

# Treatment of hydrofluoric acid exposure to the eye

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## Abstract

• **AIM:** To review the current evidence of the treatment of hydrofluoric acid (HF) exposure to the human cornea.

• **METHODS:** A comprehensive manual search of the literature was conducted through the Ovid interface to assess the mechanism and efficacy of each irrigator through a variety of clinical cases and experimental studies.

• **RESULTS:** Ocular exposure to HF is extremely damaging to the eye and swift recognition and decontamination with an appropriate agent forms the basis of treatment. Although there are various decontamination solutions that have efficacy against the corrosive action of HF, irrigation with Hexafluorine proved to be the most safe and effective treatment for the eye.

• **CONCLUSION:** In conclusion emergency departments could benefit from the availability of Hexafluorine for the treatment of HF ocular burns in patients.

• **KEYWORDS:** hydrofluoric acid; cornea; ocular; injury

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## INTRODUCTION

Hydrofluoric acid (HF) burns are becoming increasingly more common as the use of HF in industrial and domestic settings expand. Whilst considerable research has been done regarding dermal exposure, the amount of information in the literature concerning HF burns to the eye and the most effective treatment remains limited.

Comparable with other chemicals, the distinctive characteristics of HF make it highly toxic and damaging to humans. This is due to HF's "double danger" properties; corrosive because of the hydrogen ions and toxic due to the ability of fluoride ions to penetrate deep into tissue causing subsequent liquefaction necrosis<sup>[1]</sup>.

Ocular exposure to HF must be treated immediately to prevent long-term complications. Currently, the treatment recommended by TOXBASE is the immediate irrigation of the affected eye with copious water or 0.9% saline for at least 30min. Calcium gluconate may be of some use; however, evidence of efficacy is lacking. Repeated instillation of local anaesthetics, mydriatic and cycloplegic agents may also play a role in reducing discomfort<sup>[2]</sup>.

Recently however, a new decontamination solution called Hexafluorine, manufactured by Laboratoire PREVOR in France, has been made available<sup>[3]</sup>.

A literature review was performed to review the use of Hexafluorine or calcium gluconate for ocular HF burns compared with the conventional treatment of water irrigation.

## HYDROFLUORIC ACID

HF (chemical formula HF) is a solution of inorganic anhydrous hydrogen fluoride in water. It is a well-known toxic chemical used extensively in a variety of industries due to its unique corrosive properties. Some of the industries that use HF acid include glass etching, scouring metal, cleaning glazes and a leather tanning agent. In the home it is also found in rust removing agents and heavy duty cleaning products<sup>[1,4]</sup>.

HF is transported and stored under high pressure as a highly concentrated liquid. Concentrations of HF vary greatly depending on the usage, with industrial concentrations approaching 100% whereas domestic concentrations typically around 0.5%<sup>[1]</sup>. In fact the worldwide production of HF is on the increase already exceeding one million tons annually<sup>[5]</sup>. It is therefore easy to understand that hazardous situations do arise when dealing with such a chemical like HF.

HF is a particularly corrosive and toxic chemical which can induce severe tissue damage. Exposure can occur in a variety of ways including inhalation, ingestion, ocular or dermal contact<sup>[6]</sup>. Even though HF is a weak acid ( $pK_a=3.2$ ), it can cause extensive damage even more severe than other acids due to its unique ability to penetrate tissue<sup>[7]</sup>. It not only consists of the highly corrosive hydrogen ion ( $H^+$ ); responsible for local tissue necrosis, but also the cytotoxic fluoride ion ( $F^-$ ); associated with systemic toxicity<sup>[5]</sup>. Because of the strong electronegativity of the fluoride ion, HF does not readily dissociate<sup>[8]</sup>. This permits the penetration of the acid through the protective barrier of the epidermis or corneal epithelium and into the body's deeper tissue<sup>[4,5]</sup>. Once in the tissue, HF dissociates and the free fluoride ions cause liquefactive necrosis and destruction of soft tissue and bone.

