# Managing a child with an external ocular disease

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**SUMMARY** Children are affected by some common external diseases, including allergic conjunctivitis and blepharokeratoconjunctivitis. This workshop aims to familiarize readers with the clinical features of each along with common presentations and to discuss strategies for managing these conditions, with emphasis on newer drugs and therapies. The other group of external diseases that commonly present in children comprises persistent punctate erosions and persistent epithelial defects. Etiology is varied, and making the correct diagnosis requires a systematic approach with close inspection of the microenvironment of the eye. Common causes and treatment modalities will be discussed. Types of lubrication and how they may best be used also will be outlined. (J AAPOS 2010;14:68-77)

## Introduction

Children with external ocular disease pose unique challenges for the pediatric ophthalmologist. The spectrum of diseases is often different from that in the adult population, and the same disease may manifest differently in children. This, coupled with difficulties in examination and administration of eyedrops in children, especially those who may be photophobic and teary, can lead to difficult diagnostic and management issues. Early recognition and treatment of this group of diseases are critical because the visual consequences of corneal scarring in a child in the amblyogenic age group can be devastating.[1,2]

## Allergic Eye Diseases

Ocular allergy affects up to 40% of the population, including both adults[3] and children,[4] and encompasses a spectrum of disorders. Six main clinical forms have been described:

- acute allergic conjunctivitis (AAC)
- seasonal allergic conjunctivitis (SAC)
- perennial allergic conjunctivitis (PAC)
- vernal keratoconjunctivitis (VKC)
- atopic keratoconjunctivitis (AKC)
- giant papillary conjunctivitis (GPC)

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### Immunopathology

The pathophysiology of an allergic response is type 1 (immediate) hypersensitivity. This occurs when a sensitized individual is exposed to a specific antigen. Immunoglobulin E (IgE) has a strong affinity for mast cells, and crosslinking of 2 adjacent IgE molecules by antigen triggers mast cell degranulation and release of mediators such as histamine, prostaglandins, and leukotrienes. This early-phase response peaks at 20 minutes and is followed by a late phase response involving eosinophils and T cells 4 to 6 hours later.

However, only the acute and seasonal forms of allergic conjunctivitis are pure type 1 reactions. Others have a more complex immunological basis, including a delayed type 4 hypersensitivity reaction induced by T lymphocytes and macrophages, and a chronic inflammatory component. VKC is thought to be a $TH_2$-driven disease because both $TH_2$ cells and eosinophils are markedly increased in conjunctival biopsies and cytokine profiling displayed $TH_2$ activation. Products of degranulation from eosinophils, such as eosinophil cationic protein and eosinophil granule major basic protein, are thought to contribute to the more serious corneal symptoms of VKC.

### Clinical Features

Clinical features of the 6 forms of allergic conjunctivitis are presented in Table 1. Examples are shown in Figure 1.

### Therapeutic Strategies

#### Nonpharmacological Measures

Patients can be advised to avoid common allergens or other known triggers. Cold compresses are helpful in providing symptomatic relief, and the application of lubricants may help dilute allergens from the ocular surface.

#### Pharmacotherapy

Commonly used topical medications are given in Table 2.

- *Topical antihistamines*. First-generation antihistamines such as pheniramine are available over the counter

Table 1. Clinical features of the 6 forms of allergic conjunctivitis

| Disease | Age/prevalence | Causal factors | Clinical features |
|---|---|---|---|
| Acute allergic conjunctivitis | Children, especially | Large amount of allergen inoculated into the eye | Swelling of conjunctiva and lids; intense itching |
| Seasonal allergic conjunctivitis | 10-40 years | Seasonal allergens (eg, pollen) | Itchy, burning, watery eyes; conjunctival redness and edema with or without papillary reaction |
| Perennial allergic conjunctivitis | 10-40 years | Perennial allergens (eg, house dust mites) | Similar to seasonal allergic conjunctivitis but symptoms present for at least 1 year |
| Vernal keratoconjunctivitis | Onset <10 years; boys > girls; warm, dry climates (eg, Mediterranean, India); majority with family or personal history of atopy | | Self-limiting, lasting 2-10 years; may be unilateral or asymmetrical; conjunctival injection with thick, ropy discharge; giant papillae on superior palpebral conjunctiva—"cobblestone" appearance; limbitis; Horner-Trantas dots may be present at limbus; punctate epithelial erosions; macroerosions; shield ulcers; keratoconus in 15% (6% develop hydrops) |
| Atopic keratoconjunctivitis | Young adults, 20-60 years; males > females | | Associated with atopic dermatitis; chronic and more severe than other forms of allergic conjunctivitis; usually bilateral; scaly and crusty eyelids; papillae upper and lower palpebrae conjunctiva; conjunctival scarring including symblepharon; punctate epithelial erosions; corneal scarring and vascularization; anterior subscapsular cataracts (5%) |
| Giant papillary conjunctivitis | Any age; contact lens wear | | Giant papillae on superior conjunctival tarsus; cornea usually spared |

