Thermokeratoplasty (TKP) temperature profile

Edward L. Shaw and Antonio R. Gasset

Changes in corneal architecture with the application of controlled heat have been shown to be clinically useful and well tolerated. A fine hypodermic microthermistor was utilized to record the temperature at both superficial and deep levels of the rabbit cornea after the application of the thermokeratoplasty (TKP) probe at 90° C. or 130° C. These temperature readings revealed that the known corneal shrinkage temperature (T_s) of 65° C. was reached in anterior and deep stroma while the endothelial temperature was markedly lower. The temperature profiles obtained from these experiments illustrate a very rapid temperature peak with an equally rapid temperature decay. This "pulse" of high temperature shrinks the collagen without denaturing or melting it.

Key words: thermokeratoplasty, keratoconus, shrinkage temperature, corneal shape, collagen.

The hydrothermal shrinkage of collagen fibers has long been recognized as an outstanding characteristic of collagen fibers. Mammalian collagen contracts sharply at the shrinkage temperature, T_s, in this instance, 60 to 70° C. The mammalian cornea shrinks to about 3/4 of its initial length when the proper temperature is achieved. These findings agreed with our recent report in which the rabbit cornea was found to shrink at 65° C., and the amount of shrinkage varied from 40 to 50 per cent.

The significance of these observations is more than of academic interest since it has also been shown by us that in keratoconus patients, the deformities and steepness of

Fig. 1. Appearance of a keratoconus eye before and nine months after thermokeratoplasty. Notice the complete disappearance of the cone in this patient.
the cornea that significantly decreased vision secondary to progressive myopia, corneal astigmatism, and irregular corneal astigmatism can be reduced. In addition, the corneal shape can be restored and the vision improved if the precise amount of heat and time of application are used (Fig. 1).

Since the thermokeratoplasty (TKP) procedure seems most promising to achieve this purpose, additional information is necessary. It was the purpose of this study to measure temperature transmission and decay patterns across the cornea, from epithelium to endothelium after known temperatures were applied to the corneal surface. In addition, thermal gradient profiles were measured for the temperatures most commonly used clinically, those temperatures being 90°C and 130°C.

**Material and methods**

Mature albino New Zealand rabbits were used for all of the in vivo animal studies.

**Temperature delivery system.** The TKP-probe previously standardized and described by us was used throughout this study. The details of this instrument are described elsewhere. Briefly, this instrument has a 3 mm. diameter silver probe tip containing a resistance heating element and microthermistor placed within the probe head. It is connected to the heat regulating and monitoring unit by an insulated electrical wire (Fig. 2).

**Temperature measuring system.** A Baley Instrument microthermistor, 22 gauge, ½ inch long, and 0.008 inch MT-1, was used to measure corneal temperature. The probe distal to the hypodermic needle is sheathed and insulated to eliminate possibilities of errors due to convection currents or conduction of heat along the needle itself. The probe was then connected to a BAT-4 thermometer for direct reading and to a Grass Instrument Polygraph for continuous temperature read-out.

**Procedure.** All the determinations were carried out at room temperature in a small area, previously selected for stable, dry, draft-free conditions.

After intravenous injection of 40 mg per kilogram of body weight, pentobarbital sodium (Nembutal), Ophthaine (proparacaine hydrochloride) was instilled over the cornea and the conjunctiva for further anesthesia. With the help of a spring-lid speculum adequate exposure of the eyeball was maintained. The tip of the microthermistor needle was then carefully placed at the desired level of the cornea either at the anterior or posterior position. An operating microscope was used throughout to facilitate this procedure.

In one group, the needle was placed at or near the level of Bowman’s membrane; in the second group, the needle was positioned at or close to Descemet’s membrane. These positions were then confirmed by light microscopy.

After the probe temperature reached either 90°C or 130°C, the probe was gently applied to the corneal surface directly above the previously placed thermistor for a contact time of one second.

