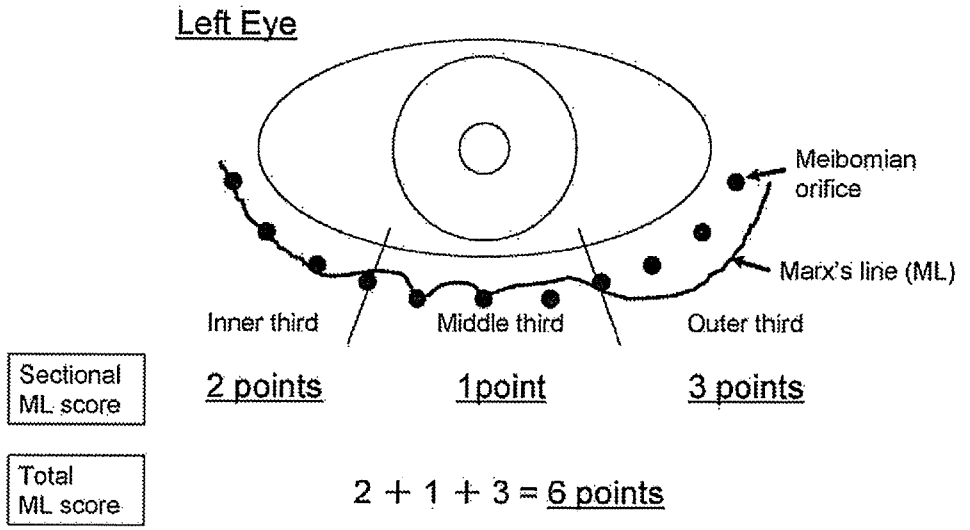


FIGURE 2. Calculation of the total ML score based on the regional scores: if the scores of the inner, middle, and outer thirds of the left eye are 1, 2, and 3, respectively, the total ML score is the sum of 1, 2, and 3, or 6 in this example.

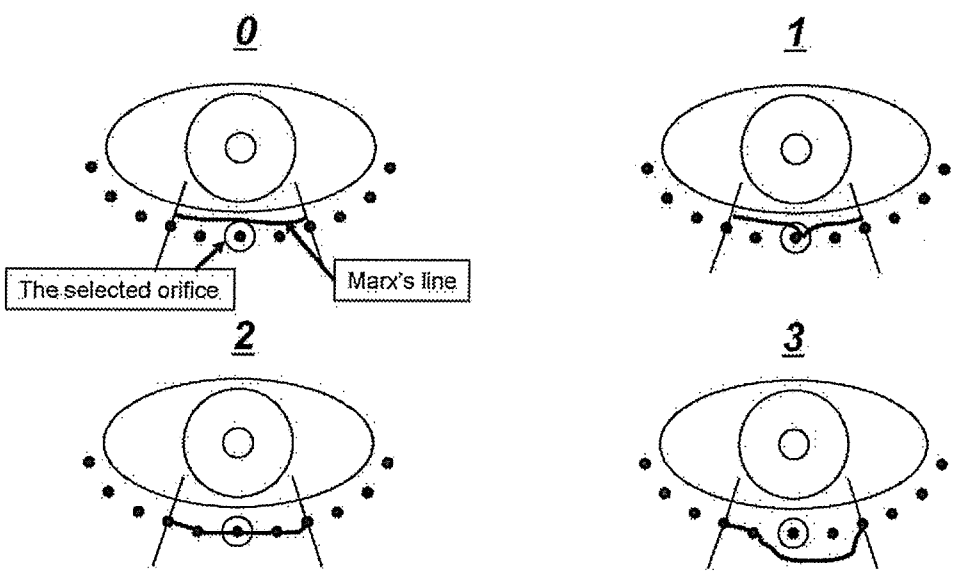


FIGURE 3. One MO was randomly selected in the center of the middle third of the lower eyelid and was scored by the ML scoring method.

Meibography, a morphologic examination of the meibomian glands that uses transillumination by a vitrectomy light probe,[4–6] was performed on one randomly selected eye of a panel of 116 subjects (51 men and 65 women, ages 56.7 ± 17.0 years). Clinical score was obtained at the outer, middle, and inner thirds of the lower eyelid according to the grading reported previously[5]: 0, no glandular loss; 1, glandular loss in less than half of each section; and 2, glandular loss in more than half of each section. Although the observation at the middle section of the lower eyelid is generally enough for screening, each of the three sections of the lower eyelid was examined as mentioned above for a more comprehensive evaluation. Then a correlation between the regional ML scores and the regional meibography scores was evaluated.

The secretion of the meibomian glands was examined in one randomly selected eye of a panel of 126 subjects (60 men and 66 women, ages 44.3 ± 20.2 years [mean ± SD]). One MO at approximately the center of the middle third of the lower eyelid was selected and its middle third ML scored, because digital pressure could be firmly and easily applied here (Figure 3). After compressing the selected meibomian gland, the color and viscosity of the secretions were scored as follows: 0, clear secretions with normal viscosity; 1, slightly yellowish with normal viscosity; 2, yellowish-white and opaque secretion with increased vis-

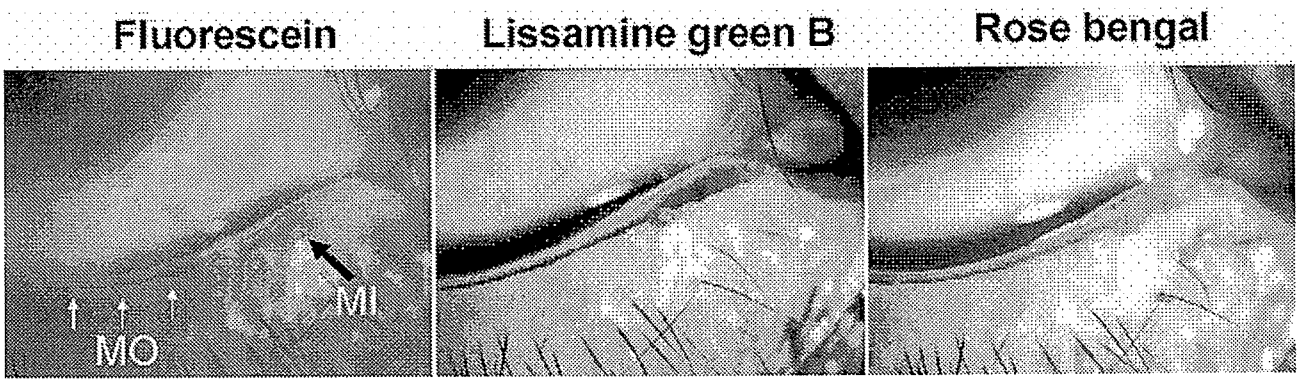


FIGURE 4. The lower eyelid margin was stained with fluorescein, lissamine green B, and rose bengal. The mucocutaneous junction is clearly stained by each solution at the same site. MO = meibomian orifice; MI = meibomian infarction.

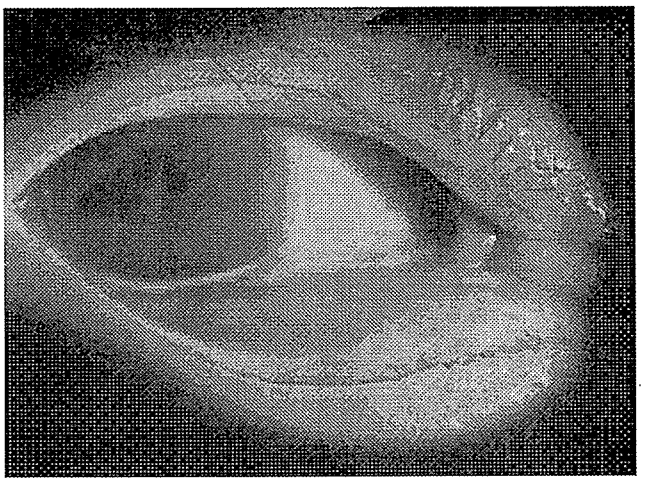


FIGURE 5. The MLs of the upper and lower eyelids are almost identical in most subjects.

cosity; 3, white and thick with a consistency of toothpaste; and 4, no secretions on compression. Then a correlation between the middle ML score and the score for the meibomian gland secretions was evaluated.

Apart from the original group of 251 subjects, the ML scores of 15 subjects (seven men and eight women, ages 44.2 ± 21.0 years) with MGD were compared with those from 15 age-matched subjects (seven men and eight women, ages 44.1 ± 20.0 years) without MGD. The subjects without MGD were defined as patients without acute ocular surface disease who had scores of one or less for the meibomian gland secretions. In the MGD group, the MOs were plugged and the meibomian gland secretion scores were two or more in all of the subjects. No one in the MGD group had been diagnosed with acute ocular surface disease.

The correlations between regional ML scores and meibography scores and between ML scores and meibomian gland secretions scores were analyzed by the Kruskal-Wallis test for analysis of variance and nonparametric Spearman rank correlation analysis among multiple groups. The

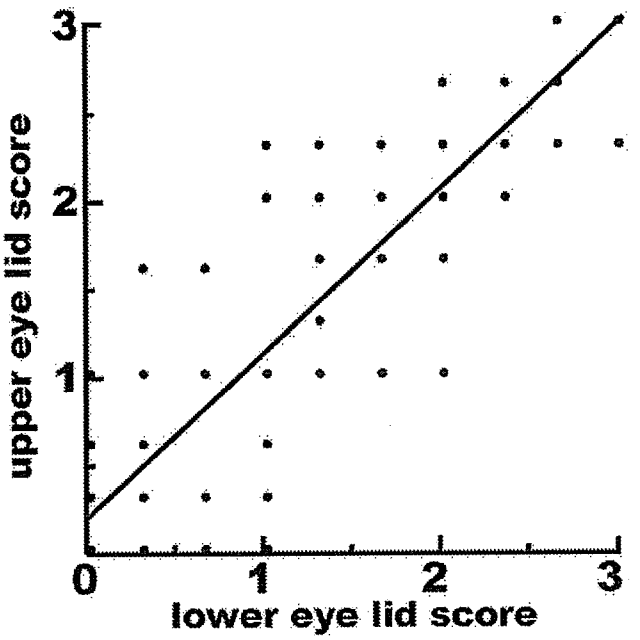


FIGURE 6. The correlation between the mean score of three parts (inner, middle, and outer thirds) for the upper eyelid and that of the lower eyelid was plotted. X axial = mean score of lower eyelid; Y axial = mean score of upper eyelid.

significance of the differences in the regional (inner, middle, outer) ML scores in different age groups was examined by the Kruskal-Wallis test for analysis of variance and the Scheffé F test for comparisons. The significance of differences in the total ML scores of eyes with and without MGD was determined by the Student *t* test.