**Table 1 Ocular chemical burn classification** (Roper-Hall) (Adapted from<sup>[7]</sup>)

Grade	Cornea	Limbal ischaemia	Prognosis
1	Clear: epithelial damage only	None	Very good
2	Corneal oedema	<1/3	Good
3	Complete corneal ulcer	>1/3-1/2	Guarded
4	Opaque cornea with iris non-visible	>1/2	Poor

**OCULAR EXPOSURE**

HF has the ability, not only to damage the superficial structures of the eye, but also to penetrate the corneal stroma. Typically after ocular contact with HF, severe pain rapidly manifests immediately followed by lacrimation and conjunctival inflammation. Although, symptoms are generally noted instantly after exposure, one case of delayed symptoms has been reported following contact with a more dilute solution<sup>[1]</sup>. Progressive opacification, vascularization and scarring of the cornea along with ischaemic changes to the conjunctival vessels may then develop. Erosion, sloughing and ulceration of the corneal epithelium may also occur<sup>[1,9]</sup>.

Roper-Hall's classification of ocular chemical burns; based on the original classification by Ballen, is simple but widely utilized (Table 1)<sup>[10]</sup>. It comprises of a simple grading system which evaluates the corneal appearance and the extent of limbal ischaemia to determine prognosis.

Potential complications after ocular exposure can occur, including a permanent decrease in visual acuity, scarring, glaucoma, uveitis, keratitis sicca and globe perforation<sup>[11]</sup>.

Currently the recommended management in the UK suggested by TOXBASE is the "removal of contact lenses if necessary, followed by the immediate irrigation of the affected eye with water or 0.9% saline for at least 30min. Repeated instillation of local anaesthetics, mydriatic and cycloplegic agents may be of use to reduce discomfort". TOXBASE also mentions the possible use of calcium gluconate and Hexafluorine; however, evidence of efficacy is lacking<sup>[2]</sup>.

Regardless of which decontamination solution is used, it is imperative that immediate action is provided as soon as possible after exposure and that the patient attends the emergency department. Whilst irrigating the eye, it is important to hold the eyelid open and for the patient to move their eyeball in every direction, thus ensuring the irrigator reaches all the surfaces. If available in the emergency department, a device such as an "Eye Irrigator" or the Morgan Lens should be utilised to help with the irrigation, with the patients then being referred to an ophthalmologist for further treatment<sup>[4,8,12]</sup>.

Various treatments have been used since the early 20th century for ocular HF burns; however, nowadays these are rarely used in modern practice. Magnesium oxide (MgO) and the quaternary ammonium compounds; Zephiran

(Benzalkonium Chloride) and Hyamine (Benzethonium chloride) were once recommended, but have since been found to be too toxic to the eye causing additional ocular damage<sup>[13-16]</sup>. It has also been established through studies that the irrigation with calcium chloride (CaCl<sub>2</sub>) increases the frequency of corneal ulceration<sup>[8,15]</sup>. Magnesium chloride (MgCl<sub>2</sub>) is occasionally still used as it has been shown to be effective for ocular HF burns; however, compared to the other newer treatments it is less effective<sup>[8,15,16]</sup>.

Although these other treatments are still around, this paper focuses primarily on the efficacy of saline, calcium gluconate and Hexafluorine decontamination.

**METHODOLOGY**

**Search Strategy** The purpose of this review is to compare and contrast the efficacy of each decontamination treatment for HF ocular exposure using a variety of clinical case reports and experimental studies collected from a comprehensive search of the English professional literature. Below is the process used to gather all the relevant data:

- 1) Medline 1946-06/2012 using the OVID interface. Searched using the standard Boolean system linking-Searched- {(HF OR HF burn OR HF) AND (eye OR ocular) AND (calcium gluconate).mp.} LIMIT (English) 15 papers found of which 4 are relevant (Table 2). Searched- {(HF OR HF burn OR HF) AND (eye OR ocular) AND (Hexafluorine).mp.} LIMIT (English) Six papers found of which three are relevant (Table 2).
- 2) Embase search from 1974-06/2012 using the OVID interface. Searched- {(HF OR HF burn OR HF) AND (eye OR ocular) AND (calcium gluconate).mp.} LIMIT (English) Sixteen papers found of which the same three are relevant (Table 2). Searched- {(HF OR HF burn OR HF) AND (eye OR ocular) AND (Hexafluorine).mp.} LIMIT (English) Nine papers found of which the same three are relevant (Table 2).
- 3) The Cochrane Library search Searched-(HF) AND (calcium gluconate) No papers found. Searched-(HF) AND (Hexafluorine) No papers found. Four papers which are relevant were found in references (Table 2).

