Production of Unilateral Reversible Cataracts in the Hamster.* (27427)

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Little is known of the pathogenesis of cataracts. For proper investigation of this problem a unilateral experimental cataract produced *in vivo* would provide great advantages because the contralateral eye would serve as a control. Unilateral cataracts have been produced by physical injury to the lens by mechanical trauma or irradiation, but the lens opacities have not been reversible(1). Reversible unilateral cataracts have been produced *in vivo* only by topical application of hypertonic solutions to the cornea(2). It is the purpose of this report to describe an atraumatic method of producing unilateral reversible lens opacities in the hamster.

Materials and methods. The lens opacities were first noted when the pupil was dilated during attempts to transplant malignant melanoma into the posterior part of the hamster eye while the animal was under general anesthesia. Syrian Golden hamsters of random age, weighing about 60 to 150 g were obtained from multiple sources. They were fed Purina Lab chow, given water *ad lib.* and kept in individual wire bottom cages.

Three general anesthetics were administered intraperitoneally. The dosages per 100 g body weight were crystalline sodium pentobarbital 15 mg dissolved in 1.0 ml distilled water, 20% ethanol 1.5 to 2.0 ml, or 1 ml of a mixture of one part sodium pentobarbital (veterinary Nembutal) to 9 parts 10% ethanol. The local anesthetic used was subcutaneous 1% procaine hydrochloride.

To vary pupillary size 4 mydriatics were used: phenylephrine HCl 10%, hydroxyamphetamine bromide 1%, cyclopentolate HCl 1% or atropine sulfate 1%. The miotic used was pilocarpine HCl 1%. The drugs administered were commercially prepared ophthalmic solutions from different companies.

Results. It was found that unilateral cataract could be produced(1) with general anesthesia, the type used being unimportant, if the level of anesthesia was deep enough to block the corneal reflex and allow the eyelids to remain open; (2) without anesthesia if the animal was placed, with the lids of one eye taped open, in a tightly fitting ventilated holder; (3) with anesthetic overdosage or sacrifice of the animal with fracture of the cervical vertebrae, with one eye open and the other taped closed; (4) with excision of the lids of one eye under local anesthesia limited to the eyelids. To produce a unilateral reversible cataract, therefore, maintenance of an open eyelid for at least 20 minutes was indispensable. If the eyelid was taped shut, no lens opacity developed (Fig. 1). Cataracts were produced in the open eye in over 90% of the experiments.

The size of the pupil affected the size of the lens opacity. If the pupil was dilated by a mydriatic the initial opacity was larger than in the undilated eye. In half an hour an eye with the pupil contracted by pilocarpine would have a cataract only in the area of the pupil while the lens in a dilated eye would be opaque over nearly the whole anterior subepithelial surface. However, if after an hour of exposure the eyes were enucleated and the lenses immediately excised the whole anterior surface was found to be opaque even if the pupil had been made miotic. Therefore, the onset of total anterior surface lens opacity was faster if the pupil was dilated than if it was constricted, but there was no difference in final intensity of the lens opacity. Little change in development of cataracts was found if light was excluded or if ambient temperature was raised or lowered.

Factors which increased local evaporation from the cornea, such as blowing air across the cornea or increasing the width of the palpebral fissure, increased the rate of onset of

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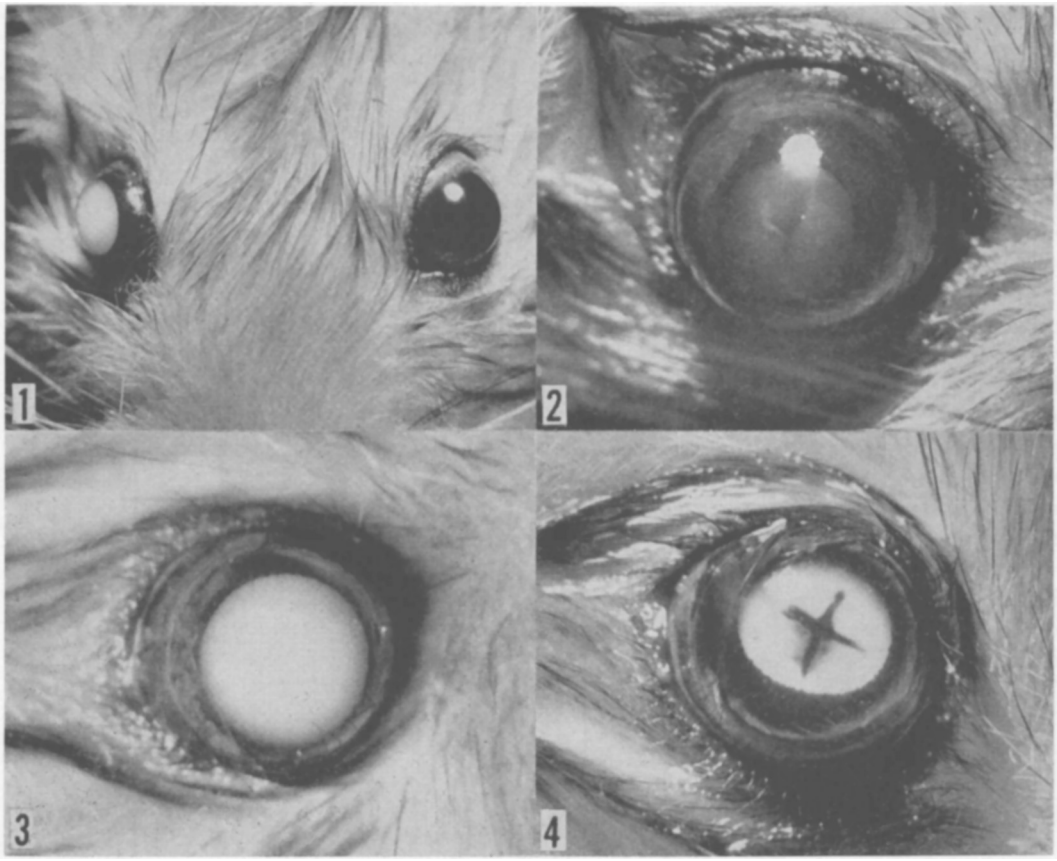

