# Acute and Chronic Conjunctivitis Due to Over-the-counter Ophthalmic Decongestants

Charles N. S. Soparkar, MD, PhD; Kirk R. Wilhelmus, MD; Douglas D. Koch, MD; Gary W. Wallace, MD; Dan B. Jones, MD

**Objective:** To describe patterns of conjunctivitis caused by ophthalmic decongestants.

**Design:** Case series.

Setting: Outpatient eye clinic.

**Patients:** We selected patients with conjunctival inflammation who were using nonprescription decongestant eyedrops, who had no other cause for conjunctivitis, and whose conditions improved after discontinuing the incriminated preparations.

**Main Outcome Measures:** Clinical characteristics of conjunctival inflammation and time to resolution of symptoms and signs after discontinuing the use of eyedrops.

Results: Seventy patients (137 eyes) were identified. Prepa-

rations containing the vasoconstrictors naphazoline, tetrahydrozoline, or phenylephrine were associated with 3 clinical patterns of conjunctivitis: conjunctival hyperemia (50 cases), follicular conjunctivitis (17 cases), and eczematoid blepharoconjunctivitis (3 cases). Decongestants were used daily for a median of 3 years (range, 8 hours to 20 years) prior to presentation. The median time to resolution of symptoms and signs was 4 weeks (range, 1-24 weeks), and patients remained asymptomatic for a median follow-up of 6 months (range, 0-12 years).

**Conclusion:** Nonprescription decongestant eyedrops can produce acute and chronic forms of conjunctivitis by pharmacological, toxic, and allergic mechanisms. Once recognized, conjunctival inflammation often takes several weeks to resolve.

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VER-THE-COUNTER ophthalmic decongestants are commonly used to control ocular redness and discomfort.<sup>1-11</sup> The

principal active ingredient in these eyedrops is an  $\alpha$ -adrenergic, vasoconstrictive amine such as naphazoline, tetrahydrozoline, or phenylephrine; some preparations also contain an antihistamine for type 1 histamine-receptor blockade.

Adverse systemic reactions to topical vasoconstrictors are uncommon but include nervousness,<sup>12</sup> headache,<sup>13-16</sup> dizziness,<sup>14</sup> nausea,<sup>14</sup> hypotension,<sup>17,18</sup> hypertension,<sup>13,14,16,19,20</sup> and cardiac dysrhythmia.<sup>14</sup> The most frequent local side effect of oph-thalmic vasoconstrictors is ocular stinging.<sup>7,21,22</sup> However, mydriasis,<sup>5,7,23-25</sup> blurred vision,<sup>7,15</sup> epithelial erosion,<sup>21,26</sup> punctal stenosis,<sup>27,28</sup> corneal epithelial pigment deposition,<sup>29</sup> iris pigment release,<sup>22,23</sup> iritis,<sup>30</sup> intraocular pressure change (ie, increase or decrease),<sup>7,13,23,24,31,32</sup> and acute angle closure<sup>15,24,25</sup> have also been described. Additionally, antihistamines may produce allergies and local irritations.<sup>33,34</sup>

Our experience indicates that decongestant eyedrops containing vasoconstrictors, with or without antihistamines, are causes of acute and chronic conjunctival inflammation.

# RESULTS

Seventy patients with ophthalmic decongestant-related conjunctivitis were identified (50 from the external disease clinic and 20 from the general clinics) (**Table 1**). The mean age at presentation was  $42.5\pm15.9$  years (range, 18-82 years). The frequency of daily eyedrop application ranged from 1 to 12 times (mean,  $3.7\pm2.2$ times per day). The duration of medication use prior to presentation averaged

See Patients and Methods on next page

From the Cullen Eye Institute, Department of Ophthalmology, Baylor College of Medicine, Houston, Tex. The authors have no commercial or proprietary interest in the products discussed in this article.

