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Letter to the Editor – Clinical Case Note

Corneal injury by formic acid: 1-year clinical course and in-vivo confocal microscopic evaluation

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## Abstract

We describe a case of severe, bilateral ocular injury by concentrated formic acid in a 38-year-old male. Complete epithelial loss, stromal edema, conjunctival hyperemia, and limbal involvement were noted initially. During the healing phase, epithelial recovery, improvement of visual acuity, and return of corneal sensation proceeded slower in the right eye. Corneal morphology was investigated by in-vivo confocal microscopy, which revealed deep stromal scarring, loss of endothelial cells and delayed re-generation of subbasal nerves in the right eye. One year following the incident, scarring, poor vision and low sensitivity persisted in the right eye, while the left eye had almost completely recovered. No thinning or ulceration had occurred, however both corneas exhibited long-term changes at both the clinical and the microscopic level.

## Introduction

Formic acid (HCOOH) is a colorless liquid which is caustic to the skin and irritating to mucous membranes of the nose and throat.<sup>1</sup> Literature describing ocular effects of formic acid is sparse, although this chemical is commonly used in laboratories and industry.<sup>1,2</sup> In a single reported human case where one drop of 90% formic acid struck the cornea, acute reaction was observed, but the limited volume of acid combined with prompt irrigation and treatment led to complete recovery after sixty hours.<sup>2</sup> We present a dramatically different outcome after severe bilateral exposure to formic acid, with abnormalities persisting one year later. In-vivo confocal microscopy enabled a cellular-level description of the recovery during the late healing and neural regeneration phase. Such information has previously only been accessible with ex-vivo histology in the most severe cases of ocular acid injury postmortem<sup>3</sup> or in cross-sectional animal studies.<sup>4</sup>

## Case Report

A man was accidentally splashed with 80% formic acid solution in both eyes and the face while at work. Within ten seconds his eyes were flushed with water, after which he left the accident scene due to breathing difficulties. Irrigation was continued at a nearby location, within an ambulance, and upon hospital arrival. Thirty minutes following the accident the eyes were irritated and chemotic and the corneal surface appeared irregular with debris. Vision was limited to counting fingers at 0.5m. Five drops of antibiotic (chloramphenicol ointment 1%, Chloromycetin, Pfizer) were applied to both eyes. The following day, vision had improved to 3m, while chemosis, subconjunctival hemorrhaging and limbal swelling were visible. The corneal stroma was clear although a large central epithelial defect and Descemet membrane folds were noted in the right cornea. The following medications were given daily: an oral antibiotic (100mg doxycycline hyclate, Vibramycin, Pfizer), six ascorbate tablets (C-vimin, 1000mg, AstraZeneca, Södertälje, Sweden), five drops of a topical steroid-antibiotic in both eyes (oxytetracycline hydrochloride 0.5 %, hydrocortisone acetate 1.5 % and 10 000 IE/ml polymyxinB sulphate, Terracortil with polymyxin B, Pfizer), and three drops of chloramphenicol in both eyes. Slit lamp examination one week later revealed early re-epithelialization, and the burn could be classified as grade 3 OD (5/35) and grade 2 to 3

OS (5/20) according to the classification system by Dua et al.<sup>5</sup> (Fig 1). Best-corrected visual acuity was 0.3 bilaterally. Three weeks after the accident the left cornea had re-epithelialized, the steroid-antibiotic was tapered to 3 drops per day, ascorbate and chloramphenicol were stopped, and the patient was instructed to use a tear substitute daily (2mg/g carbomer, Viscotears, Novartis, Täby, Sweden). In the right cornea the central epithelial lesion took two months to close. At six months, best-corrected acuity was 0.2 OD and 0.7 OS. Slit lamp examination revealed stromal opacity in the right central cornea, a clear left cornea, and bilateral conjunctivalisation in the periphery. At eight months conjunctivalisation was unchanged (Fig 1), best-corrected acuity was 0.3 OD and 0.9 OS and in-vivo confocal microscopy was performed on both eyes (HRT III-RCM, Heidelberg Engineering, Heidelberg, Germany). One year after the accident, the eyes remained unchanged from eight months. Central corneal thickness was  $524 \pm 6\mu\text{m}$  OD and  $545 \pm 4\mu\text{m}$  OS (mean  $\pm$  SD, ultrasound pachymetry). Cochet-Bonnet esthesiometry (Luneau, France) in the central cornea yielded 30mm OD and 60mm OS. A second in-vivo confocal examination was performed.