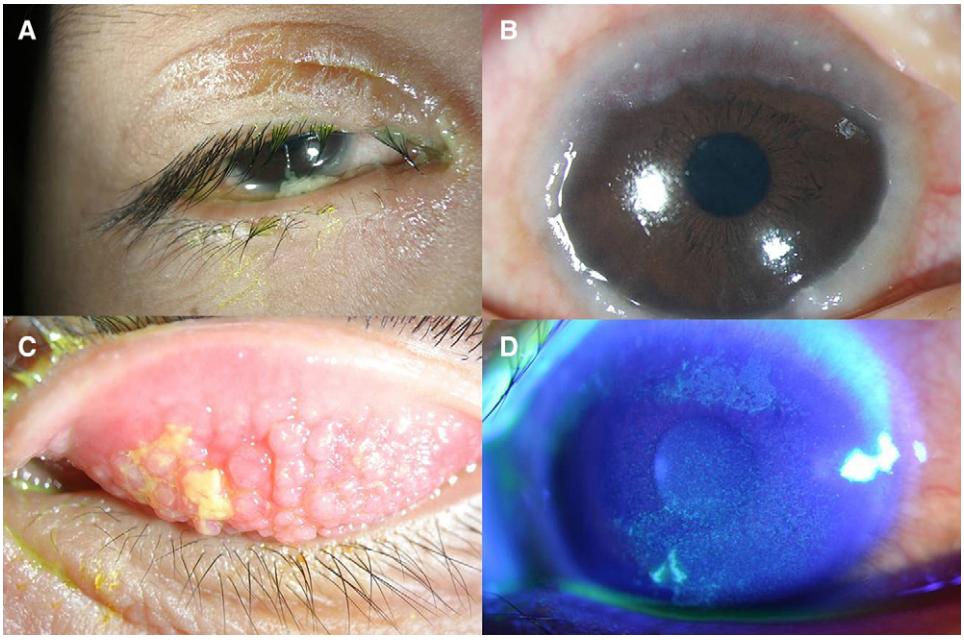


**FIG 1.** Twelve-year-old boy with VKC at various stages of his disease. A, Lid eczema with mucoid discharge; B, limbitis; C, giant papillae; and D, punctate epithelial erosions.

combined with vasoconstrictors (eg, naphazoline). Long-term use is not advised because of rebound hyperemia and inflammation. Second-generation selective H1 antagonists such as levocabastine and emedastine are better and have been shown to be effective in relieving pruritus in SAC and PAC but are relatively short-acting.[5]

Table 2. Commonly used topical medications in allergic conjunctivitis

| Drug | Trade name | Dosing | FDA approved for pediatric use? |
|---|---|---|---|
| Antihistamine (selective H1 antagonist) | | | |
| Emedastine difumarate 0.05% | Emadine[a] | 4× daily | >3 years |
| Levocabastine 0.05% | Livostin[b] | 4× daily | >12 years |
| Epinastine 0.05% | Elestat[c] | 2× daily | >3 years |
| Mast cell stabilizers | | | |
| Sodium cromoglycate 2% | Cromolyn Sodium[d] | 4× daily | >5 years |
| Lodoxamide tromethamine 0.1% | Alomide[a] | 4× daily | >2 years |
| Dual-acting agents | | | |
| Olopatadine 0.1% | Patanol[a] | 2× daily | >3 years |
| Olopatadine 0.2% | Pataday[a] | 1× daily | >3 years |
| Ketotifen 0.025% | Zaditor[b] | 2-3× daily | >3 years |
| Nedocromil 2% | Alocril[e] | 2× daily | >3 years |
| Nonsteroidal antiinflammatory drugs | | | |
| Ketorolac tromethamine 0.5% | Acular[e] | 4× daily | >12 years |
| Corticosteroids | | | |
| Prednisolone 1% | Pred Forte[e] | | No |
| Prednisolone 0.125% | Pred Mild[e] | | No |
| Prednisolone 0.5% (preservative free) | Minims Prednisolone[f] | | No |
| Dexamethasone 0.1% | Maxidex[a] | As required | No |
| Dexamethasone 0.1% (preservative free) | Minims Dexamethasone[f] | As required | No |
| Fluorometholone 0.1% | FML[e] | | >2 years |
| Rimexolone 1% | Vexol[a] | | No |
| Loteprednol etabonate 0.2% | Alrex[g] | | No |
| Loteprednol etabonate 0.5% | Lotemax[g] | | No |
| Immunomodulators | | | |
| Cyclosporine A 0.05% | Restasis[e] | 2-3× daily | >16 years |

Manufacturers:
[a]Alcon, Fort Worth, TX.
[b]Novartis, Basel, Switzerland.
[c]Allergan, Irvine, CA.
[d]Falcon Pharmaceuticals, Fort Worth, TX.
[e]Allergan, Irvine, CA.
[f]Bausch & Lomb, Kingston-upon-Thames, Surrey, UK.
[g]Bausch & Lomb, Rochester, NY.

- *Systemic antihistamines*. Oral antihistamines are extensively used to control allergic rhinoconjunctivitis but also may be helpful in patients with severe AKC and VKC. The newer antihistamines are not associated with drowsiness (eg, loratadine).
- *Mast cell stabilizers*. The mechanism of action is unclear, but there is decrease in degranulation of mast cells in response to an antigen. Therefore, it may take a few days before an effect is observed. These stabilizers can be combined with other drugs if immediate symptomatic relief is required. Sodium cromoglycate has been the gold standard for many years, but lodoxamide has been found to be more effective in VKC.[6]
- *Dual-acting agents*. Drugs such as olopatadine,[7] nedocromil, ketotifen, and azelastine combine mast cell stabilization and antihistamine (H1) effects and are the first-line drug of choice for many. They also appear to have other antiinflammatory effects, such as inhibition of cytokine release by olopatadine and inhibition of eosinophil chemotaxis by ketotifen and have convenient twice-a-day dosing.
- *Nonsteroidal antiinflammatory drugs*. Ketorolac has been shown to relieve ocular itching but is less effective than anithistamines.[5]
- *Steroids*. Topical corticosteroids are extremely effective, but potential complications include increased intraocular pressure, cataract formation, and viral or fungal infections. Short pulses are therefore recommended for acute flare-ups. Prednisolone 1% and dexamethasone 0.1% are about equipotent and are suitable, but preservative-free formulations are preferred, especially when frequent dosing up to hourly application may be required. Fluorometholone has a fluoride ion attached and is hydrophilic, making ocular penetration in a nonoperated eye unlikely. Thus, it is less likely to increase intraocular pressure, as are 2 modified steroids, loteprednol and rimexolone, which are rapidly inactivated once they enter the anterior chamber. These "soft" steroids may therefore be a good option for surface diseases but are less efficacious.
- *Immunomodulators*. Topical cyclosporine A has been shown to be effective in treatment of AKC and VKC and appears to be a useful alternative and steroid-sparing agent.[8] The 2% formulation has the longest track record, but lower concentrations (1%, 0.5%, 0.05%)[9] have been tried and shown to be effective, although only the 0.05% formulation is commercially available as a treatment for dry eye. The authors of one

