HEXAFLUORINE®

Emergency washing solution for ocular and cutaneous splashes of **hydrofluoric acid**

Updated review of current knowledge of **hydrofluoric acid** burns

Version 2009

Hexafluorine®

- Toxicological data
- Comparative studies of washing effectiveness
- User feedback
- Recommendations

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PREVOR
ANTICIPATE AND SAVE
Toxicology Laboratory & Chemical Risk Management

Hexafluorine®

Dossier

This dossier is a collection of data about hydrofluoric acid (HF) burns and Hexafluorine®. It gathers toxicological data, studies of *in vitro* and *in vivo* development of the HF burn and comparison of decontamination solution efficacy. Cases of ocular or cutaneous splashes by pure or mixed hydrofluoric acid that have occured in industry and been washed with water, water followed by calcium gluconate or Hexafluorine® are reported and analysed.

There is a glossary in chapter 7 where you will find the detailed definitions of the technical words used herein. Each term which appears in the glossary is written in blue in the dossier.

The authors would like to thank all the health and safety professionels who have been involved in this project by sharing their experience or rereading this new edition.

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November 2009 edition

Summary

- ## Introduction

Developed by Prevor, Hexafluorine® is a specific rinsing solution for application to ocular and cutaneous splashes of hydrofluoric acid (HF) and fluorides in an acidic medium.

- ## Objective

This file summarizes the data that show the efficacy of Hexafluorine® in the decontamination of HF splashes, when used as a primary care.

- ## Methodology

In vitro, *ex vivo* and *in vivo* comparative experiments compare the efficacy of various protocols: water, water followed by calcium gluconate and Hexafluorine®. The use of these washing protocols for ocular and cutaneous splashes of hydrofluoric acid that have occurred in the industrial environment are also reported in this dossier.

- ## Results

The *in vitro*, *ex vivo* and *in vivo* experiments have highlighted the efficacy of Hexafluorine® in the decontamination of HF splashes in comparison with rinsing with water only and rinsing with water followed by an application of calcium gluconate.

An *ex vivo* model of human skin explants has been used to study the tissular impact of 70 % hydrofluoric acid and to estimate the efficacy of decontaminating protocols.

A similar *ex vivo* model using enucleated rabbit eyes in association with the OCT-HR (*Optical Coherence Tomography – High Resolution*) technique, has enabled the modeling of HF penetration into the eye and of the Hexafluorine® efficacy *versus* water or 2.5 % calcium gluconate solution which is the current controversial standard.

32 cases of ocular and cutaneous splashes of hydrofluoric acid washed with Hexafluorine® have been reported in the industrial environment.

Five isolated cases

A worker fell into a tank containing 30 liters of concentrated hydrochloric acid (HCl), 233 liters of 59 % hydrofluoric acid in 1505 liters of water. He was completely immersed in this bath. Another operator was hit by an ocular 40 % hydrofluoric acid splash while filling a stainless steel stripping bath. Two workers had cutaneous 5 % hydrofluoric acid splashes. In a glassworks plant, an operator was hit on the cheek by a 70 % hydrofluoric acid vapour splash.

Two series of cases

- 11 cases of hydrofluoric acid ocular and cutaneous splashes have occurred in a German metalworks unit : 6 workers were hit by ocular and cutaneous 40 % hydrofluoric acid splashes and 5 operators were victims of 6 % HF / 15 % nitric acid (HNO_3) mixture splashes. A 40 % HF splash targeted more than 16 % of the total body surface area.

- In a Swedish metalworks company, 16 ocular and cutaneous splashes occurred between 1998 and 1999, two of which were 70 % HF splashes onto the left forearm and in the buccal cavity and the other 14 involving a pH 1 HF/HNO_3 mixture.

Those 32 workers were washed with Hexafluorine®as a primary care. There was no occurrence of a severe burn in any case. The worker whose cheek was splashed by 70 % HF vapour only developed a painless erythema. The operator who fell into a HCl/HF bath only had a minor burn on the abdomen, whereas his left eye that was washed with water developed a severe ocular burn. No secondary intensive extended treatment was necessary in any case. Most of those workers did not require lost work time. 3 of them were kept in hospital for 2 to 3 days of observation.

In this series, five potentially lethal cases of HF splashes generated no local lesion or general clinical signs.

Recently, an isolated case, initially washed with water, then later decontaminated with Hexafluorine® and having benefited from a secondary treatment with calcium gluconate, did not develop systemic effects and favorably evolved within 90 days with grafting.

- ## Conclusion

Setting emergency protocols for hydrofluoric splashes and initial rinsing with Hexafluorine® have enabled either preventing the occurrence of burns by HF or to significantly lessen their severity. Washing with Hexafluorine® can be followed by calcium gluconate treatment if it is required by the company's medical protocol or in cases of delayed use of Hexafluorine®.

Hexafluorine®

Emergency rinsing solution for the decontamination of ocular and cutaneous splashes of hydrofluoric acid

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Introduction

♦ In the industrial environment, hydrofluoric acid (HF) is extensilvely used for fluoration of organic compounds (fluorocarbons including cooling agents) and inorganic compounds (such as uranium in the nuclear industry), in processing fluoropolymers and their derivatives, in metalworks for the surface treatment of numerous metals including stainless steel, in the oil industry - specifically for refining operations -, in glass and crystal industry for engraving and polishing, in the ceramics and semiconductors industry for its action on the quartz, in the building industry for surface cleaning and obviously HF is used in chemistry labs.

In lower concentrations and smaller volumes, HF is also present in cleaning products (polishing of aluminium wheel rims, rust removing agent in laundries, wood cleaning products…).

The world production is increasing and exceeds one million tons annually.

It's therefore easy to understand that hazardous situations are numerous and diverse. While typically hands and other uncovered body parts are the targeted cutaneous surfaces, some much more extensive burns occur combining ocular and respiratory injuries with potentially lethal consequences.

♦ Nevertheless, hydrofluoric acid is dangerous whatever its concentration. Its action is both corrosive and toxic, and it can be immediate or delayed, painful or painless, depending on concentration of the involved product. It leads to severe local burns, and also to general alterations, particularly respiratory or heart lesions that can be life threatening.

All people involved in prevention in industrial environment have the experience of the hazards due to the handling of hydrofluoric acid. Therefore, the first responsibility is to set up a hazard recognition, training and prevention policy for all the operators exposed to HF, in accordance with the regulation for chemical risk assessment and management in the workplace. However, despite such care, ocular or skin splashes can occur during common operations or in critical conditions: stripping, polishing, grease-removing, immersion in baths, facilities cleaning, maintenance operations, pipe repairing, changing gates, decanting operations…

In the 1996 International Meeting about Chemical Burns in la Baule, France, Dr Gouet illustrated the severity of HF exposure with a presentation of the evolution of a cutaneous 70 % HF burn (Fig.1).

Initial 70% HF burn

70% HF burn after excisions, day + 4

70% HF burn after graft, one year after

Figure 1: Evolution of a cutaneous 70 % HF burn

Overall all these examples show that an effective decontamination device must be set up, on the accident scene itself.