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# PATIENTS AND METHODS

Adverse reactions to ophthalmic decongestants were sought in medical records coded with a primary diagnosis of conjunctivitis. These records were generated from patients examined during the past 12 years by 2 external disease specialists (K.R.W. and D.B.J.) at the Cullen Eye Institute, Houston, Tex, and from patients examined during the past 4 and 6 months at general ophthalmology clinics at Ben Taub General Hospital, Houston, and the Veterans Affairs Medical Center, Houston, respectively. Cases were excluded if other ocular surface disease was present, nondecongestant eyedrop use occurred within 2 weeks of presentation, or follow-up failed to demonstrate improvement of the conjunctival inflammation after discontinuing decongestant use. In some cases, conjunctival scrapings were obtained for cytologic examination and chlamydial infection testing (eg, Giemsa-stain examination, organism culture, or fluorescent antibody detection of the chlamydial antigen).

After resolution of decongestant-induced conjunctivitis by discontinuing use of their eyedrops, 4 patients agreed to be rechallenged for 2 weeks with new preparations of the presumed offending medications at the same frequency as used prior to presentation.

Nonparametric analyses included the Spearman rank correlation, the Wilcoxon rank sum test, and the Fisher 2-tailed exact test. Values are expressed as the mean( $\pm 1$  SD).

3.5±4.5 years (range, 8 hours to 20 years). The ocular symptoms on presentation included eyelid swelling, epiphora, ocular awareness, irritation, itching, burning, pain, foreign-body sensation, or redness. Twelve brands of ophthalmic decongestants were implicated (**Table 2**).

Three clinical patterns of conjunctivitis were identified: (1) *conjunctival hyperemia* (**Figure 1**), which is defined as diffuse hyperemia and chemosis of the conjunctiva extending beyond the interpalpebral fissure, episcleral vascular dilation, and papillae of the upper and lower pretarsal conjunctiva; (2) *follicular conjunctivitis* (**Figure 2**), which is defined as bulbar or palpebral follicles with ocular symptoms, regardless of the degree of conjunctival inflammation; and (3) *blepharoconjunctivitis* (**Figure 3**), which is defined as subcutaneous edema and hyperemia of the eyelids, diffuse chemosis, and bulbar and pretarsal conjunctival hyperemia.

Eighteen patients (including all patients with follicular conjunctivitis) were tested for chlamydial infection; the results of all tests were negative. Ten patients (4 with conjunctival hyperemia and 6 with follicular conjunctivitis) underwent conjunctival scrapings, all of which demonstrated many lymphocytes, occasional polymorphonuclear leukocytes, and few or no eosinophils.

Conjunctival hyperemia was present in 50 cases (71%); follicular conjunctivitis, 17 cases (24%); and blepharoconjunctivitis, 3 cases (4%). Ophthalmic de-

congestants, individually and as a group, were most likely to cause conjunctival hyperemia (P<.001, data not shown). Naphcon-A (naphazoline hydrochloride, Alcon Laboratories, Fort Worth, Tex), an exception, was associated with follicular conjunctivitis (P=.01, data not shown).

All patients with conjunctival hyperemia or follicular conjunctivitis were first treated by discontinuing the topical medication. After initial improvement of their conditions, 24 (36%) of these 67 patients were then prescribed a corticosteroid drop at an initial frequency of 4 times daily; this frequency was tapered during a 1- to 10week period. The corticosteroids used included 0.1% fluorometholone, 0.1% fluorometholone acetate, 0.125% or 1% prednisolone phosphate, and 1% prednisolone acetate. Patients with conjunctival hyperemia showed no difference in time to recovery whether they were treated with corticosteroids or not (Wilcoxon rank sum test, z = -0.49, P=.63, Table 1). In contrast, patients with follicular conjunctivitis showed faster improvement of their conditions with corticosteroid use (mean recovery time,  $3.3 \pm 1.0$  weeks vs  $10.3 \pm 7.2$  weeks; Wilcoxon rank sum test, z=2.58, P=.01). All patients with eczematoid blepharoconjunctivitis were treated with topical corticosteroids.