This time interval was initiated and concluded by verbal commands from an assistant using a stop-watch timing device. This one-second interval was then further controlled by calculating the distance between an initial deflection (caused by the TKP probe on the cornea) on the polygraph and the small, but noticeable, deflection when the probe was removed.

During the first part of our study, continuous polygraph tracings were made using the Grass Instrument previously mentioned. The actual polygraph curves resemble, in great part, the curves shown in Figs. 3 and 4. From these curves the (1) time of TKP probe contact, (2) start of
Results

Probe temperature (90° C.) experiments. The results obtained in 110 determinations, half at the superficial layers and half at the deeper layers of the rabbit cornea are schematically illustrated in Fig. 3 and summarized in Table I.

As can be seen, the temperature measurements carried out for every second for the initial eight seconds revealed that at a 90° C. probe temperature, the mean maximum temperature at the epithelial surface approaches its peak between one and two seconds after application of the probe. A parallel peak was obtained at the endothelial side; however, there was a significant difference in actual temperature elevation at these two levels, for the epithelial side the temperature was raised 37.2° C. and the endothelial side 21.0° C.

The maximum temperature recorded was 71.2° C. at 1.66 seconds for the epithelial side and 55.9° C. at 1.60 seconds for the endothelial side.

It should be noted that the almost identical peak temperature times at both the anterior and posterior corneal layers indicates a rapid heat transit time. The apparent faster peak time at the endothelial level reflects not only the rapid corneal transit...
Table I. Maximum temperature (time), 50 per cent decay temperature (time), and time for return to pretreatment temperatures

<table>
<thead>
<tr>
<th>TKP temperature, superficial probe (90° C.)</th>
<th>Maximum temperature (time) and S.D.*</th>
<th>50% decay temperature (time) and S.D.</th>
<th>Time to return to within 1° C. of pretreatment temperature and S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>71.2 ± 1.8° C.</td>
<td>53.0 ± 1.0</td>
<td>15.5 ± 0.50</td>
</tr>
<tr>
<td></td>
<td>(1.66 ± 0.10) seconds</td>
<td>(2.3 ± 0.08) seconds</td>
<td>seconds</td>
</tr>
<tr>
<td>TKP temperature, deep probe (90° C.)</td>
<td>55.9 ± 3.3</td>
<td>45.2° C. ± 2.5</td>
<td>18.0 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>(1.60 ± 0.2) seconds</td>
<td>(3.2 ± 0.10) seconds</td>
<td>seconds</td>
</tr>
<tr>
<td>TKP temperature, superficial probe (130° C.)</td>
<td>75.2 ± 1.4</td>
<td>54.6 ± 1.8</td>
<td>16.0 ± 0.45</td>
</tr>
<tr>
<td></td>
<td>(1.62 ± 0.20) seconds</td>
<td>(2.9 ± 0.15) seconds</td>
<td>seconds</td>
</tr>
<tr>
<td>TKP temperature, deep probe (130° C.)</td>
<td>56.7 ± 3.4</td>
<td>45.8 ± 2.2</td>
<td>18.0 ± 0.35</td>
</tr>
<tr>
<td></td>
<td>(1.54 ± 0.20) seconds</td>
<td>(3.4 ± 0.10) seconds</td>
<td>seconds</td>
</tr>
</tbody>
</table>

*S.D.—standard deviation.

time, but also the lower temperature reached at the maximum temperature point.

Similarly, a return to pretreatment temperatures was reached after 33 ± 5 seconds for both superficial and deep levels of the cornea.

In addition, at 90° C. probe temperature, it was found that a total time required to reach 50 per cent of the maximum temperature was only 2.3 seconds (53.0° C.). In contrast, the endothelial side 50 per cent decay time was found to be 3.2 seconds (45.2° C.).

**Probe temperature (130° C.) experiments.**

Table I and Fig. 4 show the same type of heat profile as shown in Fig. 3, only this time TKP temperature was 130° C. Again, the epithelial surface reached higher temperatures than the deeper layers for the first six seconds. Thereafter, however, both curves converged and finally overlapped at the pretreatment temperature in 49 ± 4 seconds.