**Table 2 Comparing calcium gluconate, water irrigation and Hexafluorine**

No.	Title and author of paper	Study type	Conclusion
1	Ocular hydrofluoric burns: animal model, mechanism of injury and therapy (McCulley 1990) <sup>[16]</sup>	Experimental study	Immediate single irrigation with H <sub>2</sub> O, NaCl or MgCl <sub>2</sub> solution was most effective. Other therapeutic agents commonly used in HF skin burn therapy were either too toxic in normal eyes or caused additive damage to burned eyes.
2	The efficacy of calcium gluconate in ocular hydrofluoric acid burns (Beiran <i>et al</i> 1997) <sup>[9]</sup>	Experimental study	HF ocular injury 1% calcium gluconate did not have any significant advantage over saline irrigation. Given subconjunctivally, 1% calcium gluconate may be toxic and worsens clinical outcome.
3	Hydrofluoric acid burns to the eye (McCulley <i>et al</i> 1983) <sup>[15]</sup>	Case report and experimental study	Immediate single irrigation with water, normal saline or isotonic magnesium chloride solution is the most effective therapy for ocular HF burns. Extrapolation of other skin burn treatments to use in the eye is unacceptable due to the toxicity of these agents in normal eyes and the additive damage caused in burned eyes.
4	The role of calcium gluconate in the treatment of hydrofluoric acid eye burn (Bentur <i>et al</i> 1993) <sup>[11]</sup>	Case report	The quick and uneventful recovery in this patient suggests that repeated instillation of 1% calcium gluconate eye drops may be efficacious in treating HF burn of the eye. They suggest that this mode of administration allows more calcium ions to reach the free fluoride ions not removed or bound by initial irrigation. However, more data are needed before recommending this procedure.
5	Ocular hydrofluoric acid burns (Rubinfeld <i>et al</i> 1992) <sup>[17]</sup>	Case reports	Patients that received immediate calcium gluconate lavage were still needed to be transferred to the burn unit for specialised monitoring. It concludes that, if an ophthalmologist is the first to treat a patient with chemical exposure, the history of HF exposure must be obtained, and the burn team and other medical specialists must be quickly consulted to avoid potentially fatal complications.
6	Hydrofluoric acid burns of the eye: report of possible delayed toxicity (Hatai <i>et al</i> 1986) <sup>[1]</sup>	Case report	Copious irrigation with water or normal saline is simple and the most effective treatment in HF ocular burns. The possible use of lactated Ringer's solution and milk as irrigants of the eye has been raised, but studies are needed to determine their practicality and effectiveness in the treatment of ocular HF exposure.
7	Analysis of hydrofluoric acid penetration and decontamination of the eye by means of time-resolved optical coherencetomography (Spöler <i>et al</i> 2008) <sup>[18]</sup>	Experimental study	Tap water and 1% calcium gluconate managed to slow the acid but couldn't prevent full penetration; however Hexafluorine stopped the acid penetration. Tap water and 1% calcium gluconate increased cornea opacification whereas the cornea remained clear after rinsing with Hexafluorine.
8	Hexafluorine for emergent decontamination of hydrofluoric acid eye/skin splashes (Hall <i>et al</i> 2000) <sup>[19]</sup>	Case report and experimental study	Hexafluorine solution has been compared with water and calcium gluconate decontamination in rabbits and rats, and was more efficacious. It worked best on the pH and pF and therefore is the best alternative for decontamination of HF eye splashes.
9	An improved method for emergent decontamination of ocular and dermal hydrofluoric acid splashes (Soderberg <i>et al</i> 2004) <sup>[20]</sup>	Series of cases and a case report	During 1998-1999 in a Swedish factory 16 cases of HF eye exposure were described. All had immediate decontamination with Hexafluorine. No damage observed in any of these patients. Mean lost work time was <1d.
10	Efficacy of hexafluorine for emergent decontamination of hydrofluoric acid eye and skin splashes (Mathieu <i>et al</i> 2001) <sup>[21]</sup>	Series of cases	During 1994-1998 PubMed in a German metallurgy factory-11 cases, with 2 cases of ocular exposure. Immediate decontamination with Hexafluorine. No eye injuries and no lost work time.