The time to resolution of signs and symptoms for all cases of conjunctivitis averaged  $6.8\pm6.7$  weeks (median, 4 weeks; range, 1-24 weeks). A positive correlation was found between the duration of decongestant eyedrop use prior to presentation and the time required for recovery (Spearman rank correlation, r=0.346, P=.01). No association was found between individual decongestant preparations or the frequency of daily eyedrop use and the time to recovery (P=.62).

Four patients in whom conjunctival hyperemia was diagnosed were rechallenged with new preparations of their vasoconstrictors. Three patients applied their decongestants (Visine [tetrahydrozoline hydrochloride], Pfizer Inc, New York, NY; Clear Eyes [naphazoline hydrochloride], Ross Laboratories, Columbus, Ohio; and Murine Plus [tetrahydrozoline hydrochloride], Ross Laboratories) in 1 or both eyes for 2 weeks and had a relapse of their signs and symptoms in the treated eye(s). The fourth patient was unavailable for follow-up.

#### COMMENT

Nonprescription ophthalmic decongestants can cause acute and chronic conjunctivitis. Three clinical patterns are described that likely represent distinct pathophysiological mechanisms.

Conjunctival hyperemia, the most common form of decongestant-associated conjunctivitis, is probably a pharmacologically induced rebound phenomenon following vasoconstrictor discontinuation. The mechanism may be either vasoconstrictor-induced tissue ischemia<sup>35</sup> with release of a vasodilating substance or constrictor tachyphylaxis.<sup>36</sup> Nasal preparations containing  $\alpha$ -adrenergic amines are well known to cause rebound vascular dilation in the nasal mucosa,<sup>7,12,37,40</sup> and such a reaction also occurs in the conjunctiva following epinephrine eyedrop use.<sup>30,41</sup> Although previous experience suggests that

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#### Table 1. Characteristics of Vasoconstrictor-Associated Conjunctivitis\*

Form of Conjunctivitis	Sex, No. of Cases (% of Total)			Frequency,		Time to Recovery, wk	
						Without	With
	M	F	Age, y	Drops/d	Duration of Use, y	Corticosteroids	Corticosteroids
Conjunctival hyperemia	24	26	41.2±16.3	3.5±2.3	3.2±3.6	6.2±6.1	9.8±8.6
	(89)	(60)	(38, 18-82)	(3, 1-12)	(3, 10 d-20 y)	(4, 2-24)	(5, 3-24)
Follicular conjunctivitis	2	15	46.1±15.7	4.5±1.9	5.0±6.7	10.3±7.2†	3.3±1.0†
	(7)	(35)	(43, 22-79)	(4, 2-9)	(2, 0.3-20)	(7, 3-20)	(3.5, 1-4)
Blepharoconjunctivitis	1	2	44.3±2.1	3.7±1.5	0.2±0.2		1.3±0.6
	(4)	(5)	(45, 42-46)	(4, 2-5)	(0.2, 8 h-0.3 y)		(1, 1-2)
All forms	27	43	42.5±15.9	3.7±2.2	3.5±4.5	7.1±6.5	6.5±7.25
		고 문화 영화	(41.5, 18-82)	(4, 1-12)	(3, 8 h-20 y)	(4, 2-24)	(4, 1-24)

\*Values are expressed as the mean ±1 SD. The median and the range are given in parentheses unless otherwise indicated. Ellipses indicate data not applicable. +Significantly different (P=.01).