Numerous works have aimed to develop an effective decontamination of hydrofluoric acid burns. The most widely used is water rinsing, combined with secondary local applications of calcium gluconate gel or gauzes, and sometimes completed with localy intra-arterial and/or intravenous infusions.

However, the research using those protocols, on animals as well as in epidemiology; show that the achieved results are not always satisfactory, particularly when HF concentrations are high. Even with early intervention there is often a burn. The situation may require surgical operations: excision of necrotic tissues, amputation of limb extremities (hands are the most oftenly exposed parts)[1]. There are few studies on deeper lesions. As for eyes, burns by concentrated HF lead to rapid opacification and ulcerations of the cornea[2].

In such conditions, severe psychological consequences may be combined with functional sequelae. Finally, some accidents due to concentrated hydrofluoric acid splashes are lethal.

The incidence of burns due to hydrofluoric acid can represent 50 % of all the burns due to acids admitted to a burn center[3].

Because of HF hazards and handling risks, PREVOR Laboratory, specialized in chemical risk, has developed a specific emergency rinsing solution, named Hexafluorine®, which can actively and effectively decontaminate ocular or cutaneous hydrofluoric acid splashes. Active rinsing with Hexafluorine® stops the diffusion of hydrofluoric acid and brings both its corrosive potential and its toxic action under control. Thus it prevents severe alterations of the biological balances of cells constituting the living tissues due to this acid.

This dossier gathers:

- *In vitro*, *ex vivo* and *in vivo* experiments supporting the comparison of the efficacy of the following common protocols respectively: water, water followed by calcium gluconate… and that of a Hexafluorine® rinsing.

- Examples of Hexafluorine® in the industrial environment. Companies using hydrofluoric acid share their experience of emergency rinsing with Hexafluorine®, either by a general account of the benefits observed by exposed staff when used, by information concerning isolated cases, or through a series of splash cases. Splashes may be ocular or cutaneous and due to hot or cold and diluted or concentrated hydrofluoric acid. Globally, more than 30 cases of ocular or cutaneous splashes washed with Hexafluorine® are described herein, three of which are cutaneous splashes with 70 % hydrofluoric acid.

1 Burns with hydrofluoric acid: a vital risk

1.1 Mechanism of hydrofluoric acid burns

Hydrofluoric acid has a double action[4,5]: corrosive and toxic (Fig.2)

Figure 2: Pictograms associated to hydrofluoric acid

- Corrosive action due to acid ions (H^+), which can attack superficial tissues (corneal epithelium or epidermis).
- Toxic action due to fluoride ions (F^-), which, due to the destruction of eye or skin superficial layers by the acid, can penetrate deeply, chelate calcium and magnesium, and thus disrupt the biological balances and lead to more or less severe biochemical, cellular and tissular disorders (Fig. 3). The disruption of various metabolic cycles is the cause of the variety of clinical signs observed: muscular, neurological, cardiac symptoms…

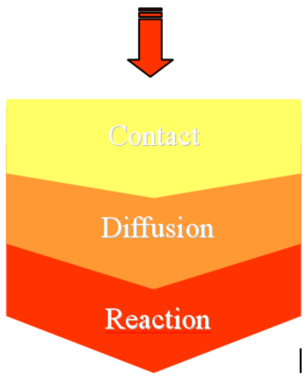


Figure 3: Process of reactivity of a chemical product

Systemic diffusion can be life threatening[6] depending on the concentration of HF solution and the percentage of altered body surface (Fig. 4).

Contact way	Body surface	HF concentration
Skin	1 %	Anhydrous
	5 %	> 70 %
	7 %	50-70 %
	10 %	20-50 %
	20 %	< 20 %
Ingestion		> 5 %
Inhalation		

Figure 4: Lethal systemic risk following a HF burn depending on concentration and altered body surface

McCulley[7] has proved the part played by H^+ ions and F^- ions in the mechanism of ocular burns. He compared burns due to:

- various concentrations of pure HF, which generates an epithelial ulceration before damaging deeper layers;
- pure hydrochloric acid, which destroys the epithelium;
- sodium and potassium chlorides and fluorides, which remain almost harmless to a safe epithelium though they are highly corrosive when put on an eye when the protecting layer of the epithelium is not present;
- fluorides in acidic medium (mixture of hydrochloric acid and sodium fluoride), which cause lesion similar to those due to HF.

Mac Culley proved that the acid action mainly destroys superficial layers, whereas the fluoride ion only slightly operates on these layers. Then the destruction of these superficial layers permits the penetration and the diffusion of HF and fluoride ions released by HF into deeper tissues which develop liquefactive necrosis. This specific mechanism differentiates HF and other acids, and particularly strong acids, which generate a coagulative necrosis with precipitation of tissue proteins[8].

These various physiopathological mechanisms due to hydrofluoric burns can be extrapolated and pictured as follows for skin (Fig.5):

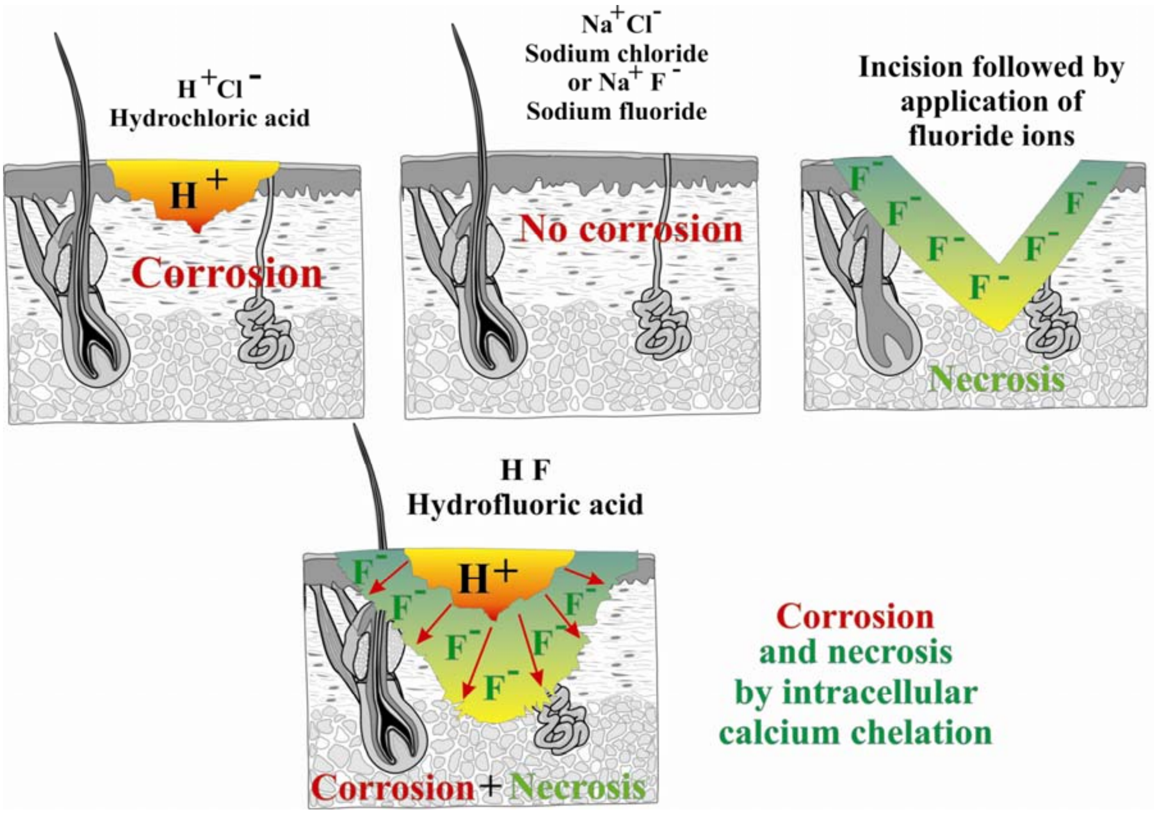


Figure 5: Mechanism of chemical burn due to HF

Boink *et al* made similar observations[9].