RESULTS

AMONG FIVE OPHTHALMOLOGISTS, INCONSISTENCY OF A score was settled in less than one for the ML score, and scores did not differ by two or more for all 20 images. There was 100% coincidence in 8 (40%) of 20 images, 80%

TABLE 1. Correlation Between Marx Line Score and Meibographic Score*

Meibographic Score	Marx Line Score 0	1	2	3
0	45	40	10	0
1	40	50	39	39
2	0	0	26	59

*A total of 348 regions in 116 subjects were studied. Regional Marx line was scored 0 to 3 (horizontal line), and regional meibography was scored 0 to 2 (vertical line).

TABLE 2. Correlation Between Marx Line Score and Meibomian Gland Secretion Score*

Meibomian Gland Secretion Score	Middle Marx Line Score 0	1	2	3
0	22	6	5	0
1	7	12	14	5
2	2	12	10	20
3	0	2	3	3
4	0	0	0	3

*A total of 126 meibomian orifices in 126 eyes were studied. Middle third Marx line was scored 0 to 3 (horizontal line), and meibomian gland secretions of one meibomian orifice at approximately the center of the middle third of the lower eyelid was scored 0 to 4 (vertical line) correspondingly.

coincidence in 10 (50%) of 20 images, and 60% coincidence in all 20 images.

The staining pattern of the eyelid margin with fluorescein is shown in Figure 4. A sharply defined line can be seen on the inner eyelid, and the staining with rose bengal and lissamine green B solutions was almost consistently seen along this particular line (Figure 4), indicating that this line appeared to represent the mucocutaneous junction (MCJ). Because fluorescein is used much more widely than rose bengal or lissamine green B solutions in clinical practice, we chose to use fluorescein alone for the staining of lid margin in subsequent assessments.

The fluorescein-stained line was observed on the inner surface of both the upper and lower eyelids with a similar pattern (Figure 5). When the ML scores of the upper and lower eyelids were determined in 65 subjects, the regression line relating the mean score of three parts (inner, middle, and outer thirds) for the upper eyelid to that of the lower eyelid was as follows: [mean score of upper eyelid = 0.234 + 0.914 × mean score of the lower eyelid] (R^2 = 0.794; $P < .0001$, Figure 6). Because of this significant correlation, we decided to evaluate the ML score of the lower eyelid alone in the subsequent study. In addition, a strong positive correlation was also found in the mean ML scores for the inner, middle, and outer thirds of the upper eyelid to those of the lower eyelid (data not shown).

To determine the correlation between ML score and other tests of meibomian gland function, we first compared ML score with the meibography score in 116 subjects. The mean ± SD meibography scores for individuals with ML scores of 0, 1, 2, and 3 were as follows: 0.47 ± 0.50, 0.55 ± 0.50, 1.21 ± 0.66, and 1.60 ± 0.49, respectively. A strong positive correlation was found between the regional ML scores and the regional meibography scores (Kruskal-Wallis test, $P < .0001$; nonparametric Spearman rank correlation analysis, $r = 0.643$, $P < .0001$; Table 1).

Next, the mean ± SD meibomian gland secretion scores for the 126 subjects with middle third ML scores of 0, 1, 2, and 3 were 0.35 ± 0.61, 1.31 ± 0.86, 1.34 ± 0.87, and 2.13 ± 0.81, respectively. A strong positive correlation was also found between ML scores and meibomian gland secretion scores (Kruskal-Wallis test: $P < .0001$; nonparametric Spearman rank correlation analysis: $r = .599$, $P < .0001$; Table 2).

Effect of aging on the ML scores was determined for the 502 eyes of 251 subjects without acute ocular surface diseases. Correlation between the total ML score and age, and the correlations between ML score for the three segments of the lower lid and age were determined.

A strong positive correlation was found between the total ML score and age in both men and women (men, $R^2 = .548$; $P < .0001$; women, $R^2 = .588$; $P < .0001$). A strong positive correlation was also found between age and the score for the outer third of the lower eyelid in both men and women (men, $R^2 = .549$; $P < .0001$; women, $R^2 = .622$; $P < .0001$); for the inner third (men, $R^2 = .446$; $P < .0001$; women, $R^2 = .425$; $P < .0001$); and for the middle third (men, $R^2 = .364$; $P < .0001$; women, $R^2 = .344$; $P < .0001$).

The mean ± SD ML scores for the outer, middle, and inner thirds of the lower eyelid were also determined for the following three groups: subjects younger than 40 years (group 1), subjects from 41 to 60 years (group 2), and subjects older than 61 years (group 3). For group 1, ML score was 0 for the three regions in men and 0.14 ± 0.35, 0.09 ± 0.29, and 0.09 ± 0.29 in women. For group 2, the respective values were 1.05 ± 1.25, 0.34 ± 0.56, and 0.39 ± 0.63 in men, and 0.86 ± 0.95, 0.33 ± 0.53, and 0.39 ± 0.47 in women. For group 3, the values were 2.42 ± 0.85, 1.18 ± 0.87, and 0.68 ± 0.89 in men and 2.55 ± 0.80, 1.18 ± 0.94, and 1.54 ± 1.09 in women. More specifically, the scores for the outer third of lower eyelid were higher in both men and women.

There were no significant differences of the regional ML scores between men and women regarding to age. No difference of the ML scores was observed between the three regions in both men and women from group 1, but differences were observed between the three regions for both men and women in groups 2 and 3 (Kruskal-Wallis tests, $P < .0001$ and $P < .0001$, respectively). In group 2,

TABLE 3. Significance of Marx Line Scores for the Outer, Middle, and Inner Lower Eyelid Regions in Men and Women in Three Age Groups*

Group	Group 1 (≤40 years)	Group 2 (41–60 years)	Group 3 (≥61 years)
Men			
Inner vs middle	NS	NS	<.005
Inner vs outer	NS	NS	<.0001
Middle vs outer	NS	<.05	<.0001
Women			
Inner vs middle	NS	NS	NS
Inner vs outer	NS	<.05	<.0001
Middle vs outer	NS	<.0001	<.0001

Inner = Marx line score for the inner lower eyelid region; Middle = Marx line score for the middle lower eyelid region; Outer = Marx line score for the outer lower eyelid region; ns = no significant difference.
*Scheffe *F* test.

a difference of the scores was observed between the middle and outer thirds among men, as well as between the inner and outer thirds and the outer and middle thirds among women. In group 3, a difference of the scores was observed between any two of the regions, except for the inner and middle thirds in women (Table 3).

The mean ± SD ML scores for eyes in the non-MGD group and the MGD group were 2.77 ± 1.59 and 5.93 ± 1.55, respectively. The difference between these two groups was statistically significant ($P < .001$).

DISCUSSION

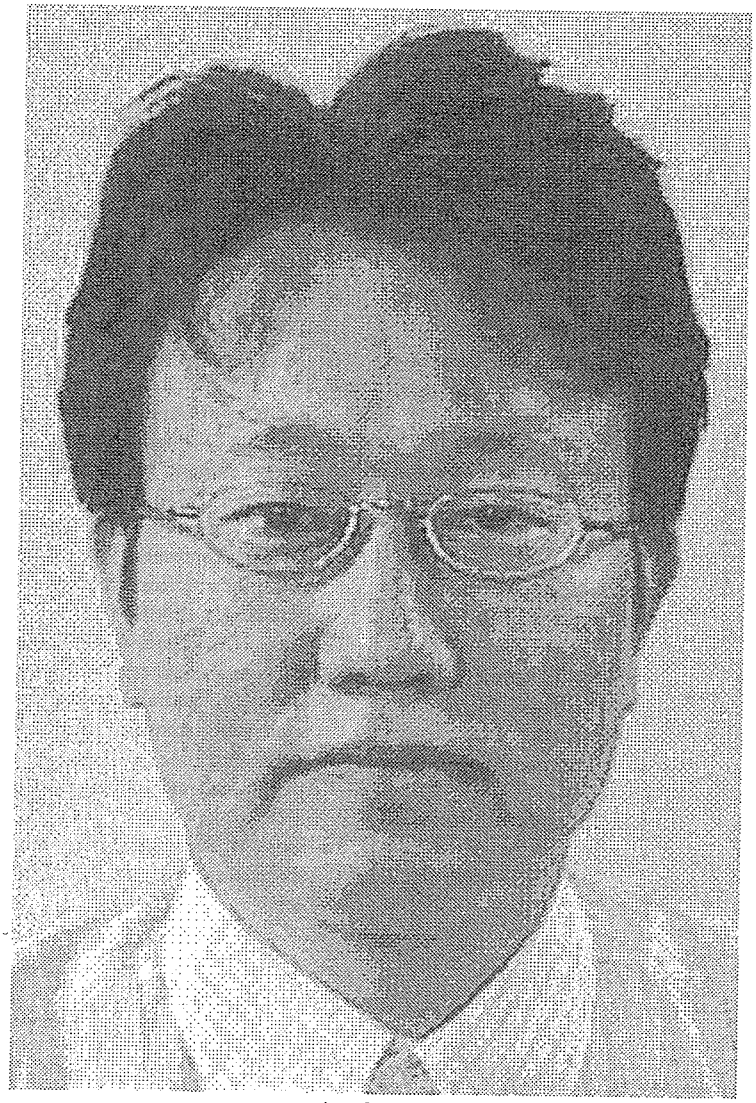
THE CONCEPT OF AN EVAPORATIVE TYPE OF DRY EYE[12] HAS become widely recognized as a result of better understanding of the pathogenesis of MGD in recent years. The importance of assessing meibomian gland function has been emphasized because lipids secreted by these glands combine with outer layers of the tear film not only to suppress evaporation of tear fluid, but also to form a hydrophobic barrier at the lid margin to prevent loss of tears.[1,2] Focusing on the latter role, we assume that the ML as revealed by fluorescein staining along the lid margin may represent such a barrier line. Because ML appears to be the interface between lipids secreted from the meibomian glands and the aqueous tear fluid, it may well be an indicator of meibomian gland function. The significance of ML was first pointed out by Norn,[13] who performed vital staining of the eyelid margin with fluorescein, lissamine green B, and Sudan III, and concluded that the stained line representing the border between tear fluid and the skin corresponded to the MCJ. In this study, we have reconfirmed Norn's observation as stated above and decided to use fluorescein for defining ML.

