

# Aqueous Humor Dynamics During the Day and Night in Healthy Mature Volunteers

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**Objectives:** To investigate the daytime vs nighttime differences in intraocular pressure (IOP), aqueous humor dynamics, central cornea thickness, and blood pressure among a cohort of healthy volunteers.

**Methods:** Thirty healthy volunteers (mean [SD] age, 57.0 [8.6] years) were enrolled in the study. Individuals underwent 1 daytime visit and 1 nighttime visit for the measurement of aqueous humor dynamics. Measurements included IOP by pneumatonometry, aqueous flow by fluorophotometry, outflow facility by fluorophotometry and tonography, uveoscleral outflow by mathematical calculation, central cornea thickness by pachymetry, and blood pressure by sphygmomanometry. Results between visits were compared by appropriate *t* test. Dependence of the pneumatonometer probe results on position was tested in enucleated rabbit eyes at set pressures and probe positions.

**Results:** Compared with daytime seated IOP, nighttime seated IOP was reduced by 16%, whereas nighttime supine IOP was increased by 17% ( $P < .001$  for both).

The IOP changes were independent of the pneumatonometer probe position. Central cornea thickness was increased at nighttime from a mean (SD) of 560 (37)  $\mu\text{m}$  to a mean (SD) of 574 (37)  $\mu\text{m}$  ( $P < .001$ ). Compared with daytime aqueous flow, nighttime aqueous flow was reduced by 49% ( $P < .001$ ). During the night, fluorophotometric outflow facility was reduced by 45% ( $P = .05$ ), and tonographic outflow facility was reduced by 17% ( $P < .01$ ). Uveoscleral outflow at night was decreased when calculated using tonographic outflow facility but not fluorophotometric outflow facility in the Goldmann equation. All other measurements were unchanged.

**Conclusions:** Significant changes in aqueous humor dynamics at night in healthy mature humans include reductions in aqueous flow, outflow facility, and possibly uveoscleral outflow. Nocturnal changes in IOP are independent of the pneumatonometer probe position and are dependent on an individual's posture during the measurement.

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**I**NTRAOCULAR PRESSURE (IOP) IS a dynamic variable that follows a circadian rhythm. Daily variation in IOP is likely a consequence of changes in aqueous humor dynamics during the same interval. It is generally agreed that aqueous humor flow decreases at night and increases during the day.<sup>1-4</sup> If this were the only change in aqueous humor dynamics at night, nocturnal IOP would be expected to be lower than daytime IOP. There remains some disagreement as to whether IOP decreases<sup>5-10</sup> or increases<sup>11-13</sup> at night. Nocturnal changes in IOP may involve a complex interplay of postural changes and changes in aqueous humor outflow (uveoscleral outflow or trabecular outflow facility) and aqueous humor inflow. In young healthy volunteers, outflow facility at night was decreased significantly in one study<sup>14</sup> but

insignificantly in another study.<sup>15</sup> Few data exist about nocturnal changes in aqueous humor dynamics among healthy mature humans in the age range that is primarily at risk for developing ocular hypertension and primary open-angle glaucoma. Insight into the normal physiological patterns of 24-hour aqueous humor dynamics can help to identify pathologic changes associated with glaucoma and potentially to determine the optimal time to administer IOP-lowering medications to achieve the best effect.

The objectives of this study were to investigate daytime vs nighttime differences in IOP, aqueous humor dynamics, central cornea thickness (CCT), and blood pressure among a cohort of healthy volunteers. In a subsequent study, patients with ocular hypertension will be compared against this patient group.

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**Table 1. Study Schedule and Procedures<sup>a</sup>**

Procedure	Daytime Visit at Days 0-1	Nighttime Visit at Days 3-4
Fluorescein sodium, 2%, instillation	6-8 Drops between 10 PM and 4 AM	3-4 Drops starting at 5 PM
Pachymetry	9 AM	2 AM
Tonometry		
Seated	9 AM to 2 PM at 45- to 60-min intervals	10 PM to 5 AM at 60- to 120-min intervals
Supine	2 PM	10 PM to 5 AM at 60- to 120-min intervals
Fluorophotometry		
Aqueous flow and outflow facility measurement	9 AM to 2 PM at 45- to 60-min intervals	10 PM to 5 AM at 60- to 120-min intervals
Seated sphygmomanometry	11:30 AM	2 AM
Tonography	3 PM	5 AM

<sup>a</sup>Times are approximate.