The attack of H^+ ions on superficial layers stops when all the aggressive ions are consumed. When there is no acid function in the chemical in contact with skin, like with fluorides (for instance sodium fluoride, NaF), there is no ulceration. The penetration of fluoride ions into the epidermis remains limited and local lesions are negligible. Any penetration route, such as an incision, shows the intrinsic action of the F^- ions. Helped by a breach of the epithelial barrier, the velocity of penetration of fluoride ions is then proportional to the chemical concentration. A tissular necrosis progressively develops, and is inexorable as long as the F^- ions are free and reactive.

When fluoride ions are in an acid solution, their hidden toxicity - which does not appear with pure fluorides - is revealed due to the concomitant aggression due to the H^+ ions of the solution, and generates specific lesions that are identical to those due to HF.

The major attacks by HF can moreover necrotize the subjacent muscular masses and even cause a decalcification of deep bone structures.

Finally, the specific severity of burns by hydrofluoric acid is definitely due to the synergic action of the acid and the fluoride ions.

What are the pathophysiological mechanisms underlying the toxicity of fluoride ions?

- The chelation of calcium and magnesium ions is responsible for metabolic disorders[10,11,12] leading to a secondary death of cells which progressively form the tissular necrosis.
- Fluoride ions also damage cellular enzymes, and particularly metalloproteinases.
- And for increasing the permeability of cytoplasmic membranes[13] of cells containing potassium.

Whereas potassium is essentially an intracellular ion, its release into the external medium might be the cause of the strong stimulation of local nerve endings, which is at the origin of the particularly intense pain of HF burns[14,15,16]. Another explanation might be that the initial corrosive action generates a secondary action of degeneration of the conjunctival tissue around vessels and nerves, thus causing painful stimulation[17]. Whatever the explanation, pain is a characteristic element and a good indication of the evolution of lesions and the efficacy of decontamination during the course of an HF cutaneous burn.

1.1.1 Cutaneous splashes

The appearance delay and the intensity of pain are relative to the HF concentration. For very concentrated solutions, pain is immediate. For low concentration solutions, pain may be delayed by a few hours to one day or more.

The Division of Industrial Hygiene of the U.S.A. National Institute of Health[18] has classified HF burns according to three classes of concentration (Fig. 7):

Concentration	Pain
50 % and more	Immediate and associated with a quickly visible destruction of tissues
From 20 to 50 %	Delayed by 1 to 8 hours after contact (with erythema developing within the same delay)
Less than 20 %	Delayed by 24 hours or more (with erythema developing within the same delay)

Figure 6 : Appearance delay of pain after contact with HF, according to concentration

Whether the concentration is high or low, the spashed surface rapidly becomes erythematous and slightly edematous. Then, there is a whitish or greyish discoloration in the middle surrounded by a purplish ring (Fig. 8), such as observed in animal experimentation by Rusch et al[19].

Figure 7 : Aspect of a 60 % HF burn, contact time 60 seconds, aspect after exposure, after 15 minutes and 2 hours (pig)

If the contact time increases, the damaged skin becomes red, then turns from grayish purple to black ish purple with an important edema (Fig. 8) and intense pain. The evolution of the burn leads to a phlyctena, which may develop over 9 or 10 days. The excision of this phlyctena releases a brown liquid or a well organized blackish blue coagulate.

The 70 % HF penetration into skin has been experimentally observed on skin sections for the first time[20,21] with the use of a new *ex vivo* model of human skin explants. This work has enabled the real time observation of the kinetics of diffusion and of the cellular damages on histological sections by optical microscopy.

The below diagram is a reminder of the different layers of normal skin as observed in low magnification optical microscopy (X40) (Fig.8).

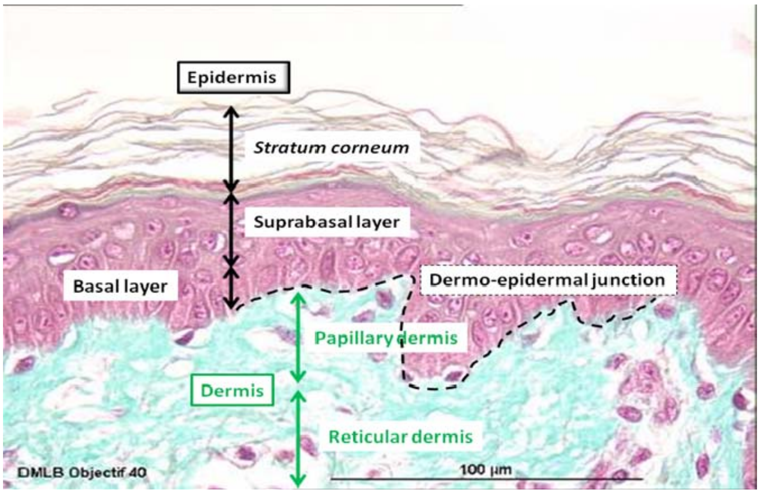


Figure 8 : The different layers of normal skin (PREVOR/BIO-EC Experiment)

The histological analysis of explants exposed to HF shows that penetration (Fig. 9) into the superficial layers of epidermis starts in the first minute of contact. It definitely increases after 2 minutes of contact, with presence of a clear acidophilic (orange-colored) cytoplasm. Lesions are greater after 3 minutes of contact with appearance of edematous cells in the epidermis and of slightly pyknotic cells in the papillary dermis. After 4 minutes of contact, epidermal lesions are clear with clearly pyknotic nuclei in the papillary dermis (Fig. 10). After 5 minutes of contact, lesions are marked in the epidermis and in the papillary dermis. They remain weak in the lower reticular dermis. Therefore lesions spread step by step after 20 seconds of contact until they reach the deep layer of dermis after 5 minutes.

