' cells are known to facilitate immune reactions in the skin by functioning as antigen-presenting cells. Although they most likely serve a similar role in the eye, their function in the cornea has yet to be clarified (4). Interestingly the Langerhans' cells of the eye are recognized by the $CD1+$ marker, but not the $CD6+$ thymocyte marker, which is commonly found on Langerhans' cells of the skin and on histiocytes from patients with Histiocytosis X (5).

As with other mucosal surfaces involved in allergic responses, neurological innervation may play an important role in modulating ocular inflammatory responses. The ophthalmic and maxillary divisions of the trigeminal nerve (Cranial Nerve V) innervate the conjunctiva, whereas the superior cervical ganglion (sympathetic) and the facial nerve (parasympathetic) innervate its vasculature. Further investigation is needed to better characterize the influence of released neuropeptides in ocular hypersensitivity disorders.

Tear Film

The conjunctival surface is bathed in a thin layer of tear film that is composed of an inner mucoprotein layer, a middle aqueous layer, and an outer lipid layer. Goblet cells that produce mucin are distributed along the conjunctival surface. Mucin is important in decreasing the surface tension of the tear film, thus maintaining a moist hydrophobic corneal surface. The lipid layer helps decrease the evaporation rate of the middle aqueous portion. The aqueous component of the tear film contains a variety of solutes including electrolytes, carbohydrates, ureas, amino acids, lipids, enzymes, tear-specific prealbumin, and

immunologically active proteins including IgA, IgG, IgM, IgE, tryptase, histamine, lysozyme, lactoferrin, ceruloplasmin, and vitronectin.

Plasmin level in tears has been found to range from 2.2–28.6 microgram/mL after ocular challenge, whereas no plasmin was detected in symptom-free atopic patients or normal patients challenged with diluent. The plasmin, similar to histamine, appeared in human tears 3–5 min after ocular challenge with allergen (6).

Cellular Components and Receptors

The cellular components of the immune system of the eye have many similarities to the systemic immune system. For example, the conjunctiva-associated lymphoid tissue (CALT) is histologically similar to gut-associated lymphoid tissue (GALT) and bronchial-associated lymphoid tissue (BALT). Lymphocytes are dispersed throughout the conjunctival epithelial layer and aggregate in follicles within the substantia propria. The epithelial cells overlying these follicles display elongated microvilli with few microplcae. The intra-epithelial lymphocytes are predominantly CD8+ while those in the substantia propria are equally distributed among the CD4+ and CD8+ populations (7). The conjunctiva is fully equipped to capture, process, and present antigen. It is generally believed that activated conjunctival lymphocytes travel to local preauricular and submandibular lymph nodes, migrate to the spleen, and then return to the conjunctiva.

Cell Adhesion Molecules

Cell adhesion molecules (CAMs) throughout the eye modulate various cellular processes including adhesion, migration, proliferation, differentiation, and activation (8). The CAMs are grouped into four superfamilies: integrins, immunoglobulin supergenes, selectins, and cadherin families. Recent work has demonstrated that CAMs are involved in the recruitment of inflammatory cells into epithelial surfaces. CAMs such as ICAM-1, VCAM-1, and E-selectin, are upregulated in allergic disorders. It is also known that mast cells are potent regulators of ICAM-1 and VCAM-1 expression, and that ICAM-1 is upregulated in an animal model of ragweed-induced allergic conjunctivitis (9). In humans, ICAM-1 expression is minimal in normal conjunctiva, whereas it has been shown to be profoundly upregulated after topical allergen challenge in allergic patients (10).

Mast Cells

Mast cells are widely distributed in connective tissue and mucosal surfaces. There are two types of mast cells: conjunctival and mucosal. Once activated, mast cells immediately extrude granule-associated mediators in a process known as mast-cell degranulation (11). Two

types of inflammatory mast cell-derived mediators are involved in this immediate-phase allergic response: preformed and “newly” synthesized. The preformed mediators include histamine, tryptase, and serotonin. Additional “newly” synthesized mediators, such as prostaglandins (PGD₂) and leukotrienes C₄ (LTD₄), D₄ (LTD₄), and E₄ (LTE₄), trigger a secondary cascade of events that produce the late-phase response.

