Horizontal Intracorneal Swirling Water Migration Indicative of Corneal Endothelial Function

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Purpose. To test our hypothesis about whether there is water migration in the horizontal corneal plane and investigate its developmental mechanism.

Methods. A fluorescein solution was intrastromally injected into normal and edematous corneas of rabbits, and the movement of the fluorescein solution was observed and recorded over time.

Results. In normal corneas, the water flow was characterized by a swirling movement from the center to the periphery in the stroma. The fluorescein solution ultimately spread and occupied the entire cornea, indicating horizontal intracorneal swirling of water. In contrast, when the corneal endothelia were injured by intracameral injection of a preservative to create corneal edema, no water migration occurred, suggesting that the integrity of the corneal endothelial function is essential for water migration. The water migration stopped with injection of a sodium-potassium pump inhibitor, indicating that the enzyme is necessary for physiologic water migration in the cornea. With recovery of corneal endothelial function, the water migration began, and focal edema remained in the periphery with no water migration in this edematous area.

Conclusions. We report for the first time the presence of horizontal water migration in the cornea in a swirling pattern (i.e., intracorneal swirling migration of water, generated by the pump function in the corneal endothelial cells), which may supplement the conventional concept of development of corneal edema in the vertical plane. This dynamic water circulatory system may be involved in increasing the efficiency of the water transfer in the entire cornea.

Keywords: water movement in cornea, corneal hydration, intracorneal water flow

The cornea, the transparent anterior portion in the eye that is highly specialized to refract and transmit light, is comprised of an outer stratified squamous epithelium, inner connective tissue stroma, and the monocellular endothelium on the posterior side that borders the anterior chamber. The corneal tissue component is regular and precisely arranged and light passing through it is bent and transmitted to the retina.[1] The cornea is avascular, with a unique local circulatory system in which essentially all the nutritional needs except oxygen are supplied via the aqueous humor with diffusion of metabolic byproducts into the aqueous humor.[2]

The cornea must maintain its water content to remain transparent; disruption can result in corneal edema.[3] Long-standing edema with irregular fluid accumulation can reduce the corneal transparency and result in bullous keratopathy with severe visual disruption resulting from edema encompassing the entire cornea.[4,5] The basic mechanisms of corneal hydration and transparency between the aqueous humor and ocular surface have been well investigated and depend on the swelling pressure of the corneal stroma, epithelial and endothelial barrier functions, active ion transport, passive transport of water across the endothelium, and evaporation from the corneal surface.[1,2,6] Stromal imbibition pressure, as well as intraocular pressure (IOP) only in the edematous cornea, promote water accumulation in the corneal stroma. However, the transport of ions across the corneal endothelium reduce the osmotic pressure of the stroma such that the semipermeable membrane properties of the endothelium balance the forces promoting corneal edema.[4,5,6–14] The corneal endothelium is principally responsible for active dehydration of the cornea, with the transport system creating an osmotic gradient that prevents the stroma from swelling excessively and becoming cloudy.[1,7,15]

To date, these mechanisms of intracorneal water movement have been reported to occur in the corneal vertical plane, that is, across the endothelium. From our clinical observation of the process of corneal edema, we propose that there exists a pattern shift of the portion of edematous cornea in between the center and periphery of the cornea. We name this phenomenon as water movement within the horizontal plane. Gothard et al.[16] reported the pattern of corneal edema in which focal peripheral corneal edema progresses to diffuse edema years after cataract surgery. The precise water dynamics of the entire cornea in the horizontal direction between the center and periphery remain to be elucidated. We hypothesized that transverse water migration may modulate the corneal water dynamics and contribute to the developmental mechanism of corneal edema. Using fluorescein as a tracing dye, we indirectly

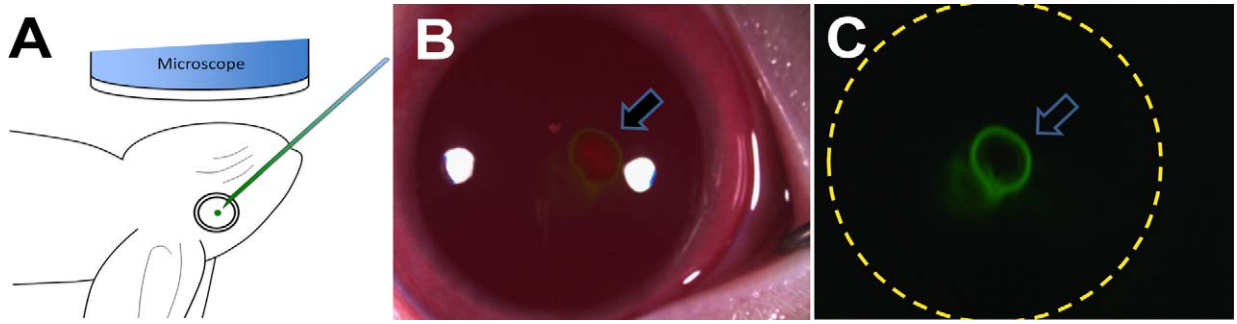

FIGURE 1. Measurement of migration of the fluorescein injected into rabbit stroma. (**A**) Schematic representation of an intracorneal injection of fluorescein solution. (**B**) A corneal photograph after stromal injection of the fluorescein. (**C**) A filtered photograph after stromal injection of stain. The *arrows* indicate the pooling of the stain.

observed for the first time the presence of intracorneal water movement from the center to the periphery in a swirling pattern in the horizontal plane, referred to as intracorneal swirling migration of water, and investigated its mechanisms in a normal cornea and an experimental model of corneal edema.