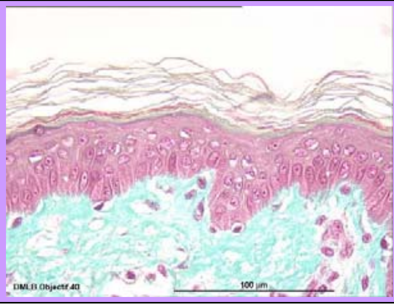
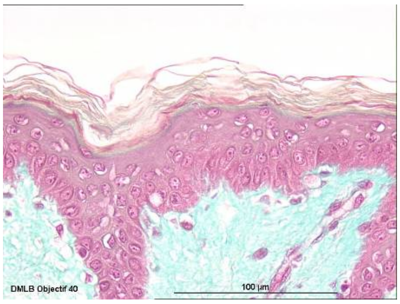
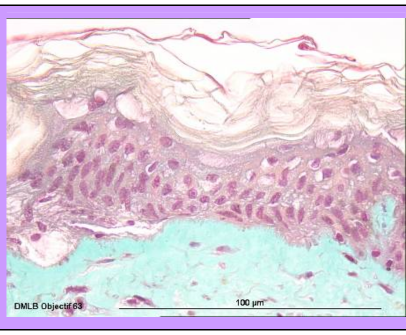
Explant exposure	Histological aspect	Comments
Not exposed		The morphology of the cellular structures of all the superficial layers of the skin (epidermis et derma) is good.
Exposure to 70 % HF for 1 minute		There are some morphological damages starting only in the upper layers of the epidermis.
Exposure to 70 % HF for 5 minutes		The epidermis presents a very damaged morphology: pyknosis of nuclei, perinuclear edema, cytoplasmic alterations (acidophilia). Same kind of marked lesions in the upper part of the derma. Lesions starting and less marked in the deeper part of derma.

Figure 9: Histological section of human skin

On the histological section (Fig.10), in order to illustrate the situation, the details of the lesions on cells an be seen with: the pyknotic aspect of the nuclei (retraction and dark color) and the acidophilic character (homogenous pink and orange-like color) of the cytoplasm (Fig. 24).

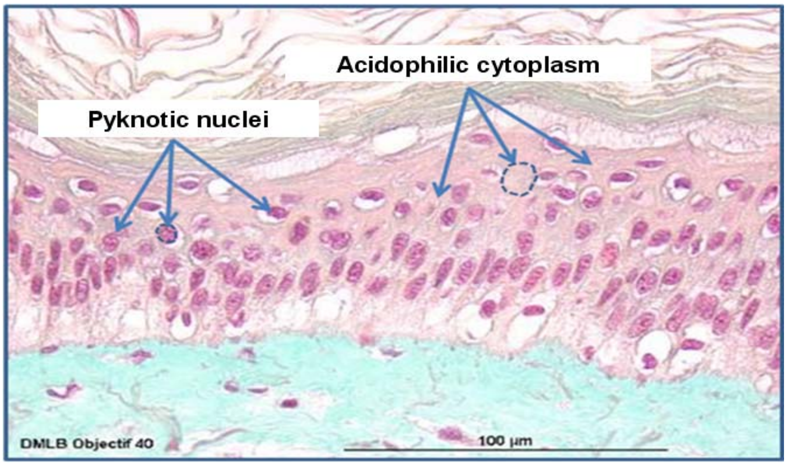


Figure 10: Histological section of human skin, 4 minute exposure to 30 µl 70 % HF

In conclusion, the hydrofluoric acid penetrates very rapidly with lesions appearing within the first minute.Therefore it is essential to perform decontamination as soon as possible. Every minute counts. The precocity and efficacy of decontamination prevent the appearance or can restrain the development of cutaneous lesions (Fig.11). Scars are often keloidal (fibrous thick tissues), coupled with pain and hypersensitivity to cold. Those physical sequelae are often associated with major psychological suffering[22].

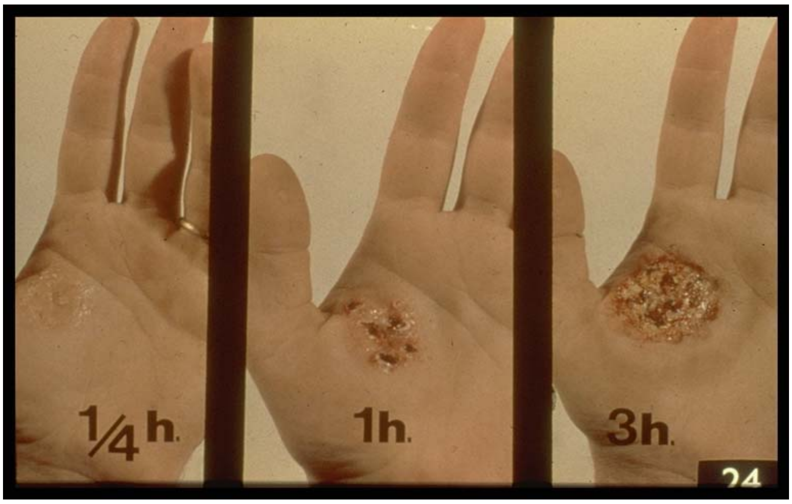


Figure 11: Simulation of the spontaneous evolution of a cutaneous HF burn

These experimental observations match the clinical observations of industrial accidents, as in the case of the spectacular aspect of a 70 % HF burn in a 45 year old worker[71] (Fig. 12). Applied treatment was: immediate rinsing with water (for 15 minutes) and saline solution during transport. Medical management in hospital: Ca and Mg I.V. infusion + local application of calcium gluconate gel. Final result: one year of sick leave.


Figure 12: 70 % HF burn

1.1.2 Ocular splashes

Ocular splashes often happen at the same time as cutaneous splashes, particularly in cases of facial contamination. The diagram below is a represents the anatomy of the eye (Fig.13).

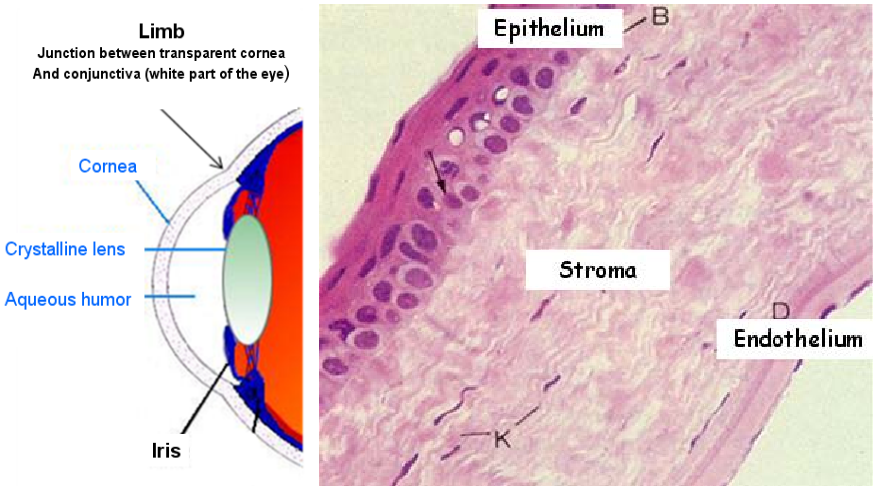


Figure 13 a) and b): a) Anatomy of the anterior chamber of an eye, b) section of the cornea

The eye is very sensitive to acid splashes. Inorganic acids (such as hydrochloric or sulfuric acids) do not penetrate beyond the corneal stroma (medium layer which is rich in collagen and the spatial structure of which maintains the corneal transparency). They induce necrosis by precipitation of the proteins and therefore restrain the extent of penetration[23,24]. The properties of hydrofluoric acid are similar to those of the other acids on the corneal surface. However, after the destruction of the epithelium, HF penetrates and fluoride ions cause severe lesions.