## RESULTS

Table 2 shows the relevant papers found. They discuss the different irrigation solutions, comparisons and outcomes after an ocular HF burn.

## DISCUSSION

The current recommended treatment for eye exposure to HF, water or 0.9% saline decontamination, works by mechanically rinsing the HF off the corneas surface. It also permits the dilution of the HF attempting to restore the pH

back to safe limits <sup>[22]</sup>. However, as water has no chemical action, it cannot control the corrosive and toxic potential of HF. Furthermore, as HF is highly permeable to the corneal surface, it is imperative that the mechanical rinsing with water is done immediately to have effect, otherwise the acid penetrates deeper and it is too late to prevent further damage. In fact, as water is hypotonic, it has been suggested it may actually favour the penetration of the acid into the tissue<sup>[20]</sup>. While it is presently the recommended treatment, the

**Table 3 Emergency decontamination of 40% HF or 6% HF/15% HNO<sub>3</sub> eye splashes with Hexafluorine** (Adapted from<sup>[21]</sup>)

Exposure	Splash area involved	Initial decontamination	Second decontamination	Sequelae	Requirement for further treatment	Lost work time
40% HF	Eye	Hexafluorine	Hexafluorine	None	None	None
6% HF/15% HNO <sub>3</sub>	Eye	Hexafluorine	Hexafluorine	None	None	None

effectiveness of water or saline has been questioned. Results from several previous experimental studies have stated that the immediate copious irrigation with water or normal saline is the simplest and most effective therapy for ocular HF burns<sup>[15,16]</sup>.

On the other hand, Hatai *et al*<sup>[1]</sup> reports a 3 years old girl who after accidentally sprayed HF into her eyes immediately rinsed them with water. Nonetheless after four days without symptoms she developed marked inflammation, corneal opacification and severe pain. Further treatment of topical ophthalmic steroids and antibiotics were needed<sup>[1]</sup>. Thus showing irrigation with water was not effective in this particular patient.

Conversely, decontamination with calcium gluconate for ocular HF exposure has brought about some controversy. Although it has been well recognised as an effective treatment for dermal HF burns, the use in the eye as an irrigator remains deliberated<sup>[12]</sup>. The irrigation with calcium gluconate works *via* two mechanisms. It not only mechanically rinses equivalent to water decontamination, it additionally creates insoluble salts by binding to the free fluoride ions<sup>[8]</sup>. This reduces the fluoride toxicity, thus improving the pain and hypocalcaemia. Nevertheless, calcium gluconate has no effect on the corrosive properties of the H<sup>+</sup> ions<sup>[23]</sup>. Calcium gluconate can be administered as a topical gel or solution, as eye drops, or as subconjunctival injections; usually in concentrations of 1% or 10%. The efficacy of each administration and concentration is debated by various authors. Bentur *et al*<sup>[11]</sup> reports the case of a patient with a HF splash to his eye treated with repeated instillation of 1% calcium gluconate eye drops to be beneficial, with no sequelae and vision returning to normal<sup>[7]</sup>. Opposing this, Rubinfeld *et al*<sup>[17]</sup> describes a patient who after HF exposure to his eyes, received 1% calcium gluconate eye drops every four hours but was left with residual corneal scarring, continuous foreign body sensation and decreased visual acuity in both eyes<sup>[17]</sup>. An experimental study on rabbit eyes was also conducted, which concluded that there was no significant advantage of adding 1% calcium gluconate eye drops to the currently accepted treatment of water irrigation, even though it had a slight benefit on the initial stage of healing<sup>[9]</sup>.

Additionally, various experiments testing the efficacy of subconjunctival injections of 1% and 10% calcium gluconate have found that they are too toxic to the eye, causing additional damage and worsening the clinical outcome<sup>[9,15,16]</sup>.