## METHODS

### STUDY DESIGN

This single-center study of 30 healthy mature volunteers was compliant with the Health Insurance Portability and Accountability Act and was approved by the University of Nebraska Medical Center Institutional Review Board. Informed consent was obtained before enrollment in the study. After a screening visit to determine eligibility, participants were scheduled for 2 study visits, 1 daytime visit (day 1) and 1 nighttime visit (day 3). The schedule of procedures performed at these 2 visits is summarized in **Table 1**.

At the screening visit, a medical and ocular history was obtained, and a complete ophthalmic examination, including slit-lamp biomicroscopy, gonioscopy, and dilated fundus evaluation, was performed. Inclusion criteria were no ocular pathologic condition other than minor refractive errors, with a spherical equivalent less than 3 diopter and baseline IOPs between 12 and 20 mm Hg. Exclusion criteria were an anterior chamber angle not exceeding Becker-Shaffer grade 2<sup>16</sup> in any part on gonioscopy, previous ocular surgical procedures, recent (within 3 months) ocular infection, and any history precluding the use of timolol maleate or acetazolamide. Using Goldmann applanation tonometry, IOP was measured 2 to 3 times in each eye and averaged.

Between 10 PM and 4 AM before the daytime visit, patients instilled 1 drop (approximately 20  $\mu$ L) of fluorescein sodium, 2%, in each eye at 5-minute intervals for a total of 6 to 8 drops. On the morning of the daytime visit, CCT and anterior chamber depth were measured by ultrasonographic pachymetry and A-Scan (Pacscan Series 300; Sonomed, Inc, Lake Success, New York), respectively. From these measurements, anterior chamber volume was calculated for each eye,<sup>17</sup> and this value was used in the determination of daytime and nighttime aqueous flow. The IOP was measured using a pneumatonometer (Classic Model 30; Reichert, Inc, Depew, New York). Four sets of duplicate fluorophotometric scans of the cornea and anterior chamber were collected using an ocular fluorophotometer (Fluorotron Master; OcuMetrics, Palo Alto, California). These values were used to calculate baseline aqueous flow (described in detail elsewhere<sup>18</sup>). Episcleral venous pressure ( $P_{ev}$ ) was measured using an episcleral venomanometer (Eyeteck, Morton Grove, Illinois)<sup>19</sup> during the morning of the daytime visit (Table 1). Two measurements were obtained per eye and averaged. Except for tonography and associated tonometry, all measurements during the daytime visit were obtained with the individual in the seated position.

After the fourth set of images, at approximately 11:30 AM, patients received 1 drop of dorzolamide hydrochloride, 2%, in each eye and oral acetazolamide (two 250-mg tablets). Be-

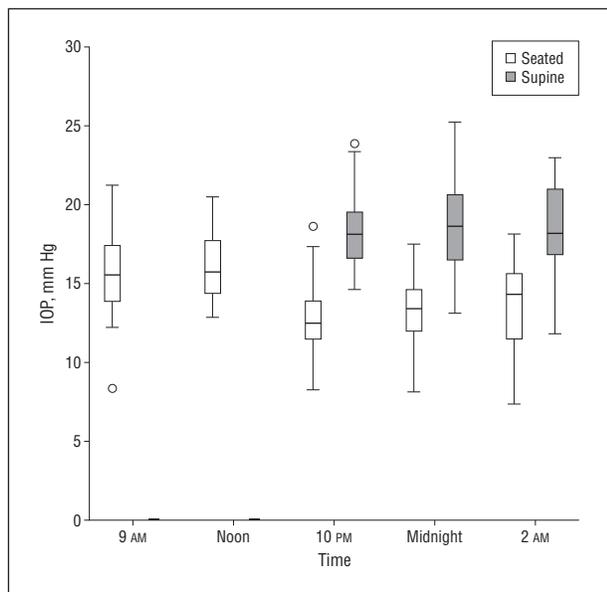
cause carbonic anhydrase inhibitors (CAIs) have been shown to decrease IOP by reducing aqueous flow<sup>20-27</sup> without affecting any outflow variables,<sup>28,29</sup> CAIs were used to facilitate calculation of fluorophotometric outflow facility ( $C_{fl}$ ). The IOPs were measured every 45 to 60 minutes during the day (2 times before and 3 times after administration of CAIs) and every 60 to 120 minutes at night (3 times before and 3 times after administration of CAIs). The  $C_{fl}$  was calculated as the ratio of the change in aqueous flow to the change in IOP induced by the aqueous flow suppressants.

