Lens

The Relationship between Body and Ambient Temperature and Corneal Temperature

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PURPOSE. Exposure to elevated ambient temperatures has been mentioned as a risk factor for common eye diseases, primarily presbyopia and cataract. The aim of the present study was to examine the relationship among ambient, cornea, and body core temperature.

METHODS. The relation between corneal temperature and ambient temperature was examined in 11 human volunteers. Furthermore, corneal temperature was measured using a thermal camera during elevation of body core temperature in three human volunteers and four rats.

RESULTS. A linear relationship between corneal temperature and body temperature was found in the rat. For humans there was an initial linear increase in corneal temperature with increasing body temperature, but corneal temperature seemed to plateau at 36.5°C to 37.0°C despite a continued increase of body core temperature. A linear relationship between ambient and corneal temperature was found in humans but with a less steep slope than that between corneal and body core temperature.

CONCLUSIONS. Corneal temperature is estimated to reach the maximum of 36.5°C to 37.0°C at ambient temperatures between 32.0°C and 34.5°C. If there is a causal relationship between elevated eye temperature, cataract, and presbyopia, the incidence of these eye diseases is predicted to increase with global warming. Importantly, the strong association between corneal temperature and body core temperature indicates that frequent infections could also be considered a risk factor for age-related lens disorders. (*Invest Ophthalmol Vis Sci.* 2010;51:6593–6597) DOI:10.1167/iovs.10-5659

Temperature is of vital importance for all biological functions. The rate of metabolic processes increases with temperature, but if temperature is elevated beyond a certain threshold proteins denature and may not function properly. Ultimately, this may lead to death. The proteins of the lens of the eye are susceptible to changes in temperature. Lowering the temperature of the lens leads to the formation of a cold cataract that disappears when the temperature is normalized. The formation of cold cataracts is seen in only certain species, not including humans, and is related to the configuration of the lens structural proteins.[1] Increasing the temperature slightly above the physiological level at 37.0°C irreversibly increases light scattering from lens proteins because of protein aggregation and denaturation.[2,3]

Exposure to elevated ambient temperatures has been proposed to be a risk factor for presbyopia[4-6] and cataract.[6,7] Cataract is a protein conformational disease.[8] The biochemical background of presbyopia is less well understood, but experimental data show that increasing stiffness of the lens content is of crucial importance,[9,10] and it has been suggested that heat-induced denaturation of lens proteins is a causal factor.[5] Logically, a relationship between heat and lens disorders could exist based on temperature-driven increased metabolic stress or thermal protein denaturation. However, a number of other factors not related to temperature may also be important. Such factors could be differences in environmental exposures, lifestyle, nutrition, and genetic background.[11]

If there is a causal relationship between eye disease and environmental temperature, eye temperature and ambient temperature must be intimately related. The association between eye temperature and ambient temperature in humans is, however, poorly understood. Lens temperature is regulated both by heat emitted from the choroidal blood flow and by cooling from the thermo-driven convectional flow of the aqueous humor in the anterior chamber.[12] Thus, both ambient temperature and body core temperature must be taken into account. We examined corneal temperature, measured on the corneal surface with a thermal infrared camera, in relation to core body temperature and ambient temperature in the rat as a model system and in humans, and we found that corneal temperature in the rat is entirely dependent on body core temperature whereas in the human we found a combined effect of body and ambient temperatures.