We have shown that the change of the location of this line was strongly correlated with meibomian gland function. We base this on the following: eyes with abnormal meibomian gland secretions or morphology had significantly higher ML scores; and ML scores were significantly higher in the MGD group than those in the group without MGD for age-matched subjects. Although a variety of methods or clinical techniques are being used to assess meibomian gland function, most of these procedures are either subjective or require special equipment. Our results demonstrated that scoring of the location of ML could be used as a rapid, efficient, less-invasive screening test for and assess of meibomian gland function. One great advantage of this procedure is that the information on the location of ML can be easily obtained during the fluorescein staining procedure in routine slit-lamp examination for patients with dry eye. Although the scoring and assessment of ML itself could be somehow subjective, the variation of the clinical score among experienced ophthalmologists was found to be reasonable and within an acceptable range.

The ML was found to shift gradually toward the outside of the eyelid margin with aging. That is, the ML generally runs in parallel and some distance away from the MOs along the conjunctival border in younger subjects. However, it becomes irregular and creeps closer to the MOs with aging, and finally extends beyond them in some subjects. This finding was consistent with the results obtained by Norn,[13] who had reported that the MOs were situated in a straight row just in front of the ML in younger normal subjects. However, the orifices were more often displaced in elderly normal subjects (>50 years)—that is, the ML might run an irregular course with increasing age.

When the ML of the inner, middle, and outer thirds of the lower eyelid was scored separately, it was found that the outward shift of the ML started earlier from the inner or outer third than the middle third, and such a shift was more common at the outer third in the elder individuals. This finding may imply that MGD are prone to develop in the inner or outer regions earlier, which is consistent with our finding that the meibomian glands at these regions are shorter and less well-developed as compared with those in the central region (data not shown). The involvement of conjunctivochalasis on the extensive outward shift of ML in elder population cannot be completely ruled out as this abnormality also occurs with aging and the redundant bulbar conjunctiva preferentially hang over the inner or outer third of the lid margin. In fact, there exists the possibility that the ML location might be modified when the lid margin become wet as a result of excessive bulbar conjunctiva. Nevertheless, ML score could still be a useful indicator for meibomian gland function unless a high degree of conjunctivochalasis is present.

In contrast to our observation, Hykin and Bron[14] reported that there were no age-related changes in the position and form of the MCJ in subjects without ocular



Biosketch

Masahiko Yamaguchi, MD, graduated from the Osaka City University School (OCU) of Medicine in 1990, and served as an ophthalmologist at the OCU Hospital from 1990 to 1995. In 1996, he joined the faculty of Ehime University School of Medicine, Department of Ophthalmology, for research on ocular surface diseases. His main area of research is in dry eye.

surface disorders. In addition, Bron and associates[15] reported that there existed two patterns of the MCJ location in eyes with MGD: an anteroplacement and a retroplacement. Especially, a retroplacement refers to a shift of the MCJ to the conjunctival side and was considered more common in eyes with MGD. We speculate that such a change might occur in patients with atopic dermatitis or other ocular surface disorders. Further careful survey would disclose this discrepancy.

In conclusion, we have demonstrated that the ML, the fluorescein staining line along the lower lid margin, is a good indicator of meibomian gland function. The evaluation is effective, less invasive, and practical as an easy screening test in daily clinical practice.

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Changes in Lumen Width of Nasolacrimal Drainage System After Adrenergic and Cholinergic Stimulation

JUNJI NARIOKA, MD, AND YUICHI OHASHI, MD

• PURPOSE: To determine the effect of an adrenergic agonist and a cholinergic agonist on the lumen width of the nasolacrimal drainage system.
• DESIGN: Prospective, nonrandomized, clinical trial.
• METHODS: The asymptomatic sides of 33 patients (23 women, 10 men) with unilateral stenosis/obstruction of the nasolacrimal drainage system were studied. The tear meniscus height of the asymptomatic side was normal, with a patent lacrimal system as reveled by dacryocystography. The nasolacrimal drainage system of the asymptomatic side was infused with 100 μL of 5% phenylephrine hydrochloride (an α-1 adrenoceptor agonist) or 100 μL of 2% pilocarpine hydrochloride (a cholinergic agonist), and dacryocystography was performed to determine the lumen width of the nasolacrimal drainage system.
• RESULTS: Phenylephrine caused a significant increase of the lumen width of the nasolacrimal drainage system, and the changes were more marked in the nasolacrimal duct (NLD), especially the upper and middle regions, than in the lacrimal sac. In contrast, pilocarpine reduced the lumen width of the NLD significantly, especially in the middle and lower regions, and the lumen width of the lacrimal sac was not significantly changed.
• CONCLUSION: The alterations of the lumen width of the nasolacrimal drainage system, especially the lumen width of the NLD by adrenergic and cholinergic agonists, suggest that the lumen width can be changed by the autonomic nervous system. (Am J Ophthalmol 2006; 141:689–698. © 2006 by Elsevier Inc. All rights reserved.)

THE ANATOMIC STRUCTURE OF THE NASOLACRIMAL drainage system (which is made up of the lacrimal canaliculus, nasolacrimal duct (NLD), and lacrimal sac (LS)) has been studied extensively, but only a few investigations have been made on the autonomic innervation to this system.[1,2] Paulsen and associates[2,3] conducted the first detailed immunohistochemical studies on the nasolacrimal drainage system and proposed a new hypothesis on the tear outflow mechanism. They found a wide vascular plexus embedded in the wall of the LS and NLD that is comparable to a cavernous body. This cavernous body-like structure was innervated densely and contained a number of neuropeptides that included substance P, neuropeptide Y, vasoactive intestinal polypeptide, and calcitonin gene-related peptide. The connective tissue and/or blood vessels in this region also were immunopositive for some neuronal markers (which included RT97, S-100 protein, and neuron-specific enolase) and for neuronal enzymes that included tyrosine hydroxylase. On the basis of these findings, Paulsen and associates hypothesized that cholinergic stimulation of the blood vessels in the cavernous body would lead to a swelling of the submucosal cavernous tissue and reduce the diameter of the lacrimal lumen and that adrenergic stimulation would relax the submucosal swelling and improve the tear flow.

The purpose of this study was to determine whether the lumen width of the LS and the NLD is altered by sympathetic and parasympathetic stimulation. Dacryocystography was used to measure the lumen width before and after the stimulations.

PATIENTS AND METHODS

• SUBJECTS: Thirty-three patients (23 women and 10 men; age, 70.8 ± 12.0 years (mean ± SD)) were studied. Because x-rays are used for dacryocystography, we ethically could not use subjects without disease of the nasolacrimal drainage system as control subjects. Instead, we selected patients who had a unilateral stenosis/obstruction of the nasolacrimal drainage system or dacryocystitis with epiphora and mucoid discharge from the medial canthal region. These patients required dacryocystography on the symptomatic side to make a definitive diagnosis and on the asymptomatic side to be certain that the lacrimal drainage system was patent and normal anatomically. All subjects were examined in the Department of Ophthalmology at

Accepted for publication Nov 18, 2005.
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0002-9394/06/$32.00
doi:10.1016/j.ajo.2005.11.040

Saijo City Shuso Hospital between April and July 2005. Approval for this study was obtained from the Institutional Review Board of the Ehime University School of Medicine. The procedures that were used conformed to the tenets of the Declaration of Helsinki; informed consent was obtained from all subjects after the nature and possible consequences of the study were explained. Patients with any ocular surface diseases, glaucoma, nasal inflammatory diseases, abnormal eyelid position, recent episode of ocular trauma, acute/chronic upper respiratory inflammation, or eye surgery were excluded. Patients with heart disease or bronchial asthma were also excluded because of the possible adverse reaction to the drugs.

The lacrimal drainage system on the asymptomatic side was examined carefully in all patients, and no signs of epiphora and mucoid discharge were recognized. Dacryocystography showed no stenosis/obstruction or dilation of the nasolacrimal system on this side. In addition, the tear meniscus height was normal, and the lacrimal system was patent on nasolacrimal irrigation.

• DACRYOCYSTOGRAPHY: All examinations were conducted by one of the authors (J.N.). Dacryocystography was performed on both sides to compare the differences between the asymptomatic and symptomatic sides to be certain that bilateral anatomic stenosis/obstruction was not present. Dacryocystography was performed with a digital radiographic system (ADR-1000A; Toshiba Medical Systems, Tokyo, Japan), and the images were stored electronically as 1024 × 1024-pixel matrix in a 6-inch image intensifier mode. Under these conditions, one pixel corresponded to approximately 0.118 mm.

To record the x-rays, the patient was placed in a supine position, and both eyes were anesthetized topically with 0.4% oxybuprocaine hydrochloride. Then, 0.5 to 1.0 ml of 61.2% iopamidol (Iopamiron 300; Nihon Schering KK, Osaka, Japan), a water-soluble contrast medium, was infused slowly and steadily under fluoroscopic guidance from the upper punctum into the nasolacrimal drainage system through the canaliculus with a 27-guage lacrimal cannula (outer diameter, 0.4 mm; inner diameter, 0.15 mm; Inami, Tokyo, Japan) that was attached to a 2.5-ml syringe. Because the lumen width can be affected by the pressure of injection, the injections were made with approximately the same low pressure. We injected the contrast medium from the upper canaliculus because the upper canaliculus joins the LS in approximately a straight line; the lower canaliculus is curved[4] and joins the caudal side of the upper canaliculus.[5] In addition, the lower canaliculus is slightly longer than the upper canaliculus.[4,6]

Because the shape of the lumen of the nasolacrimal drainage system is not completely circular but complex with many folds and ridges,[4] dacryocystography was performed from two directions, anteroposterior and oblique (45 degrees lateral oblique). Images were obtained before and after the application of the autonomic drugs. The oblique images were obtained by the rotation of the head approximately 45 degrees to the opposite direction (for example, when the right nasolacrimal drainage system was studied, the head was turned to the left). As a result, both the midsagittal and frontal plane of the patient's head made approximately a 45-degree angle with the radiation beam, although the horizontal plane was almost parallel to the radiation beam.