Fluorophotometric outflow facility was calculated at each of 3 intervals after dorzolamide or acetazolamide administration using the following formula:  $C_{flx} = (F_a - F_{ax}) / (IOP - IOP_x)$ , where  $x$  indicates the interval and  $F_a$  indicates aqueous flow. Seated IOPs were used in the Goldmann equation for calculation of daytime  $C_{flx}$ . Supine IOPs were used in the Goldmann equation for calculation of nighttime  $C_{flx}$ . The reported  $C_{fl}$  is the mean of  $C_{fl1}$ ,  $C_{fl2}$ , and  $C_{fl3}$ .

Uveoscleral outflow was calculated using the following formula:  $F_u = F_a - C(IOP - P_{ev})$ , where  $F_u$  indicates uveoscleral outflow,  $C$  was fluorophotometric ( $C_{fl}$ ) or tonographic ( $C_{ton}$ ) outflow facility, and IOP was obtained in the seated or supine position. Because of the difficulty in accurately measuring  $P_{ev}$ , several different values were used in the equation to estimate uveoscleral outflow. These values are based on 2 previous studies<sup>30,31</sup> reporting diurnal and postural variations of  $P_{ev}$ . Nighttime  $P_{ev}$  with the volunteer in the seated position was 2 mm Hg lower than the daytime seated value, and nighttime  $P_{ev}$  with the volunteer in the supine position was 1.5 mm Hg higher than the daytime seated value. Daytime  $P_{ev}$  with the volunteer in the supine position was 1 mm Hg higher than the daytime seated value. Seated systolic and diastolic blood pressures were measured by sphygmomanometry at approximately 11 AM.

At the end of the study visit, supine IOP was measured, followed by 2-minute tonography using the tonography setting on the pneumatonometer. Data were imported into a spreadsheet (Excel; Microsoft, Redmond, Washington), and a regression line of all points was generated. Tonographic outflow facility was calculated using the same formulas as in the tonometer software except that  $IOP_0$  and  $IOP_2$  were the values that fell on the regression line at 0 and 2 minutes, respectively.

Two days later (on the day of the nighttime visit) at 5 PM, 1 drop of proparacaine hydrochloride was instilled in each eye, followed by 3 to 4 drops of fluorescein, 2%, in each eye. Nighttime measurements were obtained in a hospital-based private hotel room. Fluorophotometric scans and IOP measurements were obtained throughout the night at the times listed in Table 1. The IOPs were measured in dim lighting with the volunteer in the supine position, followed by the seated position. Volunteers were instructed to return to sleep between readings. Blood pressure and CCT were measured at 2 AM. Dorzolamide, 2%,



**Figure 1.** Boxplot of the mean seated daytime intraocular pressure (IOP) and the mean seated and habitual (supine) nighttime IOPs in healthy participants ( $n=30$ ). Seated IOPs in the morning were higher than seated IOPs at night but were lower than supine IOPs at night. Seated IOPs at night were lower than supine IOPs at night ( $P<.001$ , analysis of variance). The open circles are outliers.

and acetazolamide (two 250-mg tablets) were administered immediately after the 2 AM IOP measurement. If aqueous flow and IOP did not decrease after drug treatment,  $C_{fl}$  was not calculated. The last measurement was 2-minute tonography at 5 AM.

