The influence of age on the sensitivity of the cornea. MICHEL MILLODOT.

Corneal touch threshold (CTT) was measured in 205 healthy people of different ages. It was found that CTT increased gradually throughout life, although more significantly after the fifth decade of life. The results are found to be in good accord with those of Boberg-Ans, thus refuting an earlier report asserting that corneal sensitivity (threshold) increased up to the fifth decade and declined thereafter.

The sensitivity of the cornea to mechanical stimuli has aroused a great deal of interest because of the widespread use of contact lenses. In this connection and from a purely gerontological point of view it is likewise important to know how this response varies with age.

Jalavisto and associates observed a marked decrease in sensitivity with age, using a puff of air as a stimulus. However, this is an equivocal type of stimulus which, moreover, stimulates a wide, undefined area of the cornea and even eyelids. Boberg-Ans who used a test consisting of a nylon thread of variable length confirmed qualitatively Jalavisto’s results. Boberg-Ans did not specify in his report which area of the cornea he tested. This is important because there appears to be some difference in aging of the center as compared to aging of the edge of the cornea, at least beyond 65 years. On the contrary, Zobel, using von Frey’s hairs, found that corneal sensitivity increases slowly up to the age of 45 to 50 and decreases sharply thereafter.

Thus it was believed that a systematic and statistical study of the variation of corneal sensitivity in a healthy population was warranted.

Methods. The cornea was stimulated by the Cochet-Bonnet aesthesiometer. The instrument consists of a nylon monofilament of 0.12 mm. diameter which can produce a pressure ranging from 11 to 200 mg./0.0113 mm. The aesthesiometer was mounted in a holder so that it could be moved in x, y, and z axes by means of three knobs. A corneal point near the limbus in the six o’clock position was stimulated, and the slightest bend of the nylon wire was defined as corneal contact. Stimulation of the peripheral point was chosen because this result is not affected by apprehension factors.

Measurements of touch thresholds were made subjectively. The experiment began by stimulating the cornea with the lowest pressure and continued in an ascending fashion. At each predetermined length of the nylon monofilament (with increment of 0.5 cm.) four to six contacts were made, with an occasional blank to test the subject’s reliability. From these measurements the corneal touch threshold (CTT) was defined as the length of the monofilament at which the subject responded for 50 percent of the number of stimulations. This length was converted into pressure by the use of a previously calibrated curve for the instrument.

Subjects (205) of all ages were tested. Subjects were free of any symptoms or signs of ocular conditions, and older persons with arcus senilis were not included.

Results and discussion. The mean CTT and standard deviation for the various people of all ages are shown in Table I. CTT remains practically the same between ages 7 and 40. In the fifth decade of life, however, CTT becomes significantly higher than in the fourth decade (p < 0.05), although the difference is admittedly small. But CTT continues to increase with age. By the eighth decade of life CTT has increased to almost twice what it was in children 7 to 10 years old. The latter seem to have a somewhat smaller CTT, but unfortunately it is difficult to test such young people and this result cannot as yet be conclusive, since the sample is small (n = 10). It is interesting, though, that the findings are in good agreement with those of Boberg-Ans (n = 7) as shown in Fig. 1, al-
Fig. 1. Corneal sensitivity as a function of age according to Boberg-Ans\textsuperscript{2} (solid squares) and according to the present study (open squares). The two curves are drawn by eye.

Table I. Mean (and standard deviation) peripheral CTT (mg./mm\textsuperscript{2}) obtained on healthy individuals of various ages

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>7-10</th>
<th>11-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
<th>61-70</th>
<th>71-80</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>10</td>
<td>22</td>
<td>42</td>
<td>23</td>
<td>24</td>
<td>25</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Mean CTT</td>
<td>18.3</td>
<td>20.9</td>
<td>21.3</td>
<td>19.7</td>
<td>25</td>
<td>26.7</td>
<td>33.5</td>
<td>36</td>
</tr>
<tr>
<td>S.D.</td>
<td>4.7</td>
<td>10.5</td>
<td>13.9</td>
<td>8.5</td>
<td>10.2</td>
<td>13.5</td>
<td>14.4</td>
<td>19.4</td>
</tr>
</tbody>
</table>

though the trend is more marked in his data. The fact that young children may be noticeably more sensitive than adults is of clinical significance because it may influence the type of contact lenses (soft or hard) to recommend.

The results of the present study are shown in Fig. 1 along with those of Boberg-Ans.\textsuperscript{2} The two sets of data are in good accord qualitatively, both displaying the same trend throughout life. However, Boberg-Ans\textsuperscript{2} found a greater corneal sensitivity (that is, a lower CTT) than the results of the present investigation. This discrepancy may be attributable to the fact that the subjects of his study in Denmark may have included more individuals with blue eyes than in the present study in Wales, a factor known to affect corneal sensitivity.\textsuperscript{8} Moreover, Boberg-Ans did not specify in his report whether he averaged the central and peripheral measurements, but his results are consistent with this possibility, since CTT is lower in the center than in the periphery\textsuperscript{9, 10} of the cornea.