METHODS

Animals

Female Japanese albino rabbits weighing approximately 2.5 to 3.0 kg (Japan CLEA, Tokyo, Japan) were treated according to the Institutional Animal Care and Use Committee guidelines and the ARVO Statement for the Use of Laboratory Animals in Ophthalmic and Vision Research. The rabbits with clear corneas without ocular surface abnormalities were anesthetized using a 1 mL/kg intramuscular injection with an equal mixture of 500 mg of 5% ketamine (Ketalar hydrochloride; Sankyo Co., Ltd., Tokyo, Japan) and 2% xylazine (Selactar; Bayer Ltd., Tokyo, Japan) for all procedures. The rabbits were euthanized with an overdose of pentobarbital sodium.

Reagents

Ten percent fluorescein solution (Fluorescite; Alcon Japan Ltd., Tokyo, Japan), 10% benzalkonium chloride (BAC) solution; ouabain, a sodium-potassium pump inhibitor; and physiologic saline were purchased from Alcon Japan Ltd., Wako Pure Chemicals (Osaka, Japan), Sigma-Aldrich Corp. (St. Louis, MO, USA), and Otsuka Pharmaceutical (Tokyo, Japan), respectively. The 0.01% BAC solution was prepared by adding 10 μL 10% BAC solution to 10 mL physiologic saline. The ouabain solution (100 or 500 μM) and acetazolamide solution (1%) were dissolved in physiologic saline.

Intrastromal Injection of Fluorescein Solution Into Rabbit Corneas and Intracameral Injection of BAC and Ouabain Solution Into Rabbit Anterior Chambers

Sodium fluorescein is a polar molecule at physiologic pH and is reasonably soluble in the aqueous.[17] The 10% fluorescein solution (0.2 μL) was administered by intrastromal injection into the rabbit corneas using a syringe (Hamilton, Reno, NV, USA) with a 33-gauge needle (Fig. 1A). The injected fluorescein dye appeared as ring-shaped fluorescence (Figs. 1B, 1C), because no fluorescence was observed in the center of the injected area, and the stromal fluid diluted the dye and allowed fluorescence to occur. This is considered to be due to the concentration quenching of fluorescein[18,19] as a notable characteristic of fluorescein dye; a high concentration of fluorescein would have a greater reduction in fluorescent intensity compared with a low concentration of fluorescein due to self-quenching at a high concentration. In all experiments in which fluorescein was injected intrastromally, we easily distinguished fluorescein diffusion into the corneal stroma (Supplementary Fig. S1) from that in the anterior chamber by visual examination. In addition, the fluorescein diffusion in the anterior chamber from the stromal injection point was clearly rapid and had a different pattern (Supplementary Fig. S2) compared with fluorescein diffusion into corneal stroma. We eliminated the injected eyes with fluorescein diffusion in the anterior chamber from this study. Benzalkonium chloride (0.01% in physiologic saline) and ouabain (100 or 500 μM in physiologic saline) were injected intracamerally into the anterior chamber through the sclerocorneal limbus using a 30-gauge needle.

Observation of Transverse Water Migration in the Corneal Stroma

The rabbits were positioned on their side in order to observe one eye from above. To study horizontal water migration in the cornea, the movement of fluorescein solution injected into the corneal stroma was observed and recorded over time under a fluorescence stereomicroscope (SteREO Lumar V12; Carl Zeiss MicroImaging, Tokyo, Japan). At least three rabbits were tested in each experimental group. Fluorescence images of the cornea obtained after intrastromal injection of fluorescein solution were converted into binary images by setting a threshold for pixel intensity in Adobe Photoshop (Adobe Systems, Inc., San Jose, CA, USA), and the fluorescent area was measured using ImageJ software (version 1.47, http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). The fluorescent areas were expressed as a percentage of the entire corneal area. The Mann-Whitney *U* test was performed to evaluate the statistical significance of the difference between groups. A value of $P < 0.05$ was considered significant. The time-lapse images, which were captured every 10 seconds for 20 minutes with 200-ms exposures, were converted to video format using microscopy software (AxioVision; Carl Zeiss MicroImaging).

Bullous Keratopathy Model

The rabbit model for bullous keratopathy was prepared by inducing toxicity of the corneal endothelial cells as described previously.[5] Briefly, 0.01% BAC was injected into the anterior chamber, which induced total corneal edema. A few weeks later during recovery, very mild peripheral corneal edema served as the model.