### STATISTICAL ANALYSIS

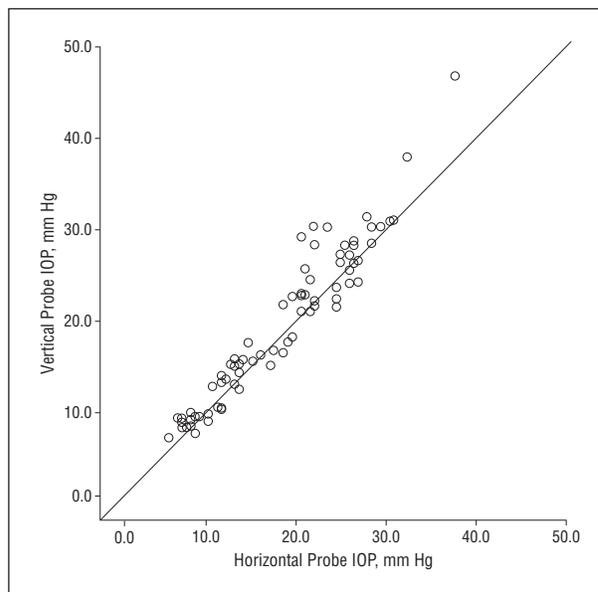
The mean values of aqueous humor dynamics for the 2 eyes were used for analysis. If measurements could be obtained for 1 eye only, that eye was used for analysis. Measurements were compared between daytime and nighttime visits using a 2-tailed paired  $t$  test and analysis of variance.  $P\leq.05$  was considered statistically significant. Unless otherwise indicated, values are reported as the mean (SD).

### DEMOGRAPHICS

Thirty individuals (5 Hispanic, 1 Asian, and 24 white) were enrolled in the study, including 10 men and 20 women. They ranged in age from 37 to 74 years, with a mean age of 57.0 (8.6) years.

### PNEUMATOMETER PROBE POSITION TEST

Nineteen enucleated rabbit eyes were used to evaluate potential variations in IOP from different probe positions. A 25-gauge needle was inserted into the anterior chamber and connected via tubing to a reservoir filled with balanced salt solution to adjust IOP (10, 20, 30, and 40 mm Hg) and to a pressure transducer (Honeywell Sensing and Control, Golden Valley, Minnesota) to continuously monitor IOP. The pressure transducer was linked to computer-running software (PowerLab; ADInstruments, Colorado Springs, Colorado). The eyes were rotated about the horizontal axis without disturbing the needle or changing the zero-pressure reference point. The IOP measurements were obtained with the pneumatonometer probe in horizontal and vertical positions in random order. Three measurements were obtained at each set pressure and probe posi-



**Figure 2.** Scatterplot showing the distribution of intraocular pressure (IOP) measured with the pneumatonometer probe in the horizontal vs vertical position at identical manometrically controlled IOPs in enucleated rabbit eyes.

tion. Intraclass correlation coefficients were used to compare the readings obtained with the 2 pneumatonometer probe positions.

## RESULTS

Thirty participants (59 of 60 eyes) were eligible for and completed the study. Screening IOPs averaged 16.6 (2.3) mm Hg.

Compared with the mean daytime seated IOP (mean of IOPs at 9 AM and 11:30 AM, 15.8 [2.4] mm Hg), the mean nighttime seated IOP (mean of IOPs at 10 PM, midnight, and 2 AM, 13.2 [2.5] mm Hg) was reduced by 16%, but the mean nighttime supine IOP (habitual position, 18.5 [2.7] mm Hg) was increased by 17% (**Figure 1**). The mean supine IOP was 5.2 (1.7) mm Hg higher than the mean seated IOP at night. Each of 3 IOP data sets (daytime, nighttime seated, and nighttime supine) differed significantly from each other using analysis of variance ( $P<.001$ ) and Bonferroni post hoc test.

In the rabbit pneumatonometry study, the position of the pneumatonometer probe did not affect IOP measurements. When plotting data from the probe placed in the horizontal position vs the vertical position, the intraclass correlation coefficient was 0.98, indicating good consistency of measurements, despite a change in the orientation of the probe (**Figure 2**).

The mean CCT was significantly greater at 2 AM (574 [37]  $\mu\text{m}$ ) than at 9 AM (560 [37]  $\mu\text{m}$ ) ( $P<.001$ ). There was no significant difference in the mean seated systolic blood pressures (129 [18] mm Hg for daytime vs 129 [17] mm Hg for nighttime,  $P=.91$ ) or the mean seated diastolic blood pressures (81 [12] mm Hg for daytime vs 79 [11] mm Hg for nighttime,  $P=.17$ ) between daytime and nighttime visits.