This is reported in a clinical case where the patient after being splashed with HF in the eyes, was given 0.5 mL 10% calcium gluconate subconjunctival injections in both eyes. Four years post-injury, vision remained significantly impaired and he continues to suffer from rare spontaneous corneal epithelial erosions<sup>[15]</sup>.

Furthermore, a promising novel emergency decontamination solution, Hexafluorine, produced by Laboratoire PREVOR in France is under review regarding its efficacy. It is an amphoteric, hypertonic, chelating agent specifically developed for the decontamination of HF ocular and dermal exposure<sup>[19]</sup>.

The amphoteric properties allow the binding of both the hydrogen and fluoride ions, thus neutralising the acidity and reducing the tissue toxicity. Chelation of Hexafluorine with these ions is not an exothermic reaction; therefore, it does not produce heat which could potentially further damage exposed tissues<sup>[7,19]</sup>. Every molecule of Hexafluorine can bind with three H<sup>+</sup> ions and six F<sup>-</sup> ions simultaneously<sup>[19]</sup>. Like water, Hexafluorine also mechanically rinses any HF off the corneas surface. Moreover, being hypertonic Hexafluorine can prevent HF penetration, and can recover some of the HF already penetrated into the tissues by creating an osmotic gradient<sup>[21]</sup>.

Hexafluorine is safe to use in the eyes, is non-toxic and non-sensitising<sup>[8]</sup>. It is already widely used in France and Germany, and gaining popularity in Italy, Ireland and Sweden<sup>[4]</sup>. Several clinical cases have been reported regarding the efficacy of Hexafluorine. In 1995, whilst working in a stainless steel factory, a patient accidentally splashed 38% HF into his eye. He rinsed the eye immediately with Hexafluorine and fortunately didn't sustain any eye injuries and was able to return to work the next day<sup>[19,23]</sup>. Moreover, in a German metallurgy facility between 1994 and 1998, any HF exposure was to be decontaminated with Hexafluorine. During this period, two workers sustained eye splashes and after immediately rinsing with Hexafluorine solution, no burns or sequelae were observed and neither lost any work time (Table 3)<sup>[21]</sup>.

Likewise, Soderberg *et al*<sup>[20]</sup> presented a case-series regarding sixteen patients who were exposed to HF in a Swedish metalwork factory over two years; five of which had ocular contact. Their affected eyes were irrigated straightaway with Hexafluorine solution and no damage was observed in any of the patients.

## LIMITATIONS OF STUDY

As HF is such a dangerous acid, information is limited involving human HF exposure, with only a handful of clinical reports available. Furthermore, because Hexafluorine is a relatively new decontamination solution, there is only a small base of evidence exploring its efficacy. In addition, in the majority of data which has been produced it is stated within their acknowledgments that the investigations were supported by the manufacturer of Hexafluorine.

In conclusion, due to HF's wide and expanding use in industry, exposure to the eye is becoming increasingly more common. Immediate emergency treatment is vital to reduce these severe symptoms and prevent long-term injury. The three decontamination solutions researched have all proven to provide some action against HF exposure to the eye.

1) Irrigation with water works by diluting and mechanically rinsing the HF off the corneas surface. Water is also widely available and at no significant cost.

2) Calcium gluconate is used extensively for HF exposure to the skin, but the use for ocular exposure has been widely disputed. In fact, numerous studies indicate that irrigation with calcium gluconate solution after HF ocular exposure may worsen clinical outcome.

3) Exploring the available clinical cases, after irrigation with Hexafluorine, no injury or long-term consequence has yet been observed. Spoler *et al*'s<sup>[18]</sup> study revealed that Hexafluorine was the only decontamination solution to preserve the transparency of the corneal surface throughout<sup>[18]</sup>.

The information collected in this study shows that Hexafluorine is the most efficacious decontamination solution for HF exposure to the eye. Whilst the currently recommended water irrigation is more widely available, and both water and calcium gluconate are significantly cheaper, it is important when dealing with a dangerous chemical such as HF, that the most effective treatment is used.

This paper concludes that emergency departments could benefit from the availability of Hexafluorine for emergency ocular exposure to HF.

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