In the eye, mast cells are classically found in the conjunctiva, choroid, ciliary body, iris, and optic nerve. Mast cells play a role in the pathogenesis of other immunological ocular disorders such as uveitis (12). Specifically, choroidal mast cells have been implicated in the pathogenesis of experimental autoimmune uveitis (13,14). Studies of this condition revealed degranulation of mast cells 9 d post immunization, peaking at 11–14 d. These findings correspond to a serum sickness-induced process. In these studies, there was minimal production of antigen-specific IgE, suggesting a non-IgE activation of mast cells, possibly by complement. Recent studies, however, have found IgE-specific antibodies in uveitis (15). In addition, mast cells have been implicated in optic neuritis (16).

Histamine

Histamine is the principal mediator involved in ocular allergy and inflammation (17). In fact, it is estimated that human conjunctival tissue contains about 10,000 mast cells per mm (3,18). Large amounts of histamine are present in several mammalian ocular structures, including the retina, choroid, and optic nerve (19–21). Histamine receptors have been found on the conjunctiva, cornea and ophthalmic arteries (22). Two separate histamine receptors, H₁ and H₂, have been identified in the conjunctiva (23). Most ocular allergic reactions are mediated through the effects of histamine on H₁-receptors (24).

Conjunctival histamine receptors have been analyzed with specific anti-H₁ and H₂ receptor immunoglobulin in order to determine the physiological significance of each of these receptors in the development of the ocular inflammatory response. Corneal endothelial cells have been found to have H₁ receptors, which when activated, permit a calcium influx and production of prostaglandin E₂ analogous to that noted during mast-cell activation.

Histamine has been shown to induce external ophthalmic artery relaxation through the release of PGI₂ through the H₁ receptor. In contrast, internal ophthalmic artery relaxation is mediated through H₂ receptors.

Histamine concentration in tears of allergic conjunctivitis patients can reach values greater than 100 ng/mL, compared to values of 5–15 ng/mL in controls (25). Histamine can induce changes in the eye similar to those seen in other parts of the body. These include capillary dilatation,

increased vascular permeability, and smooth-muscle contraction. A histamine concentration of 240 nmol/L (10 μ l of a 50 ng/mL histamine phosphate solution) caused conjunctival redness and increased vascular permeability in 50% of the subjects studied. Tear histamine levels found in nonatopic controls are similar to allergic patients in their symptom-free periods (26). Similarly, the evaluation of tear contents during ocular challenges for the release of leukotrienes has revealed increases in 8 of 9 patients, although dramatic increases were observed in only 3 of 9 patients (27).

T Lymphocytes

T-cell receptors in the normal conjunctiva are similar to those of T lymphocytes found elsewhere in the human body. Extraocular muscles, which contain an increased number of macrophages when compared to normal skeletal muscle, demonstrate relatively normal CD4 and CD8 counts with a slight preponderance of CD8 lymphocytes (28).

Complement

Complement activation in ocular inflammatory reactions may be associated with cytotoxic and antibody-mediated hypersensitivity reactions. These reactions include ocular cicatricial pemphigoid, corneal melt syndromes such as Mooren's ulcer, and marginal keratitis secondary to immune complex deposition with consequent complement activation (29).

Normal human donor corneas contain functional complement (30). Activation of the complement system, as measured by the generation of anaphylatoxins C3a, C4a, and C5a, occurs when corneas are subjected to immunologic or chemical injury (31). Immunologic injury induced by the injection of lipopolysaccharides from *Escherichia coli* or immune complexes containing ribitol teichoic acids from *Staphylococcus aureus* generate the terminal membrane attack component C5b-9. In contrast, corneas damaged by acid or alkali exposure do not produce the membrane attack complex (MAC) C5b-9 (32).

Immunoglobulins

Immunoglobulins and lymphocytes may be produced locally or may be transported from the vascular system. Immune corneal rings, which develop in rabbit animal models after an intracorneal injection of foreign antigen, are predominately composed of polymorphonuclear leukocytes, immune complexes, and complement-activated products (33,34). The measurement of antibodies in tears may be performed utilizing several methods, including the sponge technique and the capillary-tube method. There have been no quantitative differences between the sponge or capillary tube techniques in the measurement of total tear IgE (35).