Zobel's results\textsuperscript{1} showing a slow increase in corneal sensitivity up to age 45 to 50 and a sharp decrease afterwards are not in agreement with either the present results or those of Boberg-Ans.\textsuperscript{2}

Zobel's results may be accounted for by the fact that he used as a stimulus von Frey's hairs which are rather inadequate for acquiring precise and reliable data.

The cause of the decline in corneal sensitivity in the aging eye remains to be investigated. Is it due to thickening of the fibrous structure of the cornea, to a decrease of water content, or to an atrophy of nerve fibers?

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Key words: cornea, corneal touch threshold, corneal sensitivity, age.

REFERENCES


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Aldose reductase and sorbitol dehydrogenase distribution in substructures of normal and diabetic rat lens. J. G. Collins and Clinton N. Corder.

Aldose reductase (AR) and sorbitol dehydrogenase (SDH) make up the sorbitol pathway, which has been implicated in the pathogenesis of sugar cataracts. The levels of the two enzymes were determined with quantitative histochemical techniques in the epithelium, cortex, and nucleus of normal and diabetic rat lenses. The ratio of activity of AR to SDH was found to be nearly 50 to 1 in all substructures. This would strongly favor sorbitol accumulation and subsequent cataract formation.

The enzymes aldose reductase (AR) (alditol-NADP oxidoreductase, EC 1.1.1.12) and sorbitol dehydrogenase (SDH) (L-iditol:NAD oxidoreductase, EC 1.1.1.14) have been identified in the lenses of several species1−4 and make up the sorbitol pathway. Increased lens sorbitol levels in diabetic animals5 have been implicated in the pathogenesis of cataract formation.6 AR activity has been shown to vary in different areas of the calf lens.7 It has been stated that the epithelium has the highest polyol concentration7 and is the area of greatest metabolic activity.8

The study presented in this report was undertaken to evaluate the activity of AR and SDH in the epithelium, cortex, and nucleus of normal and diabetic rat lenses. The experiments were carried out in order to better understand the role of the sorbitol pathway in sugar cataract formation.

Methods. The procedures and reaction conditions were similar to those used by Corder and associates9 in a quantitative histochemical study of the sorbitol pathway in kidney substructures of normal and diabetic rats. The animals were 44-day-old rats, normal and alloxan-diabetic (intravenous injection 14 days before sacrifice) with the following serum glucose values: normal, 4.5 ± 1.1 mM and diabetic, 17.5 ± 1.7 mM (mean ± S.D.). The animals were killed by cervical dislocation, and their eyes removed and frozen. The frozen lenses were cut into sections, 30 μ thick, and dried at −20°C. Under microscopic visualization pieces of epithelium, cortex, and nucleus were dissected from the freeze-dried samples and assayed for enzyme activity by the "oil well technique."9 The assay of each enzyme's activity required a multistep procedure beginning with the introduction of a 0.5 to 1.5 μg sample in an initial reaction volume of 1.8 μl, suspended in oil. By the use of oxidation reduction of pyridine nucleotides and cycling procedures, it was possible to measure the activity of AR and SDH in the samples studied. Sorbitol was the substrate for both reactions. In the presence of AR, glucose was formed, whereas in the presence of SDH, fructose was the product. Lenses from five normal and five diabetic animals were used.

Results. The results obtained for each of the enzymes are seen in Table I.

The most obvious point is the significant difference in the levels of the two enzymes in all structures in both normal and diabetic animals. The level of AR activity is approximately 50 times higher in all cases. Statistical analysis for the difference between the means (Student's t-test) indicated the following. In normal animals there was no significant difference in the distribution of AR among the substructures of the lens, but SDH was significantly higher in epithelium than in cortex. The diabetic state was associated with some alterations in distribution of enzyme activity. AR activity in the epithelium was significantly greater than in nucleus. SDH activity increased significantly in the cortex of the diabetic relative to normal animals and was also significantly higher in the diabetic cortex than the diabetic nucleus.

Discussion. Pottinger,9 quoting literature references, shows that the Km of glucose for hexokinase is lower than the Km of glucose for AR. She proposes that with increasing levels of glucose (as in diabetes), hexokinase would be saturated and relatively more glucose would enter the sorbitol pathway. If this is the case, our data give evidence for a situation greatly favoring the accumulation of sorbitol. In both normal and diabetic animals the ratio of activity of AR to SDH is nearly 50 to 1. Since sorbitol does not