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Review

# Contact lens wear and the goblet cells of the human conjunctiva—A review

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ABSTRACT

*Purpose:* To review the reported effects of contact lens wear on the goblet cells of the human conjunctiva.
*Methods:* A literature search was undertaken to identify reports on the conjunctival health after contact lens wear, principally as assessed using the conjunctival impression cytology (CIC) technique in which cells are examined *ex vivo*, after fixation and staining. Details of technique, data on duration of contact lens wear and then CIC outcome in terms of goblet cell density (GCD) were extracted.
*Results:* Of 24 reports identified, 22 examined the bulbar conjunctiva and 2 examined the tarsal conjunctiva. A decrease in GCD was considered, directly or indirectly, to be a consequence of contact lens wear in 18 of the studies, but there was no obvious overall relationship between duration of lens wear and the GCD changes. Conversely, four reports indicated an increase in GCD or goblet cell-related mucins. Two reports concluded that there was no change in goblet cells or their mucin, a result however that is consistent with a recent conclusion that no statistically significant change in GCD was detectable in contact lens wearers assessed by *in vivo* imaging of the human conjunctiva by confocal microscopy.
*Conclusions:* The majority of published studies have concluded that contact lens wear results in a decrease in goblet cells in the conjunctiva. While there are reports that draw a very different conclusion, it should be noted that there has been limited consistency in technique or the method of reporting the results across the various studies.


## 1. Introduction

A contact lens, regardless of the material from which it is made, is manufactured and then custom fitted to align with the curvature of the ocular surface. The goodness of fit would generally be considered to be more important with a rigid or semi-rigid lens type as opposed to a soft lens which is able to conform more readily to the ocular surface curvature as it is draped across the cornea, the limbus and a small part of the adjacent bulbar conjunctiva. The back surface of the contact lens thus has some contact with the ocular surface, depending on the lens type and fit. Equally importantly, the front surface of the contact lens has some degree of contact with the eyelid marginal zone and parts of the tarsal surface, again depending on the lens type, material and size. In reality, a properly fitted contact lens does not make intimate contact with either the bulbar or tarsal conjunctiva cell surface *per se*, but is separated from the actual cells by a thin layer of tear film. This is referred to as the pre- and post-lens tear film according to whether the film is on the front or back surface of the lens. The pre-lens tear film would be expected to be part of a double layer of tear films, one on the lens and the other adjacent to the tarsal surface.

Based on most models of the micro 'structure' of the tear film and its interface with the ocular surface cells, a mucus layer or gel should form part of the normal post-lens tear film structure [1], and also be part of the double layer associated with the pre-lens/tarsal surface tear films [2]. A healthy cell surface supports the tear film and this epithelial cell layer includes the mucous-secreting cells of the conjunctiva, namely the goblet cells [3–5]. The goblet cells are considered to contain a specific mucous type called MUC5AC, a mucin that forms a gel. At least for rabbit eyes *ex vivo*, special electron microscopy preparation techniques can be used to show that the corneal (and probably the bulbar conjunctiva) surface is routinely covered with a thin layer of a porous gel-like mucous complex (Fig. 1) [6]. In contrast, a much thicker amorphous layer, with less obvious microscopic pores, appears to be present across the rabbit palpebral conjunctiva [7].

It is a reasonable assumption that the best fitting and patient tolerance of a contact lens will depend on there being a healthy conjunctiva. A thin mucous (mucin) coating was once considered a requirement for endowing reasonable wetting qualities to the surface of a contact lens [8], but this generalization and the critical amount needed may not be the same for different contact lens types. Mucin-related sialopeptides, as well as the overall protein content, have been reported to be reduced in the tears of contact lens wearers [9]. It can be speculated that any compromise in the ocular surface and/or these mucous-secreting goblet cells may

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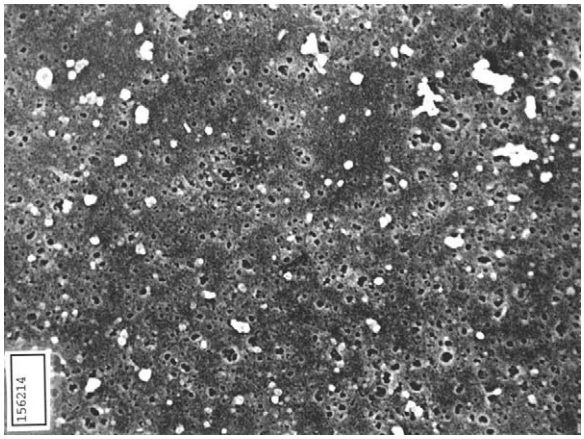


**Fig. 1.** Scanning electron microscopy appearance of the corneal surface of a rabbit after special fixation with a mucous-precipitating chemical to illustrate the presence of a mucous gel. The very high magnification image shows very large numbers of very small and dark-appearing holes in a grey film indicating pores in gel-like matrix. The irregularly shaped white flecks are presumed to be tear film microscopic debris. Length of vertical rectangular box (scale bar) = 1 μm. From Ref. [6]. Copyright Informa Healthcare.