In-vivo confocal microscopy of the central cornea eight months following injury revealed a normal-appearing epithelium bilaterally. In the right cornea, subbasal nerves were absent (Fig 2a) whereas in the left cornea, short dendrites and a few longer subbasal nerves were present (Fig 2b). The anterior stroma in both corneas was hyperreflective (Figs 2c,d). In the right cornea, the entire stromal thickness was hyperreflective, while in the left cornea the hyperreflective region was  $60\mu\text{m}$  thick below Bowman's membrane. In the right cornea, needle-like structures were observed in the mid-stroma (Fig 2e) and the posterior stroma was scarred to the endothelium (Fig 2g). In the left cornea, small, punctate deposits were observed in the mid stroma (Fig 2f) while the posterior stroma appeared normal (Fig 2h). One year after the accident, dendrites or sprouting subbasal nerves were visible in the right cornea (Fig 2i) and long, parallel subbasal nerves were observed in the left cornea (Fig 2j). In the right cornea, the entire stromal depth remained scarred (Fig 2k), while hyperreflectivity in the left cornea diminished to a  $10\mu\text{m}$ -thick region below Bowman's membrane. Peripheral conjunctivalisation was examined and revealed typical conjunctival morphology (Fig 2l) with vessels (arrow). In-vivo confocal images of the endothelium revealed a cell density of  $1562 \pm 16$  cells/ $\text{mm}^2$  (291 cells counted) in the right cornea and  $2416 \pm 31$  cells/ $\text{mm}^2$  (231 cells counted) in the left cornea.

## Discussion

Although acids typically have a milder effect than alkalis due to the acid-buffering effects of the epithelium and stromal proteins,<sup>3,6</sup> the present case illustrates that strong acids in sufficient quantity can behave similar to alkalis and elicit severe corneal damage despite prompt and adequate irrigation. The high stromal penetrability of formic acid<sup>1</sup> resulted in acid penetration through the right cornea, leading to extensive stromal scarring and endothelial damage. On a cellular level, confocal microscopy confirmed the severity of injury in the right eye, with hyperreflective tissue visible throughout the stromal thickness (likely representing precipitated or denatured extracellular glycosaminoglycans<sup>3</sup> or disrupted collagen due to fibroblastic proliferation), needle-like structures indicative of activated, migratory keratocytes<sup>4</sup> or necrotic material, and a slow

course of subbasal nerve recovery that correlated with esthesiometry. Acid exposure to the left cornea was likely milder, with epithelial recovery, recovery of stromal transparency, a normal endothelial cell density, subbasal nerve re-generation, and return to nearly normal sensitivity and acuity after one year. Although the left cornea had nearly recovered, punctate stromal opacities (possibly remnants of pyknotic or coagulated keratocytes<sup>3,4</sup>) persisted and subbasal nerves remained sparse relative to a normal, healthy cornea.

Regions of initial limbal involvement were consistent with regions of late conjunctivalization in both eyes, providing evidence of a partial limbal stem cell deficiency arising from limbal damage.<sup>7</sup> While early use of an amniotic membrane patch was considered, severe ocular inflammation and hospitalization due to respiratory problems made this option difficult. Inflammation was halted through early, intensive use of corticosteroids while local antibiotics were used to prevent infection during the epithelialization phase.<sup>7-9</sup> Additionally, early and large doses of systemic ascorbate reduced the risk of corneal thinning and ulceration.<sup>9,10</sup> Long-term corneal integrity has been maintained and ulceration was circumvented. Ascorbate was administered systemically in our case, although evidence for the superior effect of topical ascorbate has been reported.<sup>10</sup> In addition, beneficial effects of topical citrate in preventing corneal thinning and ulceration have also been reported.<sup>9,10</sup>

