Histologic Examination of Dislocated Lenses

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Purpose: To examine histological changes resulting from dislocated and subluxated lenses.

Cases: The subjects consisted of 16 patients (aged 52–89 years) who underwent total lens extraction for lens dislocation or subluxation in the Department of Ophthalmology at Fukui Medical University during the period between April 1991 and June 1998. There were 5 patients (6 eyes) with traumatic dislocation and 11 patients (11 eyes) with idiopathic dislocation.

Result: Rupture of the cortical fibers and migration of the epithelial cells toward the posterior pole of the lens were more frequently noted in patients with traumatic dislocation than in the idiopathic group, and both findings were often simultaneously observed. Rupture of the cortical fibers was considered attributable to external pressure transmitted to the lens.

Conclusion: We speculate that the concurrent migration and dislocation of the equatorial bow architecture toward the posterior pole was caused by inhibition of differentiation of the epithelial cells to fiber cells by external pressure on the equatorial region. **Jpn J Ophthalmol 2001;45:510–515** © 2001 Japanese Ophthalmological Society

Key Words: Dislocated lens, histological examination, light microscope, trauma.

Introduction

As the etiology of lens dislocation, abnormalities in the zonule of Zinn associated with hereditary systemic diseases, such as Marfans syndrome,[1,2] which is a mesodermal abnormality, Weill-Marchesani syndrome,[1,3] and homocystinuria[1] are well known. Most case reports of lens dislocation have described the small and spherical shape of the lens, complications of pupillary block and glaucoma caused by abnormal lens positions, and developmental anomalies of the zonule and anterior chamber angle. A few researchers performed histological examination of the dislocated lens. Kubo et al[3] observed the lens from patients with Weill-Marchesani syndrome under a light microscope and reported that the bow region was hypoplastic, although no abnormalities were noted in the lens epithelial cells or lens capsule. On electron microscopic observation of the lens from a patient with homocystinuria, Sakisaka and Katsume[4] reported that filaments in the zonule exhibited developmental anomalies, and that lysosomal granules were found in the cortical fibers of the lens. Histological studies[5–7] have been performed on traumatic lens opacity. Fagerholm et al reported the process of lens opacity developing after eye injuries. There have been several reports[8–13] on lens dislocation and luxation without systemic abnormalities. However, no researchers have suggested that lens dislocation can be caused by abnormalities in the zonule. Furthermore, the dislocated lens has not been investigated histologically. In cases of traumatic lens dislocation, rupture of the lens capsule and damage in the zonule were detected under a light microscope in the past. There have been few case reports of luxated or subluxated lens dropping into the vitreous body without damage to the lens capsule. In this article, we report the histological findings from dislocated or subluxated lenses after total lens extraction.

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Materials and Methods

The subjects were 16 patients (17 eyes: mean age = 69.0 ± 11.0 years; mean disease period = 49.6 ± 46.9 days) who underwent total lens extraction in

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our department during the period between April 1991 and June 1998. Traumatic dislocation was seen in 5 patients (6 eyes: mean age = 72.8 ± 9.3 years; mean disease period = 55.5 ± 69.0 days), and idiopathic dislocation of unknown etiology was seen in 11 patients (11 eyes: mean age = 66.9 ± 11.7 years; mean disease period = 46.4 ± 33.2 days) (Table 1). In the traumatic group, the disease period represented the approximate period between trauma and lens extraction. Patients with idiopathic lens dislocation visited our hospital complaining of visual loss of unknown origin. In this group, the disease period corresponded to the approximate period between the onset of visual loss and lens extraction. Causal factors for traumatic dislocation included a facial blow due to violence, collision with flying objects, and contusion of the eyeball while falling. In the traumatic cases, the cause of trauma was as follows: Lens 1, blunt injury due to a fall after heavy drinking. Lens 2, blunt injury due to a blow from a branch. Lens 3, blunt injury due to a fall. Lens 4, blunt injury due to being struck by a flying plastic bottle. Lenses 5 and 6 (in the same patient). Blunt injury because of assault. Lens extraction was performed using a loop curet or a cryoprobe. In cases of falling into the vitreous, after vitreous fibers twining around the lens were removed by vitrectomy, the lens was pulled up to the iris surface by suction using a cutter and was then removed through a sclerocorneal incision using the loop curet.