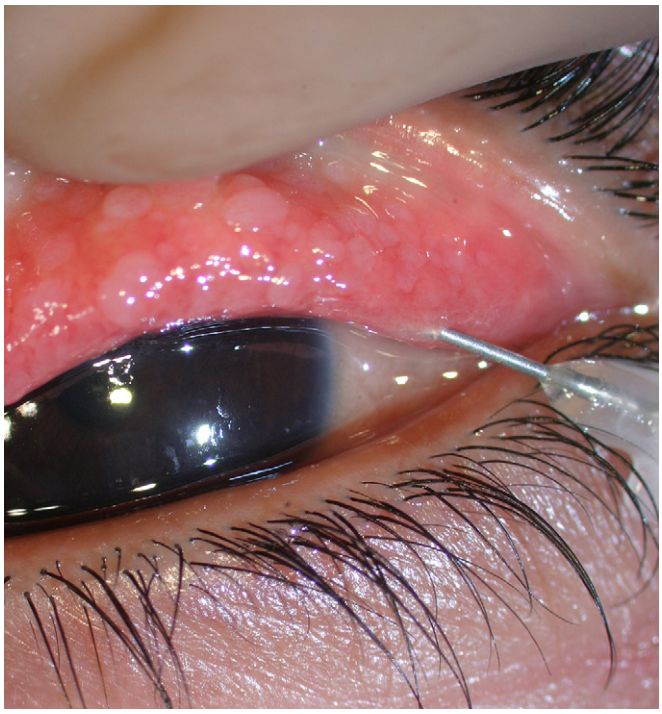

**FIG 2.** Technique of supratarsal steroid injection in the left eye of a 9-year-old boy with VKC. After eversion of the upper lid, the steroid mixture is injected into the subconjunctival space 1 mm above the superior tarsal border with a 27-gauge needle.

study[10] suggest that the minimal concentration for controlling shield ulcers associated with VKC is 1%.

Tacrolimus 0.03% ointment is licensed for use in atopic dermatitis and is useful in the treatment of eyelid involvement. It has been tried in the treatment of allergic conjunctivitis and shows early promise.[11]

- *Future therapies.* Sublingual immunotherapy describes the immunizing process in which increasing doses of specific antigens are given under the patient's tongue to induce increased tolerance. Studies have documented the clinical efficacy on allergic eye symptoms but most referred to rhinoconjunctivitis, with ocular symptoms as a secondary outcome. Other studies did not show a long-lasting effect. Montelukast, a leukotriene receptor antagonist, has been shown to improve VKC symptoms in children treated for asthma.[12] Anti-IgE therapy omalizumab administered subcutaneously is currently approved for treatment of asthma. The authors of a study,[13] when using this drug in patients with seasonal allergic rhinitis, reported improvement in ocular symptoms. Other drugs have been used in animal models and remain experimental.

### Surgical Treatment

Advanced VKC not responding to conventional therapy, especially those with cornea or limbal involvement, may be treated with supratarsal steroid injection.[14] Under general anesthesia, the upper eyelid is everted, and a mixture of triamcinolone 20 mg/0.5 mL and betamethasone 2 mg/0.5 mL or dexamethasone 2 mg/0.5 mL is injected into the subconjunctiva above the tarsus (Figure 2). Both short-acting (eg, dexamethasone) and intermediate-acting (eg, triamcinolone) steroids appear to be equally effective and have similar recurrence rates.[15,16] Symptoms improve after 1 to 5 days, but signs such as giant papillae and shield ulcers may take 2 to 3 weeks to resolve (Figure 3). It is particularly useful in patients noncompliant to topical therapy because its effect typically lasts 3 to 5 months. Increased intraocular pressure is not common but needs to be monitored closely.

Excision or cryotherapy of giant papillae help in resolution of epitheliopathy or ulcer but is of limited use as papillae tend to recur rapidly. Debridement of shield ulcer promotes reepithelialization of vernal ulcer resistant to medical therapy. Amniotic membrane transplantation can be considered for persistent epithelial defects or vernal plaques.

In the management of steroid-induced glaucoma, under certain circumstances during which the tarsal conjunctiva is severely affected and cyclosporine is not tolerated, steroid therapy may be the only option. If the child is a steroid responder, it is sometimes necessary to control the glaucoma with a trabeculectomy or tube-shunt and then treat the allergic disease with steroids.

