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Clinical and Experimental Observation of Glistening in Acrylic Intraocular Lenses

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Purpose: To determine whether or not glistening particles in implanted acrylic intraocular lenses (IOL) increase with the passage of time.

Methods: Prospective clinical study: Glistenings were evaluated in 31 patients (49 eyes) with implanted acrylic IOL, the emphasis being on when glistening first became evident and subsequent changes in the number of glistening particles. Experiment: IOLs were monitored for any changes that occurred with the passage of time as they were immersed first in a 50°C saline solution and then in another saline solution with a temperature of 35°C.

Results: Prospective clinical study: Glistening phenomenon was observed in 28 IOLs (57%) 2 to 16 months after implantation (mean = 6.6 months). Glistenings reached their peak in number within a few months of formation in all cases, showing no further increase thereafter. Experiment: Glistening particles first appeared on the 10th day of the experiment in sizes ranging from 3 to 10 μm in diameter. They remained at the same level for the next 60 days without showing any increase.

Conclusions: Glistening formation in acrylic IOLs was found to stabilize within a few months after appearance. The method of our experiment proved reliable in producing, in a relatively short period of time, glistening similar to that found in patients. **Jpn J Ophthalmol 2001;45:564–569**

Key Words: Acrylic intraocular lens, glistening, glistening particles, glistening development experiment, intraocular lens.

Introduction

Foldable intraocular lenses (IOLs) are increasingly favored in today's cataract surgery, where the small-incision, sutureless technique has become the dominant procedure. Among such IOLs, those made of acrylic material are preferred because of the reduced incidence of postoperative inflammation and posterior capsule opacification associated with their use. They are also valued on the basis of their similarity in material to polymethylmethacrylate, with its proven stability in human eyes.[1] It has been pointed out, however, that there is a phenomenon of microvacuoles, termed glistenings, which develop in implanted lenses. This occurrence, reported by Malley (AcrySof® 'glistenings' and questions of haze, *Ophthalmology Times*, May 1–7, 1995) and Dhaliwal et al,[2] as leading to reduced clarity of the affected lens, has been receiving growing attention because of its possible impact on visual function. We assessed the nature of this phenomenon through a prospective study and an experiment on implanted acrylic IOLs. The study was carried out with the objective of determining when glistening formation began and how it progressed with time, while in the experiment, we immersed acrylic lenses in heated baths to see how such microvacuoles develop and changed over time.

Materials and Methods

Prospective Clinical Study

We examined 31 patients (49 eyes), all chosen with their consent, who had undergone cataract re-

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moval by phacoemulsification and aspiration and had acrylic lenses inserted at the Miyata Eye Clinic between September 1997 and December 1998 without developing any complications. The sample comprised 11 men and 20 women aged 58 to 88 years (mean = 72 years). The acrylic lenses involved were either AcrySof® MA60BM or MA30BA produced by Alcon Laboratory, Fort Worth, TX, USA.

The pupils were dilated to 5 mm or more in diameter using the Mydrin P® mydriatic eyedrops (Santen, Osaka). We evaluated the IOLs by slit-lamp to determine when glistenings were formed and how they grew with the passage of time. Examinations were carried out every month for the first 6-month period and every 2 months thereafter. The degree of glistening formation was graded on the basis of the number of glistening particles on a scale of 0 to 3 (Figure 1), as in our earlier experiment.[3]

Glistening Development Experiment

The lenses used were Alcon's AcrySof® MA60BM (+20.OD) (n = 3 with varying lot numbers) in the Wagon Wheel Packaging system. We glued them by the haptics to a thin plastic sheet (hereafter called the "observation board"), which had holes cut out along the middle to allow space between the optics of the attached lenses and the sheet material. The observation board, thus prepared, was placed vertically in a clear screw-top bottle filled with 50 mL of saline solution with its temperature maintained at 50°C. The bottle in turn was placed in an incubator (Mini-Incubator, UI-50, Iuchi Seieido, Osaka). The temperature of the incubator was also set at 50°C. The board was left in the solution for 2 hours. Then it was removed and immediately immersed in a 35°C saline solution, also 50 cc in volume, and contained in a screw-cap bottle, which was placed inside another incubator maintaining the same temperature. Evaluation of the lenses was made from outside the bottle by slit-lamp microscope. The interval between the observation sessions was 30 minutes during the first part of the experiment involving the 50°C saline solution. It was the same for the first 3 hours of the next part using the 35°C solution, but was extended thereafter to 1 hour until the 12th hour, then 6 hours until the 24th hour, 1 day until the 10th day, and 10 days until the 60th day.