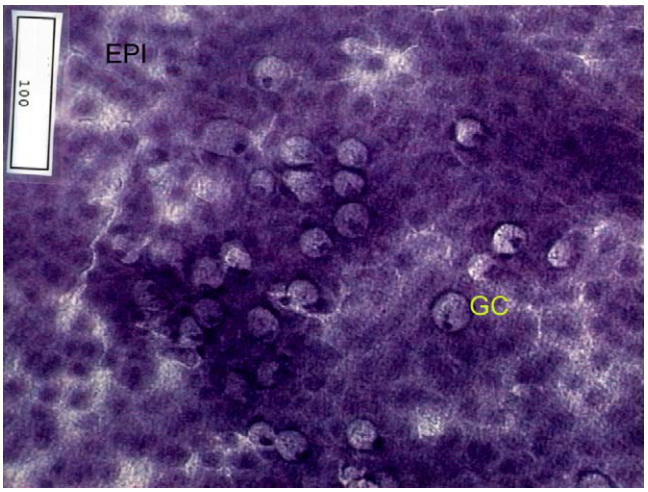


**Fig. 2.** Impression cytology sample from the nasal aspect of the exposed bulbar conjunctiva of a human soft contact lens wearer (5 years of wear) to illustrate the presence of goblet cells. The image shows a somewhat multilayered sample of smaller-sized epithelial cells (EPI) with slightly darker stained nuclei and slightly paler cytoplasm which are interspersed with a modest number of goblet cells (GC) with their typically very small and eccentrically located darker-staining nuclei. Medium power microscope field of view, 20× objective lens. Giemsa stain after glutaraldehyde fixation. Length of vertical rectangular box (scale bar) = 0.1 mm.

result in a progressive onset of contact lens intolerance [10], and even development of what are now well known complications of longer term contact lens wear, namely CLPC (contact lens papillary conjunctivitis) of the tarsal surface [11].

A number of different investigators over an extended period have reported on their assessments of the health of the bulbar or tarsal surfaces by a special research technique. This technique, widely referred to as conjunctival impression cytology (CIC), is a method of assessing conjunctival cells. CIC is now widely regarded as a simple and clinically applicable technique designed to allow for a minimally invasive investigation (as compared to a surgical biopsy being taken) of the health of the conjunctival surface [12–19]. Changes in the goblet cells of the conjunctival epithelia, as obtained by CIC sampling, have been repeatedly reported to develop in contact lens wearers [20–44]. Most of these studies have however used different sampling sites, used different grading schemes to assess the cell samples and also different methods of reporting their data.

The objective of the present review is to summarize what results have been reported for changes in goblet cells in contact lens wearers over almost a 25-year period. The conclusions from this review will hopefully demonstrate an important need for further studies that need to address the deficiencies of these previous studies as well as provide much needed information on newer contact lenses.

## 2. Conjunctival impression cytology – the technique

The basic principle of the CIC technique is generally credited to Egbert et al. [45], who noted that following the application of a cellulose acetate (Millipore) filter paper onto the bulbar conjunctiva an impression was formed of the locations of mucous-producing cells. These were visualized on the filter after removing it from the conjunctiva and staining it with a chemical (called periodic acid-Schiff or PAS) that interacted with mucous. The locations (and density) of these very small patches of mucous were thought to provide an indication of where the goblet cells were located. The technique should be distinguished from that of cytology, *per se*, generally applied to the inferior conjunctiva and lower cul-de-sac whereby a Perspex strip was used to collect epithelial cells and any inflammatory cells that might be present [46,47]; this has also been used for contact lens wearers.

Egbert et al. also, rather indirectly, noted that some cells could attach to the cellulose acetate filters, so causing them to refer to the technique as a 'simple conjunctival biopsy' [45]. The cells are collected onto the surface of a filter, usually stained with PAS and another stain called haematoxylin to visualize the non-goblet cells, and then the surface of the filter examined in a conventional light microscope. It is the latter aspect that has became popularized by use with many different investigators trying the technique over the ensuing years. There are now a number of applications that have been tried in assessing the cellular material obtained by CIC (Table 1). These will be referred to where appropriate (see later) but basically either involve treating the filter material as obtained (primary applications) or using the filter to collect cells which are then removed from the filter and analysed (secondary application). Most CIC studies on contact lens wearers have opted for primary application but, as indicated in Table 1 have used different staining methods.

Over the years a number of different filter materials have been used as well as 2 or more sets of staining to highlight cell and goblet cell features. In addition, various key investigators have reported their experiences that have led them to develop slightly different methods of grading the character of the epithelial cells and goblet cells [12–15,18,28,48–51].

The view of the cells in primary applications of CIC is, as with any cytological technique, the coronal view (as opposed to the sagittal or sectional view usually adopted when examining cells from a true conjunctival biopsy specimen). As such, the full extent of both the cells and nuclei, if in a monolayer, can be visualized (as opposed to only partial views of cells and their nuclei that may be present when a tissue sample is sectioned). The detail that is apparent will obviously depend on the magnification used; most reports on CIC samples have used a 20× or 40× objective lens so as to be able to see some or quite considerable detail in a microscope field of the view. Some confusion can arise however when only relative terms are used, e.g. different investigators may use the term 'high power field' for 40× or 100× objective lens use.

A CIC sample should contain a mixture of non-goblet conjunctival epithelial cells as well as some goblet cells, and can also contain some inflammatory cells. An example is given in Fig. 2