			Preservatives, %		
Medication† (Manufacturer, Location)	Adrenergic Agonist, %	Antihistamine, %	Benzalkonium Chloride	Edetic Acid	
Albalon Liquifilm (Allergan Inc, Irvine, Calif)	Naphazoline, 0.050		0.004	0.013	
Albalon-A Liquifilm (Allergan Inc)	Naphazoline, 0.050	Antazoline, 0.50	0.004	0.013	
Clear Eyes (Ross Laboratories, Columbus, Ohio)	Naphazoline, 0.012	영양을 만드는 것으로	0.010	0.100	
Collyrium Fresh-Eye Drops (Wyeth-Ayerst Laboratories, Philadelphia, Pa)	Tetrahydrozoline, 0.050		0.010	0.100	
Murine Plus (Ross Laboratories)	Tetrahydrozoline, 0.050		0.010	0.020	
laphcon (Alcon Laboratories, Fort Worth, Tex)	Naphazoline, 0.012		0.010	0.050	
Vaphcon-A (Alcon Laboratories)	Naphazoline, 0.025	Pheniramine, 0.30	0.010	0.010	
Naphcon Forte (Alcon Laboratories)	Naphazoline, 0,100		0.010	0.050	
Prefrin Liquifilm (Allergan Inc)	Phenylephrine, 0.120		0.005	0.015	
/asocon-A (lolab Corporation, Claremont, Calif)	Naphazoline, 0.050	Antazoline, 0.05	0.010		
/isine (Pfizer Inc. New York, NY)	Tetrahydrozoline, 0.050		0.010	0.100	
Visine AC (Pfizer Inc)	Tetrahydrozoline, 0.050		0.005	0.015	

\*Ellipses indicate data not applicable.

†Trademark names.



**Figure 1.** Conjunctival hyperemia. A 43-year-old woman who used 0.05% tetrahydrozoline eyedrops, 3 times daily, for 12 years had bilateral, symmetric hyperemia of the upper and lower tarsal conjunctiva; marked, diffuse hyperemia of the bulbar conjunctiva; and dilated superficial episcleral vessels. One week after discontinuing use of the decongestant, her conjunctival and episcleral hyperemia were diminished. A 1-week tapering course of 0.125% prednisolone phosphate drops was used. In 3 weeks, she was asymptomatic and remained so during 7 months of follow-up.

vasoconstrictors never<sup>1,2,3,7,8,42-45</sup> or rarely<sup>43,46,47</sup> incite conjunctival hyperemia, the 50 cases in this series clearly demonstrate that ophthalmic decongestants containing phenylephrine, naphazoline, or tetrahydrozoline can cause rebound dilation of conjunctival blood vessels.

Follicular conjunctivitis, which probably represents a toxic effect, <sup>34,48</sup> accounts for one fourth of the cases in this series. Follicles were most prominent in the lower palpebral conjunctiva and fornix but were also present on the bulbar and upper palpebral conjunctiva. These 17 cases are the first reports of bulbar follicles resulting from the use of decongestants. The factor(s) responsible may be any of a number of agents in the decongestant preparations: the vasoconstrictor,<sup>30,34</sup> an antihistamine (if present),<sup>34</sup> or 1 of the preservatives.<sup>33,34,49-54</sup>

Eczematoid blepharoconjunctivitis was the least common reaction in this series. Although benzalkonium chloride,<sup>21,34</sup> edetic acid,<sup>34,55</sup> and phenylephrine<sup>21,22</sup> can cause contact hypersensitivity, to our knowledge, our cases are the first reports of allergic blepharoconjunctivitis associated with preparations containing naphazoline and tetrahydrozoline.

The incidence of adverse reactions to ophthalmic decongestants is unknown. Even if the incidence is low, the

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**Figure 2.** Follicular conjunctivitis. A 67-year-old woman who used 0.1% naphazoline eyedrops, 4 times daily, for 6 months had diffuse conjunctival hyperemia and prominent follicles of the inferior tarsal conjunctiva. Follicles involving the superior tarsal and nasal bulbar conjunctiva are not shown. Giemsa-stained conjunctival scrapings showed a lymphocytic predominance with some polymorphonuclear leukocytes and rare eosinophils. After discontinuing use of the eyedrops for 2 weeks, the follicular reaction, conjunctival hyperemia, and symptoms decreased. She remained asymptomatic for 6 months of follow-up.



