THIRD EDITION

TOXICOLOGY OF THE EYE

Effects on the Eyes and Visual System from Chemicals, Drugs, Metals and Minerals, Plants, Toxins and Venoms; also, Systemic Side Effects from Eye Medications

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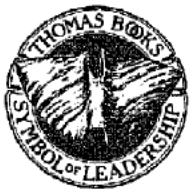

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due to accumulation of *xylitol*, electrolytes and water when D-xylose is added to the medium. Addition of an aldose reductase inhibitor prevents these effects of xylose, demonstrating the primary role of this enzyme in the cataractogenic process, similar to its role in experimental galactose cataracts.

a. Obazawa H, Merola LO, Kimoshita JH: The effects of xylose on the isolated lens. *INVEST OPHTHALMOL* 13:204–209, 1974.
b. Patterson JW, Bunting KW: Sugar cataracts, polyol levels and lens swelling. *DOCUM OPHTHALMOL* 20:64–72, 1966.
c. Schrader KE: Morphology and pathogenesis of experimental xylose cataract. *GRAEFES ARCH OPHTHALMOL* 163:422–443, 1961. (German)
d. Van Heyningen R: Xylose cataract; A comparison between the weanling and the older rat. *EXP EYE RES* 8:379–385, 1969.

Xylyl bromides and **chlorides** (including o-, m-, and p-isomers) are strongly lacrimatory.[171]

(See also Bromoxylene.)

Ytterbium chloride tested on rabbit eyes by applying 0.1 ml of 1 : 1 aqueous solution at pH 3.05 to 3.78, caused "conjunctival irritation" and ulceration which healed in ninety-six hours.[97]

Yttrium chloride applied to rabbit eyes as a 0.1 M solution (pH 5.4) for ten minutes caused no injury, but similar exposure of eyes from which the corneal epithelium had been removed to facilitate penetration of the yttrium chloride resulted in immediate slight haziness of the cornea, with subsequent increasing opacity in the next several days. Finally the corneas became completely opaque and vascularized. Exposure to 0.01 M solution after removal of the epithelium resulted in slight to mild permanent opacification.

Treatment by irrigation with neutral 0.01 to 0.1 M sodium edetate (EDTA) solutions for fifteen minutes immediately after exposure to yttrium chloride solution prevented much of the opacification and vascularization. Similar treatment with sodium chloride solution was without appreciable effect.[88] (Compare *Rare-earth salts; see INDEX.*)

Zinc chloride and **zinc sulfate** are described together because they have strong similarities in their properties, though injuries of the cornea have been more commonly related to the chloride than to the sulfate, and most animal experiments have been carried out with the chloride. Both salts are white, odorless solids, very soluble in water (1 g in 0.5 or 0.6 ml of water, forming slightly acid solutions, pH 4 or 4.5). Zinc chloride is used in high concentration in soldering fluxes, galvanizing baths, sometimes in golf balls, and in "chemosurgery" of skin cancer. Dilute solutions (0.2% to 1%) have long been used as astringent eyedrops without difficulty, but concentrated solutions and pastes such as encountered industrially have caused very severe injuries of the cornea in numerous cases of accidental splash in the eye.

The following description is organized to present information on the toxic effects in the following order: (a) human eye injuries from concentrated zinc chloride,

(b) eye injuries from concentrated zinc sulfate, (c) animal experiments with zinc chloride, and (d) clinical experience with dilute zinc salt solutions.

Human eye injuries from concentrated zinc chloride. These have been reported several times since 1903. Lewin and Guillery and Wagenmann summarized what had been reported to 1913.[153,253] Tillot, according to Wagenmann, reported the first case of corneal ulceration and iritis, but eventual partial recovery, after accidental splash of a concentrated zinc salt in 1903.

Zur Nedden reported in detail concerning a workman who splashed a zinc chloride solution of unstated concentration in one eye, causing at first only some redness, and persistent discomfort, but within six days leading to a discrete stromal opacity in the lower part of the cornea with irregularity of the overlying epithelium.[268] The opacity was grayish, located in the anterior layers of the stroma. During the next month, while some portions cleared, the remainder became dense white, and was thought to be a zinc encrustation. A discrete white opacity covered by epithelium remained, and because it was in the lower part of the cornea did not affect vision. Strader also reported a case of partial irreversible corneal opacification from zinc chloride burn.[n]

Van Lint described a workman who had splashed in one eye a liquid composed of zinc chloride, ammonium chloride, iron chloride, and hydrochloric acid, producing a burn of the cornea, and subsequently white spots in the front of the lens.[o] At six weeks after the injury the cornea still had stromal infiltration. The lens showed a great many white spots of varied shape beneath the anterior capsule, smaller than initially. From 2.5 to 6 months after injury the vision recovered only from 1/10 to 1/6, with a correcting spectacle. The impairment of vision was due to abnormality of the cornea rather than to the anterior subcapsular lens changes. The deeper parts of the lens remained normal.

