earlier study demonstrated that injections of a highly hyperosmotic solution into the vitreous rapidly caused retinal detachment and disruption of RPE apical morphology in a sequence of changes similar to (but more rapid than) the ones described herein. The solutions injected into blebs during the present experiments were essentially isoosmotic with tissue fluids, but other abnormalities of the extracellular milieu might be present.

Our method for producing non-rhegmatogenous retinal detachments in rabbit is relatively gentle insofar as morphological criteria are concerned. Comparison of our SEMs of the apical surface to published transmission electron micrographs of attached RPE-retina shows that delicate apical processes and cone sheaths survive our procedure intact, and are visible immediately following detachment. Nonetheless, the halo region was obviously highly disturbed and we think it represents the point at which the RPE was still adherent to the inflating retina. Since the retina over the bleb was necessarily stretched, there must have been considerable force acting to stretch adherent RPE processes in the halo region, thus accounting for their orientation and appearance.

Key words: RPE, apical morphology, retinal detachment

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Comparative Aqueous Outflow Facility Measurements by Pneumatonography and Schiotz Tonography

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Tonography was performed on 36 eyes of 15 normal and 3 primary open angle glaucoma patients using pneumatonography and classical Schiotz tonography. The average values of the coefficient of outflow facility (C) for the whole sample were virtually identical with both methods. However, both intersubject and interobserver variability were significantly higher with pneumatonography. Although both methods provide comparable aggregate estimates of aqueous outflow facility, we think that Schiotz tonography is more reliable than pneumatonography because of the greater mechanical stability of the Schiotz instrument on the eye. On the other hand, pneumatonography offers the advantage of a shorter test period (2 min instead of 4). Invest Ophthalmol Vis Sci 27:1776–1780, 1986

Measuring aqueous outflow facility (C) tonographically has wide applications in clinical glaucoma research. However, because tonography involves some inherent sources of error, some technical limitations and subjective approximations in estimating the C value, and because the test is usually not necessary for the management of individual glaucoma patients, it has been largely abandoned in clinical practice.
Since their introduction by Langham and co-workers, pneumatonometry and especially pneumatonography have been subject to controversy in the ophthalmic literature. While Langham considers that application of the pneumatic tonometer to the measurement of outflow facility has theoretical and practical advantages over conventional Schiotz indentation tonography, Moses and Grodzki concluded that the instrument is position and force sensitive, that it underestimates the magnitude of a change in intraocular pressure, and that it is not well suited for tonography.

In this study, we compare measurement of the C value and variability in interpreting tracings obtained by each method.

**Materials and Methods. Subjects:** Fifteen normal volunteers, aged 24 to 30 years, and three glaucoma patients, aged 42 to 67 years, were studied. All subjects were white; 11 were male and 7 female. Subjects were included in the study after written informed consent was obtained and a complete eye examination performed. The following conditions disqualified patients from entering the study: intraocular pressure higher than 22 mmHg, poor fixation in either eye, nystagmus, tropias, phorias, contact lens wear, recent eye surface infection, and corneal scarring or irregularities that prevent reliable tonometry.

**Tonography:** All subjects underwent tonography using an electronic Schiotz tonograph (V-Mueller and Co., Chicago, IL) on one eye, and a pneumatonograph (Alcon, Ft. Worth, TX) on the other eye. Three days to 1 week later, at the same hour of day, tonography was repeated with crossover use of the testing instruments. The initial method of testing on each eye was randomly chosen. In the meantime, no modification was made in the medical therapy of the glaucoma patients, which consisted of timolol 0.5% eye drops applied to each eye every 12 hours. All the test procedures were performed by one of us (Dr. Feghali, a tonographer having more than 2 years of intensive experience with both techniques), in a cool, quiet room, with the patient in the supine position. A dim red light placed at 6 feet from the patient’s eyes was used for fixation. Before each measurement, the instruments were calibrated according to the manufacturer’s instructions, the test procedure explained to the patient, and the importance of fixation stressed. Baseline intraocular pressure was determined for each eye using initial pressure (P0) determination tables for Schiotz tonography, and by taking the mean level of the recorded pulse wave in the supine position for pneumatonography. Four min tracings were then obtained with the Schiotz tonograph, and 2 min tracings with the pneumatonograph, to which probe a 10 g weight was added.