**Figure 3.** Blepharoconjunctivitis. Acute chemosis, upper-eyelid edema, and lower-eyelid eczematoid skin changes developed in a 70-year-old man 8 hours following the use of 0.05% tetrahydrozoline eyedrops in his right eye. Multiple small, sterile, peripheral infiltrates (not shown) were noted in the cornea. After 1 week of using 0.05% dexamethasone ophthalmic ointment, his signs and symptoms resolved and did not recur during 1 month of follow-up.

number of patients suffering reactions may be substantial because more than 15 million bottles of these eyedrops are sold each year in the United States.<sup>56</sup> Predisposing factors have not been determined, but some individuals may be prone to decongestant-induced conjunctivitis through sensitization or idiosyncratic susceptibility. After their initial examination and treatment, 2 patients in this series returned years later with conjunctivitis resulting from the use of a different decongestant, and recurrent conjunctival hyperemia rapidly developed in 3 patients who were rechallenged with their medications.

The diagnosis of decongestant-associated conjunctivitis relies on excluding other ocular surface conditions and asking patients specifically about the use of overthe-counter products that they may not consider to be medications. In managing vasoconstrictor-induced conjunctivitis, we recommend discontinuing all eyedrops for a "wash-out" period of 2 weeks and explaining to patients that their symptoms may temporarily worsen because of a rebound phenomenon. Rebound hyperemia and follicular conjunctivitis often take many weeks to resolve; the longer the duration of eyedrop use prior to presentation, the longer the time to recovery. In our series, topical corticosteroids did not alter the rate of recovery for cases of conjunctival hyperemia, but they did shorten the recovery time for cases of follicular conjunctivitis and were routinely used in all cases of contact hypersensitivity.

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Corresponding author: Douglas D. Koch, MD, Cullen Eye Institute, 6501 Fannin St, NC 200, Houston, TX 77030.

# REFERENCES

- Abelson MB, Allansmith MR, Friedlaender MH. Effects of topically applied ocular decongestant and antihistamine. Am J Ophthalmol. 1980;90:254-257.
- Abelson MB, Paradis A, George MA, Smith SM, Maguire L, Burns R. Effects of Vasocon-A in the Allergen challenge model of acute allergic conjunctivitis. Arch Ophthalmol. 1990;108:520-524.
- Abelson MB, Yamamoto GK, Allansmith MR. Effects of ocular decongestants. Arch Ophthalmol. 1980:98:856-858.
- Friedlaender MH. Current concepts in ocular allergy. Ann Allergy. 1991;67:5-10.
- 5. Gordon DM. Ocular decongestants. Am J Ophthalmol. 1959;48:395-396.
- Hurwitz P. Local antihistamine agents in ophthalmology. III Med J. 1950;98: 113-116.
- Hurwitz P, Thompson JM. Uses of naphazoline (privine) in ophthalmology. Arch Ophthalmol. 1950;43:712-717.
- Miller J, Wolf EH. Antazoline phosphate and naphazoline hydrochloride, singly and in combination for the treatment of allergic conjunctivitis: a controlled, double blind clinical trial. *Ann Allergy*. 1975;35:81-86.
- Nemeth L. Antihistamines in ophthalmology. Br J Ophthalmol. 1949;33:665-669.
- Salem H, Dunn BJ, Loux JJ. Conjunctival temperature: a measure of ocular decongestant and anti-inflammatory activity. *Ann Ophthalmol.* 1975;7:819-824.
- Smith JP, Lanier BQ, Tremblay N, Ward RL, deFaller JM. Treatment of allergic conjunctivitis with ocular decongestants. *Curr Eye Res.* 1982;2:141-147.
- Mertins PS. Excessive self-medication with naphazoline hydrochloride (privine hydrochloride). JAMA. 1947;134:1175.
- Caputo AR, Schnitzer RE. Systemic response to mydriatic eye drops in neonates: mydriatics in neonates. J Pediatr Ophthalmol Strabismus. 1979;15:109-122.
- Fraunfelder FT, Scafidi AF. Possible adverse effects from topical ocular 10% phenylephrine. Am J Ophthalmol. 1978;85:447-453.
- Meyer SM, Fraunfelder FT. Phenylephrine hydrochloride. *Ophthalmology*. 1980; 87:1177-1179.
- Lansche RK. Systemic reactions to topical epinephrine and phenylephrine. Am J Ophthalmol. 1966;61:95-98.
- Mindlin RL. Accidental poisoning from tetrahydrozoline eyedrops. N Engl J Med. 1966;275:112.
- 18. Rogers GW. Safe use of eye drops. N Engl J Med. 1966;275:447.
- Heath P. Neosynephrine hydrochloride: some uses and effects in ophthalmology. Arch Ophthalmol. 1936;16:839-846.
- Rosales T, Isenberg S, Leake R, Everett S. Systemic effects of mydriatics in low-weight infants. J Pediatr Ophthalmol Strabismus. 1981;18:42-44.
- Hanna C, Brainard J. Allergic dermatoconjunctivitis caused by phenylephrine. Am J Ophthalmol. 1983;95:703-704.
- 22. Mathias CGT, Maibach HI, Irvine A, Adler W. Allergic contact dermatitis to echothio-

