



# Allergic manifestations of contact lens wearing

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## Purpose of review

Contact lens-induced papillary conjunctivitis (CLPC) is a common ocular allergic disease in contact lens wearers. In its more severe form, it can cause giant papillary conjunctivitis, resulting in contact lens intolerance and the need to discontinue the use of contact lenses. This review presents the pathogenesis, clinical manifestations and management guidelines of this common disorder.

## Recent findings

Different types of contact lenses are associated with differences in the severity of CLPC. Refitting patients with silicone hydrogel contact lenses or with daily disposable contact lenses may improve the signs and symptoms of CLPC. The recent introduction of the topical immunomodulatory agent tacrolimus in other severe allergic eye diseases may apply in suppressing the allergic inflammation in CLPC as well.

## Summary

CLPC is a common ocular disorder in contact lens wearers, with a significant impact on the quality of vision. It should be promptly recognized by healthcare practitioners and managed by modifications of the types and wearing schedules of contact lenses, as well as novel treatment options with topical immunomodulators.

## Keywords

allergic conjunctivitis, allergic inflammation, contact lenses, papillary conjunctivitis, tacrolimus

## INTRODUCTION

The use of contact lenses in the general population has dramatically increased over the years. Although in 2006 about 33 million Americans were reported to be using contact lenses [1], in 2015 there were 40.9 million contact lens wearers in the United States aged 18 years and older, which is 16.7% of the US adult population [2<sup>••</sup>,3]. The use of daily wear and extended wear contact lenses is steadily increasing, with an estimated growth of 5.2% in the sales volume of soft lenses in the United States during 2015 and a similar growth of 4.9% during 2014 [3].

Allergy diseases in the United States are affecting up to 30% of the population [4]. Approximately, 15–20% of the world population is affected by some form of allergy. Of these, ocular symptoms are present in 40–60% of allergic patients [5,6].

The high prevalence of contact lens use coupled with the high incidence of systemic allergic diseases and ocular allergy exposes a high number of allergic individuals to the use of contact lenses. The use of contact lenses in patients with allergic disorders increases by five-fold their likelihood of experiencing signs and symptoms of ocular irritation [7]. The main clinical manifestation of the allergic response induced by contact lenses is contact lens-induced papillary conjunctivitis (CLPC), also termed giant

papillary conjunctivitis (GPC) [8]. This article will focus on the allergic manifestations that are associated with contact lens wear and the impact of using contact lenses in individuals suffering from allergic diseases.

## TYPES OF CONTACT LENSES

The vast majority of contact lenses in 2015 were silicone hydrogel lenses (69%), followed by hydrogels (20%) and rigid gas permeable (RGP) contact lenses (9%) [3]. Soft contact lenses include two main types of lenses: hydrogels and silicone hydrogels. The regular hydrogel lenses are made from hydroxyethyl methacrylate (HEMA). These lenses have high water content but are characterized by relatively lower oxygen permeability. The silicone hydrogel lenses, which were introduced in 1998, have better oxygen permeability but are less flexible. Hard

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**Curr Opin Allergy Clin Immunol** 2016, 16:492–497

DOI:10.1097/ACI.0000000000000311

## KEY POINTS

- Coating of contact lenses by protein and lipid deposits from the tear film is responsible for the initiation of the ocular allergic response.
- The more severe allergic responses are due to the rigid gas permeable (RGP) and hydrogel contact lenses, whereas the later designs of silicone hydrogel contact lenses are associated with a lesser degree of CLPC.
- Modifications of contact lenses wearing schedules, temporary discontinuation, refitting of contact lenses and using daily disposable lenses are the initial management strategies.
- Topical immune modulators such as tacrolimus may prove beneficial in the management of CLPC.

contact lenses are RGP lenses made from polymethyl methacrylate. The soft contact lenses have different wearing schedules. These include the daily disposable contact lenses and the extended wear contact lenses that can be used biweekly, monthly or trimonthly.