The resected tissue was immersion-fixed in 0.1 M phosphate buffer (pH 7.4) containing 4% paraformaldehyde, dehydrated with ascending grades of ethanol according to the routine method, and embedded in methacrylate resin (Polyscience, Warrington, PA, USA). Sections 1–2-μm thick were prepared, stained with toluidine blue, and examined under a light microscope. Histological samples were also taken from the extirpated lens and photographed by light microscopy.

Results

In this study, histological examination revealed that the epithelial cells were replaced by cells with flat nuclei which were stratified, in 6/17 eyes (35.3%) (Figure 1). This finding was observed in the traumatic (33.3%) and idiopathic (36.4%) groups at almost the same rate. Deep cortical regions are usually composed of cortical fibers into which the lens epithelial cells are differentiated by repeated cell division in the equatorial growth zone. Cortical fiber cells are also usually slender curved cells extending longitudinally with nuclei that form a bow region curved in an S-shape.

Migration of the epithelial cells with oval nuclei to cortical fibers in the deep cortical regions was noted on histological images in 4/17 eyes (23.5%) (Figure 2). This was more frequently observed in the idiopathic group than in the traumatic group.

Table 1. Subjects

Lens	Age	Sex	Right/Left	Period* Until Lensectomy	Extent of Dislocation	Cause
1	56	M	R	1	Subluxation	Traumatic
2	71	M	R	90	Subluxation	Traumatic
3	72	F	R	180	Subluxation	Traumatic
4	76	F	R	2	Subluxation	Traumatic
5†	81	F	R	30	Subluxation	Traumatic
6†	81	F	L	30	Subluxation	Traumatic
7	52	M	L	30	Falling into vitreous	Idiopathic
8	56	M	L	30	Subluxation	Idiopathic
9	57	M	R	30	Subluxation	Idiopathic
10	61	M	R	60	Subluxation	Idiopathic
11	64	M	R	15	Subluxation	Idiopathic
12	61	M	R	30	Subluxation	Idiopathic
13	66	M	R	15	Falling into vitreous	Idiopathic
14	80	M	R	60	Subluxation	Idiopathic
15	80	M	R	90	Subluxation	Idiopathic
16	70	F	L	30	Subluxation	Idiopathic
17	89	F	L	120	Subluxation	Idiopathic

*Approximate period (days) until lensectomy after dislocation or subluxation of lens.
†Lens 5 and 6 are in same patient.

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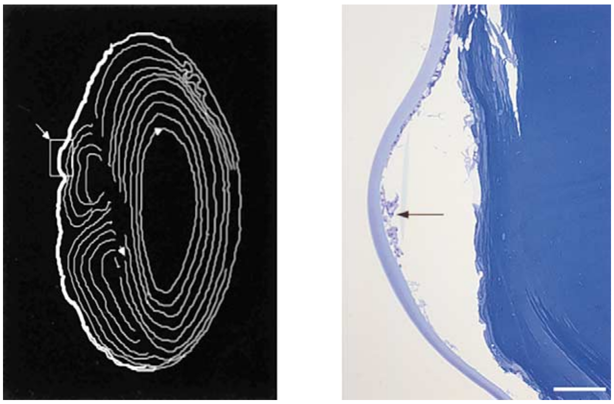

Figure 1. Histologic photograph of lens 3 (72-year-old patient, female, traumatic). Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Proliferation locally and stratification (black arrow) in monolayer of epithelial cells are observed. Space under capsule is artifact (stained with toluidine blue). Bar = 500 μm.

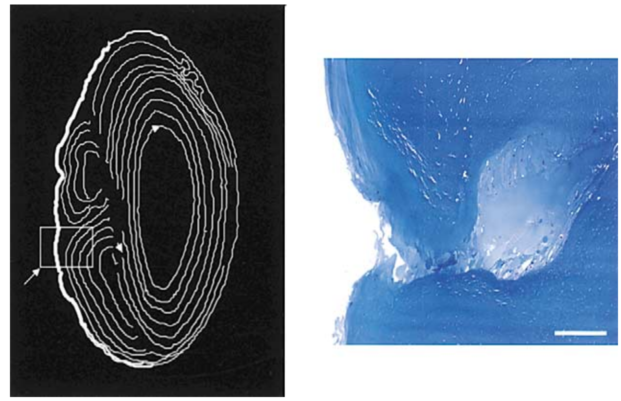

Figure 3. Same section as Figure 1. Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Anterior suture in lens cortex dehiscence. Swelling cortical fibers are seen in part of dehiscence. Part of epithelial cells appear as artifact (stained with toluidine blue). Bar = 500 μm.

