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The Effect of Instillations of Ephedrine Solution Upon the Eye.

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The sudden and great popularity of ephedrine for therapeutic purposes, chiefly in connection with mucous membrane affections, seemed to us to warrant further investigations on the action of the drug upon the eye. Experimental tests with ephedrine hydrochloride ($C_{10}H_{15}ON.HCl$) in solutions ranging from 1 to 10 per cent, were made on the eyes of 15 individuals. It was our object to determine what effect, if any, the drug has upon the acuity of vision, the sensitivity of the ocular mucous membrane, the intraocular tension, the pupil, the range of accommodation, and in producing any other symptoms, subjective or objective. Two drops of the solution were instilled 4 times into each eye at intervals of 5 minutes. Observations were made continuously over periods of several hours.

Results—1. Vision: There was no diminution of vision, but all the subjects noticed a slight fading of the test letters, which cannot be attributed to a loss of rectinal sensitivity, but rather to a lack of definition of the letters due to the enlarged pupil.

2. Anesthesia or hyperesthesia: No diminished or increased sensitivity of the cornea and conjunctiva was observed.

3. Pupils: Mydriasis occurred in all subjects. The first evidence of dilatation of the pupil was observed as early as 7 minutes after the first instillation in one case. The mydriatic action in another case did not begin until 67 minutes. Generally the first sign was observed in 15 or 20 minutes. Maximum dilatation (about 7 mm.) was attained in the great majority of subjects in 40 to 60 minutes after the first dilatation. In one case there was only moderate mydriasis. The mydriasis lasted from 3 to 5 hours, depending somewhat, but not wholly, upon the strength of the solutions used.

A distinct difference was observed between subjects with light irides and those with dark. In the subjects with light irides (all Caucasians), the mydriatic action of the drug was much more prompt than in those with dark irides (all Chinese). Furthermore, in the former the dilatation of the pupil was wider, and the weaker solutions were more effective. But the mydriasis seemed to disappear more rapidly in those subjects in which it developed more quickly. Roughly speaking, a 20 per cent solution was as effective in producing mydriasis in the light-eyed cases as a 5 per cent solution was in the dark-eyed. Apparently, there is more rapid absorption as well as quicker elimination of the drug in light-eyed persons. That this is due to an obstructive action on the part of the greater number of pigment cells in the conjunctiva and sclera in the region of the limbus, or of the chromatophores in the iris in dark-eyed persons, is only a surmise. There may be a racial difference in the rate of absorption, but that is unlikely, apart from the variation in the number of pigmented cells.

The pupils were active to light throughout all the experiments.

4. Range of Accommodation: All subjects showed a little loss of accommodation, the amount ranging from 0.25 to 2.5 diopters. The amount depended somewhat on the strength of the solution, but not wholly, for in some of the subjects on whom the stronger solutions were used, the greatest cyclopegic effect did not take place. In brief, there appeared to be an individual difference in the action of the drug upon the ciliary muscle, a difference that could not be explained by the character of the refractive error. The onset of the cyclopegia always developed a little later than the onset of the mydriasis, but generally disappeared some time before the mydriatic effect wore off.

5. Intraocular Tension: A Schiötz tenometer, which measures the tension in millimeters of mercury, was used. A solution of holocaine was used to anesthetize the cornea of both eyes, but the ephedrine solution was instilled into one eye only, the other eye being used as a control. No changes in the tension were observed during a period of more than two hours.

6. Other Symptoms: a. Subjective: All the subjects complained of a stinging and burning sensation after the instillations, the degree depending upon the strength of the solutions. The last drop caused about as much discomfort as did the first, confirming the direct test that no anesthesia developed. Several noticed a sticky, stiff feeling in the lids. Those upon whom the stronger solutions were used complained of dull frontal headache which came on towards the end of the first hour, and lasted for an hour or two; two of these sub-

jects had a little nausea. But in those subjects upon whom the weaker solutions were used, the discomfort was only mild, certainly not more than, or even as much as an individual would have following the use of such drugs as holocaine, homatropine, or zinc sulphate.

b. Objective: All the subjects developed a mild congestion of the superficial vessels of the palpebral and bulbar conjunctiva, which lasted for about 20 or 30 minutes. There also developed a pericorneal or ciliary injection, which was quite marked in two subjects which had strong solutions instilled. The appearance of the conjunctiva became normal generally in about half an hour, but was not followed by blanching, as occurs with adrenalin. The corneal epithelium was examined with a corneal microscope and a slit lamp, but no changes, such as occur following the use of cocaine, were observed. Neither was there any protosis of the eyeball, nor a widening of the palpebral fissure, as occur with cocaine.

Summary—1. Ephedrine hydrochloride, in solutions from 1 to 10 per cent, is a mydriatic, quite uniform in action. The mydriasis lasts from three to five hours.

2. Ephedrine is more effective as a mydriatic in individuals with light irides than in those with dark. Weak solutions of the drug produce approximately the same effect on light eyes, as solutions in about double the strength produce on dark eyes.

3. It has a slight or a moderate cycloplegic effect, which passes off in an hour or two.

4. Ephedrine hydrochloride, when instilled into the eye, is somewhat similar in its physiologic action to atropine, homatropine and cocaine respectively, but its action is more like euphthalmine hydrochloride, although not as prolonged as the latter.

5. It seems to be the best drug that is available for use in making ophthalmoscopic examinations, since its mydriatic and slight cycloplegic effects wear off so quickly.

6. It is somewhat toxic when instilled into the eye in solutions stronger than 5 per cent.

7. A solution of 20 per cent ephedrine hydrochloride is recommended for individuals with light irides, and a 4 per cent solution for those with dark irides.

8. These experiments, on the whole, confirm the work of Miura,[1] and of Chen and Schmidt,[2] but are somewhat more comprehensive and specific in their findings.

[1] Miura, K., *Berlin Klin. Wockenschr.*, 1887, xxxviii, 707.

[2] Chen, K. K., and Schmidt, C. F., *J. Pharm. and Exp. Therap.*, 1924, xxiv, 339.