All types of contact lenses can induce GPC, which varies in the location and extent of the area involved in the upper tarsal conjunctiva [8]. The papillary reaction caused by HEMA-based lenses is located at the upper and middle parts of the tarsal conjunctiva (zones 1 and 2), whereas that caused by RGP lenses is located in the middle and lower parts of the tarsal conjunctiva (zones 2 and 3), closer to the lid margin. The reaction in RGP lenses is more localized, whereas the reaction to HEMA lenses is more diffuse. The silicone hydrogel contact lenses have both a localized and a diffuse GPC, but the localized form is more common in this type of contact lenses, and the symptoms are usually milder in silicone hydrogel lenses compared with the hydrogel and the RGP lenses [8].

## CONTACT LENS-INDUCED PAPILLARY CONJUNCTIVITIS

The most common form of allergic response to contact lenses is an inflammatory disease of the upper tarsal conjunctiva. This was initially described by Spring [9] and by Allansmith [10] as a reaction to soft contact lenses. It was suggested that the proteinaceous deposits on the contact lenses served as antigens that elicited the allergic immune response. The condition was initially termed GPC. However, GPC can be caused by other factors such as ocular prosthesis, exposed sutures, extruded scleral buckles, filtering blebs and exposed corneal

deposits. In addition, in most of the patients, the papillae are small and uniform rather than the giant papillae that are encountered in vernal keratoconjunctivitis (VKC). Therefore, the term CLPC is more appropriate for the ocular allergic manifestations that are induced by contact lenses.

## PATHOPHYSIOLOGY OF CONTACT LENS-INDUCED PAPILLARY CONJUNCTIVITIS

The cells that participate in allergic inflammation – namely mast cells, plasma cells, neutrophils and lymphocytes, eosinophils and basophils – are all increased in numbers in the conjunctival epithelium and subepithelial tissue [11]. In addition, many cytokines and chemokines are elevated in the tear film of patients with CLPC, including IL-6 and IL-6-soluble receptor, monocyte chemoattractant protein-1 and monokine-induced gamma interferon, eotaxin-2, IL-11 macrophage inflammatory protein-1 delta and tissue inhibitor of metalloproteinases-2 [12]. Of these, the levels of eotaxin, a major chemoattractant of eosinophils, were correlated with the severity of the papillary reaction [13]. Another mediator that is elevated in tears of patients with GPC is leukotriene C4, which correlates with signs of redness, edema, mucoid discharge and papillary formation that are common in CLPC [14]. The tear immunoglobulins, IgE and IgG, are elevated in these patients, with a correlation between the amount of elevation and severity of symptoms. Following cessation of lens wear, the levels of the tear immunoglobulins return to normal levels [15].

The major process that is responsible for the initiation of the allergic inflammatory response to contact lenses is the coating effect. Contact lenses are coated with various lipid and protein deposits, which are derived from the tear film (Fig. 1). This coating not only varies according to the types of



**FIGURE 1.** Protein deposits on the surface of a soft contact lens, and hyperemic thickened upper tarsal conjunctiva.

polymers in the lenses, but also changes between different individuals. High water content contact lenses tend to coat more compared with low water content lenses. The HEMA hydrogels attract more protein and lysozyme deposits compared with the silicone hydrogel lenses, whereas the silicone hydrogel lenses accumulate more lipid deposits [16,17].

The development of the allergic inflammatory response starts with deposition of protein substances on the surface of contact lenses. Studies with contact lenses have shown that within 30 min of lens insertion, 50% of its surface can be coated with protein deposits, and within 8 h, 90% of its surface is coated [18]. The coating process is affected by the polymer content and structure of the various contact lenses. This process is common to all lens wearers, even those who do not develop CLPC. However, contact lens wearers who develop GPC have more coating on their lenses. In addition, lenses from GPC patients that were inserted into eyes on monkeys, promoted papillary reaction in the tarsal conjunctiva of these monkeys [19]. This animal model is evidence for the existence of antigens in the contact lens coatings that produces the allergic inflammatory response. The finding of IgG, IgA and IgM in the contact lens protein deposits also supports the allergic mechanism in contact lens-induced CLPC [20].