FIG. 1. Unilateral cataract produced by taping left eye shut while right eye remained open. Left eye opened for picture.
FIG. 2. Stage II cataract showing anterior Y suture and gray appearance of anterior cortex.
FIG. 3. Stage IV cataract showing milky white opacity of lens cortex.
FIG. 4. Stage IV cataract with X formed by direct pressure on lens through intact cornea.

lens opacities. Factors that inhibited local evaporation, such as an air tight layer of silicone high vacuum grease (Dow-Corning), a 1 cm column of Hanks' balanced salt solution or normal saline, or an air tight cup, placed over the open eye, prevented formation of cataracts. One drop of Hanks' balanced salt solution placed on the cornea every 15 seconds stopped cataract formation, while one drop every 60 seconds did not.

Description of lens opacities. The normal hamster lens was found to be transparent except for anterior and posterior embryonal Y sutures. Lens opacities could be graded into 4 stages of severity. Stage I was mild haziness of the anterior cortex with increased visibility of the anterior Y suture. In Stage II a definite thickening of the anterior Y suture occurred with a gray appearance of the anterior cortex (Fig. 2). Stage III was a white opacity of the anterior cortex. Stage IV was a milky white total opacity of the anterior lens cortex (Fig. 3). Dissection of the lens revealed the opacity to involve a layer less than one millimeter thick underneath the anterior capsule. The rest of the lens was comparatively clear.

Depending on the method used, the lens opacities usually began 20 to 30 minutes after induction of the experiment and became maximal in 100 to 120 minutes. Depending on depth and length of the anesthesia or other experimental procedure the opacities would clear in either the dead or living animal between 100 to 400 minutes even though the eyelid remained open. If the eyelid was

closed after the cataract developed the opacity cleared completely in about 60 minutes, even in a dead animal. Usually the opacity cleared first in the center of the anterior cortex, but occasionally random eccentric areas cleared first. Focal pressure on the opaque lens, through the intact cornea, immediately cleared that area of the lens compressed (Fig. 4).

Biomicroscopy with a slit beam 20 to 30 minutes after a cataract was well formed, showed that the anterior chamber or space between the iris and the cornea was narrowed very markedly in the cataractous eye as compared to the control eye. After maximal cataract development, the cataractous eye was notably softer and there was roughening of the corneal epithelium.

Discussion. Dehydration appears to be important in the pathogenesis of these lens opacities but may not be the only factor, since the opacity reverses while the dehydrating stimulus is still active. Investigations of lens and aqueous humor changes as well as atmospheric factors are in progress.

Summary. Several highly effective methods for production of unilateral reversible cataracts in hamsters are described. With each method, the eyelids must remain open to expose the cornea, and the lens opacity which develops will clear even if the eyelids remain open, but will clear more rapidly if the lids are closed. No cataract develops if the eyelids are kept closed or protected by an air tight seal. The mechanisms involved are being investigated.

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1. Pirie, A., Heyningen, R. V., *Biochemistry of the Eye,* Blackwell Scientific Publications, Oxford, 1956, 92.

2. Heubel, Emil, *Arch. f. Physiol.,* 1879, v20, 114.

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Acute Systemic and Coronary Hemodynamic Effects of Trimethidinium Methosulfate.* (27428)

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Ganglionic blocking agents have been used extensively in treatment of essential hypertension; however, none seem to be universally effective and all have limitations. The search for better blocking agents has led recently to development of a new synthetic compound, trimethidinium methosulfate, an asymmetric bis-quaternary amine. Pharmacological studies of this compound showed that ganglion blocking properties and hypotensive responses do not run necessarily parallel. Furthermore it has been suggested that the drug may have a central component of action(1). Clinical evaluation of trimethidinium methosulfate showed that it has a hypotensive action similar to that of other ganglionic blocking agents(2,3,4,5,6,7). Associated side effects on the gastrointestinal tract are reported to be mild and easily controlled when compared with those of pentapyrrolidinium and mecamylamine(5).

The following study of the hemodynamic effects of trimethidinium methosulfate on systemic and coronary circulations was undertaken in the hope that the information obtained would be of some value in guiding the clinician in his selection of therapeutic agents.

Material and methods. The present study was carried out in 10 mongrel dogs weighing

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