TABLE 1. Results of Dacryocystography in the Symptomatic Sides

Variable	N (%)
Nasolacrimal stenosis	11 (33.3)
Chronic dacryocystitis caused by nasolacrimal obstruction	9 (27.3)
Functional nasolacrimal obstruction	8 (24.3)
Internal common punctum obstruction	3 (9.1)
Canaliculitis	1 (3.0)
Upper canalicular obstruction + punctal stenosis	1 (3.0)
Total	33 (100)

• EFFECT OF ADRENERGIC AND CHOLINERGIC AGONISTS ON NASOLACRIMAL DRAINAGE SYSTEM: To evaluate the effect of gender, male and female patients were studied separately. Phenylephrine was assigned to the patients whose clinical record ended with an odd number, and pilocarpine was assigned to those patients with an even number. We stopped this study after 10 male patients had been studied, at which point, 23 female patients (12 patients with phenylephrine and 11 patients with pilocarpine) had been studied already.

Group A consisted of 12 women and 5 men with a mean age of 71.4 ± 12.3 years (range, forty-eight to ninety-one years); each patients received 100 μl of 5% phenylephrine hydrochloride, an α-1 adrenoceptor agonist that is used for mydriasis (Neosynesin eye drop solution; Kowa, Tokyo, Japan). Group B consisted of 11 women and 5 men with a mean age of 70.3 ± 11.9 years (range, forty-three to eighty-four years); each patient received 100 μl of 2% pilocarpine hydrochloride, a cholinergic agonist that is used as a topical medication for glaucoma (2% Sanpilo eye drop solution; Santen Pharmaceutical, Osaka, Japan). Both drugs contained chlorobutanol as a preservative agent.

After the control pretreatment dacryocystography images were recorded, approximately 100 μl (which corresponded to 2 or 3 drops) of phenylephrine or pilocarpine was infused into the asymptomatic side from the upper punctum into the nasolacrimal drainage system through the canaliculus with the use of a procedure that is similar to that used to infuse the contrast medium. During the infusion, the lower punctum was compressed to prevent a reflux of the agonists. The patients were asked not to blink and to keep their eyes closed for 15 minutes to reduce the

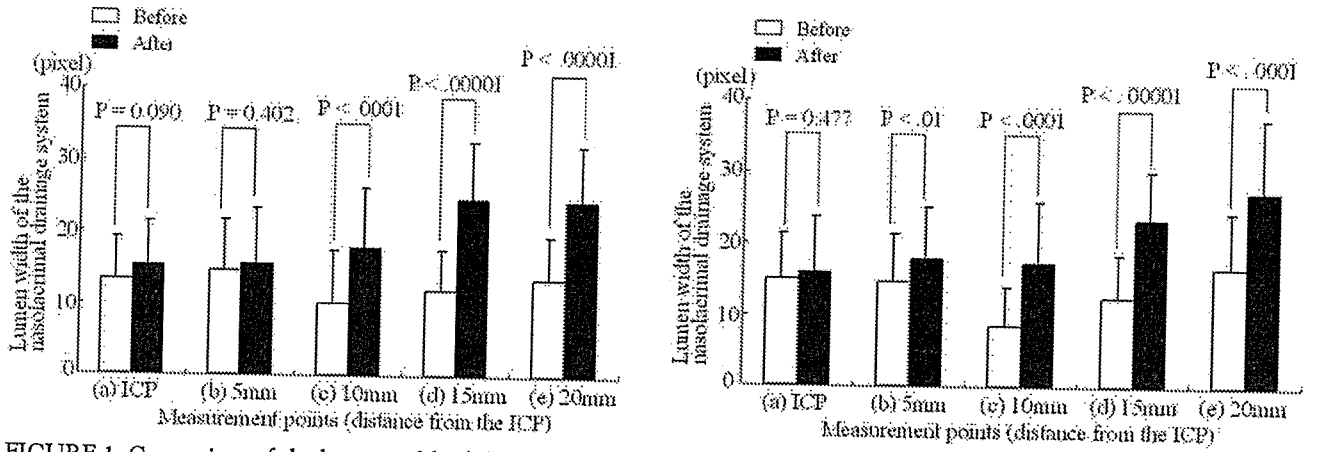

FIGURE 1. Comparison of the lumen width of the nasolacrimal drainage system at five points before and after phenylephrine. The anteroposterior images are shown in Left panel, and the oblique images are shown in Right panel. Analysis was performed with paired *t* tests. (a) = point 1; (b) = point 2; (c) = point 3; (d) = point 4; (e) = point 5; ICP = internal common punctum.

outflow of the drug by lacrimal pumping. Fifteen minutes later, dacryocystography was performed in the anteroposterior and oblique directions to obtain the posttreatment images.

The lumen width of the nasolacrimal drainage system was measured from the dacryocystography images before and after the autonomic agonists. For all measurements, the electronic images were magnified by six times on the basis of the scale required to give 1-cm squares that were nontransparent to radiation. The lumen width was measured by identification of one edge of the duct and the anchoring of one end of an adjustable line at this point. Then the other end of the line was dragged to the other edge of the duct. The length of the line was calculated automatically on the basis of the number of pixels, and the data were displayed. This method is used generally to measure the size of blood vessels in coronary angiograms.[7]

In addition to the absolute size, the ratio of the lumen width before and after drug administration was calculated using the following formula: ratio (%) = $(\alpha - \beta)/\beta \times 100$, where α equals the width after drug administration and β equals the width before drug administration.

It was very difficult to identify the exact borders of the LS, the intraosseous part of the membranous NLD, and the meatal part of the NLD on the dacryocystography. Whitnall[4] reported that the length of the lacrimal sac in cadavers averaged approximately 12 mm and that the distance from the upper end of the LS to the internal common punctum was approximately 2.5 mm. For the NLD, the average length of the intraosseous part of the NLD was 12.4 mm, and the length of the metal part averaged 5.3 mm.[4] Because the vertical axis of the LS and the long axis of the NLD are slightly posterior,[4] the lumen width of the nasolacrimal drainage system was measured at the following five points: point 1 at the level of the internal common punctum, which is approximately the upper LS; point 2, 5 mm below point 1, which is approximately the middle LS; point 3, 10 mm below point 1, which is approximately the lower LS or upper membranous NLD; point 4, 15 mm below point 1, which is approximately the middle membranous NLD; and point 5, 20 mm below point 1, which is approximately the lower membranous NLD.

• STATISTICAL ANALYSES: The Student *t* test was used to compare the values that were obtained from the two groups before drug administration. Paired *t* tests were used to compare the lumen widths before and after the administration at each of the five points, and one-way analysis of variance with a post hoc Tukey test was used for within-group analysis at each measurement point and for analysis of the ratio of the lumen width after drug administration. Repeated-measures analysis of variance were used to compare the drug effects between women and men in each group. A probability value of $<.05$ was taken to be significant. In these calculations, the actual measured pixel-based width was used.

RESULTS

EXCEPT FOR A MILD AND TEMPORARY MYDRIASIS OR MIOSIS that was caused by a reflux of a small amount of the drugs from the punctum, no other complications were seen during the study. After the measurements, there were no complications such as ocular hypertension, nasolacrimal stenosis/obstruction, or dacryocystitis. The results of dacryocystography on the symptomatic side are shown in Table 1.

• DACRYOCYSTOGRAPHY BEFORE AGONISTS: Because the pretreatment lumen widths for the anteroposterior images in group A were not significantly different from that in group B, the values were combined. The mean pretreatment lumen widths that were obtained from the anteroposterior images of the combined group were 1.49 ±

TABLE 2. Comparison of the Lumen Width of the Nasolacrimal Drainage System at Five Points Before and After Phenylephrine (Pixel)

Variable	Anteroposterior Imaging		Oblique Imaging	
	Before	After	Before	After
Internal common punctum	13.4 ± 5.9	15.4 ± 6.1	14.9 ± 6.4	15.8 ± 7.8
5 mm	14.5 ± 7.2	15.4 ± 7.9	14.6 ± 6.6	17.8 ± 7.3*
10 mm	10.2 ± 7.3	17.9 ± 8.3†	8.5 ± 5.5	17.2 ± 8.6†
15 mm	11.8 ± 5.9	24.7 ± 8.0‡	12.5 ± 5.9	23.2 ± 7.0‡
20 mm	13.5 ± 6.1	24.6 ± 7.7†	16.6 ± 7.6	27.1 ± 10.3†

*$P < .01$.
†$P < .0001$.
‡$P < .00001$.

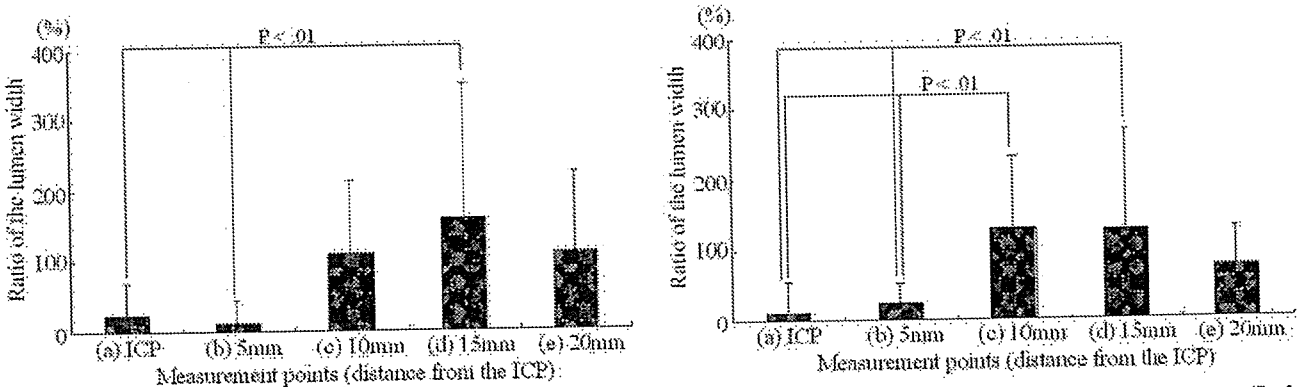

FIGURE 2. Comparison of the change in the ratios of the lumen width after phenylephrine from anteroposterior images (Left panel) and oblique images (Right panel) with the use of one-way analysis of variance with a post hoc Tukey test. (a) = point 1; (b) = point 2; (c) = point 3; (d) = point 4; (e) = point 5; ICP = internal common punctum.