Another suggested mechanism for CLPC is the mechanical damage, caused by the constant friction between the lens surface and the epithelium of the tarsal conjunctiva. This friction damages the epithelial cell membranes and releases various chemotactic factors that initiate the allergic inflammatory response [21].

The association between meibomian gland disease (MGD) and CLPC is inconclusive. Although early reports associated meibomian gland obstruction with contact lens intolerance [22], later studies [23,24] failed to establish a significant association between MGD and CLPC. However, a recent study [25] did find a role for MGD in CLPC. Significant distortion of the meibomian glands was found not only in contact lens wearers who had CLPC, but also in patients with different types of allergic conjunctivitis who did not use contact lenses. It was therefore suggested that the morphological changes in meibomian glands were associated with the allergic disease and not with the use of contact lenses [25].

### CLINICAL MANIFESTATIONS OF CONTACT LENS-INDUCED PAPILLARY CONJUNCTIVITIS

The major symptoms of CLPC include itching, redness, burning, foreign body sensation and increased mucous discharge, mainly when opening the eyes

after sleep. There is no clear correlation between the severity of complaints and the clinical findings, particularly at the early evolution of GPC, when the symptoms are more prominent than the appearance of the papillary response.

The signs of CLPC include fine papillae that are smaller than 0.3 mm in the mild or early stages of the disease. This may be accompanied by thickening and mild hyperemia of the tarsal conjunctiva. The bulbar conjunctiva may be mildly inflamed. In later stages, large papillae greater than 0.3 mm develop [10].

To help describe the location of the tarsal papillae, the tarsal plate was divided into three zones, in which zone 1 lies along the tarsal border, zone 2 describes the central area of the tarsal plate and zone 3 borders the area along the lid margin [15].

The clinical course of CLPC may be divided into four stages:

Stage 1 – Preclinical stage: characterized by minimal mucous discharge upon awakening, occasional itching, mild protein coating on contact lenses and mild hyperemia of the tarsal conjunctiva.

Stage 2 – Mild CLPC: increased mucous and itching, increased coating of the contact lenses, mild injection of the tarsal conjunctiva, variable sized small papillae in the tarsal conjunctiva, mostly less than 0.3 mm (Fig. 2).

Stage 3 – Moderate CLPC: more prominent itching and mucous production, difficult to tolerate contact lenses, excessive lens movement on blinking, increase lens awareness, marked thickening and injection of the tarsal conjunctiva, larger and more elevated papillae, measuring more than 0.3 mm (Fig. 3).

Stage 4 – Severe CLPC: inability to wear contact lenses, intense discomfort, excessive lens movements, excessive mucous production and giant



**FIGURE 2.** A mild contact lens-induced papillary conjunctivitis showing small papillae sized less than 0.3 mm and diffusely located in zones 1 and 2 of the tarsal conjunctiva.

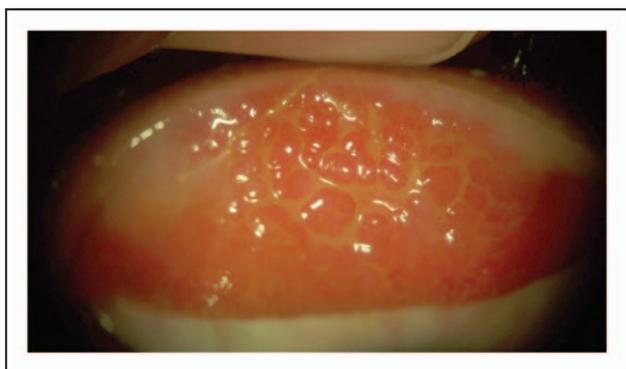


**FIGURE 3.** A moderate contact lens-induced papillary conjunctivitis with moderate papillae sized more than 0.3 mm and located at zones 1 and 2, with mucous secretion.