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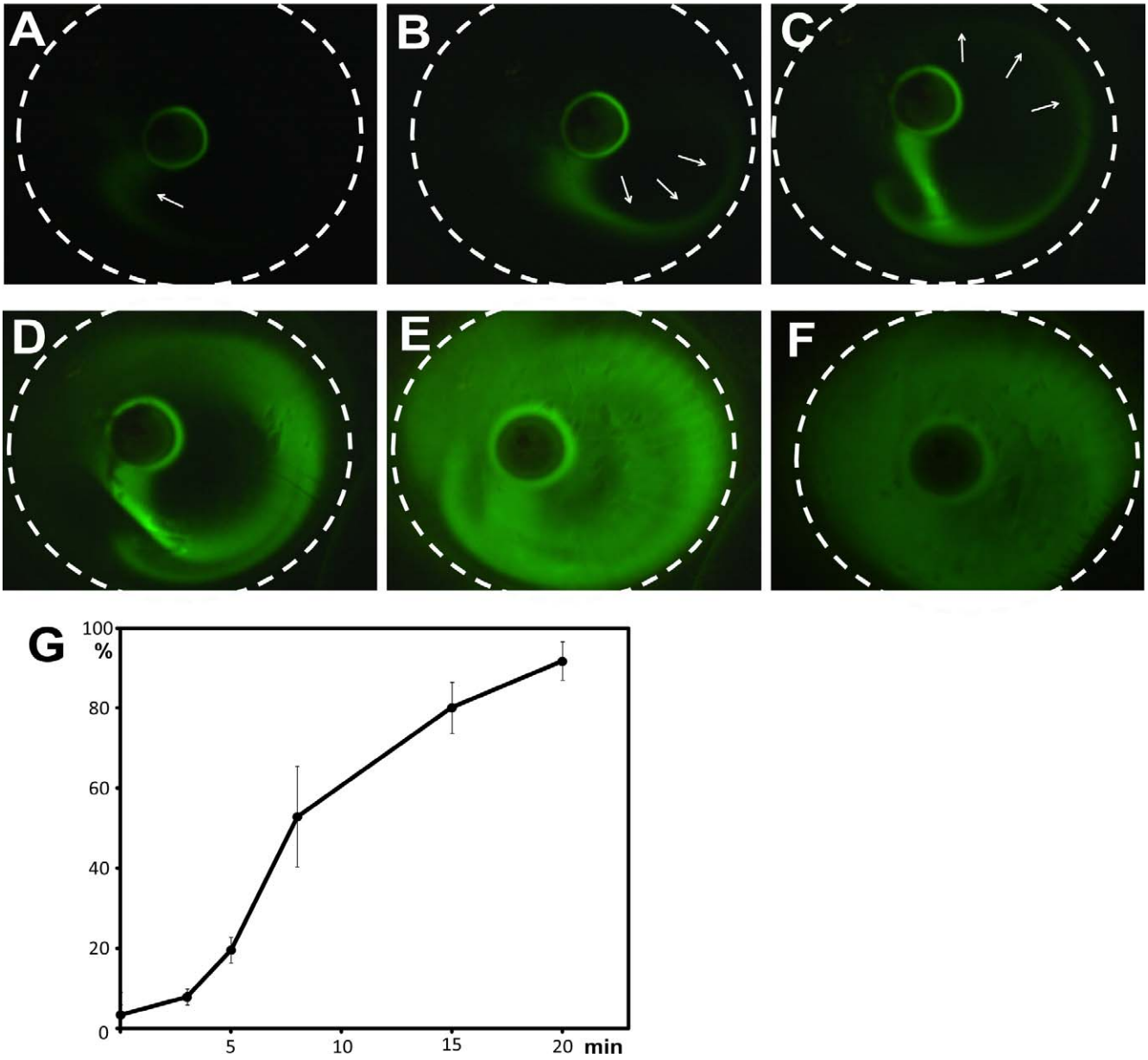

FIGURE 2. Intracorneal swirling flow of water in a normal cornea after fluorescein injection in the central area. (**A**) A photograph obtained 3 minutes after injection. The movement of the stain (*arrow*) begins in a linear fashion from the central pooling of the stain to the periphery. (**B**) A photograph obtained 4 minutes after injection. The fluorescein (*arrows*) reaches the most peripheral cornea. (**C**) A photograph obtained 5 minutes after injection. The movement (*arrows*) of the fluorescein swirling in an arc along the periphery. (**D**) A photograph obtained 8 minutes after injection. The movement of the fluorescein has expanded. (**E**) A photograph obtained 15 minutes and (**F**) 20 minutes after injection. The fluorescein covers the entire cornea. (**G**) The fluorescent area over time as a percentage of the entire cornea. The *y*-axis shows the percentages of the fluorescent area in relation to the entire cornea. The *x*-axis shows the time after injection (minutes). The movement of the water indicates the presence of horizontal water flow in the entire normal cornea, namely, the intracorneal swirling flow of water. The *error bars* indicate the standard error of the mean.

RESULTS

Corneal Water Migration in the Horizontal Plane in Normal Corneas

Using a fluorescence microscopic camera, we observed pooling of the fluorescein solution in the central cornea (Figs. 1B, 1C) after the stromal injection. The injected dye appeared as ring-shaped fluorescence due to the concentration quenching of fluorescein.[18,19] In normal corneas, the water began to flow from the point of central pooling to the corneal periphery in a linear fashion (Fig. 2A) 3 minutes after the injection. Upon reaching the peripheral cornea (Fig. 2B) 4 minutes after the injection, the water swirled in an arc along the most peripheral area (Fig. 2C) 5 minutes after the injection, and the range of the fluorescence flow (Fig. 2D) expanded 8 minutes after the injection and ultimately covered the entire cornea (Figs. 2E, 2F) 15 and 20 minutes, respectively, after the injection. These results indicated the presence of horizontal water migration in the entire normal cornea. Although we observed slow centrifugal diffusion of the fluorescein from the point of injection in all directions to the peripheral cornea, we primarily observed a rapid unidirectional spiral pattern of

fluorescein originating from the point of injection. The spiral pattern was driven by in vivo intracorneal water migration. The values of IOP measured by a tonometer (Icare Finland Oy, Vantaa, Finland) before the experiment (average ± SEM, 7.8 ± 0.5 mm Hg; $n = 5$) did not differ significantly from those measured after the experiment (8.5 ± 0.8 mm Hg). The measurements of the fluorescent area and estimations of their extent over time as a percentage of the entire corneal area were 3.4% ± 0.2%, 7.8% ± 1.1%, 19.6% ± 3.2%, 52.9% ± 12.6%, 80.1% ± 6.3%, and 91.8% ± 4.8% (average ± SEM; $n = 5$) at 0, 3, 5, 8, 15, and 20 minutes, respectively. Analysis of the expansion of the flow of water (Fig. 2G) indicated that the fluorescent-positive area gradually increased and encompassed the entire cornea throughout the time of observation. Supplementary Video S1 is a time-lapse video of the normal cornea after intrastromal injection of the fluorescein solution. The video shows the details of the dynamic appearance of the swirling flow of water.

To investigate the relation between the point at which the fluorescein solution was injected into the cornea and the patterns of the swirling water, we observed the patterns starting from the corneal periphery. After the fluorescein solution was injected into the peripheral cornea (Fig. 3A), the swirling flow of water appeared from that point in an arc (Fig. 3B), moved toward the center after one rotation (Figs. 3C–E), and gradually spread (Fig. 3F). There was no direct linear movement toward the center from the point of injection. With the injection into the peripheral cornea and that in the center, the horizontal swirling water eventually covered the entire cornea. After the initial linear flow reached the most peripheral area, the fluorescence intensity in the limbus increased, indicating partial movement of the water from the cornea to outside the cornea (i.e., the sclera).