0.6 mm, 1.65 ± 0.7 mm, 1.20 ± 0.8 mm, 1.45 ± 0.7 mm, and 1.77 ± 0.9 mm at points 1 through 5, respectively. The mean pretreatment lumen widths for these same points in the oblique images were 1.71 ± 0.7 mm, 1.86 ± 0.8 mm, 1.07 ± 0.5 mm, 1.42 ± 0.7 mm, and 1.98 ± 1.2 mm, respectively. Most importantly, the lumen widths in the anteroposterior images did not differ significantly from those measured on the oblique images, which would indicate that the nasolacrimal drainage system at these points was approximately circular.

• EFFECTS OF PHENYLEPHRINE AND PILOCARPINE: After phenylephrine infusion, the lumen width was significantly larger than the pretreatment widths at points 3 through 5 in the anteroposterior images (Figure 1, Left panel; Table 2) and at points 2 through 5 in the oblique images (Figure 1, Right panel; Table 2). The lumen widths after drug administration at points 4 and 5 were significantly greater than at points 1 and 2 in the anteroposterior images and at point 5 than at points 1 through 3 in the oblique images. The ratio of the lumen widths before and after drug administration was larger at point 4 than at points 1 and 2 in the anteroposterior images (Figure 2, Left panel) and at points 3 and 4 than at points 1 and 2 in the oblique images (Figure 2, Right panel).

These findings indicate that phenylephrine dilated the lumen width of the nasolacrimal drainage system significantly but that the changes were not uniform along the NLD. Our findings demonstrated that the changes in the lumen width of the NLD were more marked in the upper and middle region of the NLD than in the LS (Figure 3).

In group B, the lumen widths of the nasolacrimal drainage system decreased significantly at points 3 through 5 (Figure 4, Left panel; Table 3); the oblique images showed a significant decrease at points 4 and 5 (Figure 4, Right panel; Table 3). After pilocarpine, the lumen widths at points 3 and 4 were significantly smaller than at points 1 and 2, and the lumen width at point 5 was significantly smaller than that at point 2 in the anteroposterior images. In the oblique images, the lumen widths at points 4 and 5 were significantly smaller than at points 1 and 2, and the lumen width at point 3 was significantly smaller than at point 2. The ratio of the lumen widths showed that the ratios at points 3 through 5 were smaller than at points 1 and 2 in the anteroposterior images (Figure 5, Left panel),

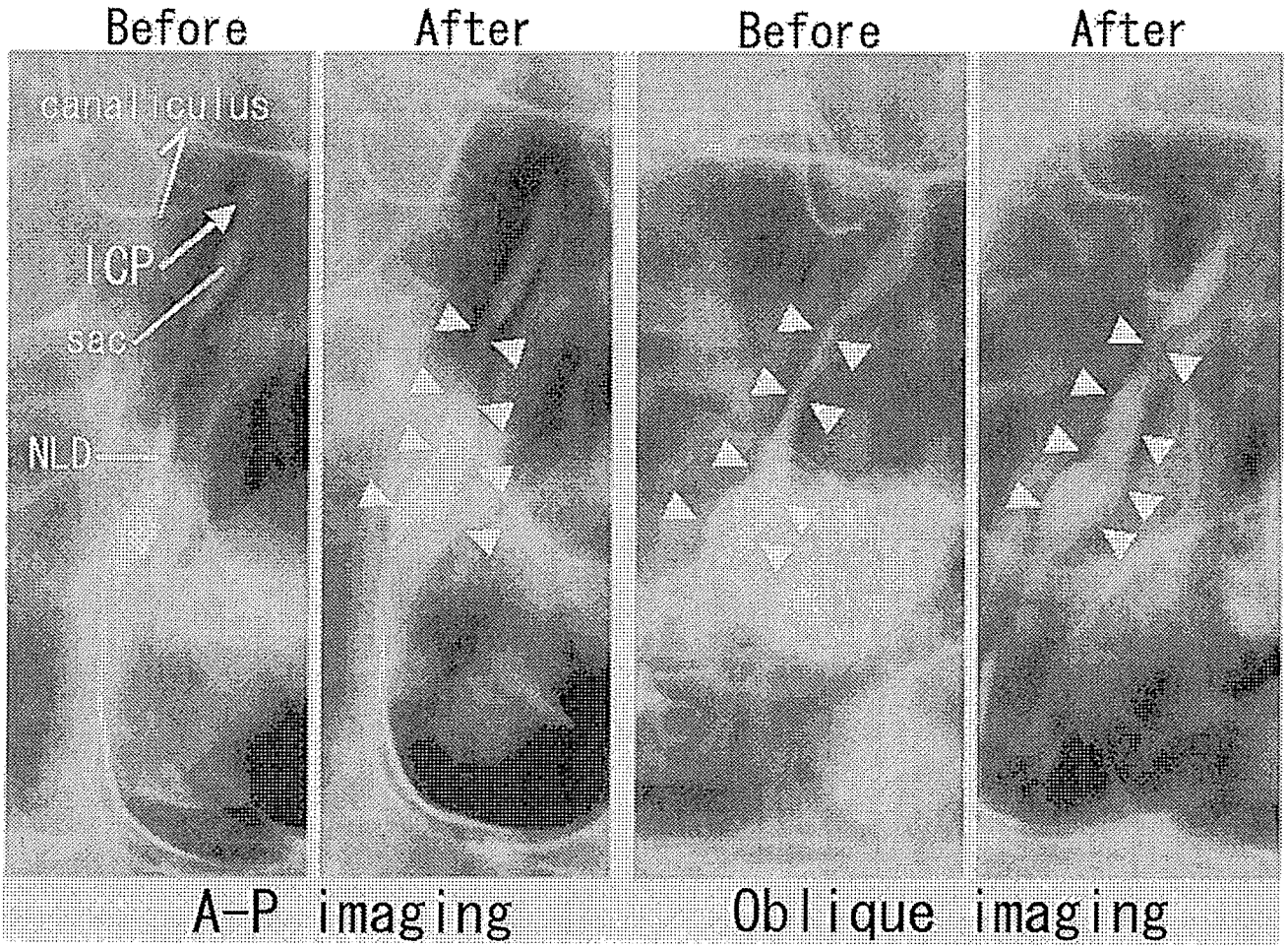

FIGURE 3. Dacryocystography shows dilation of the lumen width of the nasolacrimal drainage system after phenylephrine administration in anteroposterior (A-P) and oblique views (arrowheads), right side. ICP = internal common punctum; NLD = nasolacrimal duct.

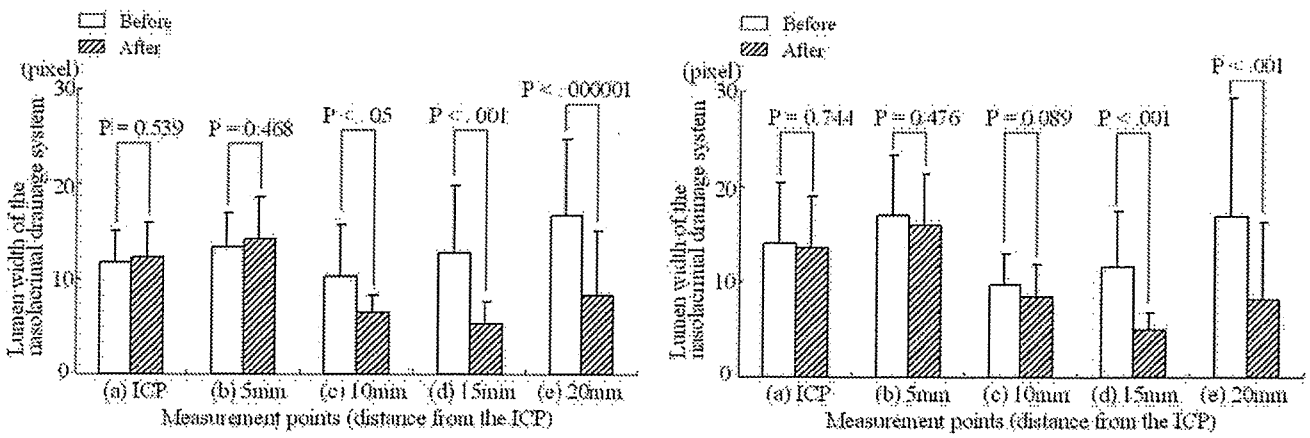

FIGURE 4. Comparison of the lumen width of the nasolacrimal drainage system at five points before and after pilocarpine. The anteroposterior images are shown in Left panel, and the oblique images are shown in Right panel. Analysis was performed with paired *t* tests. (a) = point 1; (b) = point 2; (c) = point 3; (d) = point 4; (e) = point 5; ICP = internal common punctum.

TABLE 3. Comparison of the Lumen Width of the Nasolacrimal Drainage System at Five Points Before and After Pilocarpine (Pixel)

Variable	Anteroposterior Imaging		Oblique Imaging	
	Before	After	Before	After
Internal common punctum	11.8 ± 3.4	12.3 ± 3.7	14.0 ± 6.3	13.7 ± 5.4
5 mm	13.4 ± 3.6	14.3 ± 4.3	17.0 ± 6.4	16.0 ± 5.3
10 mm	10.3 ± 5.6	6.6 ± 1.8*	9.8 ± 3.2	8.5 ± 3.4
15 mm	12.9 ± 7.0	5.4 ± 2.3†	11.6 ± 5.8	5.0 ± 1.8†
20 mm	16.7 ± 8.1	8.3 ± 6.9†	16.9 ± 12.5	8.2 ± 8.2†

*$P < .05$.
†$P < .001$.
‡$P < .000001$.