Aqueous flow was significantly reduced from a mean of 2.05 (0.87)  $\mu\text{L}/\text{min}$  during the day to a mean of 1.04

**Table 2. Aqueous Flow and Outflow Facility Measurement During the Daytime and Nighttime**

Measurements	No. of Volunteers	Mean (SD)		P Value <sup>a</sup>
		Daytime	Nighttime	
Aqueous flow, $\mu\text{L}/\text{min}$	30	2.05 (0.87)	1.04 (0.42)	<.001
Outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$				
Fluorophotometric	17	0.29 (0.12)	0.16 (0.14)	.05
Tonographic	30	0.23 (0.05)	0.19 (0.08)	.009

<sup>a</sup>Daytime vs nighttime, 2-tailed paired *t* test.

**Table 3. Uveoscleral Outflow Calculation**

Daytime			Nighttime			P Value <sup>a</sup>
Time and Posture	No. of Volunteers	Uveoscleral Outflow, Mean (SD), $\mu\text{L}/\text{min}$	Time and Posture	No. of Volunteers	Uveoscleral Outflow, Mean (SD), $\mu\text{L}/\text{min}$	
<b>IOP and Fluorophotometric Outflow Facility<sup>b</sup></b>						
11:30 AM seated	30	0.29 (0.89)	2:00 AM seated	17	0.06 (0.27)	.59
11:30 AM seated	30	0.29 (0.89)	2:00 AM supine	17	-0.41 (1.62)	.06
<b>IOP and Tonographic Outflow Facility<sup>b</sup></b>						
3 PM seated	30	1.38 (1.06)	5:00 AM seated	30	0.07 (0.74)	<.001
3 PM supine	30	0.52 (1.03)	5:00 AM supine	30	-0.08 (0.75)	.01

Abbreviation: IOP, intraocular pressure.

<sup>a</sup>Daytime vs nighttime uveoscleral outflow, 2-tailed unpaired *t* test.

<sup>b</sup>Variables used in the modified Goldmann equation.

(0.42)  $\mu\text{L}/\text{min}$  at night, a reduction of 49% ( $P < .001$ ). These results are summarized in **Table 2**.

Fluorophotometric outflow facility calculations could not be obtained in some eyes because of the lack of any IOP or aqueous flow effect by the aqueous flow suppressants, especially at night. During the daytime, outflow facility calculations could be obtained in 59 of 60 eyes. Using supine nighttime IOP for the same calculations at night, outflow facility values could be obtained in 10 right eyes and 12 left eyes of 17 individuals (Table 2). Among these 17 individuals, the mean outflow facility was significantly lower at night than during the day (0.16 [0.14] vs 0.29 [0.12]  $\mu\text{L}/\text{min}/\text{mm Hg}$ ,  $P = .05$ ). Using seated nighttime IOP, outflow facility values could be obtained in 11 right eyes and 10 left eyes of 14 individuals. Among these 14 individuals, a statistically significant decrease in the mean outflow facility at night was not achieved (0.17 [0.19] vs 0.26 [0.11]  $\mu\text{L}/\text{min}/\text{mm Hg}$ ,  $P = .14$ ). This may have been owing to the larger spread of data in this group.

Tonographic outflow facility was significantly lower at nighttime (0.19 [0.08]  $\mu\text{L}/\text{min}/\text{mm Hg}$  at 5 AM) compared with daytime (0.23 [0.05]  $\mu\text{L}/\text{min}/\text{mm Hg}$  at 2 PM) ( $P = .009$ ). These results are summarized in Table 2.

Daytime and nighttime fluorophotometric uveoscleral outflow values were not statistically significantly different (**Table 3**). However, uveoscleral outflow values calculated using tonographic outflow facility in the modified Goldmann equation were significantly lower at nighttime compared with daytime irrespective of IOP (seated or supine) or  $P_{ev}$  (measured or adjusted for time and posture) used in the calculation.