When we injected the fluorescein into the sclera near the corneal limbus (Fig. 4A), no fluorescein signals in the cornea were recorded throughout the time course, indicating no horizontal water migration into the cornea from the periphery (Figs. 4B, 4C).

The animals were euthanized and fluorescein was injected into the corneal center 1 hour later when blood flow is interrupted and body temperature decreases. A few hours post mortem, the horizontal intracorneal swirling flow of water was still present as in a living normal eye (Figs. 5A, 5B), indicating that the swirling flow of water in the cornea does not result from blood flow in the peripheral limbus.

Corneal Endothelial Function Controls the Intracorneal Swirling Flow of Water

Over time, the linear flow of water to the peripheral cornea and the swirling flow of water to the entire cornea identified in a normal cornea were not seen in this model of bullous keratopathy (Fig. 6A). The fluorescein spread diffusely and was not immersed in the peripheral cornea. Active intracorneal swirling was not seen and only spread slowly in the bullous model (Figs. 6B–E). The values of IOP in eyes with bullous cornea before the experiment (average ± SEM, 9.2 ± 1.3 mm Hg; $n = 3$) did not differ significantly compared with those after the experiment (8.4 ± 0.5 mm Hg). The percentages of the fluorescent area in relation to the entire cornea were 7.4% ± 1.6%, 9.6% ± 2.0%, 11.3% ± 2.0%, 14.2% ± 2.0%, 18.1% ± 2.0%, and 22.1% ± 0.7% (average ± SEM; $n = 3$) at 0, 3, 5, 8, 15, and 20 minutes, respectively. Analysis of the amount of fluorescein in the bullous corneas (Fig. 6F) indicated that there were significantly ($P < 0.05$) fewer fluorescent areas in the bullous cornea compared with normal corneas. Supplementary Video S2 is a time-lapse video of a bullous cornea in which there is no intracorneal swirling migration and only diffusion. In this experiment in the bullous model, no horizontal water migration was seen, suggesting that the source of the horizontal water migration in the cornea may be associated with corneal endothelial function.

To determine which endothelial cellular function affected the horizontal water migration in the cornea, ouabain was infused to suppress the corneal endothelial pump function. The endothelial cellular pump function and the horizontal water migration were suppressed when 1000 μM of ouabain was injected into the anterior chamber. After injection, there was no active intracorneal swirling migration but only slow diffusion (Figs. 7A–D) as in the corneas with bullous keratopathy, indicating that the swirling flow of water is controlled by the corneal endothelial pump function. To investigate this in more detail, we performed an experiment using a low concentration of ouabain (100 μM) and compared the intracorneal swirling flow of water with that in a normal cornea (Figs. 7E–H). Analysis of the extent of the fluorescein showed that the percentages of the fluorescent area in relation to the entire cornea after treatment with 1000 μM of ouabain were 3.8% ± 0.5%, 7.6% ± 0.7%, 12.7% ± 0.6%, 11.4% ± 0.9%, 25.3% ± 5.6%, and 34.3% ± 8.2% (average ± SEM; $n = 4$) and after treatment with 100 μM of ouabain the percentages were 3.2% ± 0.5%, 9.6% ± 2.6%, 11.3% ± 2.4%, 23.0% ± 4.4%, 57.0% ± 10.0%, and 82.0% ± 5.4% (average ± SEM; $n = 4$) at 0, 3, 5, 8, 15, and 20 minutes, respectively (Fig. 7I). The speed with which the stain moved in eyes treated with 1000 μM of ouabain was suppressed significantly compared with normal eyes. With the lower concentration of ouabain, the area of diffusion increased significantly compared with the higher concentration. These results indicated that the driving force of the intracorneal swirling flow of water is dependent on the corneal endothelial cellular pump function.

When we then examined the relation between the intracorneal horizontal flow of water and partial peripheral corneal edema that remained during the recovery period after induction of corneal edema, the edema was confided to the upper periphery (Fig. 8A). The figure also shows horizontal water movement in a normal cornea, that is, in the area opposite to that with the peripheral edema, from the center to the periphery. Figure 8B also shows linear flow to the periphery and the swirling flow of water that gradually spread to the entire cornea over time as well as a normal pattern. However, no water flow was seen in areas with peripheral edema (Figs. 8C, 8D). Analysis of the amount of stain moving around the cornea showed that the percentages of the fluorescent area in relation to the entire cornea were 2.9% ± 0.6%, 7.7% ± 2.2%, 11.6% ± 1.8%, 22.1% ± 5.8%, 41.7% ± 11.2%, and 48.7% ± 6.9% (average ± SEM; $n = 3$) at 0, 3, 5, 8, 15, and 20 minutes, respectively; Fig. 8E). The fluorescent-positive area in the cornea with peripheral edema significantly decreased compared with that in normal cornea in the late phase of the observation (15 or 20 minutes).

Discussion

Although exacerbation and improvement of the corneal edema in the horizontal plane can be observed in clinical samples,[16] the reason for the preferential water retention in the peripheral cornea is unknown and has never been investigated. One attractive hypothesis is the presence of water migration from the center to the periphery in the horizontal corneal plane. The current experiments using fluorescein dye as a tracer showed for the first time the horizontal migration of water in normal corneas. The water movement was characterized by a swirling motion in the stroma and the fluorescein solution ultimately spread and encompassed the entire cornea.