As a minimally dissociated acid ($pK_a = 3.2$), hydrofluoric acid can:

- penetrate into ocular tissues much deeper than the other acids,
- precipitate cations (Ca^{2+}, Mg^{2+}),
- quickly produce an opacification of the cornea and more severe lesions at the level of the anterior chamber of the eye (Fig. 13a et 13b) and at the level of the lens.

Ocular splashes of hydrofluoric acid destroy the corneal epithelium (Fig. 14) then generate an edema of the stroma and an ischaemia in the zone of the pericorneal limbus and of the adjacent conjonctiva. The deep penetration of fluoride ions causes an important inflammatory reaction.

- with the formation of edema of the stroma, not a good prognosis for the tissular regeneration as known in cases of chemical ocular burns[25],
- opacification of the cornea (Fig.14) and even
- necrosis of the structures of the anterior chamber[26].

Figure 14: Opacification of the lens

1.2 Serious consequences of the penetration of fluoride ions

The chelation properties of the fluoride ions are the cause of the toxic potential specific to HF damage. The local chelation of calcium and magnesium ions triggers ionic dysequilibriums which changes the physiological biochemical cellular cycles. Initially limited to the tissues of the contact zone, those dysequilibriums spread and quickly become generalized as indicated by the concentration of electrolytes in the peripheral blood[27].

Thus, in addition to the dehydration (for anhydrous HF) and to the corrosive action on the surface, there are systemic (in the whole body) hypocalcemia and hypomagnesia, in the case of concentrated solutions or in the case of an extended contact surface. The hypocalcemia triggered by the chelation of fluoride ions is difficult to reverse and can be lethal for splashes of very concentrated HF, even when they are not extensive (from about 2 % of the body surface) [28]. Coupled with hyperkalemia (release of intracellular K^+ ions during the phenomenon of necrosis), hypocalcemia can lead to lethal cardiac rhythm disturbances (ectopic arrythmia, tachycardia and ventricular fibrillation[29]).

The rapidity of the phenomenon, from a few minutes to few hours, prevents the body from mobilizing its calcium resources, even though they are extensive.

In conclusion, whereas burns by strong acids do not produce specific lethal risks, burns by hydrofluoric acid can have severe or even lethal consequences[27, 30, 31, 53, 54, 55].

1.3 First aid rinsing after a hydrofluoric acid splash

After a chemical splash, the first actions are rinsing to decontaminate and undressing the victim[31]. If the victim wears contact lenses, they must be removed without causing any additional ocular trauma. Given the double danger of hydrofluoric acid, it is vital to decontaminate as soon as possible with an effective rinsing method.

Camarasa[22] reports the case of a worker who had unscrewed with bare hands, for better dexterity, some screws soiled by HF which sealed the window of a HF gas cylinder. Feeling extensive stinging, he washed with water after 3 hours and was treated with calcium gluconate after several hours. This accident had severe consequences: large physical and psychological sequelae: the ends of the stumps remain painful and sensitive to the cold; he now wears fingerless gloves permanently. The accident led to one year of sick leave, a 40 % permanent partial disability, and a professional re-qualification with change of position.

1.4 Limits of the mechanical effect of rinsing

Having no chemical action, water only acts by mechanical sweeping and dilution effects. Mechanical rinsing or external decontamination with water permits the removal of the chemical only from the surface. Water cannot control the double aggressive potential of hydrofluoric acid, which is both corrosive and toxic.

With a 280 mosmoles/kg osmotic pressure, 0.9 % saline solution is isotonic to blood but remains hypotonic to eye (corneal osmotic pressure is about 420 mosmoles/kg). Therefore, saline solution, like water, can only achieve a mechanical rinsing.

1.5 Principle and advantages of hypertonicity of washing

The effect of the hypotonicity of water was highlighted on a fibroblast cell culture. This experiment allowed the comparison of the effect of two rinsing liquids: water (20 mosmol/kg) and a hypertonic solution (800 mosmol/kg). The pictures below show the results (Fig. 15): culture a) before rinsing, b) when rinsing begins, c) after rinsing[32].

With water, the cell volume increases progressively until they « explode ». With the hypertonic solution, there is a small retraction with no deleterious effect.

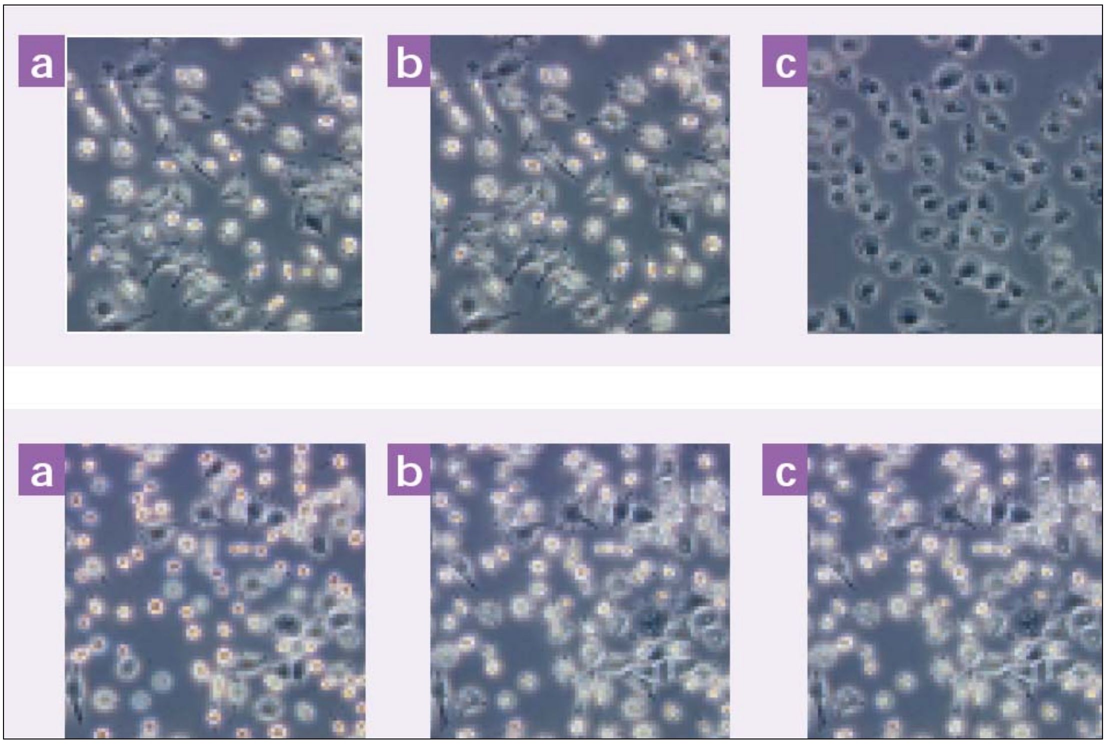


Figure 15: Effects of osmolarity onto a cell culture of fibroblasts

Passive rinsing does not have any positive osmotic force that could reverse the flow of the aggressive chemical and pull it outside the tissues. Only rinsing with a hypertonic solution can generate a flow from the inside of tissues towards the outside. Drained by this flow, the aggressive chemical can thus come out of the tissues. The influence of the rinsing hypertonicity is shown by the following diagrams (Fig. 16):