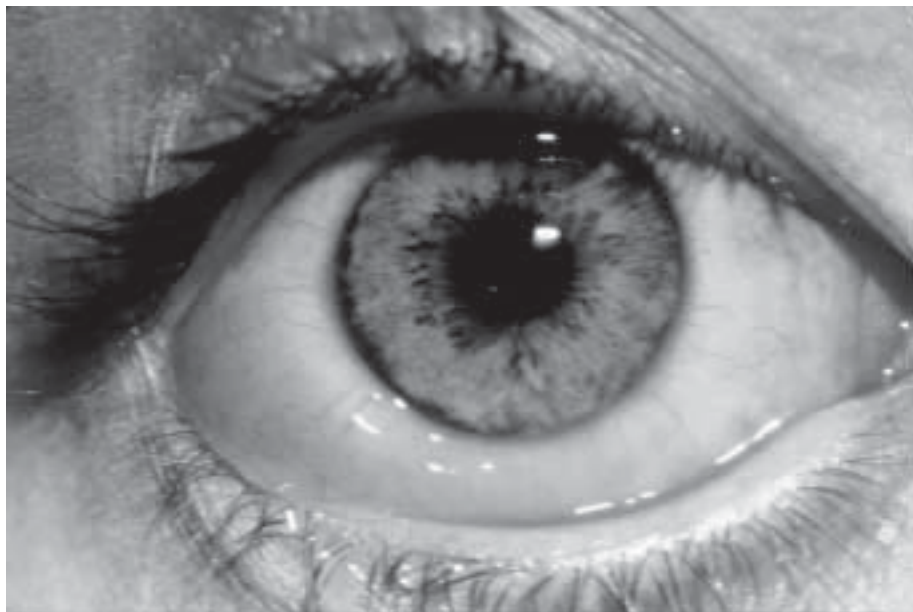


Fig. 2. Chemosis seen in Allergic Conjunctivitis.

Clinical Presentations

Allergic Conjunctivitis (AC)

Mast cell and IgE-mediated reactions are the most common hypersensitivity responses of the eye (36). Allergic conjunctivitis (AC) symptoms are due to the direct exposure of the ocular mucosal surfaces to the environment. At the interface of the conjunctiva there are an estimated 50 million mast cells.

The symptoms of itching, tearing, and burning may also include corneal symptoms of photophobia and blurring of vision. Clinical signs of AC include a milky or pale-pink conjunctiva with vascular congestion, which may progress to conjunctival swelling (chemosis) (Fig. 2). A white exudate may form during the acute state, which becomes string-like in the chronic form.

The differential diagnosis of ocular allergic disorders includes infectious causes (chlamydia, molluscum contagiosum, Parinaud's oculoglandular syndrome), chronic forms of conjunctivitis (GPC, VC, AKC, superior limbic conjunctivitis, follicular conjunctivitis), and miscellaneous disorders including keratoconjunctivitis sicca, acne rosacea, and ocular cicatricial pemphigoid.

AC is characterized histologically by infiltration of the conjunctiva with inflammatory cells, including neutrophils, eosinophils, lymphocytes, and macrophages. In contrast to asthma, which has eosinophilic

infiltration as a predominant feature, AC has a paucity of eosinophilic infiltration in the acute stage. However, there are a large amount of eosinophils in the more chronic forms. Tear fluid from these patients has been found to contain a small amount of eosinophils and histamine.

Seasonal and Perennial AC

Seasonal and perennial AC are the most prevalent forms of ocular allergy. Although its conditions tend not to be severe, they are prevalent. It is estimated that 5–22% of the population suffer from this condition (37).

Seasonal Allergic Conjunctivitis (SAC)

Clinical Features

SAC is the most common form of AC and represents half of all cases of AC. The onset of symptoms is seasonally related to specific circulating aeroallergens. Grass pollens have been noted to be associated with increased ocular symptoms noted during the spring and fall ("Indian summer"). The ocular symptoms are frequently associated with nasal and pharyngeal complaints. Common ocular complaints include itching, burning sensation, and watery discharge. A white exudate may form during the acute state; it becomes string-like in the chronic form. Rarely, SAC may also include symptoms of photophobia and blurring of vision. The conjunctival surfaces are mildly injected with various levels of chemosis or conjunctival edema. Lid edema may sometimes occur, as well as papillary hypertrophy along the tarsal conjunctival surface.