Results

Prospective Clinical Study

The evaluation period for each specimen varied from 5 to 20 months (mean = 13.1 months). In all, glistenings of Grade 1 or above were found in 28 of the 49 eyes (57%) examined. Assuming that we detected the glistenings as they formed (Figure 2), our findings indicate that glistening formation began at varying points after the first postoperative month, never earlier, with the latest reported in the 16th month after surgery.

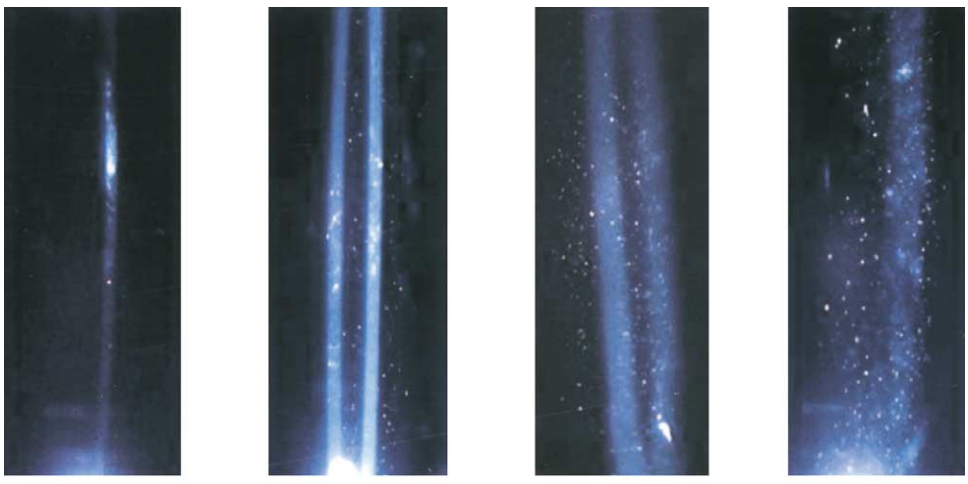

Figure 1. Grading of glistening in acrylic lenses.

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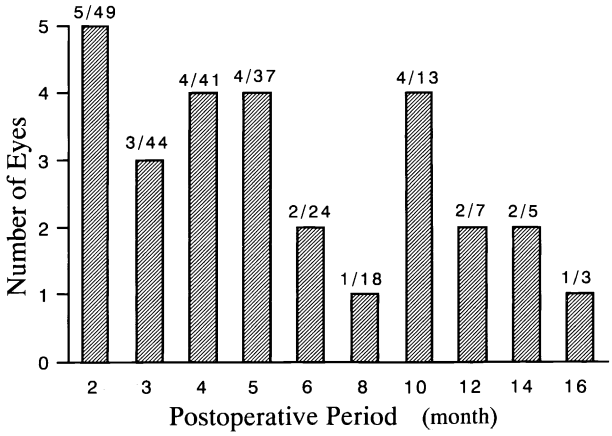

Figure 2. Timing of glistening formation. Horizontal axis represents length of time elapsed since surgery (months) while vertical axis indicates number of eyes in which glistening formation was detected. Fraction above each bar representing a time span is: number of eyes in which glistening formation was detected/number of eyes being evaluated, with the latter excluding eyes that had already developed glistenings. Glistenings did not form during first postoperative month, but started to form at varying points thereafter, the latest in the 16th month after surgery.

In the 28 eyes that developed glistenings, the average period between the operation and the appearance of glistening particles was 6.6 months. Of those eyes, 13 belonging to 9 patients were available for evaluation for periods of 6 months or longer. Monitoring them for changes in the degree of glistening (Figure 3), we found that the formation of Grade 1 glistenings tended to peak after 1 month, whereas

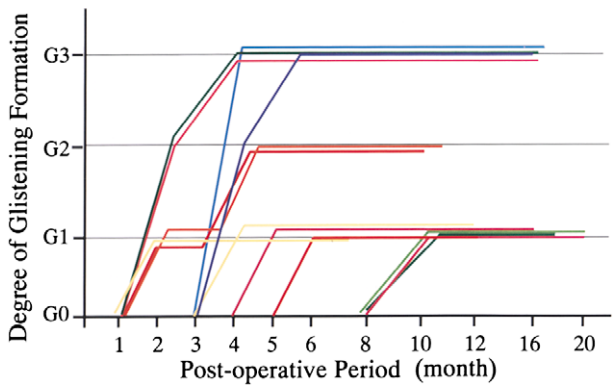

Figure 3. Changes in glistening formation over time. This chart covers the 13 eyes that were studied for 6 months or more after formation of glistenings had been detected. Each line represents one eye. In all lenses studied, the number of glistenings stopped increasing after a few months. G0–G3 indicates grade of glistening.

