



What are the factors contributing to the occurrence of contact lens induced peripheral ulceration (CLPU): A study of its pathogenesis in a rabbit model



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Introduction

CLPU is one of the major complications of contact lens wear with unknown aetiology, and occurs mostly in extended hydrogel contact lens wearers⁽¹⁾. It has been described as an acute, sudden onset corneal lesion characterized by circular full-thickness epithelial defect in the periphery or mid-periphery of the cornea, accompanied by moderate bulbar and limbal redness. Photophobia, tearing and minor pain are the main symptoms of CLPU. It mostly resolves upon removal of contact lens without the use of antibiotics, leaving behind a scar. Both *S. aureus* and *S. epidermidis* are frequently isolated from the eye of CLPU patients (although not necessarily from the ulcer itself), and hypersensitivity to staphylococcal antigens has been suggested to be responsible for the formation of CLPU.

Bacteriological studies have demonstrated that carriage of Gram positive bacteria, particularly *Staphylococci*, is associated with an increased risk of having CLPU. A case of CLPU, reported by Jalbert *et al*, with regular microbiological monitoring of 6 years demonstrated a direct relation of *S. aureus* with CLPU, as *S. aureus*, found in large amount in this patient, had never been isolated prior to the CLPU event⁽²⁾. A previous study of the bacterial strains isolated from contact lens wearing subjects showed that *S. aureus* more frequently produced an array of potentially pathogenic toxins and enzymes than *S. epidermidis*⁽³⁾. These indicate *S. aureus* is more likely to cause CLPU. The aim of this experiment is to investigate whether antigens from dead cells of *S. aureus*, or its secretory products were responsible for CLPU, or whether live bacteria and corneal surface trauma were necessary to cause CLPU.

Materials & Methods

Can immunized rabbit model (*S. aureus* 031) induce CLPU?

Bacterial antigens: phenol-inactivated *S. aureus* suspension (1×10^{10} cells/ml) and *S. aureus* supernatant

Immunization of rabbits: with the phenol-inactivated *S. aureus* suspension

Contact lens wear: 2 - 4 weeks

Challenged agents: Bacterial antigens and live bacterial cells (see table 1)

Examination: slit-lamp

Does extended wear of contact lens induce CLPU?⁽⁴⁾

Duration of contact lens wear: 7 weeks

Bacterium: *S. aureus* (031)

Examination: slit-lamp

Is corneal epithelial trauma necessary for CLPU?

Agents (see table 1): live *S. aureus* (031), live *S. epidermidis* (019) and bacterial antigens (as above)

Contact lens coating: with bacterial cell suspension OD₆₆₀ 2.0.

Epithelial trauma: 1-2mm scratch at corneal periphery

Examination: slit-lamp examination, histology

Results



Figure 1. Phlyctenules at the limbal region, seen in immunized rabbits of *S.aureus*, that were fitted with contact lens coated with live *S. aureus*.

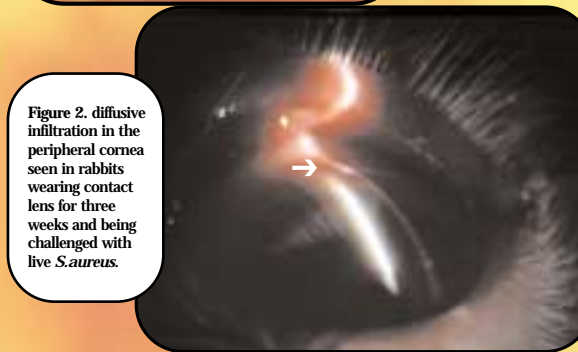


Figure 2. Diffusive infiltration in the peripheral cornea seen in rabbits wearing contact lens for three weeks and being challenged with live *S.aureus*.

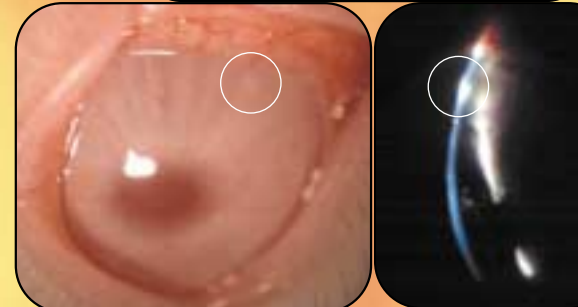


Figure 3. A rabbit CLPU, seen in rabbits fitted with live *S. aureus* coated lenses. An artificial epithelium defeat was made prior to fitting of the lens.