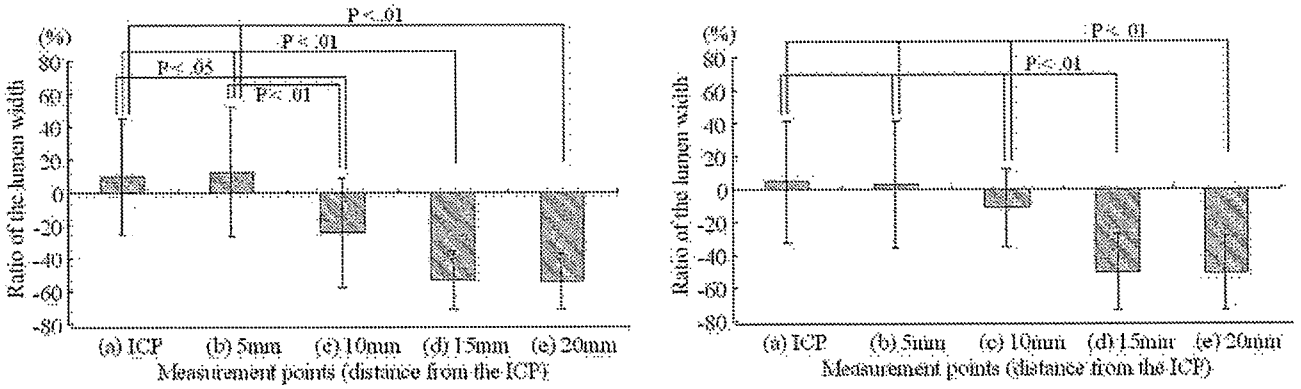

FIGURE 5. Comparison of the change in the ratios of the lumen width after pilocarpine in anteroposterior images (Left panel) and oblique images (Right panel) with the use of one-way analysis of variance with a post hoc Tukey test. (a) = point 1; (b) = point 2; (c) = point 3; (d) = point 4; (e) = point 5; ICP = internal common punctum.

and the ratios at 4 and 5 were smaller than at 1 through 3 in the oblique images (Figure 5, Right panel).

These findings indicate that pilocarpine reduced the lumen width of the NLD significantly and, as with the anteroposterior images, that the changes were not uniform. The changes were more marked in the middle and lower regions, and the lumen width of the LS was unchanged essentially (Figure 6).

• COMPARISON OF DRUG EFFECTS IN WOMEN AND MEN: No significant difference in the degree of change in the lumen width was found between the men and women in either group. These findings indicate that the effects of phenylephrine and pilocarpine are not gender-dependent.

DISCUSSION

OUR RESULTS CLEARLY DEMONSTRATED THAT THE LUMEN width of the NLD is increased by an adrenergic agonist and reduced by a cholinergic agonist. These findings have confirmed the suggestion of Paulsen and associates[2,3] that there is an autonomic network in the NLD. We used 5% phenylephrine and 2% pilocarpine eye drop solutions because these drugs are used widely at these concentrations in daily clinical practice and in general, have no serious adverse reactions. Moreover, this is highest concentration that is available commercially in Japan.

It is well known that the wall of the membranous NLD is thicker than the wall of the LS[4,8,9] and that this cavernous body is well-developed in the NLD and to a lesser extent in the LS. Because the membranous NLD is embedded in the osseous NLD,[4] a change in the lumen width most likely resulted from a change in the thickness of the wall of the membranous NLD rather than a change in the outer diameter. Thus, our observations can be attributed most likely to changes in the cavernous body within the wall of the NLD, and the thick cavernous wall of the NLD may be a key requisite for these changes to occur.

The flow and volume of blood in the nasal mucosa are known to be under autonomic control,[10–13] and there are anastomoses between the dense plexus of the nasal mucosa, the LS, and the NLD.[6] This is significant because the mucosa of the membranous NLD gradually attains the characteristics of the nasal mucosa as it approaches the nasal cavity[4]; thus, the membranous NLD may possess

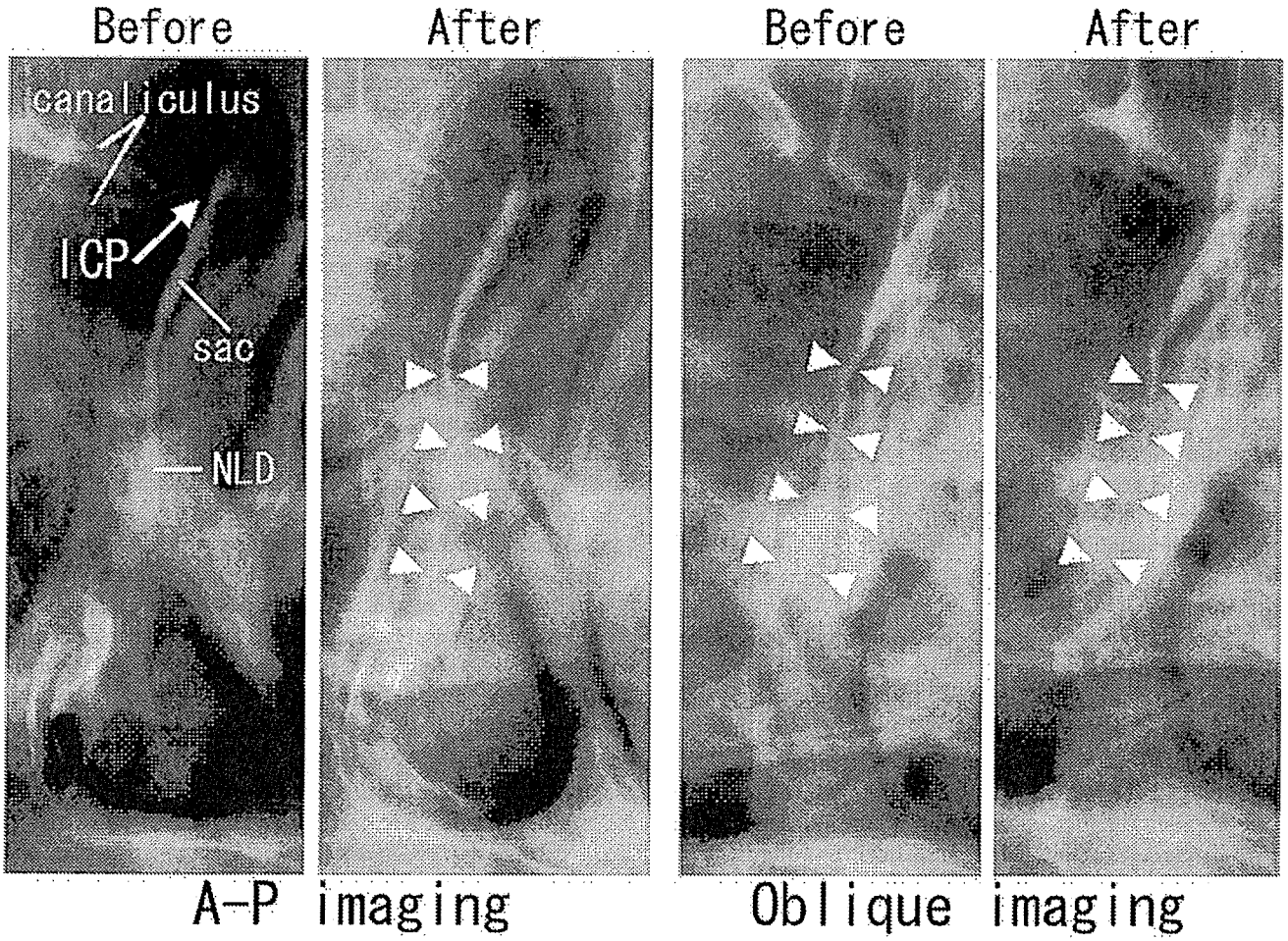

FIGURE 6. Dacryocystography shows reduction of the lumen width of the nasolacrimal drainage system after pilocarpine administration in an anteroposterior (A-P) image and oblique image (arrowheads). ICP = internal common punctum; NLD = nasolacrimal duct.

physiologic characteristics that are similar to those of the nasal mucosa.

Fischer and associates[13] reported that somatostatin and neuropeptide Y (nonadrenergic vasoconstrictors) were present in the human nasal mucosa. Vasoactive intestinal polypeptide and substance P, which are potent mediators of vasodilation, have also been detected in the nasal mucosa.[14] Because some of these peptides are contained in the nasolacrimal drainage system,[2] further investigations on the effect of these peptides on the lumen width of the nasolacrimal drainage system are necessary. The ocular surface and nasal mucosa have sensory innervations, and mechanical[15] and sensory[16] stimulation of the nasal mucosa induces aqueous tear production and vasodilatation of the blood vessels in the nasal mucosa.[17] In addition, the sensitivities of the corneal and conjunctival are correlated with tear clearance.[18] These sensory innervations of the ocular surface and nasal mucosa may play a role in changes of the lumen width of the nasolacrimal drainage system. There are thermoreceptors in the nasal mucosa,[19] and stimulation of these receptors induced a vascular response in the nasal mucosa.[17,20] It is also known that the body surface cooling causes a reflex swelling of the nasal mucosa and that body surface heating induces the shrinkage of the nasal mucosa.[21] These observations indicate that there are many factors that can alter the lumen width of the nasolacrimal system.

Whitnall[4] has shown that the nerves to the LS are derived from the infratrochlear branch of the ophthalmic division of the fifth nerve and that the lower part of the NLD receives axons from the anterior superior alveolar branch of the maxillary division of the same nerve. In addition, the contribution of the seventh cranial nerve, through the Nervus intermedius, to the facial autonomic innervation should be considered.[22–25] The parasympathetic preganglionic fibers arise from the lacrimatory nucleus of the facial nerve, run in the Nervus intermedius of the facial nerve, and then travel in the greater petrosal branch of the nerve. The greater petrosal nerve then joins the deep petrosal nerve to form the nerve of the pterygoid canal. The deep petrosal nerve arises from superior cervical sympathetic ganglion through the internal carotid plexus

and passes without interruption through the pterygopalatine ganglion. Although a detailed map of the innervation of the nasolacrimal drainage system has not been determined, these pathways also may supply innervation to the nasolacrimal drainage system.

A limitation of this study was that we assumed that an increase in the lumen width indicated an increase in the area of the lumen. This assumption would be correct if the lumen was circular, but it is known that the shape of the lumen varies and contains numerous folds and ridges. To test this assumption, we photographed the nasolacrimal drainage system from two directions and measured the width at five different points. The fact that the lumen widths that were obtained with anteroposterior images were not significantly different from those obtained from oblique images would suggest strongly that our assumption was correct. However, additional anatomic studies of the nasolacrimal drainage system will be required to determine the exact relationship between the width and area of the lumen.

Amanat and associates[26] reported that 30% of the patients with unilateral epiphora had a physiologic obstruction in the lower part of the NLD of the asymptomatic side by lacrimal scintigraphy, which indicates that the anatomically asymptomatic side may not be completely physiologically normal in our patients. Even though our use of asymptomatic sides may have introduced some bias to our data, we chose not to use healthy volunteers for ethical reasons. We also believe that a cross-over design with the use of phenylephrine and pilocarpine on the same patient would have increased the statistical power of our conclusions; however, repeated x-ray radiation would have to be performed on the same patient.