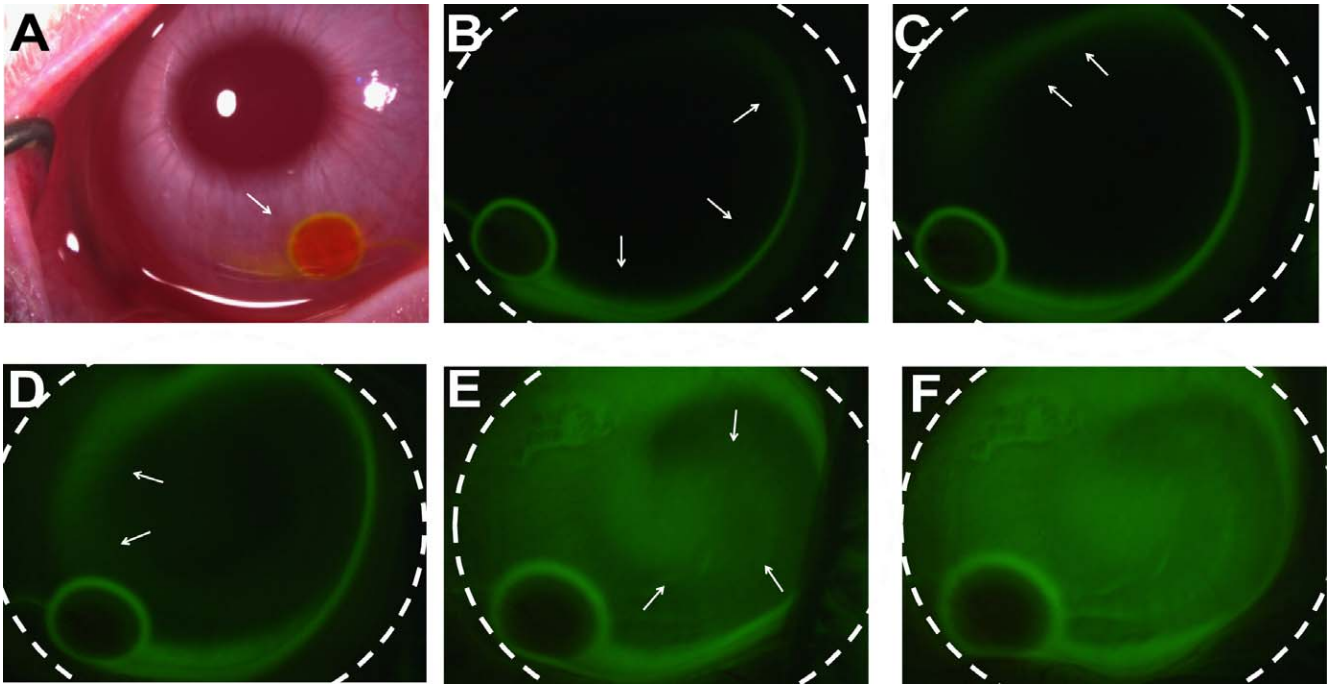

FIGURE 3. Intracorneal swirling flow of water after a fluorescein injection into the peripheral cornea. (**A**) A photograph obtained after fluorescein injection into the peripheral cornea. The *arrow* indicates the pooling point. (**B**) A photograph obtained 3 minutes and (**C**), 4 minutes after injection. The intracorneal swirling flow of water (*arrows*) begins to move from the injection point in the periphery along an arc. (**D**) A photograph obtained 5 minutes after injection. The arrows indicate the swirling flow of water. The swirling motion continues toward the center after one rotation. (**E**) A photograph obtained 8 minutes after injection. The *arrows* indicate the swirling flow of water. (**F**) A photograph obtained 15 minutes after injection. The swirling flow of water has expanded to the entire cornea.

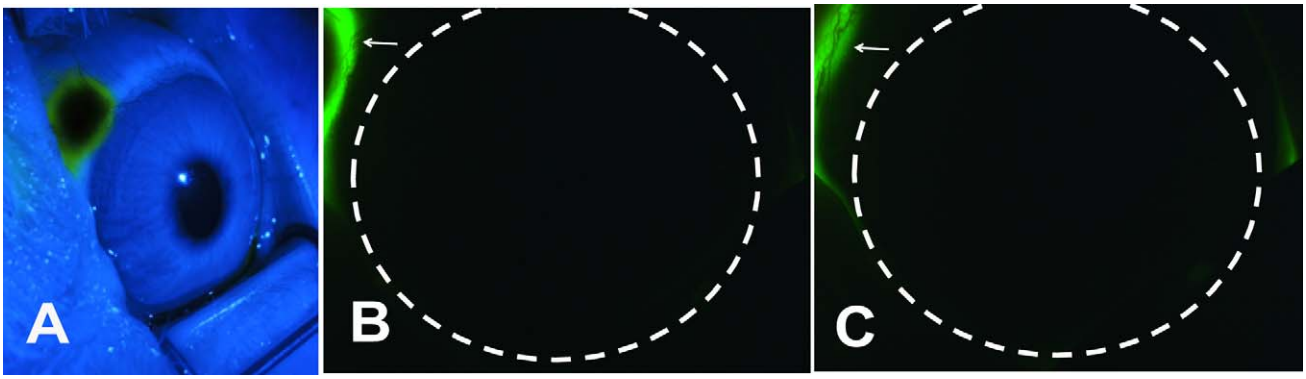

FIGURE 4. The intracorneal swirling flow of water is not induced by a fluorescein injection into the sclera near the corneal limbus. (**A**) The fluorescein solution is injected into sclera the near the corneal limbus. (**B**) A photograph obtained 5 minutes after injection and (**C**) 20 minutes after injection. No water stream from the sclera to the cornea is detected.

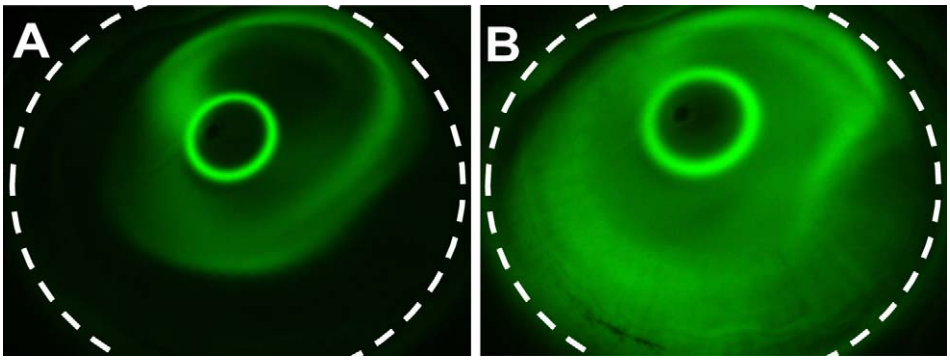

FIGURE 5. Intracorneal swirling flow of water after fluorescein injection in a postmortem cornea. The intracorneal swirling flow continues after death. (**A**) A photograph obtained 5 minutes and (**B**), 15 minutes after the injection.