Symptoms are usually bilateral, although the degree of involvement may not be symmetrical. Affected individuals usually have a history of atopy. AC is seldom followed by permanent visual impairment.

Pathophysiology

Conjunctival cytology has revealed eosinophil infiltration in 25% of SAC patients. Elevated serum IgE levels have been noted in 78% of SAC patients, and tear fluid IgE is present in almost 96% of tear fluid samples.

Perennial Allergic Conjunctivitis (PAC)

Clinical Features

PAC is considered to be a variant of SAC that persists throughout the year, although 79% of PAC patients experience a seasonal exacerbation. Dust mites, animal dander, and feathers are the most common airborne allergens implicated in PAC. The prevalence of associated symptoms of asthma or eczema is lower than for SAC (3.5:10,000) (38). PAC is similar to SAC in age range and duration of symptoms, although

SAC is subjectively more severe. When patients with PAC are compared to those with SAC, a history of exposure to house dust was more common (42 vs 0%), as well as the association of perennial rhinitis (75 vs 12%).

Pathophysiology

SAC and PAC are typical mast cell-mediated hypersensitivity reactions affecting the eye in which the allergens react with specific IgE antibodies bound to the surface of conjunctival mast cells. The activation of mast cells leads to the release of powerful vasoactive amines that are responsible for the itching, vasodilatation, and edema encountered in AC.

Patients with SAC and PAC have been noted to have aeroallergen sensitivity and elevated IgE in both tears and serum. One difference between PAC and SAC includes the finding that 89% of PAC had specific serum IgE for house dust as compared to 43% of SAC patients. Similarly, 78% of PAC patients had tear-specific IgE for house dust, whereas none of the SAC patients had measurable IgE specific for house dust in tears. Tear samples of SAC and PAC patients have also been shown to contain elevated levels of eosinophil major basic protein.

Eosinophils have been demonstrated in conjunctival scraping in 25–84% of PAC patients and in 43% of SAC patients. Various mediators from eosinophils, such as Eosinophil Cationic Protein (ECP) and ICAM-1, have been detected in tears. However, serum levels of ECP and ICAM-1 have not been found to be increased in children with allergic conjunctivitis (39).

Atopic Keratoconjunctivitis (AKC)

AKC is a chronic inflammatory process frequently involving the lower tarsal conjunctiva. A family history of atopy, including conditions such as eczema and asthma, is common. Approximately 95% of patients with AKC have eczema and 87% have a history of asthma. AKC typically begins in the late teens or early twenties and may persist until the fourth and fifth decades of life. This disorder only occasionally presents before the late teens.

In one study evaluating pediatric atopic dermatitis patients from 1–10 yr of age, only 21% had symptoms localized to the eyelids (40). In contrast, severe AKC associated with complications such as blepharoconjunctivitis, cataract, and ocular herpes simplex was observed in 40% of older patients, with the peak incidence occurring in the 30–50 year-old age group (41–43).

Clinical Features

Ocular disease activity has been shown to correlate with exacerbations and remissions of the dermatitis as well as with tear levels of eosinophil cationic protein (44,45). Ocular involvement has been reported



Fig. 3. Atopic Keratoconjunctivitis demonstrating eczematoid lid changes ("Dennie-Morgan lines").

in 41 of 128 patients with atopic dermatitis: 13 had severe conjunctivitis, and 3 had severe keratitis (46). In another study, 85 out of 200 patients with atopic dermatitis were reported to have ocular involvement including blepharoconjunctivitis, cataract, corneal scarring, pannus formation, keratoconus, and ocular herpes simplex (47).

The symptoms of AKC commonly include itching, burning, and tearing. These symptoms are more severe than in SAC or PAC and tend to be present throughout the year. Symptoms may worsen in the winter and summer months and may be exacerbated by exposure to animal dander, dust, and certain foods (48).

The periorbital skin, skin, and cheeks may demonstrate eczematoid changes including erythema and thick scales. The skin of the eyelid is frequently affected by eczema that results in a single or double infraorbital crease ("Dennie-Morgan lines") secondary to edema or thickening (Fig. 3). The absence of the lateral eyebrow present in many older patients ("de Hertoghe's sign") may be owing to the extensive chronic eye rubbing in response to severe itching (49). Corneal scarring and neovascularization may result in blindness.