Rzehulka described in detail a patient who had an eye accidentally burned by instillation of one drop of 50% zinc chloride solution.[m] There was immediate severe pain, which persisted despite immediate irrigation with water. The corneal epithelium became eroded. Large folds developed in Descemet's membrane, and the corneal stroma was turbid. This was accompanied by severe iritis with small hemorrhages in the iris. Deep and superficial vascularization of the cornea followed. The eye was treated with mydriatic and cortisone eyedrops and 5% neutral ammonium tartrate eye bath. In four months the cornea cleared sufficiently to permit 6/8 vision.

De Rose described a workman who splashed a reaction mixture of zinc and hydrochloric acid in one eye, causing great pain.[a] After irrigation of the surface, the cornea was found to have lost its epithelium but the stroma appeared transparent. Two days later most of the cornea was transparent, but for the first time small opacities appeared in the anterior cortical layers of the lens. Vision was reduced to 1/12 and the intraocular pressure was subnormal. At six days the anterior cortical lens opacity was more diffuse and the aqueous turbid. At ten days the surface of the cornea was almost healed, but the lens opacity and turbidity of the aqueous were more accentuated, and much pigment became deposited on the posterior surface of the cornea. The intraocular pressure remained low, and treatment with mydriatics and local corticosteroid was continued. At twenty days the patient had acute glau-

coma with pain, corneal edema, and tension of 50 mm Hg, responding to treatment with oral acetazolamide during several days, but at about thirty days from the injury the glaucoma and pain returned. The cornea was diffusely clouded by edema and much pigment on the posterior surface. A scleral staphyloma developed. Vision was so low and pain so great that the eye was enucleated. Histologic examination confirmed extensive dissemination of pigment on the back surface of the cornea and in the trabecular meshwork. Also, iridocorneal synechias were present irregularly. The iris was mostly degenerated, with nearly complete loss of pigment. The lens had become cataractous. It was believed that these extensive injuries were attributable to the action of zinc chloride. The glaucoma was believed to have been due to infiltration of the trabecular meshwork with pigment.

Houle and Pavan-Langston have reported on two patients who had severe damage to their eyes from concentrated zinc chloride.[e,k] One of these patients had zinc chloride solder-flux paste splashed into one eye. The other patient had his eyes accidentally drenched by concentrated zinc chloride solution used in galvanizing steel. Both patients within the next day or two developed changes in the appearance of their eyes that was remarkably similar to the appearance of eyes that have very recently undergone severe acute attacks of angle-closure glaucoma. These eyes had extensive corneal edema, with wrinkling of the posterior surface, cells in the aqueous humor, and small discrete spots of gray opacity on the front of the lens, exactly like Glaukomflecken. Both patients took many months for subsidence of their corneal edema and for recovery of useful vision. Glaucoma was not a problem in these patients, but acetazolamide was given with the hope of making the intraocular pressure lower than normal. Corticosteroids given systemically seemed to help relieve discomfort and photophobia that developed after the corneal epithelium (and presumably the corneal nerves) regenerated. In these cases, as in those previously described in the literature, the spots in the lenses that were evident within the first few days after injury not only looked like Glaukomflecken, but also subsequently behaved like Glaukomflecken, persisting, but tending to become smaller, and causing no significant trouble. The corneas were the great problem.

In treatment of cancer of the eyelid and closely neighboring skin, Mohs has used a saturated solution of zinc chloride made into a paste by addition of powdered stibnite (antimony trisulfide) and sanguinaria powder.[g,h] Fortunately, injury to the eye has not occurred. This may be explained by the fact that the paste has been applied to the outer surface of the eyelid, and care has been taken not to bring the paste into direct contact with the eye.

Human eye injuries from concentrated zinc sulfate solutions. These seem all to have been reported in the 1950's as a complication of use of 20% zinc sulfate solution for treatment of dendritic keratitis, recurrent erosion, and ulcus serpens. Prior to 1955 the application of 20% zinc sulfate solution on a swab directly to such ulcers was considered to be fairly safe, and though some cursory mention had been made of occasional delicate branching opacities which had developed under the anterior lens capsule, such complications were considered to be rare.[c,i] Pillat presented the first detailed description of cases of white flecks induced in the lens after cauterization of the cornea with 20% zinc sulfate, having the characteristic appear-

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