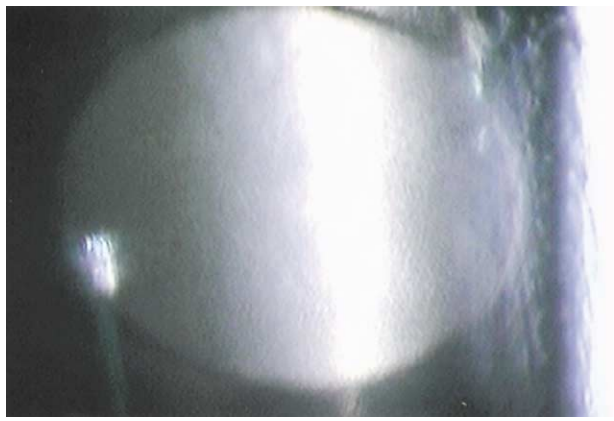

Figure 4. Lens in 50°C saline solution. Optic remains clear with no detectable change.

Grades 2 and 3 glistenings were likely to continue increasing in number for a few months before stabilizing. No further glistening formation was noted after these stabilizing points in any of the IOLs.

Glistening Development Experiment

Immersion in a 50°C saline solution alone did not cause any change to the IOLs (Figure 4) Once transferred to a 35°C solution, however, they immediately developed opacities (Figure 5). Left in this condition for about 30 minutes, the optics of lenses gradually began to recover clarity from the periphery and developed a round transparent region spreading from the center. In the core of this round region were large glistening particles (Figure 6). Several hours later, there was no trace of opacity left in the lenses while the glistenings remained (Figure 7). However, these microvacuoles began to fade in time, com-

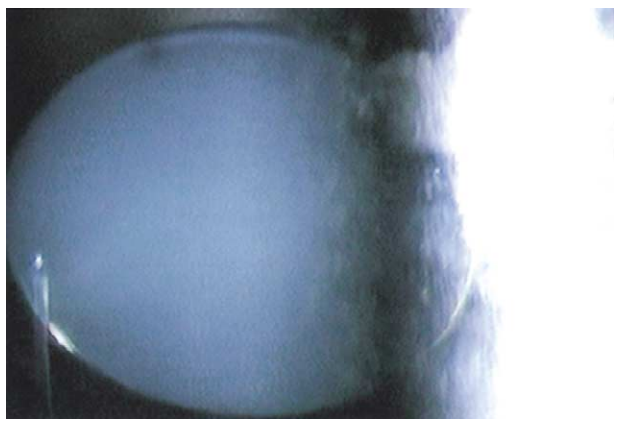

Figure 5. Lens immediately after immersion in 35°C solution. Optic clouded upon hydration in solution.

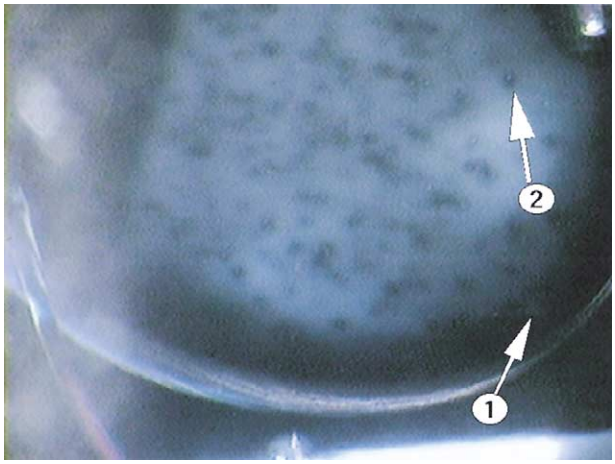

Figure 6. Lens after 90 minutes of immersion in 35°C solution. Opacity begins to dissipate from periphery (arrow 1). In center of optic round transparent region containing large glistening particles (arrow 2) remains.

pletely dissipating by the third day (Figure 8). No further change was observed after this development.