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## Figure Captions

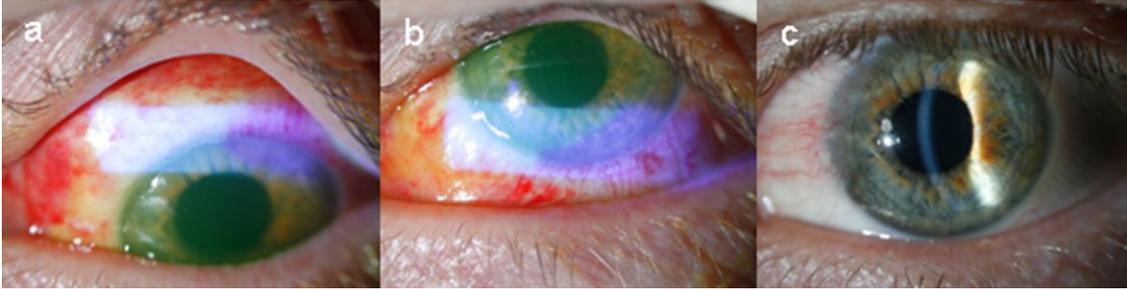


Figure 1. (a), (b) clinical appearance of right eye one week after formic acid burn. This eye had 5 clock hours of limbal involvement and 35% conjunctival involvement. (c) eight months after formic acid burn, conjunctivalization in the temporal superior quadrant of the right eye. Stromal haze was also visible in the central cornea.

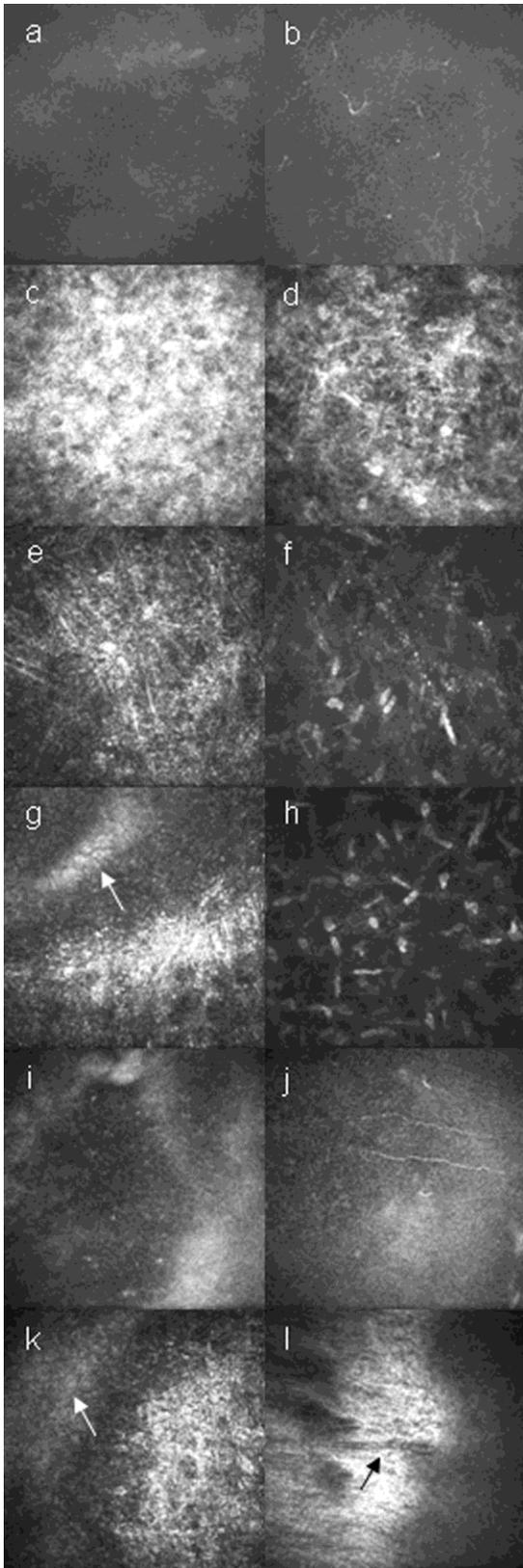


Figure 2. In-vivo confocal microscopy OD (left column) and OS (right column) eight months (a-h) and one year (i-l) following formic acid injury. An absence of subbasal

nerves OD (a) and a few subbasal nerves with dendrites OS (b). Anterior stromal hyperreflectivity (c,d). Sharp needle-like structures in the mid-stroma (e) and mid-stromal keratocytes and punctate deposits (non contact-lens wearer) OS (f). Posterior stromal scarring with endothelial cells visible (arrow) OD (g) and normal-appearing posterior stromal keratocyte nuclei OS (h). One year after injury, sprouting subbasal nerves OD (i) and long, parallel subbasal nerves OS (j) were visible. Posterior stromal scarring to the endothelium (arrow, k) and bilateral peripheral conjunctivalization with blood vessels (arrow, l) persisted after one year. All images, 400 x 400 $\mu$ m.