MATERIALS AND METHODS

Animal Studies

The relationship between corneal temperature and body core temperature was examined in four male Zucker Diabetic Fatty (ZDF) rats 19 weeks old. The rats were sedated for the procedure with 85 mg/kg ketamine (Intervet International B.V., Boxmeer, The Netherlands), 4 mg/kg xylazine (Intervet International B.V.), and 1.5 mg/kg acepromazine (Pharmaxim Sweden AB, Helsingborg, Sweden). The core body temperature of the rats dropped approximately 3°C immediately after sedation. To normalize body temperature, the rats were placed on a heating table. Normal body temperature was achieved in 5 to 10 minutes. Corneal temperature was measured on the undilated eye using an infrared thermal camera (Fluke Ti25; Fluke, Everett, WA) at regular intervals during the heating procedure (Fig. 1). The average temperature reading of the corneal area was used. Core body temperature was measured as the highest temperature viewed in the ear region on the infrared photographs (Fig. 1). The infrared camera works by measuring heat emitted from surfaces, and it was calibrated by photographing objects of a known temperature. Temperature readings were accurate within <0.1°C. Room temperature was constant during
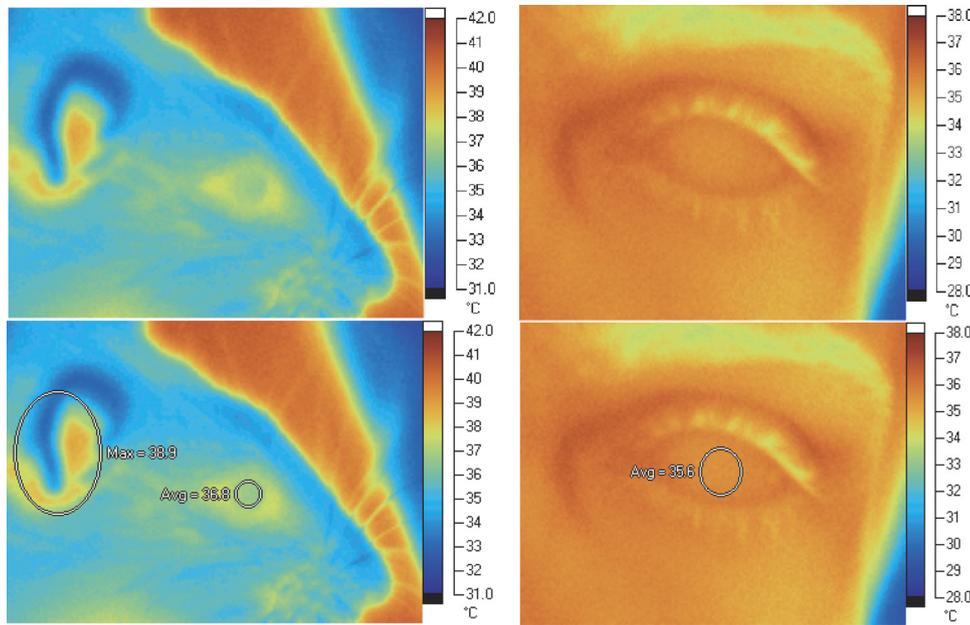
FIGURE 1. Infrared thermal photographs of a rat eye and a human eye. The markers used for determining ear temperature (rat only, the maximum value was used) and corneal temperatures (both rat and humans, the average values were used) are shown. The heating table used in the rat experiments can be observed as the hot area behind the rat. Note that the temperature color code is not identical between the human and animal photographs.

the experiments. The animal studies adhered to the ARVO Statement for the use of Animals in Ophthalmic and Vision Research.

Human Studies

The relationship between corneal temperature, core body temperature, and ambient temperature was examined in three healthy volunteers (two men, one woman; age range, 27–29 years). Body core temperature was elevated ~1°C in the volunteers. Compensating thermoregulatory mechanisms are less effective in warmer and more humidified surroundings.[13] Thus, body core temperature was elevated by preventing loss of heat by wrapping the volunteers in a layer of household cling film to isolate sweat, followed by a layer of aluminum foil to prevent heat loss from skin radiation. Subsequently, the volunteers were wrapped in warm blankets, ensuring passive heating.

Core body temperature was measured by placing the tip of a modified skin probe (model no. 10-1600-030; Novamed, Elmsford, NY)

4 cm distal in the nasal cavity and connecting it to a temperature monitor (LS-1400 D Temperature Monitor; Novamed). Nasal respiration was prevented by compressing the alae nasi by a nasal clip at least 10 minutes before and during the experiment. Distal nasal temperature has been proven to be a reliable measurement of body core temperature.[14] Corneal temperature was measured on the undilated eye at regular intervals during the elevation of body temperature by using the same thermal camera as was used for the animal experiments (Fig. 1). Room temperature was measured with a thermometer (LT Lutron TM-926; Scan Instruments, Roskilde, Denmark) during the experiments.