# ARCH OPHTHALMOL/VOL 115, JAN 1997

Slayback Exhibit 1096, Page 4 of 5 Slayback v. Eye Therapies - IPR2022-00142 phate iodide and phenylephrine. Arch Ophthalmol. 1979;97:286-287.

- Epstein DL, Boger WP III, Grant WM. Phenylephrine provocative testing in the pigmentary dispersion syndrome. Am J Ophthalmol. 1978;85:43-50.
- Rumelt MB. Blindness from misuse of over-the-counter eye medications. Ann Ophthalmol. 1988;20:26-30.
- Weiss DI, Shaffer RN. Mydriatic effects of one-eighth percent phenylephrine: a potential cause of angle-closure glaucoma. Arch Ophthalmol. 1962;68:41-43.
- Komi T, Maeda I, Uno Y, Otsuka H. Inhibitory effect of sodium chondroitin sulfate on epithelial keratitis induced by naphazoline. *Nippon Geka Gakkai Zas*shi. 1964;68:154-158.
- Lisch K. Conjunctival alterations by sympathomimetic drugs. Klin Monatsbl Augenheilkd. 1978;173:404-406.
- Saraux H, Offret H, de Rancourt de Mimerand E. Pseudo-perniphigus oculaire induit par les collyres: a prpos de 3 observations. *Bull Soc Ophtalmol Fr.* 1980; 80:41-45.
- Herman DC, Bartley GB. Corneal opacities secondary to topical naphazoline and antazoline (Albalon-A). Am J Ophthalmol. 1987;103:110-111.
- Aronson SB, Yamamoto EA. Ocular hypersensitivity to epinephrine. Invest Ophthalmol. 1966;5:75-80.
- 31. Hill K. What's the angle on mydriasis? Arch Ophthalmol. 1968;79:804.
- Lee PF. The influence of epinephrine and phenylephrine on intraocular pressure. Arch Ophthalmol. 1958;60:863-867.
- 33. Cohen SC. Antistene eyedrops. Am J Ophthalmol. 1952;35:1704-1705.
- Wilson FM. Adverse external ocular effects of topical ophthalmic medications. Surv Ophthalmol. 1979;24:57-88.
- Isenberg SJ, Green BF. Effect of phenylephrine hydrochloride on conjunctival Po<sub>2</sub>. Arch Ophthalmol. 1984;102:1185-1186.
- Kully BM. The use and abuse of nasal vasoconstrictor medications. JAMA. 1945;127:307-310.
- Feinberg SM, Friedlaender SJ. Nasal congestion from frequent use of privine hydrochloride. JAMA. 1945;128:1095-1096.
- Fennenbaum JI. Allergic rhinitis. Paterson R, ed. Allergic Diseases: Diagnosis and Management. 2nd ed. Philadelphia, Pa: JB Lippincott; 1980:87.
- Schiller IW. Deleterious effects of privine hydrochloride. N Engl J Med. 1945; 232:333-335.
- 40. Sternberg L. The abuse of vasoconstrictors in hay fever and vasomotor rhi-

nitis. N Y State J Med. 1944;44:1573-1574.