As a change in the lens cortex, anterior suture dehiscence (Figure 3) was noted in 10/17 eyes (58.8%). More than half the patients in both the traumatic (50.0%) and idiopathic (63.6%) groups showed this change. Rupture of the cortical fibers (Figure 4) was observed in 5/17 eyes (29.4%), with a slightly higher incidence in the traumatic group (33.3%) than in the idiopathic group (27.3%).

As an abnormal finding in the lens capsule, interlaminar detachment (Figure 5 in the posterior capsule of the region to which the zonule of Zinn was attached was noted in 7/17 eyes (41.2%). The incidence was higher in the idiopathic group (45.5%) than in the traumatic group (33.3%).

Four of the 17 eyes (23.5%) showed migration of the equatorial bow architecture toward the posterior pole (Figure 6) and rupture of the cortical fibers. With migration of the equatorial bow architecture toward the posterior pole, a monolayer of flat epithelial cells was noted in the equatorial region. In lenses extirpated early (within 1 month) after luxation, the equatorial bow architecture was preserved without abnormalities to the lens epithelial cells. These above six histological findings are summarized in each patient (Table 2).

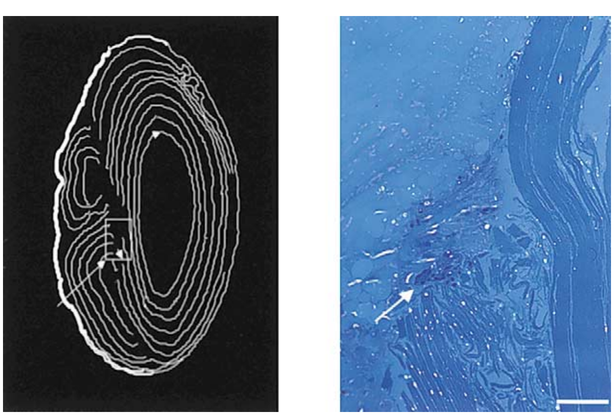

Figure 2. Same section as Figure 1. Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Epithelial cells (white arrow) are migrating in deep cortical regions through anterior suture dehiscence (stained with toluidine blue). Bar = 500 μm.

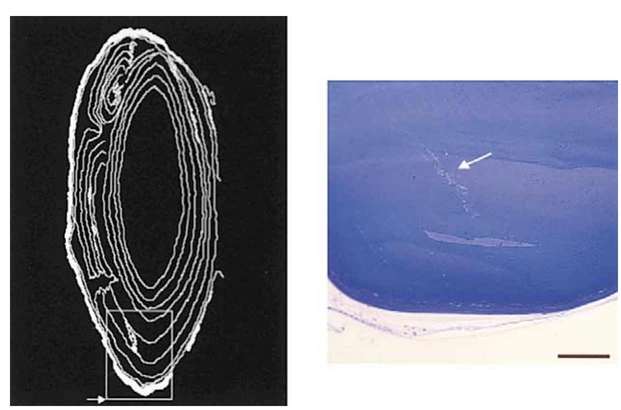

Figure 4. Histologic photograph of lens 12 (61-year-old patient, male, idiopathic). Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Lines of the cortical fibers which have irregular parts, and rupture (white arrow) of cortical fibers are observed (stained with toluidine blue). Bar = 100 μm.