In addition, the relation between ambient temperature and corneal temperature was measured in 11 healthy volunteers (six men, five women; age range, 26–58 years). Volunteers were placed in three different indoor surroundings—typical office-type rooms (22°C–28°C), a sauna (43°C), and a cooling room (2°C)—for at least 5 minutes before
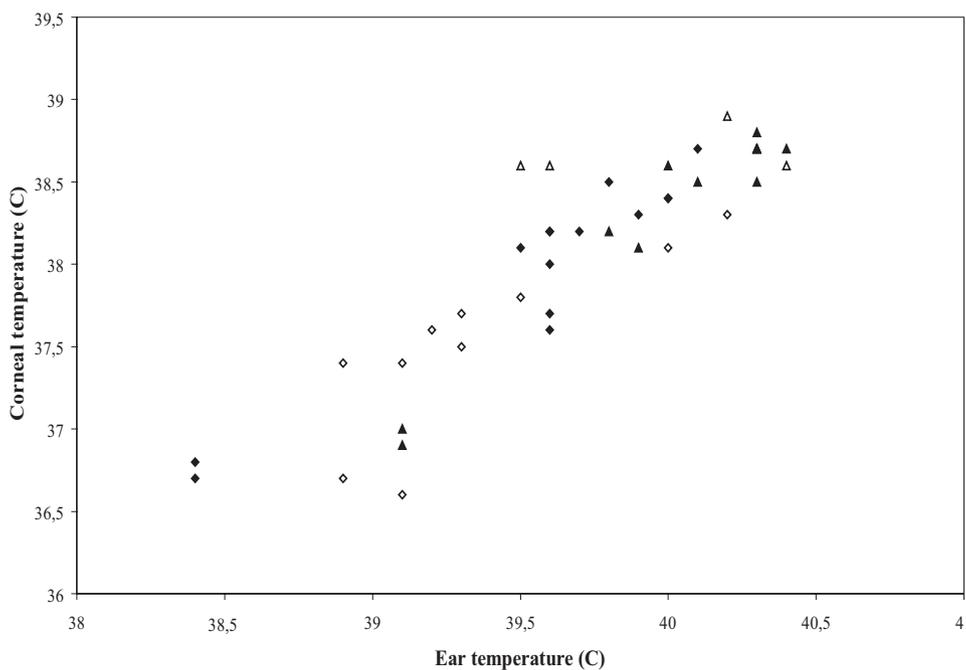

FIGURE 2. Corneal temperature as a function of ear temperature for rats. Symbols represent the four rats used for the experiments.
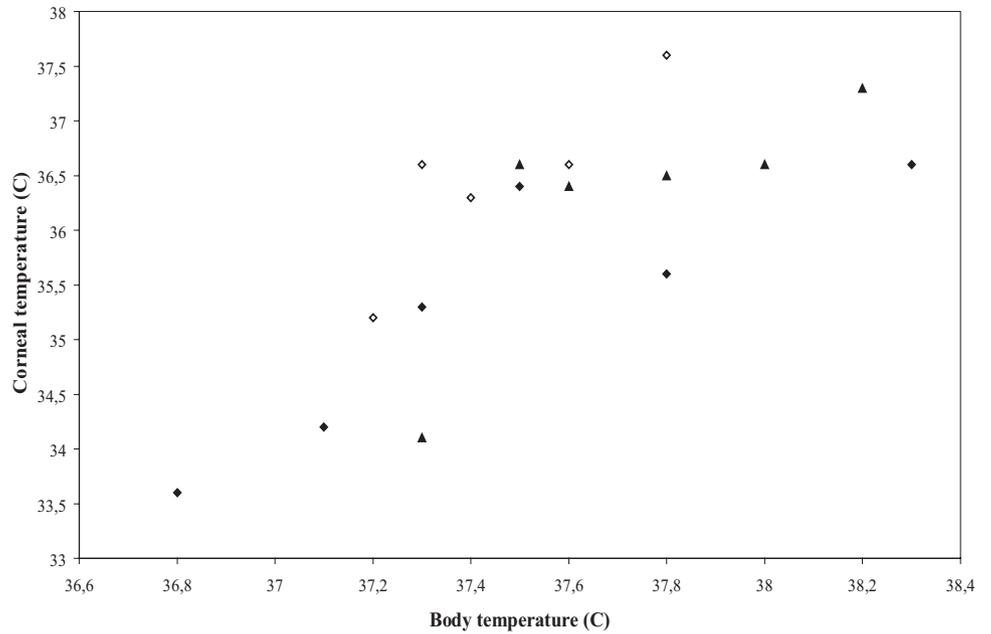
FIGURE 3. Relation between core body temperature (measured 4 cm distal in the nasal cavity) and corneal temperature in humans. Different markers are used for the three healthy volunteers.

corneal temperature was measured with the infrared camera. Ambient temperature was measured with the same thermometer used in all other experiments.