## Blepharoconjunctivitis

Blepharoconjunctivitis (BKC) is a common but underrecognized problem in children. The condition is similar to that found in adults, including an association with acne rosacea, but there are important differences in terms of clinical presentation and treatment. BKC is primarily an eyelid margin disease with secondary corneal and conjunctival involvement. It is traditionally divided into anterior and posterior blepharitis, although the conditions often coexist. Anterior disease involves the anterior lid margin, hair follicles, and associated oil glands, whereas posterior disease is associated with meibomian gland dysfunction (Table 3).

### Important Features in Children

Age of presentation is around 6-7 years,[1,17-19] although there is usually a delay of 1 to 2 years between the onset of symptoms and diagnosis. Presenting symptoms include red eye, photophobia, epiphoria, and recurrent chalazia or sties.

Cornea involvement is common (up to 81%).[1,17,18] This includes punctate epithelial erosions, subepithelial infiltrates, phlyctenules, marginal keratitis and ulceration, or corneal opacity. Location of cornea involvement tends to be central or paracentral in younger children[1] rather than the classical peripheral or marginal inflammation seen in adults. Cornea scarring and vascularization may develop (Figure 4). Adequate management requires both topical and systemic treatment, but there may be frequent exacerbations requiring prolonged steroid treatment.

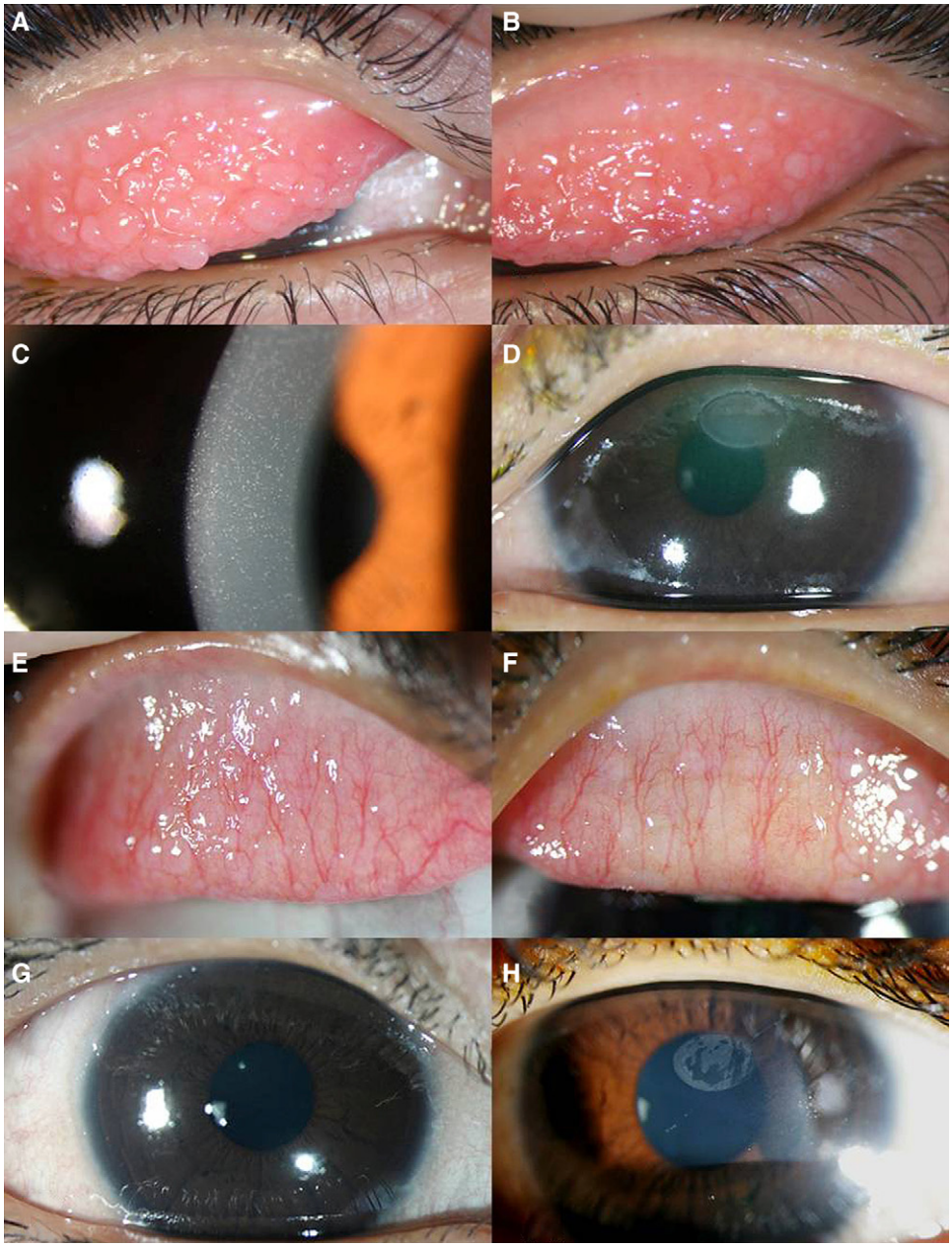


**FIG 3.** Same patient as in Figure 2 showing giant papillae in both upper lids (A,B); punctate epithelial erosions in right eye (C); shield ulcer in left eye (D). Three weeks after injection, with flattening of papillae (E,F); resolution of keratopathy (G); and healing of shield ulcer (H).

Table 3. Comparison of clinical signs in anterior and posterior blepharitis

| Anterior blepharitis | Posterior blepharitis |
|---|---|
| Inflamed eyelids | Meibomian gland pouting, capping, hypertrophy, or inflammation |
| Lid margin telangiectasia | Posterior lid margin telangiectasia |
| Scales and collarettes at base of lashes | Posteriorization of gland orifices |
| Madarosis | Incongruity of posterior lid margin |
| Trichiasis | |
| Lid notching | |

Visual impairment is common. Superimposed amblyopia attributable to prolonged corneal opacification and/or refractive changes (in particular astigmatism due to cornea scarring) frequently is present. Delayed treatment may result in decreased final vision.