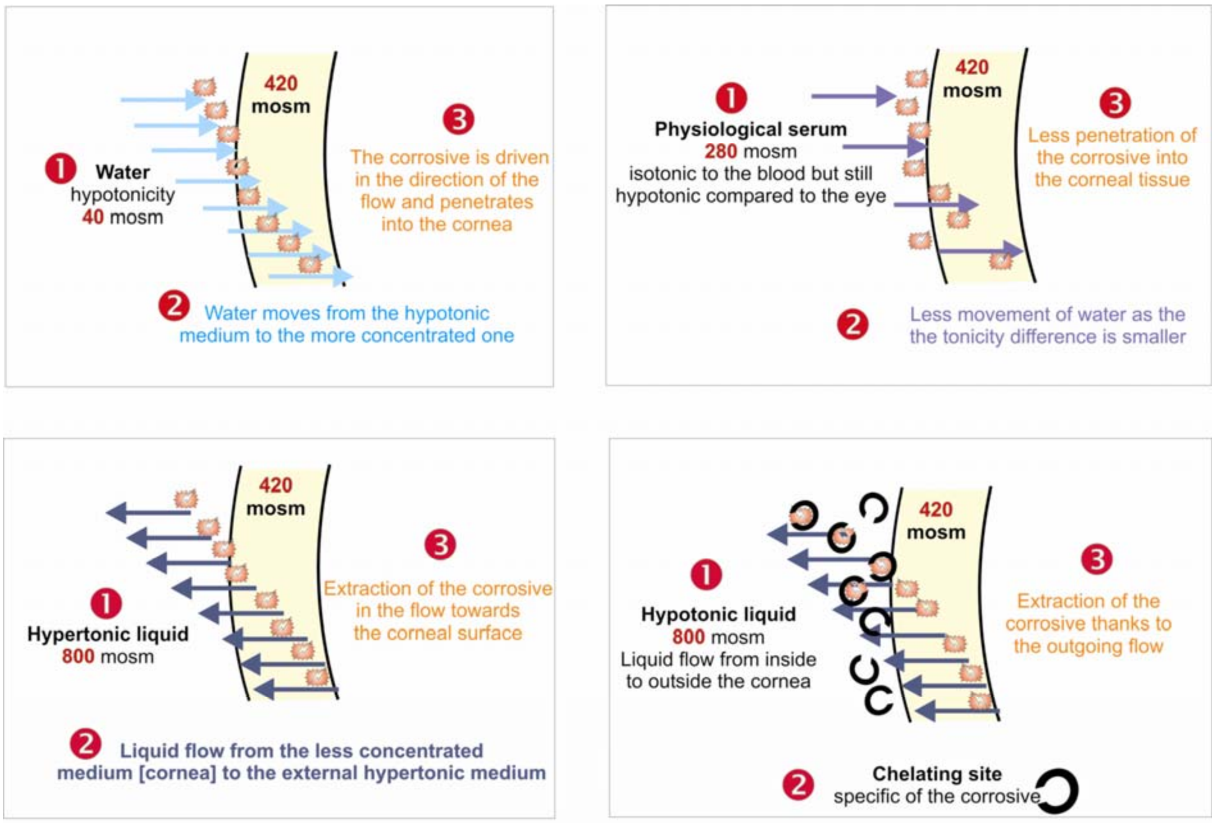


Figure 16: Role of the hyperosmolarity of an ocular rinsing solution

This phenomenon of osmosis permits the restriction of the burn severity but it must be coupled with a direct action on the chemical in order to stop the burn. To put it plainly, in addition to being hypertonic, the rinsing solution must also be able to control the aggressive potential of the chemical.

In case of a hydrofluoric acid splash, the rinsing solution must act on the acidity, which is the cause of the superficial attack of tissues, and it must chelate the fluoride ions, the penetration of which into the deep layers generates a toxic hypocalcemia. The hypertonicity of the rinsing solution makes the chemical aggressor already inside come out and thus permits the chemical and chelating properties of this solution to act on the double aggressive potential of the chemical. The principle of hypertonicity of a rinsing solution applies to ocular and cutaneous splashes.

Thus, in an *in vivo*[33] experiment simulating a 15.3 % ammonia splash, the appearance of a stromal edema has been highlighted in three situations: after rinsing with saline solution, after use of a hypotonic solution and obviously when not rinsing.

The lacunae which appeared at the level of the stroma, are quickly populated by inflammatory cells in an anarchical way. The evolution is correlated with the constitution of a sequelar cicatricial opacity which is the origin of the decline of sight[34]. This confirms the conclusions of work by Paterson[35, 36].

1.6 Results and analysis of the classic rinsing protocols

Experimental works[37, 38, 39, 40, 41, 42] and treatment protocols [13, 43, 44, 45, 46] of HF accidents have found and evaluated solutions to decrease the severity of these burns. The treatment of "rinsing with water followed by local application or injection of calcium gluconate" is by far the most used. As stated above, water permits removing HF from the surface by mechanical sweeping. Then calcium gluconate:

- Locally applied as a gel,
- in hypodermic injections,
- in local or regional intra-arterial (I.A.) or in intravenous (I.V.) injections,

chelates the fluoride ions that have spread over. The repeated applications of calcium gluconate often depend on the re-appearance of the feeling of pain for the patient.

Examples of decontamination with the water plus calcium gluconate protocol, has proved its efficacy for low or medium concentrations[47, 48, 49, 50, 51] but its use on high concentrations does not always prevent the development of severe lesions, or even the patient's death.

There are lethal cases of cutaneous burns by concentrated hydrofluoric acid due to splashes on about 10 % of the body surface, even though they had been immediately washed with water.

- Mayer[52] et al. reported a case of 70 % HF splash, over 9-10 % of the body surface (posterior side of thighs), which lead to the patient's death, even though he had been immediately washed with water. He had severe hypecalcemia and cardiac arrest.
- Mullett[53] et al. reported a case of 70 % HF splash over 8 % of the body surface (right leg), immediately washed with tap water for 15 minutes. A late I.V. injection of 10 % calcium gluconate did not prevent the patient from dying from cardiac arrest.
- Tepperman[54] and coll. described a pure HF splash over 2.5 % of the body surface, on the face, complicated by a small intoxication by inhalation. The victim had been washed with water after 10 minutes. 10 % calcium gluconate was injected under hospital supervision two hours after the splash. Cardiac arrest followed.

Applied topically or injected after water rinsing, calcium gluconate mainly acts on the chelation of fluoride ions. We have seen above that the origin of the penetration of the fluoride ions is the acid attack. If the acid is not removed thoroughly, then it keeps destroying the corneal epithelium or the epidermis, and thus it facilitates deeper tissular destruction by the fluoride ions. With only a limited action on the acid (see 2.1.1 in *vitro* experiments), calcium gluconate cannot stop both the corrosive action of the acid ions and the toxicity of the fluoride ions. This is why it is recommended to apply calcium gluconate several times, thoroughly massaging the area in order to facilitate its penetration. However, such applications cannot neutralize highly concentrated fluoride ions (concentrated HF solution and/or large body surface splashes). In serious cases, calcium gluconate can slow down the development of the burn, but progressive complications can occur.