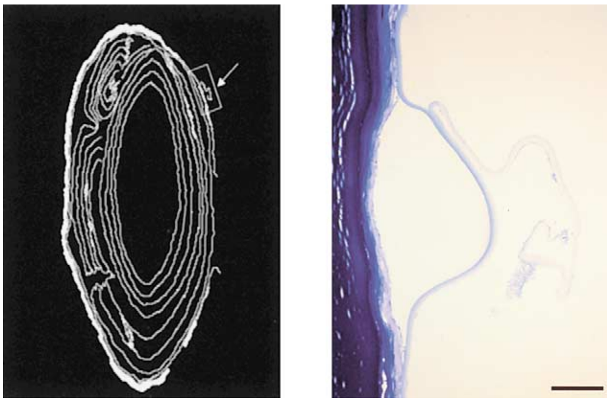

Figure 5. Same section as Figure 4. Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Bar = 500 μm. Abnormal findings in lens capsule. Interlaminar detachment in posterior capsule of region, to which the zonule of Zinn is attached, is observed (stained with toluidine blue).

Discussion

The lens, as a whole, functions like a single cell, although it consists of various cell structures including epithelium, cortical fibers, and capsule. It is well known that lens opacity occurs even when ocular metabolism is slightly disturbed by trauma, disease, and aging.[14–16] In patients with Weill-Marchesani syndrome, Kubo et al[3] reported hypoplasia of the bow region and migration of nuclei toward the posterior lamellar cortex of the lens. They speculated that decreased tension in the zonule caused an extension disorder of the lens in the equatorial direction and, therefore, uniform elongation of lens fibers was disturbed in the anterior-posterior direction.

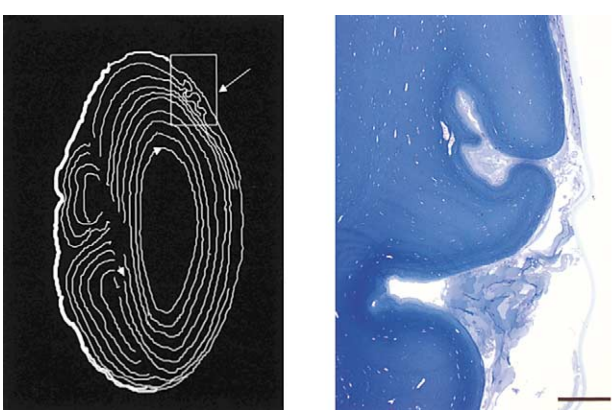

Figure 6. Same section as Figure 1] Outlines of observed lenses are shown at left, and microscopic findings in area indicated by rectangle and white arrow are shown at right. Migration of equatorial bow architecture toward posterior pole is observed, monolayer of flat and swelling epithelial cells is noted in equatorial region. Swelling of epithelial cells increases toward posterior pole (stained with toluidine blue). Bar = 500 μm.

In a study of tissue reactions, repair processes and development of lens opacity after traumatic rupture of the lens capsule, Fagerholm et al speculated that the normal functioning of epithelial cells was essential for lens transparency. They reported marked swelling of the lens fibers at the injury site in cases of traumatic cataract and the proliferation of lens epithelial cells, especially spindle cells, in cases of capsular rupture.[5,6] In cases of posterior subcapsular cataract, they reported posterior migration of epithelial cells, melting and liquefaction of lens fibers at the posterior pole, and the appearance of a granular substance. Anterior and posterior subcapsular swelling of lens fibers was also reported in cases of traumatic cataract without capsular rupture.[5,6]

Yoshida et al[17] investigated age-related changes in the histological features of lens fibers consisting of the anterior, superficial layer because the anterior cortex is hardly affected by aging or disease. The regular arrangement of lens fibers was disturbed, swollen, and broken with age. They also reported that the space between fibers increased with age. In the traumatic group, we also observed swollen fibers in the anterior suture of the lens (Figure 3) Dehiscence in the anterior suture, through which epithelial cells migrated into a deep part of the lens cortex (Figure 2), was characteristic of traumatic cataract and not found in nontraumatic cases. Although capsular rupture was not encountered, these findings suggest that considerable traumatic force was applied to the lens tissue.