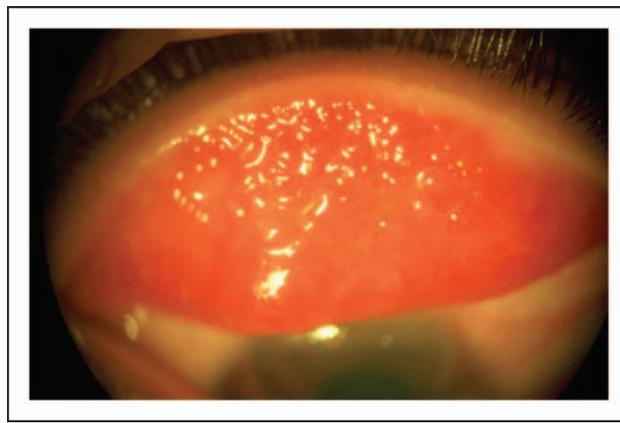
papillae of 1 mm or bigger (Figs 4 and 5). There may be subconjunctival scarring. The term GPC should probably be reserved for this late stage of severe CLPC.

### DIFFERENTIAL DIAGNOSIS

Giant papillae occur also in VKC. The clinical history helps to distinguish between these two entities. VKC is a disease in children, which develops in early childhood and persists until late puberty, whereas CLPC is a common reaction to chronic lens wear in all ages. In addition, the papillae in VKC are much larger, more variable in shape and size, with typical rough surfaces (Fig. 6). There is sometimes secondary damage to the cornea, manifested by shield ulcers, vernal plaques, microbial keratitis and keratoconus [26,27]. In addition, VKC is sometimes characterized by the occurrence of limbal hypertrophy and multiple limbal inflammatory nodules, which do not occur in CLPC.



**FIGURE 4.** A severe form of contact lens-induced papillary conjunctivitis showing big papillae with distinct borders in all zones of the tarsal conjunctiva.



**FIGURE 5.** A severe form of contact lens-induced papillary conjunctivitis showing big papillae with markedly thickened hyperemic tarsal conjunctiva.

The location of the papillae in VKC is in all zones of the tarsal conjunctiva. The location of papillae in CLPC varies with the type of lens used. Soft lens wearers have a papillary response mainly at zones 1 and 2, whereas RGP lenses and silicone hydrogel contact lenses have papillary response in zones 2 and 3 (closer to the lid margin) [15]. Soft contact lenses are associated with a generalized papillary response, whereas those wearing RGP or silicone hydrogels have papillae that are more localized.

### MANAGEMENT

The management strategy of CLPC is modification of the various aspects in the use of contact lenses: changing the lens cleaning solutions, changing the type of the contact lens, refitting the patient with a new lens, decreasing wearing time throughout the day or shortening the replacing intervals for extended wear contact lenses. One study [15] looked



**FIGURE 6.** Vernal keratoconjunctivitis has a severe tarsal inflammatory response with prominent coarse giant papillae, mainly in zones 1 and 2, with prominent mucous discharge.

at the effect of each of these modifications in reducing contact lens intolerance. When only the cleaning procedure was changed, only 50% of affected patients were able to continue wearing their contact lenses. A decrease in the wearing time only resulted in 20% of patients who could continue wearing lenses. Refitting the patients with new contact lenses resulted in 68% of patients who could tolerate wearing their lenses if they were refitted with the same type of lens, a change to an RGP (gas permeable hard) lens resulted in 82% of patients returning to contact lens wear and frequent replacement of a daily wear lens resulted in a 91% success rate [15].