Other ocular findings include bilateral involvement of the conjunctiva in the form of fine papillary hypertrophy of the upper and lower tarsal conjunctiva, chemosis, limbal hyperemia, and limbal gelatinous hyperplasia. Cicatricial conjunctivitis with subepithelial fibrosis, fornix

shortening, and symblepharon formation are observed in more severe cases. These findings are similar to the ocular manifestations of cicatricial pemphigoid (50,51).

Bilateral involvement with abundant mucoid discharge is common. Secondary staphylococcal blepharitis is prevalent owing to the eyelids becoming indurated and macerated. AKC patients have a higher incidence of bilateral superinfection, especially with *Staphylococcus* (52,53). The corneal epithelium reveals punctate staining with fluorescein and limbal infiltration with Horner-Trantas Dots. AKC patients are at risk for herpes simplex keratitis, which may be bilateral, severe, and recurrent (54). Keratoconus occurs in approx 1.5–16% of patients with atopic dermatitis; conversely, eczema was reported to occur in 16% of patients with keratoconus (55–57).

Cataract as an ocular complication of atopic dermatitis was first reported in 1914 (58,59). Cataracts associated with AKC occur in 8–12% of patients in conjunction with severe forms of atopic dermatitis. Typically they occur in young adults approx 10 yr after the onset of the atopic dermatitis (60,61). A unique feature of AKC cataracts is that they predominantly involve the anterior portion of the lens in the form of anterior subcapsular cataracts. AKC patients have also been shown to develop posterior polar cataracts. Prolonged topical corticosteroid therapy may increase progression of cataract formation. There is no correlation between the severity of the atopic dermatitis, distribution of lesions, or serum IgE levels and the development of cataracts (62).

Pathophysiology

The histopathologic findings of AKC include a mixture of mast cell, eosinophil, and lymphocyte infiltration into the conjunctival epithelium. In situ hybridization studies of ocular tissue demonstrate that chronic forms of ocular allergy, such as VC, demonstrate increased levels of mRNA for IL-3, IL-4, and IL-5, as compared to normal tissue. Specifically, IL-2 mRNA expression was significantly higher in subjects with AKC than those with VKC ($p = 0.004$) or GPC ($p = 0.02$). However, IL-5 mRNA expression was significantly higher in patients with VKC ($p = 0.004$), AKC ($p = 0.04$), and GPC ($p = 0.02$) than in normal controls. In addition, gamma interferon (IFN- γ) mRNA expression was greater in patients with AKC than in patients with VKC ($p = 0.01$), GPC ($p = 0.01$), or control subjects ($p = 0.005$). These findings reflect that AKC appears to have a slight shift in mRNA expression to the Th2-like T-cell cytokine profile (63).

Conjunctiva from patients with AKC contain a marked increase of CD3+ lymphocytes in the substantia propria. Levels of IL-4 and IL-5 have been found to be increased in the conjunctiva as well (64). In addi-



Fig. 4. Vernal Keratoconjunctivitis with upper tarsal plate hypertrophy.

tion, there is an increase in CD1+ (lymphocytes) noted in the epithelium and the substantia propria.

Serum IgE levels are commonly elevated in patients with AKC but poorly correlate with the severity of disease (65–67). Tears from AKC patients may have IgE, eosinophils, and MNCs but display a paucity of basophils and mast cells.

The mechanism of corneal damage in this disorder is poorly understood, but it appears to be related to eosinophilic activation and mediator release.

Vernal Keratoconjunctivitis (VKC)

VKC is a severe bilateral recurrent chronic ocular inflammatory process of the upper tarsal conjunctival surface. It has a marked seasonal incidence, classically occurring in the spring or vernal season. It occurs in children and young adults who have a history of atopy, including seasonal allergy, asthma, and eczema. VKC is observed typically in pre-pubescent males. Its incidence becomes equally distributed. VKC may threaten sight if it involves the cornea.