## Therapeutic Strategies

Primary treatment is targeted at the lid disease. Lid hygiene or warm compresses with the use of cotton wool-tipped swab sticks and warm water, diluted baby shampoo,

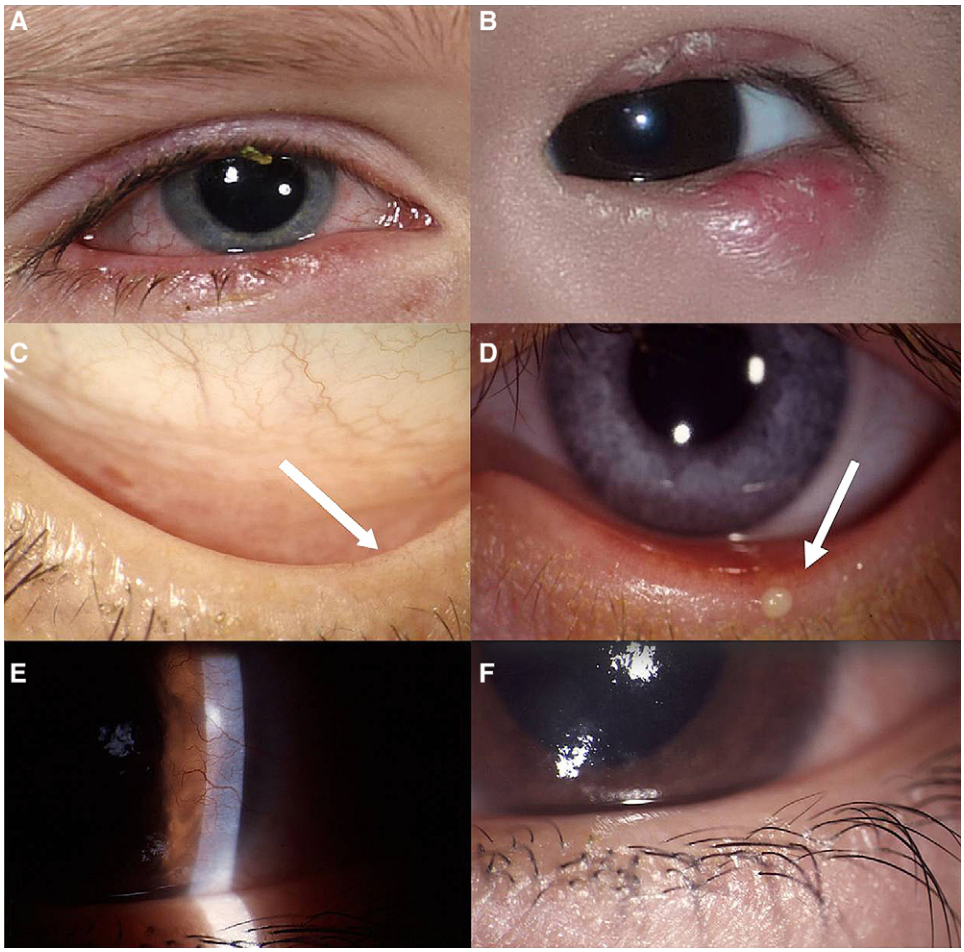


**FIG 4.** Clinical features of BKC. A, Crusting and collarettes in anterior blepharitis. B, Multiple chalazia. C, Lid margin telangiectasia and rounding. D, Meibomian gland capping. E, Corneal opacity with vascularization. F, punctate epithelial erosions and surface irregularity.

or special eyelid cleansers are the mainstay of treatment. However, modified lid hygiene with the use of a clean fingertip or warm damp flannel to rub the eyelids at the base of lashes during showering may be more easily implemented in small children.[1]

*Staphylococcus aureus* and *Staphylococcus epidermis* are common organisms cultured from conjunctival or lid swabs taken in patients with BKC. A variety of topical antibiotics can be used, including chloramphenicol, erythromycin, ciprofloxacin, gentamicin, and fusidic acid.

Systemic antibiotics often are necessary to control the lid disease, but tetracycline is contraindicated in children younger than 8 years because of its effect on dental enamel. Oral erythromycin is an effective and well-tolerated alternative, although it is unclear whether the mechanism of action is a direct effect on lipid synthesis or influence on the microflora. Recommended dosage ranged from 25% to 80% of the recommended dose for treatment of moderate infections in children (50 mg/kg per day). Treatment is usually required in the long term but should be reduced quickly to the minimum dose required to control lid margin disease. We have shown that even doses as low as 125 mg once weekly can control the lid margin disease adequately.[1]

Flaxseed oil ($\alpha$-linolenic acid) can be considered for children unable to tolerate or reluctant to use long-term systemic antibiotics. It is a source of omega-3 essential fatty acids, which have been found to have antiinflammatory effects and improve dry eye syndrome. In addition, it appears to have a thinning effect on meibomian secretions. The dosage recommended is 2.5 mL once a day for up to 12 months with a reduction to alternate days according to clinical improvement.[1]

Topical steroids are required for acute exacerbations and secondary corneal involvement. Prednisolone 1%, prednisolone 0.5%, or fluoromethalone can be used depending on severity but should be converted to fluorometholone or rimexolone once the disease is under control because they are less likely to induce glaucoma.