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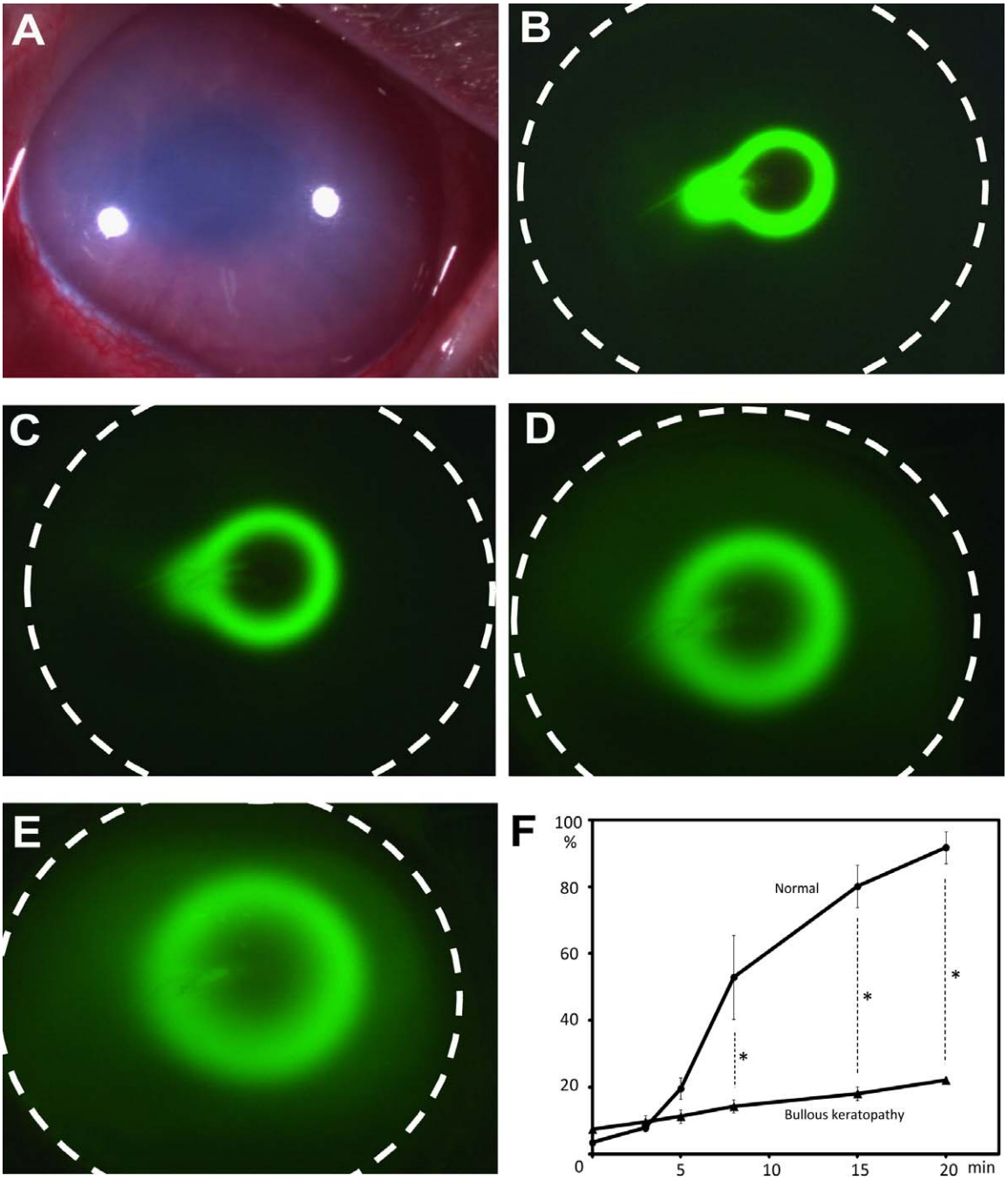

FIGURE 6. Intracorneal swirling flow of water after fluorescein injection into the cornea in the bullous keratopathy model. (**A**) A photograph obtained 7 days after the intracameral BAC injection in the bullous keratopathy model. (**B**) A photograph obtained 3 minutes, (**C**) 8 minutes, (**D**) 15 minutes, and (**E**) 20 minutes after injection. (**F**) Analysis of the fluorescent area over time as a percentage of the entire corneal area. $^*P < 0.05$. The intracorneal swirling flow of water seen in normal corneas is not seen over time. The stain only spreads diffusely and has not reached immersion in the corneal periphery. The *error bars* indicate the standard error of the mean.

In contrast, when the corneal endothelia were injured by intracameral injection of a preservative to create corneal edema, no swirling water migration was seen, suggesting that the integrity of the corneal endothelial function is essential for this water movement. The swirling migration of the water also stopped with injection of the sodium-potassium pump inhibitor, indicating the need for this enzyme for physiologic water migration in the cornea. When corneal endothelial function recovered, the swirling migration resumed while focal edema remained at the periphery, and no water migration occurred in the edematous area. These results suggested that water retention in the peripheral cornea may be related to the intracorneal swirling flow of water. The intracorneal water migration weakened with decreased corneal endothelial function and may result in partial peripheral corneal edema progressing to total corneal edema (Fig. 9).