## COMMENT

That there is a circadian rhythm of IOP in humans has been well established and accepted, but there is little consensus as to whether IOP increases or decreases at night. Some studies<sup>11,12</sup> have reported that IOP increases at night vs during the day with the individual in a seated or supine position, whereas other studies<sup>5,10</sup> have reported that IOP decreases at night. The difference in study findings may be because of methodological differences, including actual variations in nocturnal IOP among the individuals studied (age, race/ethnicity, and disease influences<sup>32</sup>), the position of the individual (seated vs supine), and the type of tonometer used. Using pneumatonometry, our study found that (compared with daytime IOP) nocturnal IOP increased in the supine position and decreased in the seated position. Based on our rabbit study data, these results cannot be explained by differences in pneumatonometer probe position. Higher supine IOP may be secondary to vascular engorgement of the orbit and consequently an increased hydrostatic  $P_{ev}$ .

The present study is in agreement with other studies<sup>3,4,33</sup> in that the rate of aqueous flow at night is significantly lower than that during the day. Our finding of a 49% reduction in nocturnal vs diurnal aqueous flow is similar in magnitude to that found in these earlier studies.

Our study found that outflow facility of healthy adults aged 37 to 74 years, whether determined by tonography or fluorophotometry, significantly decreased from day to night. Studies of younger healthy individuals, aged 21

**Table 4. Comparison of Measurable Variables Between 17 Eyes in Which CAI-Induced Reductions in Nocturnal IOP and Aqueous Flow Could Be Obtained (Group 1) and 13 Eyes in Which CAIs Failed to Work (Group 2)**

Variable	Mean (SD)		P Value <sup>a</sup>
	Group 1 (n=17)	Group 2 (n=13)	
<b>Daytime</b>			
9 AM seated IOP, mm Hg	15.9 (2.6)	15.5 (2.1)	.64
CCT, $\mu\text{m}$	552 (42)	571 (28)	.17
Aqueous flow, $\mu\text{L}/\text{min}$	2.07 (0.91)	2.03 (0.86)	.90
Fluorophotometric outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$	0.26 (0.11)	0.33 (0.12)	.10
Fluorophotometric uveoscleral outflow, $\mu\text{L}/\text{min}$	0.32 (0.89)	0.26 (0.93)	.86
Tonographic outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$	0.23 (0.04)	0.24 (0.05)	.55
Tonographic uveoscleral outflow, $\mu\text{L}/\text{min}$	0.52 (1.00)	0.52 (1.11)	.98
<b>Nighttime</b>			
2 AM IOP, mm Hg			
Seated	14.0 (2.3)	12.2 (2.3)	.04
Supine	19.4 (2.5)	17.2 (2.4)	.02
CCT, $\mu\text{m}$	566 (39)	585 (32)	.16
Aqueous flow, $\mu\text{L}/\text{min}$	1.09 (0.54)	0.94 (0.24)	.36
Tonographic outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$	0.18 (0.07)	0.20 (0.09)	.49
Tonographic uveoscleral outflow, $\mu\text{L}/\text{min}$	-0.11 (0.90)	-0.04 (0.51)	.79

Abbreviations: CAI, carbonic anhydrase inhibitor; CCT, central cornea thickness; IOP, intraocular pressure.

<sup>a</sup>Two-tailed unpaired *t* test.

to 23 years<sup>14</sup> and 18 to 45 years,<sup>15</sup> also reported possible decreases in outflow facility at night. Not all of these decreases were statistically significant at  $P < .05$ . In the present study, this reduction was measurable between 2 and 5 AM as determined by fluorophotometry and at 5 AM as determined by tonography. The reason for this substantial reduction in outflow facility on a daily basis is a subject for future study. Understanding the regulatory mechanisms underlying this circadian fluctuation will provide valuable insight into how outflow facility is controlled physiologically and why daily fluctuation is important for the health of the eye.

For successful determination of outflow facility by the fluorophotometric method, a drug must reduce aqueous flow and IOP yet have no effect on the other variables in the Goldmann equation,<sup>18,29</sup> especially outflow facility, uveoscleral outflow, and  $P_{ev}$ .  $\beta$ -Blockers work well for this purpose during the day, but at night they fail to reduce IOP and aqueous flow<sup>3</sup>; as a result,  $C_{Tl}$  cannot be calculated. Another option is CAIs. These inhibitors reduce aqueous flow without affecting outflow facility or uveoscleral outflow.<sup>23,28,29</sup> Carbonic anhydrase inhibitors reduced IOP and aqueous flow at night in 1 study,<sup>21</sup> prompting us to select drugs of this class for the present project. However, dorzolamide and acetazolamide failed to lower IOP at night in 13 of 30 participants in our study. Failure of CAIs to reduce IOP at night is not a novel finding.<sup>3,8</sup> Until a drug is found that quickly, consistently, and substantially reduces (or alternatively increases) aqueous flow and IOP at night (without affecting the other variables), the fluorophotometric method has limited usefulness to determine nocturnal outflow facility.