The average lumen width of the upper orifice of the osseous NLD is 4.6 mm[4]; the lumen width of the membranous NLD is smaller, because the wall of the membranous NLD becomes thicker in this area.[4,8,9] The lumen width of the LS and the NLD that were measured at the five points tended to be slightly smaller than those reported by Malik and associates[27] (2.43 ± 0.95 mm for the LS, and 2.30 ± 0.83 mm for NLD), who also used dacryocystography with a water-soluble agent. This discrepancy may be because they may have exerted excessive pressure on the LS and NLD by direct insertion of a cannula into the LS, or it may simply reflect racial differences.[28]

It is possible that not using a standardized pressure of infusion of the contrast medium through the canaliculus can lead to artificial distention of the nasolacrimal drainage system on dacryocystography measurements. However, we performed dacryocystography under fluoroscopic guidance and stopped the infusion when the contrast medium was detected in the nasal cavity. In addition, after phenylephrine infusion, 98.0% (50/51) of the lumen width at points 3 through 5 in the anteroposterior images and 94.1% (64/68) at points 2 through 5 in the oblique images were significantly larger. Conversely after pilocarpine infusion, 87.5% (42/48) of the lumen width at points 3 through 5 in anteroposterior images and 96.9% (31/32) at points 4 and 5 in the oblique images were reduced significantly. Moreover, the lumen widths of the LS were not changed significantly, except for one point after phenylephrine infusion. These findings, coupled with our statistical analysis that shows that the changes were statistically significant, indicated that the changes were not due to the injection protocol.

Dacryocystography is the most common and useful method to obtain anatomic information of the nasolacrimal drainage system.[29,30] We selected to use dacryocystography because it is readily available and safe and because the results can be obtained quickly and at low cost.[31–34] Other imaging techniques (e.g., lacrimal scintigraphy,[35] computed tomography,[36,37] and magnetic resonance imaging[29,31,32]) have been used to evaluate the nasolacrimal drainage system. Among these, lacrimal scintigraphy is useful in the evaluation of the physiologic condition of the tear flow dynamics[33,35] but gives limited anatomic information.[33] Conventional computed tomography and magnetic resonance imaging are used to analyze the structure of orbit and the paranasal sinus[33]; however, these procedures cannot distinguish the point of nasolacrimal obstructions precisely.[33,36,37] Although computed tomography dacryocystography provides functional information,[38] a small stenosis or obstruction can be missed between slices.[39] Magnetic resonance dacryocystography is a noninvasive procedure that is used for the functional assessment of the nasolacrimal system.[29,31,32] However, it is expensive, with long image acquisition time, frequent image degradation with patient movement,[32,39] and lower spatial resolution.[29] Helical computed tomography dacryocystography[39] and three-dimensional rotational dacryocystography[40] are new methods for the evaluation of the nasolacrimal drainage system in detail; however, these methods have not yet been established as routine tests and are also expensive.[39] Furthermore, because of the sensitivity, it is difficult often to distinguish between anatomic variations and true filling defects.[39]

O'Donnell and Shah[41] recommended dacryocystorhinostomy (DCR) in cases with a "functional" NLD obstruction and obtained highly successful results after DCR, which suggests a necessity of appropriate lacrimal drainage surgery for this abnormality. This suggested that a dysfunction in the tear outflow in cases of functional NLD obstruction may be attributed to an abnormal autonomic control that reduces tear outflow rather than a weakness of the lacrimal pump. In this respect, the topical application of adrenergic agonist may be useful in the treatment of the functional NLD obstruction. Further studies are necessary to determine the relationship between functional NLD obstruction and the reaction of the nasolacrimal drainage system to adrenergic or cholinergic agonists by topical instillation. In addition, an intentional dilation of the NLD by sympathetic stimulation may be beneficial in the

prevention of the false passage formation at the time of nasolacrimal intubation.

François and Neetens[42] suggested that sensitive receptors were present in the wall of the LS. These receptors would then control tear secretion, because lacrimation can decrease in the absence of inflammation of the LS. Moreover, Yen and associates[43] reported that tear secretion decreased after temporary punctal occlusion in normal subjects, which suggests that there are some receptors on the ocular surface, lacrimal outflow tract, or nasal mucosa that are part of a feedback mechanism that controls tear production. The innervations to the lacrimal gland,[44,45] accessory lacrimal gland,[46,47] meibomian gland,[48] and conjunctival goblet cells[49] have been studied extensively; tear production is believed to be regulated by autonomic and sensory nerves. Earlier, tear outflow was believed to be regulated mainly by the lacrimal pump through the canaliculus and LS that accompanies blinking.[50–54] However, our results suggest that tear outflow may also be affected by changes in the lumen width of the NLD. Because tear fluid contains norepinephrine and epinephrine,[55,56] the innervation of the LS and NLD may be involved actively in this feedback system.

Further studies are needed to determine the relationship between the lumen width in the nasolacrimal drainage system and the kinetics of tear outflow. This is important because these findings are related closely to the differential diagnosis of nasolacrimal stenosis/obstruction and dry eye disorders. The critical question of whether a wide or narrow nasolacrimal drainage system is preferable for smooth tear outflow is now underway.

In summary, our data show that an adrenergic agonist increased the lumen width of the nasolacrimal drainage system, especially the lumen width of the NLD, whereas cholinergic agonist reduced its width. These findings indicate that the drainage of tears through the NLD is controlled, in part at least, by the autonomic nervous system.

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Biosketch

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強い硝子体混濁を認めたHuman T-Cell Lymphotropic Virus Type 1関連ぶどう膜炎の1例

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A Case of Human T-Cell Lymphotropic Virus Type 1-Associated Uveitis with Severe Vitreous Opacity

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背景：Human T-cell lymphotropic virus type 1（HTLV-Ⅰ）関連ぶどう膜炎（HAU）はHTLV-Ⅰキャリアに発症するぶどう膜炎で通常，軽度～中等度の硝子体混濁を呈する場合が多いといわれている。今回我々は，片眼性の非常に強い硝子体混濁を認め，網膜の観察が困難であったHAUの1例を経験したので報告する。

症例報告：症例は19歳女性。左眼視力低下。血清中のHTLV-Ⅰ抗体の上昇，前房水のpolymerase chain reaction法におけるHTLV-Ⅰプロウイルス陽性，他のぶどう膜炎の否定によりHAUと診断した。治療として副腎皮質ステロイド薬の全身投与を行ったところ，急速に硝子体混濁は軽快した。

結論：HAUのなかには非常に強い硝子体混濁を示す症例もあり，診断に注意が必要である。

（眼　紀　57：691－694，2006）

キーワード：Human T-Cell Lymphotropic Virus Type 1関連ぶどう膜炎，硝子体混濁，Polymerase Chain Reaction，副腎皮質ステロイド薬治療

Background : Human T-cell lymphotropic virus type 1 (HTLV-Ⅰ)-associated uveitis (HAU) has been reported to occur in HTLV-Ⅰ carriers, and many cases of HAU have mild or moderate vitreous opacity. We report 1 case of HAU in which vitreous opacity was severe. In this case, we could not see the retina well because of vitreous haze.

Case Report : A 19-year-old female complained of loss of vision in her left eye. HAU was diagnosed based on a high serum HTLV-Ⅰ antibody level, detection of HTLV-Ⅰ DNA provirus in the aqueous humor, and lack of evidence for other possible causes for uveitis. Systemic corticosteroid therapy was initiated and vitreous opacity decreased.

Conclusion : It is necessary to consider HAU as a possible cause of severe vitreous opacity.

(Folia Ophthalmol Jpn 57 : 691－694, 2006)

Key Words : Human T-Cell Lymphotropic Virus Type 1 (HTLV-Ⅰ)-Associated Uveitis, Vitreous Opacity, Polymerase Chain Reaction, Steroid Therapy

緒　　言

Human T-cell lymphotropic virus type 1関連ぶどう膜炎（以下HAU）は全身疾患を有さない成人T細胞白血病ウイルス1型（human T-cell lymphotropic virus type 1 以下HTLV-Ⅰ）無症候キャリアに発症するぶどう膜炎と定義されている。日本での感染率は地域性があり，南九州，沖縄で比較的高いと報告されている[1,2]。臨床所見として多くが中間部にぶどう膜炎を呈し，硝子体混濁は軽度～中等度であることが大多数であり，非常に強い硝子体混濁を示した症例の報告は少ない[3]。今回我々は，急激な硝子体混濁のため，診断に苦慮した片眼性のHAUを経験したので報告する。

症　　例

症　例：19歳，女性。

主　訴：左眼視力低下と霧視。

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既往歴：特記すべきことなし。

家族歴：母親，姉2人がHTLV-Ⅰキャリア。

出身地：愛媛県。

現病歴：2002年7月25日より急激な左眼視力低下を自覚し，近医眼科を受診した。同時に微熱も出現していた。ぶどう膜炎の診断にて0.1%リン酸ベタメタゾン点眼を1日4回投与されるが症状は軽快せず，8月2日，精査目的にて愛媛大学医学部附属病院眼科を紹介され受診した。

初診時所見：矯正視力は右眼1.0，左眼光覚弁であった。眼圧は右13mmHg，左23mmHgであった。左眼前眼部において，多数の角膜後面沈着物，前房内炎症性細胞を認め，虹彩後癒着も全周に観察された。硝子体混濁は非常に強く，とくに鼻側下方に乳頭径大の塊状の混濁を多数認めた（図1）。網膜は硝子体混濁のため詳細な観察はできなかった。超音波Bモード検査では硝子体腔に強い膜様の反射を認め，高周波超音波生体顕微鏡（ultrasound biomicroscopy以下UBM）では毛様体の浮腫を観察できた（図2）。フルオレセイン蛍光眼底造影（以下FA）では，初期像より乳頭および乳頭周囲の強い漏出と，静脈の軽度怒張・拡大を示し（図3），インドシアニングリーン蛍光眼底造影（以下IA）では，初期像で脈絡膜血管の透過性亢進を示す過蛍光が認められた（図4）。右眼は前房，眼底ともにとくに異常を認めなかった。