Among the six histological findings (Table 3 reported in this article, although stratification of epithelial cells and migration of the equatorial bow architecture toward the posterior pole can be associated with nontraumatic cataract and aging, the remaining four findings are considered to be attributable to the loss of lens elasticity due to traumatic damage or laceration of the zonule. However, compared with the idiopathic group, laceration of the cortical fibers and migration of the equatorial bow architecture toward the posterior pole were more frequently found in the traumatic group (Table 3). In lenses resected in the early phase (within 1 month) after lens dislocation, the equatorial bow architecture was preserved, and there were no abnormal findings in the lens epithelium. Nishida reported that even though the lens was damaged by trauma, lens dislocation hardly changed with time.[10] However, we

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Table 2. Histologic Findings in 17 Eyes in This Study

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Stratification of epithelial cells			+	+					+	+				+	+		
Migration of epithelial cells			+						+	+						+	
Anterior suture dehiscence			+	+		+	+		+	+	+	+		+		+	
Rupture of cortical fibers			+	+								+			+	+	
Abnormal findings in lens capsule			+	+			+		+		+	+				+	
Migration of bow architecture toward posterior pole			+	+											+	+	

consider that external pressure due to trauma inhibits its normal cell division in lens tissue, resulting in abnormalities in the bow architecture. This seems to be the reason that migration of the bow architecture toward the posterior pole and local proliferation and migration of the lens epithelial cells were frequently observed with time, after lens dislocation, in patients other than those undergoing early lens extraction (within 1 month). In all patients showing migration of the epithelial cells toward the posterior pole, rupture of the cortical fibers was simultaneously observed, while in patients not showing migration, the incidence of concurrent rupture of the cortical fibers was as low as 7.7% (Table 4), suggesting that these two histological findings are closely correlated, in that the rupture of the cortical fibers was attributable to external pressure transmitted to the lens, and that concurrent migration of the epithelial cells toward the posterior pole was caused by inhibition of differentiation of the epithelial cells to fiber cells by external pressure on the equatorial region.

All findings other than migration of the bow architecture toward the posterior pole and rupture of the cortical fibers were more frequently noted in the idiopathic group than in the traumatic group, and the incidences were similar to those in patients overall (Table 3). Age-related changes in the lens include, in addition to enlargement and coloration of the lens nucleus, loss of epithelial cells, their dislocation toward the posterior pole of the lens, and disappearance of mitosis in these cells. In the cortical fibers, swelling of the fiber cells, disordered arrangement, rupture, and narrowing of the bow architecture, and in the lens cortex, hypertrophy, disappearance of the layered structure, and protrusion toward the epithelial cells are noted.[14–16,18,19] Even in normal lenses, migration is often observed when cataract develops, and fiber collapse is present.[18] Stratification of epithelial cells and migration of the bow architecture toward the posterior pole can be caused not only by trauma but also by aging. These findings suggest that age-related changes are factors in tissue change, thereby resulting in the high incidence of tissue changes in the idiopathic group (mean age = 66.9 years).

The findings in this study suggest that rupture of the cortical fibers was attributable to external pressure transmitted to the lens, and that concurrent migration of the epithelial cells toward the posterior pole was also induced by inhibition of differentiation of the epithelial cells to fiber cells by external pressure on the equatorial region. The orderly tissue ar-

Table 3. Frequency of Histologic Findings in Dislocated Lenses

	% Traumatic (n = 6)	% Idiopathic (n = 11)	Average % (n = 17)
Stratification of epithelial cells	33.3	36.4	35.3
Migration of epithelial cells	16.7	27.3	23.5
Anterior suture dehiscence	50.0	63.6	58.8
Rupture of cortical fibers	33.3	27.3	29.4
Abnormal findings in lens capsule	33.3	45.5	41.2
Migration of bow architecture toward posterior pole	33.3	18.2	23.5

Table 4. Frequency of Histologic Findings in Dislocated Lenses

	% Migration of Bow Architecture Toward Posterior Pole (+) (n = 4)	% Migration of Bow Architecture Toward Posterior Pole (−) (n = 13)
Stratification of epithelial cells	75.0	23.1
Migration of epithelial cells	50.0	15.4
Anterior suture dehiscence	75.0	53.8
Rupture of cortical fibers	100.0	7.7
Abnormal findings in lens capsule	75.0	30.8

chitecture of lens tissue appears to be elaborately regulated by traction from the zonule of Zinn and by its physical relationship to the surrounding tissue.