**Statistical analysis:** The tonography tracings were randomly and separately presented to one of us (Dr. Azar) and to four other assistants, each of whom was asked to draw a best fitting line along each curve and to determine the initial and final readings on the scale. Tracings which two or more observers found difficult to fit with a line because of multiple irregularities, and those which failed to display ocular pulsations over more than one quarter of their total span, were considered technically unsatisfactory and the corresponding eyes excluded from the analysis. Thirteen tracings out of 72 (18%) were considered technically unsatisfactory (8 pneumatonograms and 5 Schiotz tonograms), causing exclusion of 11 eyes and 2 patients (both with normal eyes), as well as 9 satisfactory tonograms in the 11 excluded eyes. If two satisfactory tracings were obtained from only one eye of an individual, only data from that eye were analyzed; if both tracings from both eyes were satisfactory, data from the two eyes were averaged for each tonographic method, and the averages used in the analysis. The comparison of the techniques is thus based on 25 eyes of 16 patients, with each patient contributing one value for each technique and constituting a single statistical unit. Determination of outflow facility from the tracings was done using Schiotz and pneumatonography tables, with no additional correction for scleral rigidity. Analysis of the first 2 min of the Schiotz tonography tracings, for comparison with the 2 min pneumatonography, data was not attempted. Analyses of such abbreviated Schiotz tracings are fraught with a variety of uncertainties and were abandoned by investigators years ago (personal communication with Dr. Robert Moses), so that 4 min Schiotz tonography remains the accepted standard.

For each individual subject, the C values determined from the pneumatonography tracing by each of the five observers (CiP) were averaged to give a mean C and standard deviation for that individual subject with that technique (CiP ± SDiP). The individual means (CiP) were averaged to give a mean C and standard deviation for the entire group of subjects (n = 16) with that technique (C± SDp). The individual standard deviations (SDiP) were averaged to give a mean standard deviation for the entire group of subjects with that technique (SDp). The same calculations were done for the C values obtained from the Schiotz tonography tracings, generating C1S, C± SD1S, C± SD2S, and SD1S. These parameters permitted statistical comparison of mean facility, intersubject variability and interobserver variability with the two techniques, using t- or F-tests, as described below.

**Results.** Mean outflow facility for the entire group of 16 subjects was similar with the two techniques. For
pneumatonography, $C_{2P} \pm SD_{2P} = 0.242 \pm 0.114 \mu l \times min^{-1} \times mmHg^{-1}$; for Schiotz tonography $C_{2S} \pm SD_{2S} = 0.220 \pm 0.070 \mu l \times min^{-1} \times mmHg^{-1}$. Paired t-test comparison confirmed the absence of any statistically significant difference between these values. However, intersubject variability was greater with pneumatonography, as evidenced by the larger standard deviation. This difference in intersubject variability was statistically significant by the F-test of the variance ratio $[SD_{2P}^2/(SD_{2S})^2 = 2.652; P < 0.05]$. In Figure 1, the mean facilities for each individual subject obtained by pneumatonography and Schiotz tonography ($C_{1P}, C_{1S}$) are plotted against one another. While the correlation is statistically highly significant ($r = 0.635; P < 0.001$), it is far from complete. Indeed, only 40% ($r^2 = 0.403$) of the intersubject variation about the mean pneumatonographic facility ($C_{2P}$) is accounted for by the intersubject variation about the mean Schiotz tonographic facility ($C_{2S}$). Note also the greater scatter of the data along the y (pneumatonography) axis, despite the similarity of the mean facilities.