Recurrent chalazia are a common presentation, and a history of such in a child necessitates the exclusion of eyelid and corneal disease. Medical treatment such as lid hygiene, warm compress, and topical and systemic antibiotics can result in improvement or resolution within 1 to 3 months.

Table 4. Causes of persistent epithelial erosion in children

| |
|---|
| Trauma |
| Exposure keratitis secondary to lagophthalmos or proptosis |
| Viral keratitis, especially molluscum contagiosum |
| Herpetic keratitis |
| Vernal keratoconjunctivitis |
| Trichiasis |
| Epiblepharon common in Asian children: relatively high proportion require surgical correction |
| Circatricial entropion secondary to infection or immune disease |
| Dry eyes |
| 1. Primary (very rare in children) |
| 2. Secondary (eg, blepharokeratoconjunctivitis) |
| Neurotrophic keratitis |
| Cornea dystrophies: can present as painful erosions |
| 1. Reis-Buckler dystrophy |
| 2. Meesman dystrophy |
| 3. Lattice dystrophy |
| Epidermolysis bullosa |
| Cystinosis |
| Microsporidia keratitis (rare): can present as punctate epithelial erosions, but usually a slightly raised area in the center of the lesions (Figure 6) |

Surgical treatment is considered for nonresolving lesions, particularly if large and multiple. Incision and curettage can be augmented by intralesional triamcinolone injections in selected cases. In older cooperative children, an intralesional injection under local anesthesia may circumvent the need for surgery, but the chances of recurrence are greater.[20]

Lubricants are important because of the evaporative drying that accompanies meibomian gland disease. If the child cannot tolerate frequent lubrication, punctal plugs should be considered. Managing only the inflammatory lid margin disease is insufficient, and the secondary dry eye must also be addressed. Finally, optical correction of any induced refractive error and amblyopia treatment must be instigated if necessary.

## Persistent Epithelial Erosions

Punctate epithelial erosions may cause pain, watering, photophobia, and difficulty in opening eyes. Children usually present with rubbing of eyes. Vision is mildly reduced in the acute stage, but healing may be associated with scarring, which can lead to astigmatism.

### Causes

Persistent epithelial erosions may occur for a variety of reasons and include exposure, toxic, inflammatory, and mechanical causes (Table 4). The pattern and location of fluorescein staining as well as close inspection of the lids and corneal sensation can provide important clues to the etiology. Molluscum contagiosum, for example, is a common cause of follicular conjunctivitis that can easily be missed (Figure 5).

### Treatment

Lubricants are an important adjunctive treatment. A plethora of products is available, but the choice can be guided by some simple considerations, and different formulations may be used in combination to achieve the desired effect in individual patients (Table 5).

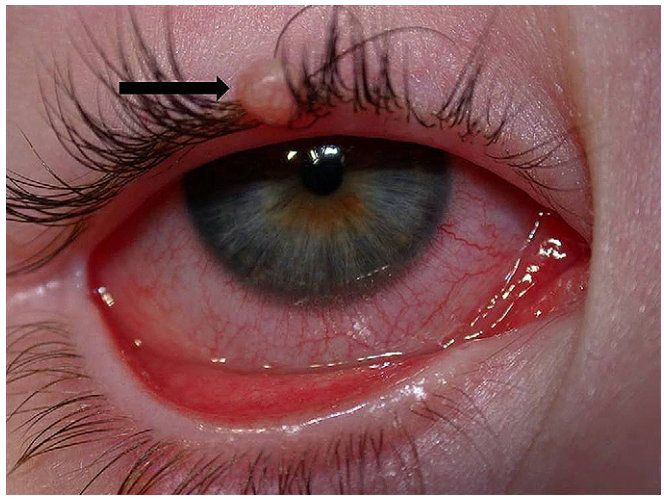

**FIG 5.** Molluscum contagiosum on right upper lid of a 12-year-old child with chronic unilateral conjunctivitis and punctate erosions.

Standard artificial tears have hydrogels (eg, methylcellulose) added to enhance viscosity and retention time, but despite this their effects may be short-lived. Formulations with greater viscosity (eg, Refresh Celluvisc [Allergan, Irvine, CA] and Refresh Liquigel Allergen, Irvine, CA) are longer lasting but often cause transient blurring lasting up to 20 minutes. Thus, a balance must be made. Systane (Alcon, Fort Worth, TX) uses HP-Gual, which forms a soft get once exposed to the eye, with increased viscosity and bioadhesive properties. For nighttime use, or for the treatment of lagophthalmos, petroleum-mineral oil-based ointments are the best because they maintain prolonged contact with the cornea.

Preservatives are added to increase the shelf life of lubricants. The commonly used benzalkonium chloride can cause irritation and epithelial toxicity, so the newer preservatives, such as sodium perborate and polyquaternium-1, are preferable. Preservative-free solutions are the best choice, especially if given more than 4 times a day. Tonicity may be a further consideration because tear osmolarity increases in dry eyes, and moderately hypotonic artificial tears have been show to promote ocular surface healing.

In severe dry eyes, other alternatives must be considered, including punctal plugs and omega-3 essential fatty acids supplementation. However, in cases in which the inflammatory component is predominant, a short course of topical corticosteroids or long-term use of cyclosporine 0.05% drops is often helpful.

## Persistent Epithelial Defects

Persistent epithelial defects (PEDs) can be extremely difficult to treat. The key is to improve the microenvironment of the ocular surface.