None of the human volunteers were contact lens wearers because contact lens wear was found to influence the temperature readings of the cornea. The study followed the tenets of the Helsinki Declaration, and all volunteers gave their written informed consent after the procedures had been explained. The study was approved by the Medical Ethics Committee of the Capital Region of Denmark (no. H-A-2009-014).

RESULTS

In the rats, the corneal temperature was approximately 2°C lower than the central body temperature, with a linear relationship between corneal and body temperature (Fig. 2). The relationship can be expressed by equation 1 ($P < 0.0001$; $R^2 = 0.86$):

$$Temp_{cornea} = 1.15 \times Temp_{ear} - 6.50 \qquad (1)$$

In the human volunteers, corneal temperature and core body temperature initially were also linearly related (Fig. 3), but corneal temperature seemed to plateau at 36.5°C to 37.0°C in spite of the continued increase in body core temperature. This was in contrast to the rats, in which corneal temperature did reach an upper limit.

The relationship between corneal temperature and ambient temperature was assessed in 11 healthy volunteers (Fig. 4). Interindividual variation in corneal temperature was approximately 3% of the mean value for a given ambient temperature. Ambient temperatures ranged from 2°C to 42°C, but the cor-
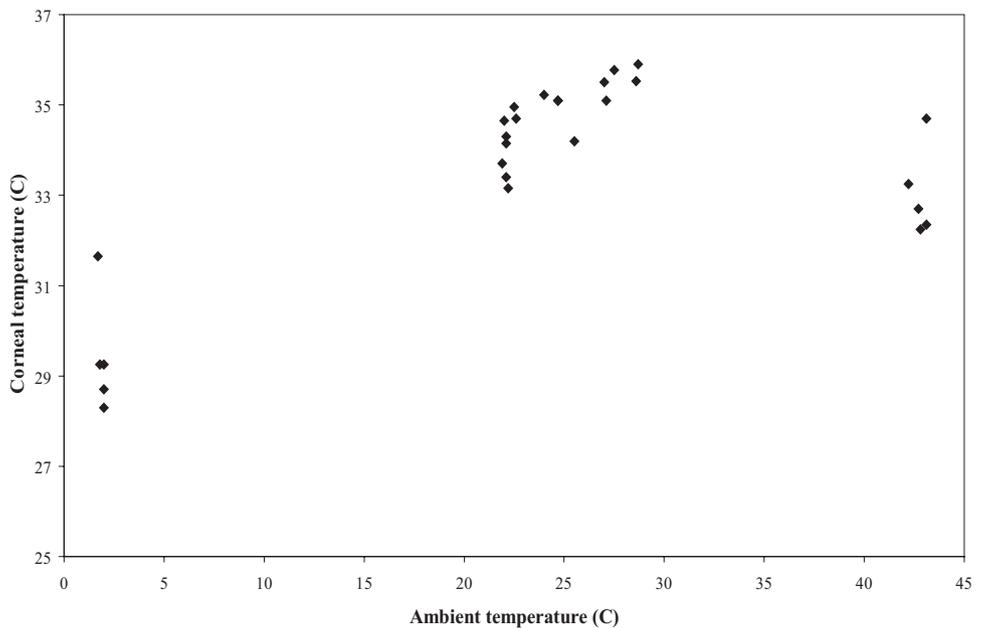

FIGURE 4. Corneal temperature (°C) as a function of ambient temperature (°C) in 11 human volunteers.

neal temperature seemed to plateau at ambient temperatures around 22°C. Increasing ambient temperature by 20°C from 2°C to 22°C increased corneal temperature by 3°C ($P = 0.002$, rank sum test), whereas increasing ambient temperature another 20°C, from 22°C to 43°C, did not increase corneal temperature ($P = 0.065$, rank sum test; Table 1).

DISCUSSION

We investigated the relationship among corneal temperature, core body temperature, and ambient temperature. Most important, we found that corneal temperature was intimately related to body core temperature in the rat and in the human. In humans, the corneal temperature seemed to plateau at 36.5°C to 37.0°C in spite of a continued increase in body core temperature. Similarly, a plateau of corneal temperature was also found in humans when ambient temperature was increased, but this plateau occurred at a lower level of corneal temperatures at 33°C to 35°C. Changes in body core temperature had a dramatic effect on corneal temperature; for example, corneal temperature increased 2°C when core temperature increased 0.4°C, whereas a 20°C increase in ambient temperature, from 2°C to 22°C, was required to increase corneal temperature by 3°C.