For the 130° C. probe temperature, 1.5 seconds were needed to reach a maximal temperature of 75.2° C. on the endothelial side. The 50 per cent decay time from the...
peak temperature was found to be 2.9 seconds (54.6° C.) for the epithelial side and 3.4 seconds (45.8° C.) on the endothelial side.

A comparison of both curves revealed that around 17 seconds was required to get to within one degree of the pretreatment temperature.

The plotted curves shown in Figs. 3 and 4 were subjected to computer analysis, the projected curves from which are shown in Figs. 5 and 6, respectively. As can be seen, the computer-drawn curves from the given formulas are remarkably similar to the actual data in Figs. 3 and 4.

A comparison of 130° C. versus 90° C. reveals that the epithelial or superficial temperature increases at 130° C. were not significantly greater than at 90° C. between two to six seconds (p < 0.05). The temperature change at the endothelial side at 130° C. was not significantly greater than at 90° C. The temperature differences between the increases at 90° C. and 130° C. were more pronounced from the second to the sixth seconds for the superficial versus deeper layers. Fifty per cent temperature decay time was significantly longer at the endothelial level compared with the epithelial level (p < 0.01).

Discussion

If heat is applied to the cornea, changes in the collagen fiber, ground substance, and cell components can be expected.

The changes which occur with the application of 90° C. are characterized by first, rapid degenerative changes in the epithelium, then anterior stroma followed by endothelial cell damage. Finally, cells in the deeper areas of the stroma are also affected. However, regeneration occurs at all levels within three to four days and is characterized by first, regeneration of the epithelium followed by endothelium and finally by stroma. Within seven days the cornea appears normal. These findings paralleled the metabolic activities of the heated cornea as evaluated by analysis of the different enzymes related to glycolysis.

A substantial decrease or absence of enzymes was found throughout the cornea beginning almost immediately after the heat application. Forty-eight hours after heat application, an almost normal enzymatic pattern was found in the corneal epithelium; whereas stromal cells in the anterior half of the corneal stroma showed markedly reduced enzymatic level. The enzymatic pattern gradually returned to normal by the fourteenth day after treatment.

Since quantity and duration of the temperature elevation at different layers of the cornea should parallel the effect of heat on the different cell components, this study indicates that because of the short and modest elevation in temperature at the endothelial side, little if any endothelial damage can be expected with this brief application at controlled temperature. This agreed with our previous morphologic evaluations. It should be emphasized that, although controlled temperature application produces little damage, excessive heat will produce irreversible destruction and melting of the cornea as the denaturation temperature of the protein is reached.

This study also indicates that shrinkage temperature is attained in the anterior half of the cornea without reaching the melting point of the corneal collagen or the "toxic" temperature of the endothelium.

Our studies show that even though our TKP-probe tip temperature was 130° C., both the anterior and posterior corneal levels do not exceed the shrinkage temperature. This is felt to be due to the rapid dissipation of heat through the cornea and by the "heat sink" effect of the anterior chamber and iris which allows a 50 per cent temperature decay to occur at the endothelium within 1.5 seconds. The temperature in the anterior chamber never rose more than a few degrees even at maximum temperatures, and in numerous measurements near the anterior lens capsule, only a transient rise in temperature of a few degrees could be seen.

It is obvious that studies done on the
rabbit are not exactly equal to studies done in man. However, after many experiments similar to the present one, using human eye-bank eyes, a great degree of parallelism could be found. The similarity and clinical appearance in both rabbit and human corneas has already been mentioned. The TKP-temperature profile for human corneas, although statistically too small, was also amazingly similar to the profile noted previously in this report.

It is felt that the rabbit offers a suitable animal model for TKP research as it has already proved valid for lamellar and penetrating keratoplasty, drug penetration, corneal ulcers, and numerous other studies.

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REFERENCES