In order to gain a clearer view of a lens for detailed analysis, on the 10th day we removed one of the specimens from the solution, which was interfering with the view, and inspected the specimen by slit-lamp. In doing so, we were careful to keep the lens at a constant temperature by adjusting the room temperature to 35°C. We used purified water of the same temperature to rinse any saline residues off the lens surface to prevent crystallization. The slit-lamp examination, thus conducted, revealed tiny glistenings in the lens optic (Figure 9 identical to those clinically observed. We returned the lens to the 35°C saline solution in the screw-top bottle to resume evaluation from the outside, again using a slit-lamp microscope. The 60-day observation period ended with no further change to this specimen. When lifted out of the bath again and inspected by slit-lamp on the 60th day, however, the lens was found to have retained glistening particles similar to those observed on the 10th day. Using an optical microscope, we identified them as microvacuoles measuring 3 to 10 μm (Figure 10). They dissipated in 30 to 60 minutes when the lens was left drying in the room at 35°C or below. The same procedure was performed on three samples with good reproducibility.

Figure 8. Lens after 3 days of immersion in 35°C solution. Large glistenings have disappeared. Optic appears completely clear.

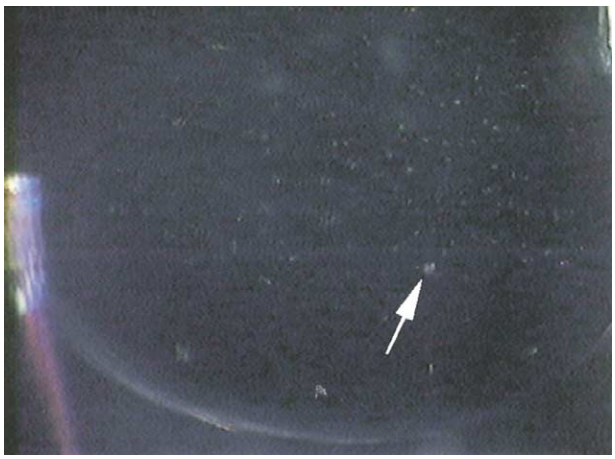

Figure 7. Lens after 3 hours of immersion in 35°C solution. Opacity has dissipated but some large glistenings (arrow) remain.

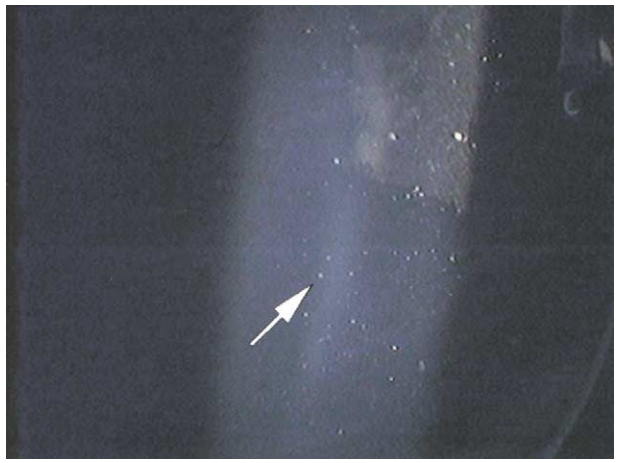

Figure 9. Lens after 10 days of immersion in 35°C solution, seen through slit-lamp microscope. Tiny glistenings (arrow) identical to those observed in clinical situations can be seen.

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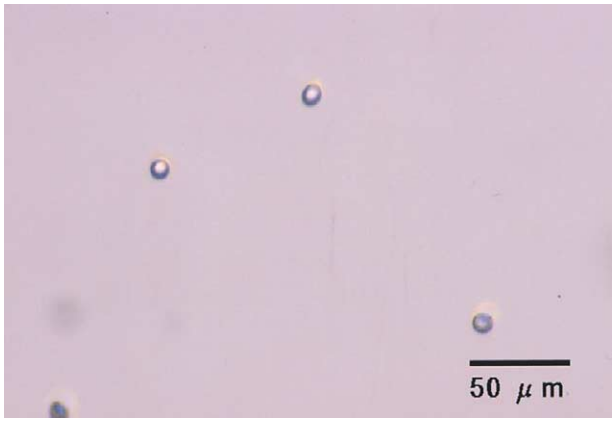

Figure 10. Lens after 60 days of immersion in 35°C solution, seen through optical microscope. Microvacuoles measuring 2 to 10 μm in diameter are found in optic. They dissipated as lens dried.