The standard deviation of the five readings obtained...
for each subject by each technique (SD_{IP}, SD_{IS}) gave an average standard deviation (SD_{IP}, SD_{IS}), reflecting interobserver variability in reading the tracings generated by each technique. For pneumatonography, SD_{IP} = 0.048 \mu l \times \text{min}^{-1} \times \text{mmHg}^{-1}; for Schiotz tonography, SD_{IS} = 0.022 \mu l \times \text{min}^{-1} \times \text{mmHg}^{-1}. Analysis of variance confirmed significantly greater interobserver variability with pneumatonography (F = 2.182, P < 0.01). In Figure 2, the standard deviations for each individual subject (SD_{IP}, SD_{IS}) are plotted against one another; there is virtually no correlation (r = 0.026), and the greater scatter along the y (pneumatonography) axis is apparent.

Discussion. The 13 tonograms which were considered technically unsatisfactory could not be fitted with a proper line because of multiple irregularities in the tracings. These disorderly recordings were often due to involuntary squeezing of the patient’s eyelids, sudden blinking movements, or temporary shift of the contralateral eye from the fixation target. Less frequently, they were caused by fine movements of the examiner’s hand or arm. The relatively high frequency (18%) of unsatisfactory tracings could be partly attributed to the young age of the study population. Young patients are usually more tense during an eye examination, and have more brisk blinking reflexes than older individuals.

The average C values obtained by both methods were not statistically different. However, both intersubject and interobserver variability were significantly higher for pneumatonography. We attribute this wider scatter to a greater mobility of the pneumatonography probe tip on the corneal surface, and more transmission of eye and hand movements to the transducer. Unlike the tip of the Schiotz instrument which is concave, has an external diameter of 10.0 mm and rests steadily on the cornea, that of the pneumatonograph is flat, has a 5.3 mm. external diameter, and can slide on the corneal surface (Figs. 3-4). Furthermore, the presence of a guide ring (Fig. 3) with an internal diameter of 11.5 mm around the Schiotz tonograph probe leaves a free space on the sides preventing transmission to the probe of fine horizontal movements of the patient’s eye or examiner’s hand. In the case of the pneumatonograph, which lacks such a ring and has greater mobility on the cornea, more hand and eye movements are trans-
Inhibition of Lens Opacification in X-Irradiated Rats Treated With WR-77913

Thomas D. Osgood,* Thomas W. Menard,† John I. Clark,‡ and Kenneth A. Krohn§

Radiation induced cataracts are models for studying mechanisms of lens opacification. WR-77913, S-3-(amino-2-hydroxypropyl) phosphorothioate (NCS-318809), has been identified as a radioprotective agent. Injection of WR-77913 (1160 mg/kg, i.p.) 15 to 30 min before exposure to 15.3 gray of x-irradiation inhibited rat lenses from developing radiation cataracts. X-Irradiated rats which did not receive the drug developed dense cataracts. Lenses from control rats which received no radiation remained transparent. Individual lenses for over 40% of the lens weight in control and drug-treated rats. Proteins below 25K daltons accounted for over 25% of the soluble protein in control and drug-treated cataractous lenses. Inhibition of protein ranged from 12 to 17% of the total lens weight for each group. The ratio of insoluble to soluble lens protein was 0.40 for control, 0.65 for drug-treated, and 11.28 for cataractous rat lenses. HPLC confirmed a dramatic loss of soluble protein and a complete absence of protein below 25K daltons from developing radiation cataracts. Irradiated rats which did not receive the drug developed dense cataracts. Lenses from control rats which received no radiation remained transparent. Individual lenses were weighed, homogenized, and assayed for protein content using the Lowry method. The molecular weight distribution of soluble protein was determined by HPLC. Mean lens weights were: controls 48.2 mg; irradiated, drug-treated 45.9 mg; and irradiated, nontreated 45.5 mg. Protein accounted for 40% of the lens weight in control and drug-treated rats and less than 20% for the nontreated cataractous lenses. Water was less than 60% of the lens weight in control and drug-treated rats and over 80% in cataractous lenses. Insoluble protein ranged from 12 to 17% of the total lens weight for each group. 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The results of this study were obtained within the normal intraocular pressure range (<22 mmHg); their applicability at higher pressures remains to be determined.

Key words: aqueous humor, tonography, pneumatonography, Schiotz tonography, aqueous outflow facility

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