It has recently been reported that lens epithelial cells and fiber cells produce cytokines, humoral molecules that participate in the proliferation of epithelial cells and signal transmission for pseudometaplastic collagen production.[20] McAvoy and Chamberlain[21] studied fibroblast growth factor (FGF) in lens epithelial cells, and suggested that the FGF concentration in the ocular media is involved in controlling and maintaining lens polarity and lens growth patterns. It is necessary to investigate what kind of cytokines are produced by external force on the lens, how cytokines are related to various lens functions and tissue changes, and how cytokines participate in the healing process of the lens after trauma.

References

1. Kubota Y. Systemic diseases and eyes. In: Masuda K, ed. Current encyclopedia of ophthalmology, 4th-B ed. Tokyo: Nakayama-Shoten, 1994:177–8.
2. Meire FM, Van Egmond J, Hassens M. Congenital Marfan syndrome with contractures. A clinicopathological report. Bull Soc Belge Ophthalmol 1992;245:91–7.
3. Kubo E, Hirai R, Fujii C, Mori K, Akagi Y, Ishiguro H. A case of Marchesani syndrome. Nihon Ganka Kiyo (Folia Ophthalmol Jpn) 1994;45:337–40.
4. Sakisaka H, Katsume Y. Electron microscopic examination in the lens of homocystinuria. Ganka Rinsho Iho (Jpn Rev Clin Ophthalmol) 1980;74:483–91.
5. Fagerholm PP. The response of the lens to trauma. Trans Ophthalmol Soc UK 1982;102(Pt 3):369–74.
6. Fagerholm PP, Philipson BT. Human traumatic cataract. Acta Ophthalmol 1979;57:20–32.
7. Jonse WL. Traumatic injury to the lens. Optom Clin 1991;1:125–42.
8. Morimoto N, Oshima K, Date S, Matsuo N, Sakaguchi N. Lens dislocation into anterior chamber in two siblings. Nihon Ganka Kiyo (Folia Ophthalmol Jpn) 1989;40:2631–7.
9. Nishi O, Nishi K, Yamada Y. Explantation of endocapsular posterior chamber lens after spontaneous posterior dislocation. J Cataract Refract Surg 1996;22:272–5.
10. Nishida S. Anatomy of ectopic lens. In: Honda Y, ed. Practical ophthalmology, 6th ed. Tokyo: Bunkodo, 1995:100–3.
11. Seland JH. The lenticular attachment of the zonular apparatus in congenital simple ectopia lentis. Acta Ophthalmol. 1973;51:520–8.
12. Shawaf S, Noureddin B, Khouri A, Traboulis EI. A family with a syndrome of ectopia lentis, spontaneous filtering blebs, and craniofacial dysmorphism. Ophthalmic Genet. 1995;16:163–9.
13. Yatsuka Y, Yatsuka H, Imaizumi M, Seguchi Y, Nakatsuka K. Two cases of bilateral lentis without systemic disorders. Rinsho Ganka (Jpn J Clin Ophthalmol) 1998;52:891–4.
14. Kuwabara T, Imaizumi M. Denucleation process of the lens. Invest Ophthalmol Vis Sci 1974;13:913–81.
15. Takehana M. The age changes of the lens. In: Honda Y, ed. Practical ophthalmology, 22nd ed. Tokyo: Bunkodo, 1995:194–7.
16. Uga S. The lens. In: Masuda K, ed. Current encyclopedia of ophthalmology, 2nd-B ed. Tokyo: Nakayama-Shoten, 1993:3–13.
17. Yoshida S, Shoji E, Obara Y. In vivo biomicroscopy of the human lens fiber. Atarashii Ganka (J Eye) 1991;8:77–80.
18. Kuwabara T. The maturation of the lens cell: a morphologic study. Exp Eye Res 1975;20:427–43.
19. Yajima Y, Mizukawa A, Okisaka S. Structure of the lens. Atarashii Ganka (J Eye) 1984;1:3–17.
20. Nishi O, Nishi K, Fujiwara T, Shirasawa E, Ohmoto Y. Effects of the cytokines on the proliferation of and collagen synthesis by human cataract lens epithelial cells. Br J Ophthalmol 1996;80:63–8.
21. McAvoy JW, Chamberlain CG. Fibroblast growth factor induces different responses in epithelial cells depending on its concentration. Development 1989;107:221–8.