That aqueous flow and outflow facility are reduced at night may support the observation that drugs acting on outflow pathways more effectively reduce IOP at night than drugs suppressing aqueous flow. For example, pros-

taglandin  $F_{2\alpha}$  analogues reduce IOP by increasing uveoscleral outflow, outflow facility, or both<sup>8,34-38</sup> during the day. They also reduce IOP at night,<sup>8,14,39-42</sup> possibly by returning outflow to normal daytime levels. On the other hand, inflow drugs such as  $\beta$ -blockers do not reduce IOP at night<sup>3,4,42</sup> because they cannot reduce aqueous flow below the normally low nighttime rate.

A decrease in uveoscleral outflow at night was found when using  $C_{ton}$  in the Goldmann equation. This provides evidence that nocturnal decrease in outflow is not confined to the trabecular meshwork. A decrease in nocturnal uveoscleral outflow was not found when using  $C_{Tl}$  in the Goldmann equation. This may be owing to a smaller sample size, a larger spread of data in the fluorophotometry assessment, or both.

A comparison of measurable variables between 17 eyes in which CAI-induced reductions in nocturnal IOP and aqueous flow could be obtained (group 1) and 13 eyes in which CAIs failed to work (group 2) is given in **Table 4**. No difference was seen between the 2 groups in any of the daytime variables. At night, group 2 had significantly lower seated and supine IOPs, which explains the inability to further lower IOP with CAIs. There was no difference between the groups in any other nighttime variables. This suggests that the inability to obtain fluorophotometric measurements in group 2 likely does not introduce a selection bias in the results obtained from group 1.

Blood pressure is another systemic circadian factor that may contribute to nocturnal changes in the eye. Reportedly, blood pressure is lower at night than during the day. Nocturnal hypotension is thought to be involved in reduced perfusion pressure of retina and optic nerves and in visual field deterioration in normal-tension glaucoma.<sup>43-45</sup> Blood pressure is lower when measured in the supine position compared with the seated position.<sup>46</sup> Noc-

turnal blood pressure reduction was not observed in our study, perhaps because our diurnal and nocturnal measurements were obtained when individuals were seated.

In our study and other studies,<sup>13,47-51</sup> the central cornea is thicker at night compared with during the day. The thickening may be associated with relative hypoxia, decreased osmolarity, and increased temperature that occur under the closed eyelid during sleep.<sup>47,48,52</sup> Other investigators have reported a strong correlation between CCT and IOP.<sup>53</sup> That circadian changes in CCT potentially contribute to any part of the circadian variation in tonometrically measured IOP is a concern, as nocturnal IOP may be higher because the cornea is thicker. However, in the present study, despite the thicker cornea at night, corresponding seated IOPs were decreased compared with daytime values. Posture strongly affects IOP, as can be seen by the increased supine IOP at night, but posture is unlikely to affect CCT. Therefore, our IOP findings cannot be explained by CCT changes.

In summary, our study of healthy individuals aged 37 to 74 years found that normal ocular changes from diurnal to nocturnal periods include decreases in seated IOP, aqueous inflow, and outflow facility and increases in central corneal thickness and supine IOP. A less consistent finding was a nighttime decrease in calculated uveoscleral outflow, found when  $C_{\text{ton}}$  but not  $C_{\text{fl}}$  was used in the Goldmann equation.

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#### Correction

**Error in Byline.** In the Clinical Sciences article titled "Effect of Prophylactic Intraocular Pressure-Lowering Medication on Intraocular Pressure Spikes After Intravitreal Injections" by Frenkel et al, published in the December issue of the *Archives* (2010;128[12]:1523-1527), Max P. C. Frenkel should not have a degree listed after his name. The article was corrected online.