Clinical Features

Although VKC is a bilateral disease, it may affect the eyes asymmetrically. Symptoms of VKC include intense pruritus exacerbated by exposure to wind, dust, bright light, hot weather, or physical exertion associated with sweating. Symptoms include photophobia, foreign-body

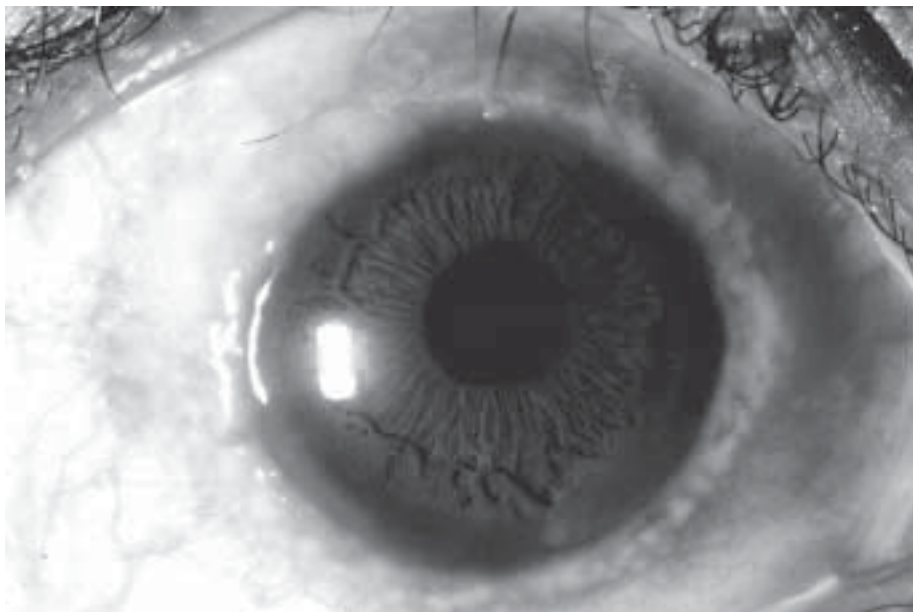


Fig. 5. Horner-Trantas dots seen in Vernal Keratoconjunctivitis.

sensation, and lacrimation. Examination of the eye in VKC reveals conjunctival hyperemia with papillary hypertrophy or “cobblestoning” of the upper tarsal plate (Fig. 4). A milky-white fibrinous secretion composed of eosinophils, epithelial cells, and Charcot-Leyden crystals may be present. The mucus may be so abundant that a pseudomembrane forms on the upper lid when everted and exposed to heat (Maxwell-Lyon’s sign). Transient limbal or conjunctival yellowish-white nodules lasting between 2–7 d (Horner-Trantas dots) may also be seen (Fig. 5). Other signs include an extra lower eyelid crease (Dennie’s Line) and corneal ulcers.

Late in the course, subepithelial fibrosis may externally appear as white, linear scarring running parallel to the lid margin (“Arlt’s line”). Two forms of the disease, limbal and palpebral, exist and are named according to the region of the conjunctiva more extensively affected. In severe cases, an oval-shaped keratitis or “shield ulcer” develops superiorly on the cornea (Fig. 6). This condition may result in severe discomfort and photophobia.

Pathophysiology

Histopathologically, VKC is characterized by conjunctival infiltration with eosinophils, degranulated mast cells, basophils, plasma cells, lymphocytes, and macrophages. The effectiveness of topical cyclosporine, an inhibitor of lymphokine release, supports the hypothesis that VKC is a combined mast cell, eosinophil and lymphocyte-mediated hypersensitivity reaction. Mucosal-type mast cells are increased in the conjunctiva