The advantages and disadvantages of the water plus calcium gluconate application methods are in the following table (Fig.17):

Protocol	Avantages	Disadvantages
Water rinsing	▪ External rinsing by sweeping ▪ Effect of dilution	▪ Risk of hypothermia for extended lesions ▪ Hypotonic rinsing favouring the penetrating flow of fluoride ions from the outside to the inside of tissues
Calcium gluconate application	▪ Chelation of the fluoride ions when migrating towards deep layers	▪ Limited action on acidity (H^+ ions) ▪ Multiple applications required ▪ Factor depending on the victim's pain

Figure 17: The advantages and disadvantages of the water plus calcium gluconate application

- Other protocols recommend, after a primary emergency rinsing with water, the application of salts such as: magnesium chloride ($MgCl_2$), magnesium sulfate ($MgSO_4$), magnesium oxide (MgO)… Sodium chloride (NaCl) [55], calcium chloride ($CaCl_2$)[56], 0.2 % Hyamine and 0.03 or 0.05 % Zephiran which are quaternary ammonium salts, or even lanthane chloride ($LaCl_3$)[57,58] may be used for rinsing. These protocols have been studied in rabbit eyes by McCulley[59] and coll.

In practice, these treatments may cause secondary effects on normal and burned eyes.

- Experiments on primary rinsing using sodium chloride followed or not by ocular irrigation or by sub-conjunctival injection of 1 % calcium gluconate diluted solution have been realized by Beiran et al.[60]. Local applications of MgO or $MgSO_4$, irrigations with 0.2 % Hyamine or 0.05 % Zephiran as well as sub-conjunctival injection of 10 % calcium gluconate have proved responsible for the appearance of ocular lesions in normal eyes.

- Comparative studies[61] have experimentally estimated treatments containing Zephiran, Hyamine, calcium acetate and calcium gluconate on cutaneous burns by 38 % hydrofluoric acid.

- At the same time, replacing water rinsing by rinsing with saline solution (0.9 % sodium chloride) has been suggested. This is in accordance with the idea of involving positive osmotic pressures in order to try to make the aggressive chemical go out. However, as shown in Fig. 16, the osmotic pressure of saline solution is too weak. Therefore this kind of rinsing remains clearly passive.

Conclusion

Classic rinsing (external rinsing with water or saline solution, followed by treatment with calcium gluconate or with other salts meant to chelate calcium or magnesium), are essentially based on the principle of mechanical rinsing. Thus, those rinsing methods cannot have the properties of an active rinsing, which are necessary for the achievement of an optimal decontamination, meaning acting simultaneously on acidity and on toxic fluoride ions. With these classic methods, hydrofluoric acid can start its corrosive and toxic action, burns can appear and one can only try to minimize their extent and depth.

1.7 Advantage of active rinsing

In addition to the rinsing effect by simple mechanical sweeping, rinsing must also enable one to, quickly and simultaneously:

- Stop the progression of the quantity of chemical product that has penetrated inside the tissues. This quantity of the aggressive product is the origin of the chemical burn.

- Stop, due to the osmotic pressure mechanism, the HF penetration by creating a flow from the inside towards the outside of tissues.

- Absorb simultaneously all the aggressive potential of the chemical.

These three properties constitute the concept of active rinsing. They must be combined for the decontamination to be optimal.

2 Results of rinsing with Hexafluorine®

2.1 Comparative studies of various rinsing methods

Developed by PREVOR laboratory, Hexafluorine® was created to improve water rinsing and to permit an active rinsing in case of hydrofluoric acid splashes. Its action mechanism is multiple:

Sweeping effect

Like water, Hexafluorine® rinses the exposed surface quickly. By experience, 90 % of the rinsing effect is due to the mechanical effect. Therefore, only a small quantity of chemical remains on the surface or penetrates into the layers of skin. However this small quantity is sufficient to induce a chemical burn, which will develop until the complete inactivation of all the corrosive molecules.

Absorption of H^+ ions

Due to its chemical properties, Hexafluorine® can inactivate the acidity still available quickly and thus prevent the destruction of the epithelial layers and restrains the penetration of fluoride ions.

Every molecule of Hexafluorine® can bind with 3 H^+ ions simultaneously[62]. The absorption power of H^+ ions was highlighted by *in vitro* experiments (Fig.19).

Thanks to this almost immediate inactivation of the acid (20 seconds), the pH is quickly lowered back into the zone of acceptable physiological limits (over 5.5) and thus the corrosive attack is stopped.

Chelation of F^- ions

Hexafluorine® traps the F^- ions on the surface, and does not allow them time to penetrate towards deeper tissues.

Every molecule of Hexafluorine® can chelate 6 F^- ions at once. This results in a residual concentration of fluoride ions of less than 10^{-6} mol/l (pF= 6), which is not dangerous as it below the limit concentration of toxicity (10^{-5} mol/l, pF = 5) (Fig. 20).

Hypertonicity

Unlike water, Hexafluorine® is a hypertonic liquid: rinsing with Hexafluorine® enabmes the penetration of fluoride ions into tissues to be stopped and so contributes to the complete decontamination of the tissues in contact.

Conclusion

Considering active rinsing, the properties of Hexafluorine® enable it to perform:

- An external rinsing by sweeping mechanism,
- an internal rinsing by stopping the penetration of hydrofluoric acid when making HF come out of the tissues, thanks to its hypertonicity,
- a complete rinsing by controlling both the corrosive and the toxic dangers of HF, due to its chemical properties.

2.1.1 *In vitro* experimentation

The estimation of the efficacy of Hexafluorine®, in comparison with other rinsing methods such as water by itself or 10 % gluconate calcium has been based simultaneously on the corrosive potential (pH measurement) and on the toxic potential of hydrofluoric acid (pF measurement).

Material and method

PREVOR laboratory has developed a method for the *in vitro* testing of the efficacy of rinsing solutions for chemical splashes (Fig. 18).

Figure 18 : PREVOR *in vitro* dosage protocol to test the efficacy of rinsing solutions

The protocol realizes the dosage of a normal (1N) solution or 10 ml of a 0.1N solution by an increasing volume of a decontaminating solution.

10 ml of 0,1 N (0.2 %) hydrofluoric acid are poured into a beaker. An increasing volume of rinsing solution: water, 10 % calcium gluconate or Hexafluorine® is added milliliter by milliliter. Then the evolution of concentration in acid (pH measurement) and in fluoride ions (pF measurement) is observed.