全身検査所見：血液・生化学検査に著変を認めず，単純ヘルペスウイルス（以下HSV），帯状ヘルペスウイルス（以下VZV），サイトメガロウイルスの血清抗体価の上昇はみられなかった。Human leukocyte antigen（HLA）typingはA11，A24（9），B51（5），B62（15），Cw4，DR4であった。また，ツベルクリン反応は陰性で，胸部X線撮影では両側肺門リンパ節腫脹などの異常は認めなかった。

経　過：初診当日入院となった。母親がHTLV-ⅠキャリアであったことからHAUを最も疑ったが，患者は健康な青年者であり，また片眼性であることからヘルペスウイルスによる急性網膜壊死も否定できないと考え，8月2日より

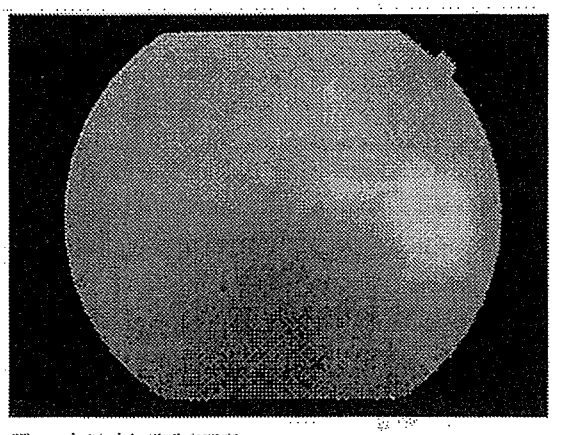

図1　初診時左眼眼底写真
強い硝子体混濁があり，とくに鼻側下方に乳頭径大の塊状の混濁を多数認めた。

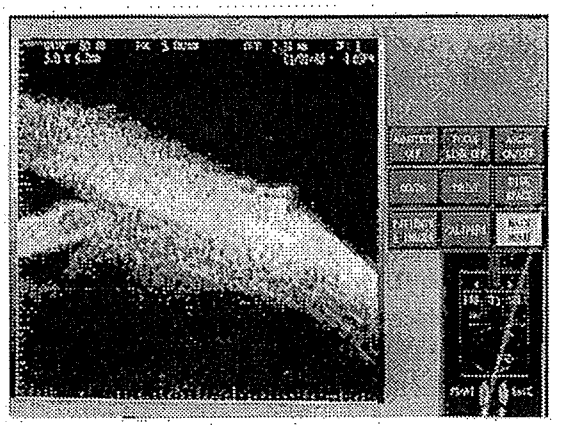

図2　初診時左眼高周波超音波生体顕微鏡所見
毛様体の浮腫を認めた。

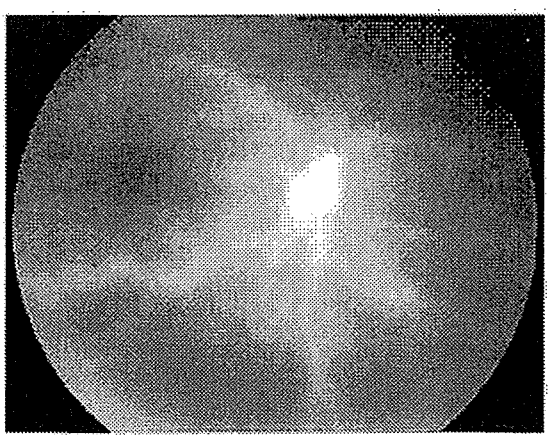

図3　左眼フルオレセイン蛍光眼底造影所見
造影1分11秒後。乳頭および乳頭周囲の強い漏出と，静脈の軽度怒張，拡大を認めた。

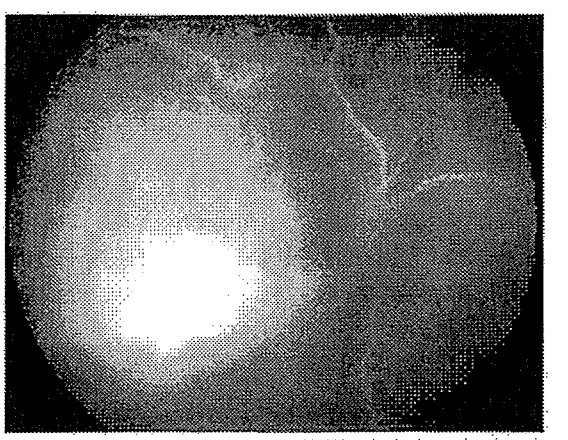

図4　左眼インドシアニングリーン蛍光眼底造影所見
造影1分19秒後。脈絡膜血管の過蛍光を認めた。

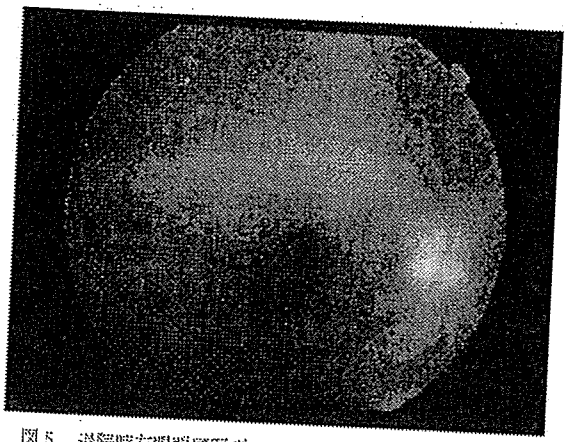

図5　退院時左眼眼底写真
硝子体混濁は下方に一部遷延したが，ほぼ消失した。

アシクロビル1,500mgの点滴，ソルメドロール250mgの点滴，0.1%リン酸ベタメタゾンの点眼で治療を開始した。血清抗HTLV-Ⅰ抗体価をparticle agglutination法（セロディア® HTLV-Ⅰ使用）にて測定したところ，8,192倍以上を示したため，100倍希釈血清を用いて400倍から定量した結果，51,200倍となった。Polymerase chain reaction（以下PCR）法にて前房水中にHTLV-Ⅰプロウイルス DNAを検出したことに加えて，血液検査，全身検索および前房水におけるHSV，VZVのDNAが陰性という結果より，他のぶどう膜炎を除外できたためHAUと診断し，急性網膜壊死は否定的と考え，アシクロビル点滴を中止した。その後副腎皮質ステロイド薬（以下ステロイド）の全身投与を漸減したところ，硝子体混濁は徐々に軽快した。治療開始後16日目には，左眼眼底下方に硝子体混濁が遷延するものの，視力も左眼矯正1.2と向上し，血清抗HTLV-Ⅰ抗体価も25,600倍と1管のみ低下した。その後も経過良好につき8月20日，退院となった（図5）。以後，外来通院にてステロイドを漸減し中止したが，再発は認められなかった。

考　　察

HTLV-Ⅰ関連ぶどう膜炎は，HTLV-Ⅰキャリアに発症するぶどう膜炎で，キャリアの約1,000人に1～2人発症するといわれている[3]。病態としては，HTLV-Ⅰ感染T細胞がサイトカインを過剰に分泌し[4]，炎症を引き起こすと考えられており，HTLV-Ⅰにより生じ異型リンパ球の浸潤を主徴とする成人T細胞白血病とは異なる病態を示している。特徴的な臨床所見としては，ベール状，数珠状の混濁を示す中等度の硝子体混濁が認められ，ときに網膜眼底には血管に沿って小さな白色顆粒状の混濁を示す場合もある[5]，本症例では初診時，すでに眼底が透見不能なほどの非常に強い硝子体混濁を示していたため，ベール状，数珠状の混濁や血管に沿う小さな顆粒状の混濁などの，HAUに特徴的な所見は詳細には観察できず，臨床所見のみでの診断は困難であった。また，患者は愛媛県南部の出身で，母親がHTLV-Ⅰキャリアであったことから，初診時よりHAUも考慮したが，片眼性の非常に強い硝子体混濁が主体であるため，転移性眼内炎，急性網膜壊死などの可能性について完全に除外することができなかった。そのため，少しでも原因ウイルスとしての可能性が高いと考えられるHTLV-Ⅰ，ヘルペスウイルス群の前房水のPCR法による検出を試みた。しかしながら，進行が急であったため，初診時に行った血液検査や，HTLV-Ⅰ，ヘルペスウイルス群の前房水のPCR法の結果を待つことなく，鑑別すべき疾患のなかで最も重症と思われる急性網膜壊死の治療を最優先した。

経過中に得られた検査結果として，HTLV-Ⅰ抗体価が51,200倍と高値で，PCR法にてHTLV-Ⅰプロウイルス DNAが前房水より検出されたこと，また各種ヘルペス属DNAは陰性であったことから，HAUを強く疑いアシクロビルの全身投与を中止し，ステロイドによる治療を続行した。HAUは，特徴のある硝子体混濁，HTLV-Ⅰキャリアの確認，他のぶどう膜炎の否定により診断が可能であるとされているが，本症例では，非常に強い硝子体混濁のため，初診時の診断は容易ではなかったと考える。

今回の患者の出身地である四国地方南部では，九州地方と同様，HTLV-Ⅰキャリアが比較的多い[6]。本症例では患者自身がキャリアであるかどうかを自覚していなかったが，母親がキャリアであったことが診断を進める上で大きな参考となった。HTLV-Ⅰは母乳感染により15～20%が垂直感染するといわれている[3]。そのため，本人がキャリアであることを確認できなくても，母親がキャリアである場合は本疾患を疑い，血清抗体価や前房水のPCR法を施行するのが望ましいと思われる。

本症例が片眼性の非常に強い硝子体混濁を示した原因は明らかではない。本症例では，全身検索においては眼以外の場所には異常を検出できなかったことから，炎症の主座は左眼にあった可能性が高いと思われるが，片眼のみ強い炎症が出たという病態については，今後の検討が必要である。HAUの場合，甲状腺機能異常を合併する場合が多いとされている[7,8]が，本症例ではthyroid-stimulating hormone，thyrotropin-releasing hormoneなどは正常値であり，エコー検査においても異常は認めなかった。同様に神経系など合併すると思われる器官の異常も認めなかった。

本症例のIA検査においては，脈絡膜血管の拡張が認められた。渡邊らは，HAUの蛍光眼底造影検査所見として，FAとIAでみられる過蛍光の部位が一致し，FAでみられる過蛍光の一部は脈絡膜～網膜にかけての炎症の波及をあらわしていることを報告しており[9]，本症例においても同様の結果が得られた。

なお，初診時のUBM所見において毛様体浮腫，脈絡膜下腔を認めた点が注目される。HAUのUBM所見について