Table 5. Commonly available lubricants

| Product | Active ingredient(s) | Preservative |
|---|---|---|
| Carboxyl methylcellulose (CMC) artificial tears | | |
| Refresh Tears[a] | 0.5% CMC | Purite |
| Refresh Plus[a] | 0.5% CMC | None |
| Refresh Liquigel[a] | 1% CMC | Purite |
| Refresh Celluvisc[a] | 1% CMC | None |
| *Thera Tears[b] | 0.25% CMC | None |
| Hydroxypropyl methylcellulose (HPMC) artificial tears | | |
| Bion Tears[c] | 0.3% HPMC, 0.1% dextran 70 | None |
| Tears Naturale Forte[c] | 0.3% HPMC, 0.1% dextran 70, 0.2% glycerin | Polyquad |
| Tears Naturale II[c] | 0.3% HPMC, 0.1% dextran 70 | Polyquad |
| Tears Naturale Free[c] | 0.3% HPMC, 0.1% dextran 70 | None |
| Genteal[d] | 0.3% HPMC | Genaqua |
| Genteal Mild[d] | 0.2% HPMC | Genaqua |
| Visine Tears[e] | 0.2% HPMC, 0.2% glycerin, 1% polyethylene glycol 400 | Benzalkonium chloride |
| Visine Pure Tears[f] | 0.2% HPMC, 0.2% glycerin, 1% polyethylene glycol 400 | None |
| Polyvinyl alcohol (PVA) artificial tears | | |
| Murine Tears[g] | 0.5% PVA , 0.6% povidone | Benzalkonium chloride |
| Hypotears (hypotonic preparation) [d] | 1% PVA , 1% polyethylene glycol 400 | Benzalkonium chloride |
| Akwa Tears (hypotonic preparation) [h] | 1.4% PVA | Benzalkonium chloride |
| Propylene glycol and/or glycerin | | |
| Advanced Eye Relief "Environment"[i] | 1% propylene glycol, 0.3% glycerin | Benzalkonium chloride |
| Advanced Eye Relief "Rejuvenation"[i] | 0.95% propylene glycol | Benzalkonium chloride |
| Advanced Eye Relief "Rejuvenation PF"[i] | 0.95% propylene glycol | None |
| Systane[c] | Polyethylene glycol 400 0.4%, propylene glycol 0.3%, hydroxypropyl guar (gel-forming matrix) | Polyquad |
| Ointments and gels | | |
| GenTeal Gel[d] | 0.3% HPMC, carbopol 980 | GenAqua |
| Refresh PM ointment[a] | 57.3% white petrolatum, 42.5% mineral oil | None |
| Tears Naturale P.M. ointment[c] | 56.8% white petrolatum, 42.5% mineral oil | None |
| Lacrilube ointment[a] | White petrolatum, mineral oil | Chlorobutanol |
| Advanced Eye Relief Night Time[i] | White petrolatum, mineral oil | None |

Manufacturers:
[a]Allergan, Irvine, CA.
[b]Advanced Vision Research, Woburn, MA.
[c]Alcon, Fort Worth, TX.
[d]Novartis, Basel, Switzerland.
[e]Pfizer, New York, NY.
[f]Pfizer, New York, NY.
[g]Prestige Brands, Irvington, NY.
[h]Akorn, Lake Forest, IL.
[i]Bausch & Lomb, Rochester, NY.

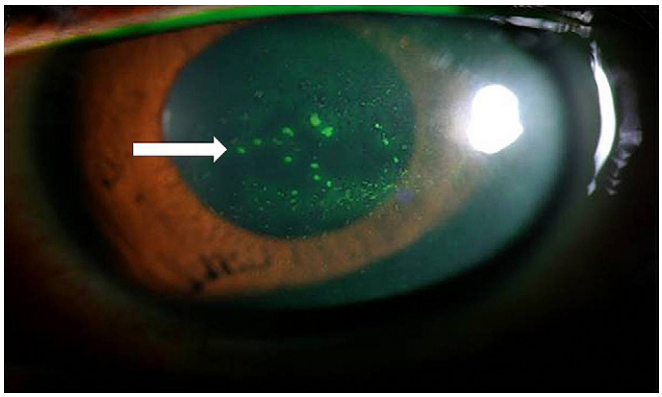

**FIG 6.** Superficial punctate lesions in a case of culture-proven microsporidial keratoconjunctivitis in the left eye of a 13-year-old boy.