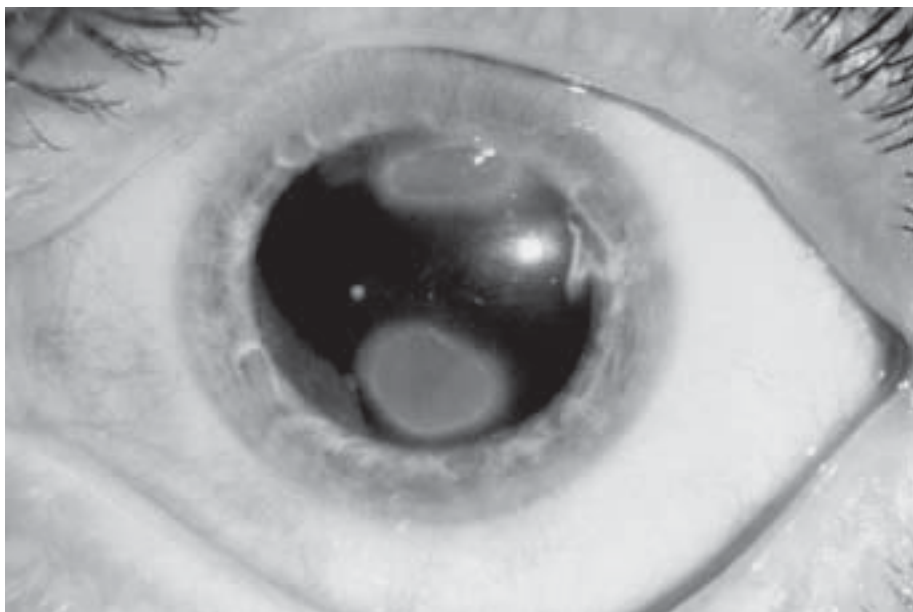


Fig. 6. Vernal "shield ulcers."

of these patients (68). Degranulated eosinophils and their toxic enzymes, such as major basic protein, have been found in the conjunctiva and in the periphery of corneal ulcers. These findings suggest a pathogenic role of these cells in complications associated with VKC (69,70).

Tears from VKC patients contain higher levels of histamine (16 ng/mL) when compared to controls (5 ng/mL) (71). Patients with VKC have demonstrated an increased responsiveness to topically applied histamine when compared to healthy controls (0.01 mg/mL vs 0.05 mg/mL of histamine) (71). The effect of topically placed histamine may be due to the decreased amount of histaminases in tear fluid of VKC patients when compared with normals (72). Tears from VKC patients also contain major basic protein, eosinophil cationic protein (73–75), Charcot-Leyden crystals (76), basophils, eosinophils, and IgE- and IgG-specific for aeroallergens such as ragweed pollen. Eosinophil cationic protein levels found in tears were noted to be directly correlated with patient symptoms and were reduced when anti-inflammatory treatment was initiated with cyclosporine or dexamethasone (77).

Giant Papillary Conjunctivitis (GPC)

Clinical Features

GPC, characterized by upper tarsal papillary hypertrophy or "cobblestoning," is associated with continued use of contact lens

and ocular prosthetics (Fig. 7). Pruritis and tearing associated with GPC tends to aggravate during the spring, when pollen counts are high. Signs include a white or clear exudate, which often becomes thick and rope-like.

Pathophysiology

GPC is associated with infiltration of basophils, eosinophils, plasma cells, and lymphocytes, suggesting a mixed mast-cell and lymphocyte-mediated process. The contact lens preservative thimerosal and proteinaceous deposits on the surface of the lens have been implicated as causes of GPC, but their specific role in the etiology of disease remains controversial.

Analysis of glycoprotein deposits on disposable soft contact lenses have revealed that protein deposition is more likely to occur on the tarsal surface of the lens, and protein integration is directly proportional to the lens's water content. Corneal deposits have been shown to contain lysozyme, tear-specific pre-albumin, and the heavy-chain components of IgG (78). In one case of lens-associated GPC, plasma cells and mast cells were found to be elevated (79). Tear histamine levels have not been found to be increased (80), whereas elevations of leukotrienes (LTC₄) have been reported (81). A recent study compared normal tear-fluid leukotiene C4 levels to tear fluid from soft-contact lens wearers with and without GPC (82). The LTC₄ levels reported in that study were 210 pg/mL for control patients, 221 pg/mL for normal soft-contact lens wearers, and 550 pg/mL for contact-lens wearers with evidence of GPC.

GPC may develop in both rigid and soft contact lens wearers. GPC is estimated to affect 1–5% of rigid contact lens wearers and up to 15% of soft contact lens patients (83). Disposable contact lenses have been proposed as an alternative treatment for GPC (84,85).

Conclusion

In conclusion, allergic ocular disease is an important clinical entity that is commonly encountered. Improved understanding of the pathogenesis of ocular allergies and increased awareness of the clinical features of various allergic ocular conditions will facilitate their prompt recognition by clinicians.

Acknowledgments

The authors thank Peter S. Hersh, MD, Professor of Ophthalmology at the University of Medicine and Dentistry of New Jersey, New Jersey Medical School, for use of his slide photos (Figs. 2–7).

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