Discussion

Foldable IOLs with their ease of insertion are preferred in today's cataract surgery, which is increasingly marked by the small-incision, sutureless technique. Those of acrylic material are especially popular for their promise of minimum postoperative inflammation and the low risk of posterior capsule opacification associated with their use.[1] However, the problem of microvacuoles forming in implanted acrylic IOLs has attracted attention with concerns about the possible impact on visual function. Fortunately, we have encountered no incident as yet in our daily practice confirming such a threat. There has been, in fact, no evidence so far questioning our earlier finding that there was no significant disparity between the two groups of glistenings—Grade 0 and Grades 2 and 3—in their effect on contrast sensitivity (without glare).[3] It should be noted, however, that there have been later reports, presented by Mitooka et al[4] and Minami et al[5] among others, on cases of severe glistening formation resulting in decreased contrast sensitivity at high spatial frequencies as demonstrated in glare testing. These findings point to the possibility that a high density of glistenings can cause intraocular light scatter, which in turn results in glare disability. This theory suggests that if glistening particles kept increasing as time progressed after surgery, insertion of an IOL would inevitably affect visual function in the end. What is reassuring in this regard is that in our clinical research, glistening formation has been found to stabilize within a few months with no further increase thereafter. It is worth noting, however, that given the limited amount of time spent on our prospective clinical study, where the longest observation period lasted 20 months, or 14 months after the formation of glistenings, the need for further research is quite evident.

We also tried to determine the long-term stability of glistenings in simulated conditions, by immersing IOLs in constant-temperature saline solution and monitoring for changes. In the preliminary stage of the experiment, intended to produce glistenings, we kept acrylic IOLs in a 35°C saline solution for a period of 6 months (n = 3). However, this procedure proved unreliable as a method for replicating the phenomenon with the glistening particles forming in only one of the three samples. Dogru et al[6] reported that glistenings did not occur during a 6-month immersion test. Similarly, the experiment conducted by Omar et al[7] involving a 14-day immersion test, found that glistenings appeared only following a change in temperature, not while the lenses, Wagon Wheel-packaged IOLs marketed in Japan, were kept in a solution at a constant temperature. What these results seem to indicate is that it would take very long for glistening formation to begin in a lens in a constant-temperature fluid environment. We decided therefore to accelerate the process by causing a change in temperature, as in our earlier experiment.[3] Whereas the change in the previous experiment had been from 37°C to 25°C, with the final temperature of 25°C chosen to match that of the room where the conclusive examination of the lens was to be conducted, we set the final temperature at 35°C this time to simulate the condition of long-term immersion in aqueous humor. The microvacuoles produced this time exceeded in size those from our previous experiment, which measured 20 μm on average. A possible explanation for this difference is the greater drop in temperature: 15°C this time compared with 12°C in the earlier attempt.

The glistening particles produced in this experiment, which appeared to be microvacuoles of the same type as those observed in the last experiment, gradually shrank in size while the lens was left soaking in a 35°C saline solution, finally stabilizing at 3 to 10 μm in diameter, the same range in size as that of clinically developed glistenings. Having diminished to this size, they remained the same for the next 60 days. Our explanation for this process is as follows: the drop in temperature from 50°C to 35°C caused water to rush into voids (tiny cavities) in the lens material, temporarily filling them, and then to gradually seep out, leaving the voids to stabilize in a certain size range, as glistening particles. In other words, at 35°C, voids in an IOL seem to reach stability in the

form of water vacuoles measuring 3 to 10 μm in diameter. Accordingly, glistenings in clinical situations are likely to stabilize at a certain point instead of growing indefinitely in size.

Although glistenings in acrylic lenses may not affect visual function when present in small numbers, it is obviously preferable to have none at all. With manufacturers expected to introduce more and more new soft materials—not only acrylic but other types as well—for use in IOLs, it is critical that effective methods of testing newly developed products be established to assess the possibility of developing glistenings. One way of simulating the intraocular environment is to keep the lens immersed continuously in a saline solution with the temperature maintained at around 35°C. The problem with this method is that one would need to wait indefinitely for the formation of glistenings to begin. The formation process can be hastened through a change in temperature. Although there is no way that glistenings will ever develop where there is no void in the lens material, voids when present will certainly be filled with water as the temperature changes. It is not certain, however, that the glistenings produced in this manner are of the same kind as those observed in patients. Our previous experiment yielded an unusually large number of glistening particles following a drop in temperature. This result may hint at the existence of voids that do not turn into glistenings in clinical situations. These considerations add to the importance of replicating as closely as possible clinically induced glistenings (microvacuoles measuring 10 μm or less in diameter) in establishing the reliability of such a procedure. That said, we consider the method of our experiment as described above to be, despite its reliance on temperature control, highly effective in replicating clinically developed glistenings in a short period of time. Useful also in identifying the presence of voids in lens material, this method should serve as an effective way of testing new materials for the possibility of developing glistenings. We intend to use it on new soft materials to be introduced.

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Figure 1 is reproduced here with the permission of Igaku Shoin, the publisher of *Rinsho Ganka*, see Miyata et al.[3]

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