- 41. Shaffer RN. Autonomic ocular drugs. Invest Ophthalmol. 1964;3:498-499.
- Abelson MB, Butrus SI, Weston JH, Rosner B. Tolerance and absence of rebound vasodilation following topical ocular decongestant usage. *Ophthalmol*ogy. 1984;91:1364-1367.
- Grossmann EE, Lehman RH. Ophthalmic use of tyzine: a clinical study of this new vasoconstrictor. Am J Ophthalmol. 1956;42:121-123.
- Menger HC. New ophthalmic decongestant, tetrahydrozoline hydrochloride: clinical use in 1,156 patients with conjunctival irritation. JAMA. 1959;170:178-179.
- Stokes JJ. Clinical evaluation of tetrahydrozoline ophthalmic solution. J Med Assoc Ga. 1958;47:540-541.
- 46. Mamelok AE. Allergic conjunctivitis. Cutis. 1976;17:244-248.
- Spector SL, Raizman MB. Conjunctivitis medicamentosa. J Allergy Clin Immunol. 1994;94:134-136.
- Liesegang TJ. Bulbar conjunctival follicles associated with dipivefrin therapy. Ophthalmology. 1985;92:228-233.
- Fisher AA, Pascher F, Kanof NB. Allergic contact dermatitis due to ingredients of vehicles: a 'vehicle tray' for patch testing. *Arch Dermatol.* 1971;104:286-290.
- Fisher AA, Stillman MA. Allergic contact sensitivity to benzalkonium chloride: cutaneous, ophthalmic, and general medical implications. *Arch Dermatol.* 1972; 106:169-171.
- Gasset AR, Ishii Y, Kaufman HE. Cytotoxicity of ophthalmic preservatives. Am J Ophthalmol. 1974;78:98-105.
- Lemp MA, Zimmerman LE. Toxic endothelial degeneration in ocular surface disease treated with topical medications containing benzalkonium chloride. Am J Ophthalmol. 1988;105:670-673.
- Sussman JD, Friedman M. Irritation of rabbit eye caused by contact-lens wetting solutons. Am J Ophthalmol. 1969;68:703-706.
- Theodore FH, Schlossman A. Ocular Allergy. Baltimore, Md: Williams & Wilkins; 1958:64-77.
- Raymond JZ, Gross PR. EDTA: preservative dermatitis. Arch Dermatol. 1969; 100:436-440.
- IMS America Ltd staff. Ophthalmic decongestants, in US pharmaceutical market: drug store and hospital purchases. Presented at the Plymouth Meeting of IMS America Ltd; January 1990-June 1991; Plymouth, Pa.

## Notes From Our Ophthalmic Heritage

#### A look at the past . . .

he knowledge which the ancient Surgeons professed was not very extensive. Their theory was confined—their practice consequently rude; but in *Ophthalmic* operations, they were particularly unskillful. It is not till very recently that the operation of the Cataract has been performed. A more wonderful Ophthalmic cure, however, has been effected within the space of a few days, than ever was effected before.

A Mr Lauvent, belonging to Astley's Company, in a combat with another Performer, had the misfortune to have the point of a small sword run in under his right eye. He was under the care of several eminent Oculists for seven months, during which period it was not thought that a piece of the sword remained in his head. Mr Lauvent one day discovered it, and applied to an Oculist to extract it, but without effect.

Mr Dehors, of Poland Street, was at length applied to. He immediately extracted a piece of sword three inches and a quarter long. It had entered the corner of the eye, passed through the top of the nose, and lodged its extensive point in the maxillary or jaw bone.

Mr Lauvent is now perfectly cured, without any injury being done to the sight.

Reference: Ophthalmic operations. The Morning Post and Daily Advertiser. Thursday, November 8, 1792.

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