A beneficial effect of daily disposable contact lenses on allergic eye disease was recently demonstrated in two studies. These studies were based on the ability of the contact lens to act as a physical barrier against airborne antigens. Changing the regular regimen of extended wear contact lenses to daily disposable contact lenses in individuals with CLPC was associated with significant reduction of signs and symptoms of papillary conjunctivitis [28]. Using daily disposable contact lenses following acute exposure to grass pollen in one clinical trial resulted in a significant reduction in the various signs and symptoms of CLPC compared with those who kept using their current contact lenses [29].

The topical treatment of CLPC is not different from that of any other form of allergic conjunctivitis. Topical mast cell stabilizers, topical antihistamines and topical corticosteroids are currently the main drug categories that are employed in most of the ocular allergy diseases. Mast cell stabilizers were found to be up to 70% successful in moderate-to-severe GPC [30]. Topical corticosteroids, such as loteprednol are also used in CLPC, markedly reducing the presence of papillae, itching and contact lens intolerance [31]. However, topical corticosteroids are limited because of their significant side effects and the need to monitor the intraocular pressure during treatment.

A recent study presented a novel biomimetic lens that was developed to release olopatadine, an H1-receptor blocker. This lens was designed to include functional monomers that match with the chemical groups of the H1-receptor, thereby binding olopatadine to the lens. Thus, this contact lens can slowly release olopatadine on the ocular surface, thereby creating a local slow release delivery system of antihistamines [32].

Tacrolimus is a topical calcineurin inhibitor, with a potent effect on allergic eye diseases. Many studies have demonstrated the efficacy and safety of tacrolimus in VKC [33,34,35] and in atopic keratoconjunctivitis [36,37]. Unfortunately, the

literature on tacrolimus in CLPC is scarce. One recent study [38] found that 0.05% tacrolimus was as well tolerated and as effective compared with 0.1% fluorometholone in CLPC. A case report claims that topical 0.03% tacrolimus ointment given twice daily completely resolved the signs of GPC within 1 month [39]. As topical tacrolimus was demonstrated to be an extremely potent anti-inflammatory agent in the most severe forms of ocular allergy, it is strongly believed that tacrolimus will also play a major role in the management of CLPC.

The management of CLPC is tailored to the different stages and should be performed as a team work by both the optometrist and the ophthalmologist. Stage 1 of CLPC needs just routine observation. In stages 2 and 3, the contact lens must be discontinued for 2–4 weeks, and then other types of contact lenses should be refitted, such as daily disposable lenses. Those who use extended wear lenses for periods of 1 month should change their cleansing solutions and consider a solution based on hydrogen peroxide [15]. If there are still allergic signs and symptoms, the lens must be discontinued for another period of a few weeks and then refitted with a daily wear disposable lens or RGP. Topical treatment with H1-receptor blockers or by corticosteroids should be considered according to the severity of the signs of tarsal inflammation. In addition, as MGD is found in many contact lens wearers, topical preservative free tear substitutes, lid hygiene and systemic doxycycline may be added to the treatment protocol.

Stage 4 disease requires cessation of lens use for a month and fitting with a different type of lens: daily disposables or RGPs. Following resolution of the inflammatory response, refitting the patient with new lenses is the best option. Wearing daily wear contact lenses that are replaced every 4 weeks reduces the rate of GPC [40]. In addition, those who use daily disposable lenses do not develop GPC. Some patients must discontinue using contact lenses indefinitely and consider other options such as spectacles or laser vision correction surgery.

## CONCLUSION

As contact lens wearing becomes more prevalent, as well as the prevalence of allergic diseases in the general population, the incidence of contact lens-induced papillary conjunctivitis is increasing. Prompt recognition of this common disorder is needed by primary care physicians, ophthalmologists and optometrists. Modification of contact lens wearing schedules, specifically shifting to daily disposable lenses may improve the manifestations of contact lens intolerance. Newer topical drugs

such as tacrolimus may help to significantly alleviate the signs and symptoms of CLPC.

## Acknowledgements

None.

## Financial support and sponsorship

None.

## Conflicts of interest

There are no conflicts of interest.

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- of special interest
- of outstanding interest

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