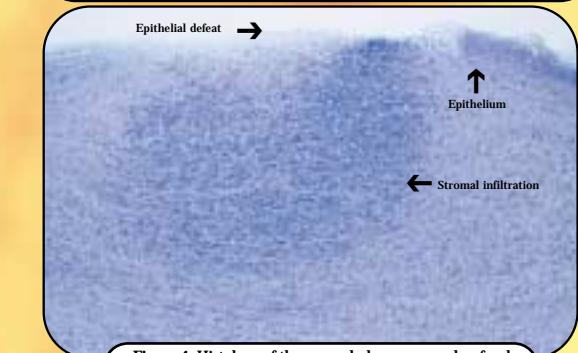


Figure 4. Histology of the corneal ulcer, appeared as focal epithelial defeat with underlying infiltration.

Results cont.

Table 1. Experimental designs and observations

Treatment of rabbits	Challenging agents	Contact lens wear	Observation on cornea
Immunization with <i>S. aureus</i>	<i>S.aureus</i> supernatant (n=6)	Yes	No lesion
	Killed <i>S.aureus</i> (n=6)	Yes	No lesion
	Live <i>S.aureus</i> (n=6)	Yes	Limbal phlyctenule
Extended wear ⁽⁴⁾	Live <i>S.aureus</i> (n=10)	Yes	Diffusive infiltration
	Live <i>S.aureus</i> (n=6)	No	No lesion
Trauma of corneal surface	Live <i>S. epidermidis</i> (n=9)	Yes	No lesion
	<i>S.aureus</i> supernatant (n=12)	Yes	No lesion
	Killed <i>S.aureus</i> (n=12)	Yes	No lesion
	Live <i>S.aureus</i> (n=35)	Yes	CLPU-like lesion

Table 2. Number of bacteria isolated

	Number of <i>S. aureus</i> colonies	Number of <i>S. epidermidis</i> colonies
Conjunctival swap	6 - 25	0 - 5
Corneal scrapings	0 - 20	N/A
Contact lens	0 - 25	2 - 8

In an immunized rabbit model of *S. aureus* (031) :

Phlyctenules were observed in the immunized rabbits challenged with live *S. aureus* cells (4/6), (see figure 1).

No obvious reactions occurred in the rabbits challenged with other *S. aureus* antigens.

No CLPU-like lesion formed.

In an extended contact lens wear model:⁽⁴⁾

Extended wear caused diffusive non-ulcerative keratitis (6/10), (see figure 2).

No CLPU-like lesion formed.

A rabbit CLPU model with corneal epithelial trauma:

18/35 rabbits challenged with live *S. aureus* showed ulceration (CLPU-like lesions) in the peripheral cornea in 24 h (see figure 3).

2/35 rabbits challenged with live *S. aureus* showed focal infiltrates in the peripheral cornea in 24 hours.

No corneal lesions were observed in rabbits challenged with live *S. epidermidis* or *S. aureus* antigen preparations.

These corneal lesions were accompanied with mild to moderate inflammatory reactions, and healed quickly upon removal of contact lens without the need of antibiotics.

Discussion

Immunization with *S. aureus* probably stimulated an autoimmune reaction as made evident by phlyctenules. Pre-sensitization with *S. aureus*, however, was not required for the formation of CLPU. Contact lens induced peripheral ulceration may be induced by the colonization of *S. aureus* on the ocular surface as well as on contact lens, but only in the presence of traumatic change in corneal surface. However, only small number of bacteria were recovered from the ulcers (table 2). The contact lens induced ulceration in this rabbit model presented with mild to moderate inflammatory reaction and healed upon discontinuation of CLW with scar formation, mimicking the CLPU in human.

Conclusions

A corneal epithelial defect and *S. aureus* are crucial factors in the formation of contact lens induced peripheral ulceration (CLPU).

References

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