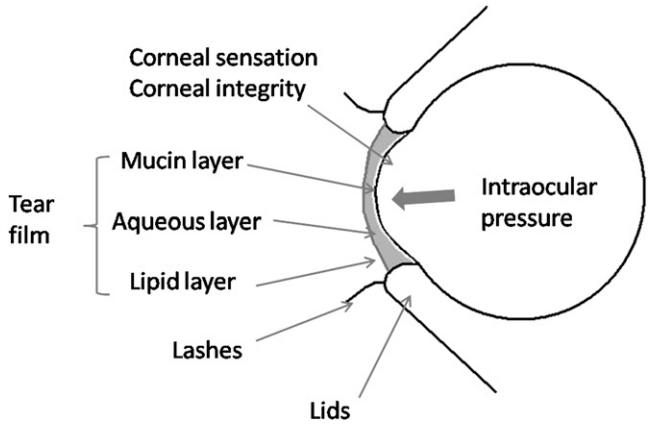


**FIG 7.** Factors that may contribute to ocular surface disruption.

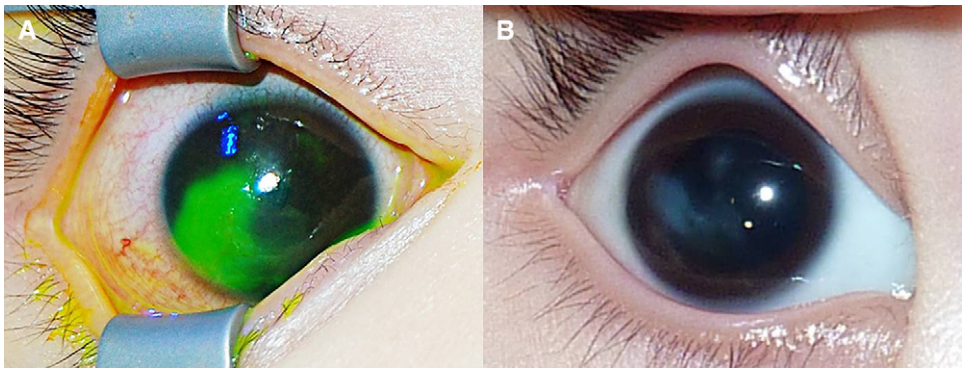


**FIG 8.** A, Shown is an 18-month-old girl with a 3-month history of red eye found to have an epithelial defect in her right eye, which failed to heal with topical antibiotics. B, Corneal scraping was positive for herpes simplex virus, and the defect healed with scarring and 4D of induced astigmatism after treatment with topical acyclovir.

## Causes

Contributing factors are shown in Figure 7 and include tear film problems, corneal anesthesia, limbal stem-cell deficiency, lid and lash anomalies, and increased intraocular pressure.

A problem in any layer of the tear film can lead to or contribute to PEDs. The lipid layer is disturbed in meibomian gland dysfunction, leading to reduced tear break-up time. Primary aqueous deficiency is rare in children and may indicate underlying pathology. Goblet cell destruction as in Stevens-Johnson syndrome affects the mucin component.

The trigeminal nerve is important for corneal healing. Congenital corneal anesthesia is rare and can occur in isolation or in association with certain systemic conditions. In acquired cases, trigeminal nerve injury or compressive lesions should be excluded. Herpes simplex keratitis is an important differential in any nonhealing epithelial defect in children. In contrast to adults where diagnosis is often clinical, virological confirmation is very helpful (Figure 8). There is a high risk of visual impairment and recurrences, and prolonged systemic treatment may be required.[2]

Limbal stem cell deficiency can be primary, as in aniridia, or secondary, such as in chemical injuries or Stevens-Johnson syndrome. The hallmark is conjunctivalization of the corneal surface, and it may lead to PEDs and scarring. The diagnosis can be confirmed with impression cytology.

Lid incongruity such as lagophthalmos caused by facial paralysis or proptosis can cause exposure keratopathy. Inturning lashes such as in trichiasis or entropion must also be excluded.

## Treatment Options

Lubrication options are discussed previously. Other topical treatments are considered as follows:

- *Autologous serum*. Serum contains a variety of growth factors, vitamins, and immunoglobulins, and these epitheliotrophic factors are thought to exert a therapeutic effect on nonhealing epithelium. Autologous serum has been used with some success but procuring it can be difficult.[21,22] The problem in a young child is the relative large volume of blood needed to acquire sufficient serum.
- *Albuminate*. As an alternative to serum, this substitute also has been reported to promote healing of the epithelium.[23]
- *Healon* (AMO, Santa Ana, CA). Before the advent of commercially available hyaluronic acid, viscoelastic with hyaluronic acid component could be used to promote healing of the defect.
- *Hyaluronic acid drops*. These are now available commercially but can leave white sediment in the base of the defect.
- *Punctal plugs*. These reduce the need for very frequent lubricating drops by increasing the tear reservoir. Dissolvable collagen plugs (lasting 7 to 10 days) can be used to determine efficacy of punctal occlusion before the placement of semipermanent silicon plugs. Silicone punctal plugs have been used in children and are typically retained for weeks to months but can be retained for years. (Subbu R, Nischal KK, Jones S, Moore W. The use of punctal plugs in children. E-poster, World Congress of Paediatric Ophthalmology and Strabismus. Barcelona 2009.) Permanent punctal occlusion, if desired, is best performed by the use of thermocautery.
- *Amniotic membrane transplant (AMT)*. Human amniotic membrane promotes epithelialization and decreases inflammation, neovascularization, and fibrosis. AMT may be used as patch graft to fill in defects, as bandage contact lens, or for treatment for tarsal conjunctival scarring.
- *Tarsorrhaphy*. For AMT in children, central tarsorrhaphy must be performed to prevent the amniotic membrane from being dislodged by rubbing. However, lateral tarsorrhaphy decreases the area of the eye exposed to the environment and allows healing in cases of exposure keratopathy.
- *Botulinum toxin–induced ptosis*. This well-described method of protecting the cornea[24] can be combined with other modalities. This lasts 6 weeks, so if there is any doubt about amblyogenic insult it is best avoided.

- *Lid surgery*. Tarsal eversion or anterior lamellar repositioning for trichiasis may be required.
- *Limbal stem cell transplant*. Conjunctival limbal autografts from the healthy contralateral eye can be performed for unilateral cases. In bilateral cases, tissue may be harvested from a cadaver or a living related donor, and it is now also possible to cultivate limbal stem cells in vitro.[25]

## Conclusions

External diseases may be difficult to manage in children. In a child presenting with pain, photophobia, redness, and tearing, the differential diagnoses can be varied. However, close inspection of the ocular surface and lids, measurement of intraocular pressure, and appropriate microbial investigations will lead us to the correct diagnosis. In uncooperative children, there should be no hesitation in proceeding with examination under anesthesia.

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