Although we suggested that the driving force of intracorneal swirling migration of water is the endothelial cellular pump function, there are other possibilities. First may be the centrifugal force from the corneal center to the periphery.

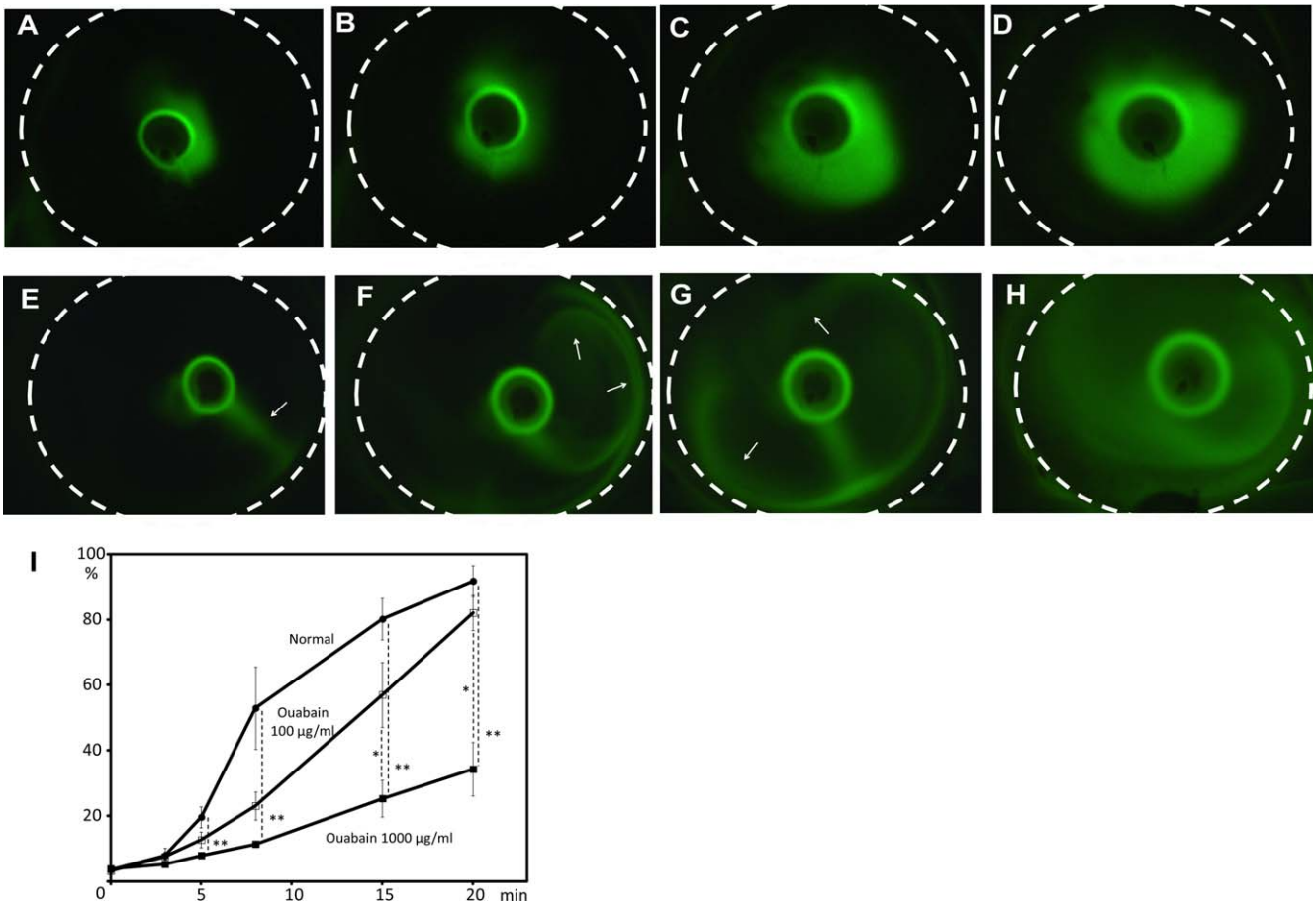

FIGURE 7. (**A–D**) Intracorneal swirling flow of water after fluorescein injection into the cornea after a 1000-µM intracameral injection of ouabain. (**A**) A photograph obtained 3 minutes, (**B**) 8 minutes, (**C**) 15 minutes, and (**D**) 20 minutes after the injection of stain. No active intracorneal swirling flow of water is seen over time. (**E–H**) The intracorneal swirling flow of water after fluorescein injection into the cornea of a 100-µM intracameral injection of ouabain. (**E**) A photograph obtained 3 minutes, (**F**) 8 minutes, (**G**) 15 minutes, and (**H**) 20 minutes after stain injection. The *arrows* indicate the flow of water. A weak intracorneal swirling flow of water is seen compared with that in normal corneas. (**I**) Analysis of the spread of the fluorescent solution. The speed of immersion of the fluorescein in eyes treated with a 1000-µM intracameral injection of ouabain is suppressed significantly compared with normal eyes. With the 100-µM concentration of ouabain, the diffusion increases significantly compared to the 1000-µM concentration. $^{*}P < 0.05$. $^{**}P < 0.01$. The *error bars* indicate the standard error of the mean.

However, when the fluorescein solution was injected into the peripheral cornea, the swirling flow of water generated from the injection in the periphery moved toward the center in an arc-shaped rotation contrary to the centrifugal force from the center to the periphery. Further investigations of the developmental mechanism of intracorneal swirling migration of water are needed. A second possibility may be the corneal structure. Water transfer from the center to the corneal periphery may occur because of structural differences between the two areas. Water absorbency varies depending on the nature of the proteoglycan and collagen fiber organization, which may affect water transfer in the cornea. The concentration of acidic glycosaminoglycans such as keratan sulfate and chondroitin is highest in the central cornea.[20] Further, the force behind the intracorneal swirling migration of water may result directly from a functional difference, such as the electrophysiologic activity between the periphery and the center. Further research is needed to clarify the difference between the center and the periphery.