Corneal temperatures of rats and humans showed remarkable differences in response to changes in body core temperature. These findings might be explained by the differences in the geometry of the eyes of the two species, as can be appreciated by looking at Figure 5.[15] In rats, the corneal temperature is in greater equilibrium with the blood temperature because of the short distance ($\sim$0.6 mm[15]) between the vascularized iris and the avascular cornea. In humans, anterior chamber depth measures approximately 3 mm,[16] which is enough to allow for a significant thermally driven convectional flow of the aqueous humor[17] and, hence, a cooler cornea. Humans are adapted to living in all climate zones, ranging from freezing arctic areas to hot deserts, without any noticeable difference in visual performance. The deep anterior chamber in humans may serve to protect the interior eye, especially the lens, from large temperature variations caused by changing ambient temperatures.

Increased eye temperature has been implicated as a risk factor for lens disorders such as presbyopia and cataract. Our measurements of corneal temperature were an indirect measurement of lens temperature because direct measurements would require invasive procedures. Internal eye temperature measurements have been performed in rabbits[18,19] showing that there is an intraocular gradient in temperature from the cool cornea to the warm retina and that lens temperature is a mixture of corneal and retinal temperatures. Not surprisingly, we found that corneal temperature never exceeded body core temperature, but unexpectedly we found that corneal temperature plateaued both when ambient temperature and body core temperature were increased at 33°C to 35°C and 36°C to 37°C, respectively.

FIGURE 5. Schematic drawing of a human eye (*left*) and a rat eye (*right*) showing the differences in geometry. The length of the adult human eye is 23 mm, and the length of a 4-month-old rat eye is 6.3 mm.[15] Human eye redrawn from Paterson CA, Delamere NA. The lens. In: Hart WM, ed. *Adler's Physiology of the Eye*. 9th ed. 1992:348–390. Copyright 1992, with permission from Elsevier. Rat eye redrawn from Hughes A. A schematic eye for the rat. *Vision Res.* 1979;19:569–588. Copyright 1979, with permission from Elsevier.

Others have found a corneal temperature of 36°C at an ambient temperature of 40°C, supporting our observations of a plateau.[20] This could indicate that the eye has thermosensors that regulate the corneal temperature, though we have not found evidence of such sensors in the literature. However, the thermoregulation of the cornea may be self-regulatory to some extent because increased ambient temperature will increase the cooling of the cornea by accelerating the evaporation of the tear film. Changing the blinking rate also affects corneal temperature.[21]

In the face of global warming, the question of a link between eye disease and ambient temperature is more relevant than ever. Interestingly, the implication of our data is that the effect of global warming on the prevalence of eye disease will be worse for those living in cold climates getting warmer than for those in hot climates getting hotter.

In conclusion, with the prospect of increased global temperatures in the future, the prevalence of cataract may increase and the onset age of presbyopia may decrease if a causal relationship between lens disorders and eye temperature exists. However, our results clearly demonstrate that the effects of increased body temperature, such as experienced during fever caused by infections, must not be overlooked as a risk factor. Whereas global temperatures may prove difficult to change, it is in our hands to reduce the burden of infection with the use of medical therapy and improved sanitation and nutrition.

Acknowledgments

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TABLE 1. Corneal Temperature versus Ambient Temperature

Ambient Temperature (°C)	Corneal Temperature (°C)
1	31
22	34
25	35
28	35
43	33

Corneal temperature (mean of all the measurements for a given ambient temperature) was measured with an infrared camera in relation to ambient room temperature.
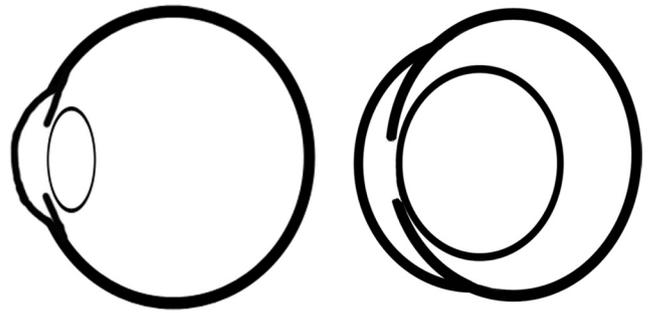
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