Although the developmental mechanism of corneal edema and water migration in the cornea has been explained in terms of water movement in a vertical cross section of the cornea,[1,7] we showed the presence of horizontal water migration. A stain injected into the central cornea first moved linearly from the central cornea to the periphery in the flow of water. After reaching the periphery, the stain moved by circulating along the corneal edge and along the arc and diffused into the cornea as an intracorneal horizontal swirling migration of water. When the fluorescein solution was injected in the periphery, the swirling flow of water began along an arc and diffused into the entire cornea. These results may be evidence of an efficient dynamic water circulatory system that covers a large area and contributes to water retention, nutrient supply, and waste removal in the avascular corneal tissue. Transverse movement of a macro in the cornea would increase the efficiency of the metabolism of the entire cornea, which may be biologically reasonable. In this study, we indirectly observed the water migration using the fluorescein agent. However, there is no direct evidence whether the fluorescein agent can represent the natural water movement itself in the cornea. The local gradient in inhibition pressure created artificially in these experiments may not necessarily represent the natural physiologic process. This is the limitation of our investigation. Although the intracorneal swirling migration of water represents water flow in the corneal stroma, it remains to be determined which part of the corneal stroma this flow moves through. The specific composition of the corneal fibers

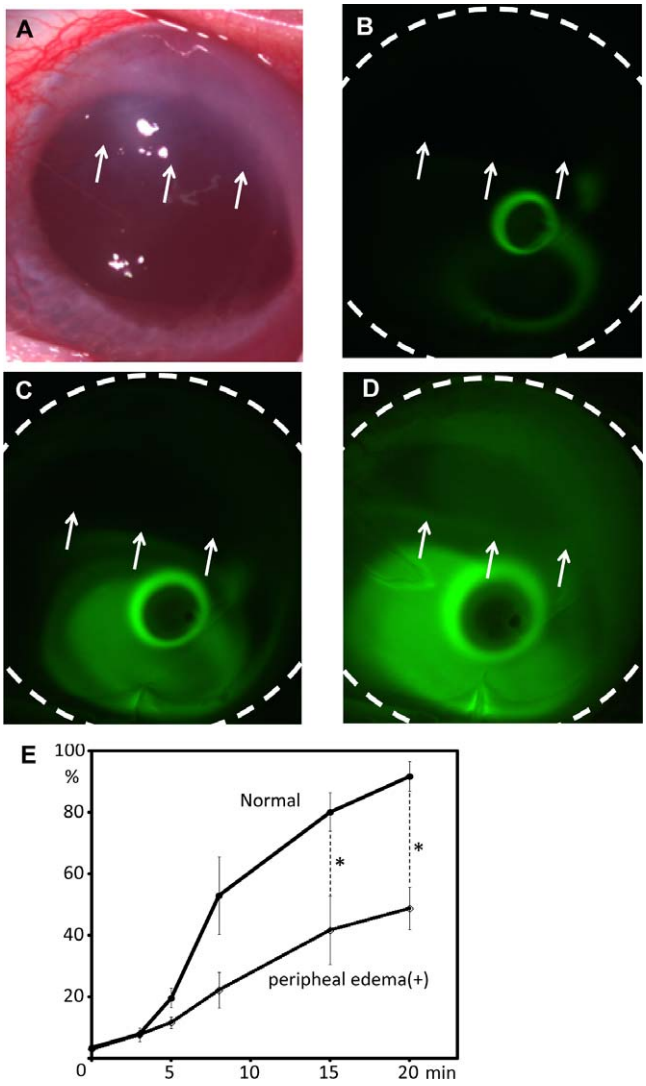

FIGURE 8. (**A**) A photograph of a cornea with peripheral edema confined to the upper area. (**B**) A photograph obtained 5 minutes, (**C**) 8 minutes, and (**D**) 20 minutes after the fluorescein injection. The *arrows* indicate peripheral edema. (**A**) Although the intracorneal swirling flow of water began and (**C**, **D**) spread gradually to the entire normal cornea on the side opposite the peripheral edema, no water flow is seen in areas with peripheral edema. (**E**) Analysis of the movement of the stain. The speed of the movement of the stain in the corneas with peripheral edema is significant compared with normal eyes 15 or 20 minutes after injection. $^*P < 0.05$. The *error bars* indicate the standard error of the mean.

coursing through the corneal stroma has been investigated.[21] Further investigations are needed to clarify these issues.

Corneal edema is one of the most representative human corneal diseases characterized by water pooling in the cornea. Since our results suggested that intracorneal swirling migration of water as a physiologic phenomenon may be related to development of corneal edema, the variations in this horizontal water migration in the early progression stage or recovery process of corneal edema remain to be elucidated. Further investigations that continuously monitor the intracorneal swirling migration of water in different degrees of corneal edema may clarify the developmental mechanism of corneal edema.

In summary, we report for the first time the presence of horizontal intracorneal swirling flow of water in the cornea.

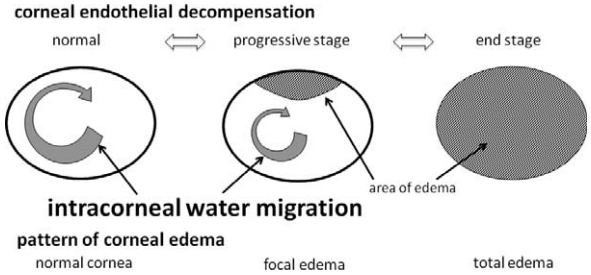

FIGURE 9. Schematic representation of the relation between the intracorneal swirling flow of water and corneal endothelial decompensation. The intracorneal water migration weakens with decreased corneal endothelial function and may result in partial peripheral corneal edema progressing to total corneal edema.

The water migration was generated by the sodium-potassium pump function in the corneal endothelial cells. This novel phenomenon may be the key to new interpretations of several pathological findings and/or treatments for corneal diseases in the future.

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