The pH and pF measurements are made with a *HEITO* pHmeter-fluorimeter. The two following graphs show the experimental results (Fig.19 and 20):

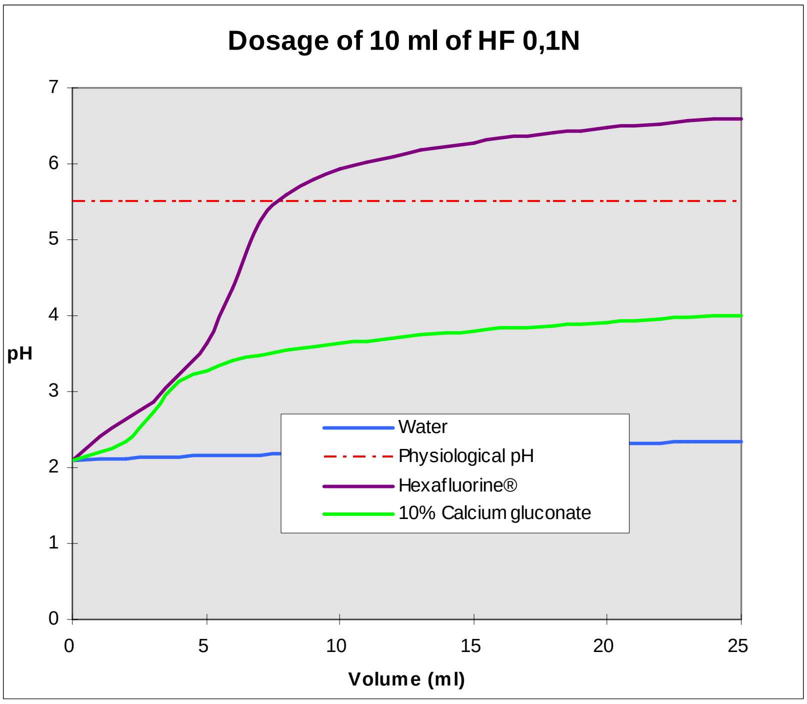


Figure 19: Evolution of the corrosive potential (pH) of a HF solution in presence of an increasing volume of various rinsing solutions

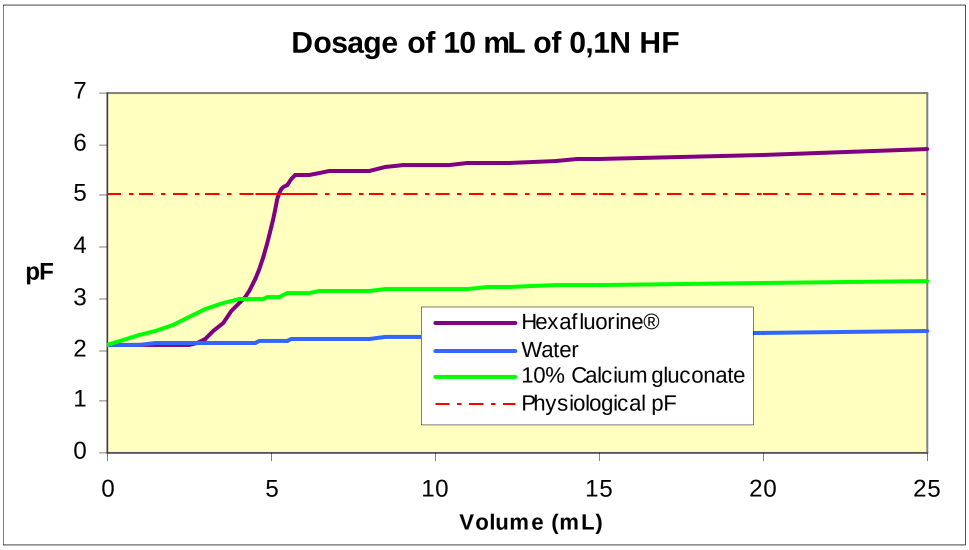


Figure 20: Evolution of the toxic potential of a HF solution in presence of an increasing volume of various rinsing solutions

Discussion

In the first graph, the pH scale permits the observation of the zones in which acids are aggressive. In the pH zone between 5.5 and 9, the product is harmless (pH in the zone of physiologically acceptable level). In the case of acids, the lower the pH value is, the more corrosive the acid is; it is then called a strong acid.

After addition of a small volume of Hexafluorine® (8 ml), the 10 mL solution of 0.1 N hydrofluoric acid returns to the "physiologically acceptable" zone. The resulting mixture is no longer aggressive.

25 mL of water added to the 10 ml 0.1 N HF only has a weak effect of dilution. The pH remains under 2.5, so the solution is still corrosive.

The addition of 8 ml of 10 % calcium gluconate decreases the concentration in protons (H^+) by 100 times ; the pH reaches 3.5 (the pH being a logarithmic unit, a 10^2 decrease is equivalent to 2 units on the scale: 1.5 + 2 = 3.5). However, this pH value remains in the zone of chemical aggressiveness.

In the second graph, the pF notation expresses the concentration in released fluoride ions, which thus reveals its toxic potential. The lower the pF value is, the higher the concentration in fluoride ions is and the stronger its toxic potential gets.

The mathematical relation between pH and concentration in protons $[H^+]$ is:

$$pH = -\log [H^+]$$

By analogy, the mathematical relation between pF and concentration in fluoride ions $[F^-]$ is:

$$pF = -\log [F^-]$$

For a pF value above 5, the product is said to be harmless (pF in the physiologically acceptable zone). On the graph of the evolution of the hydrofluoric acid pF in presence of an increasing volume of various rinsing solutions, we can observe that a small volume of Hexafluorine® (5 mL) enables the 10 ml of 0.1N HF to be brought back to the zone of no danger.

It is remarkable that the progressive addition of water only dilutes the hydrofluoric acid solution. The residual mixture HF/ water remains aggressive with a pF value near 2 after a 25 mL additional volume of water.

The addition of an increasing volume of a 10 % calcium gluconate solution reduces (by a factor of 10) the concentration of released fluoride ions (final pF = 3 for 5 ml added) and in doing so, to lower the toxic potential. In the specific and comparative conditions of our experiment, the addition of 25 ml of 10 % calcium gluconate does not enable the pF to return to the zone of non-aggressiveness.

2.1.2 Ex *vivo experimentation*

2.1.2.1 Ocular burns

Experimental methods for ocular burns

New models have been developed for the valuation of the chemical contamination / decontamination of the eye. The EVEIT® model (*Ex vivo Eye Irritation Test*) has specifically been used in order to visualize the diffusion of HF into the cornea and to compare various rinsing methods[63]. Performed by a German team, the study compares the following situations:

- No rinsing
- Water rinsing
- Rinsing with a 1 % calcium gluconate solution, which is the reference suggested by the literature for the specific decontamination of ocular HF splashes
- Rinsing with Hexafluorine®

The EVEIT® model is confirmed for its capacity to act similarly to living ocular tissues when in contact with corrosive chemicals[64]. It is made of enucleated rabbit eyes maintained in a 4 °C humid atmosphere in order to conserve all the qualities of the corneal epithelium. They are treated within 12 hours after slaughtering.

The diffusion of chemical inside the cornea was observed by OCT-HR (*Optical Coherence Tomography – High Resolution*), in spatial and temporal high resolution[65]. This method visualizes the kinetics of the penetration of the corrosive molecules during the initial stage of an ocular chemical burn. The OCT-HR technique permits the observation and the measurement in real time of the diffusion velocity and of the penetration depth. This method also measures the thickness of the cornea, with a resolution of a micrometer (Fig. 21).

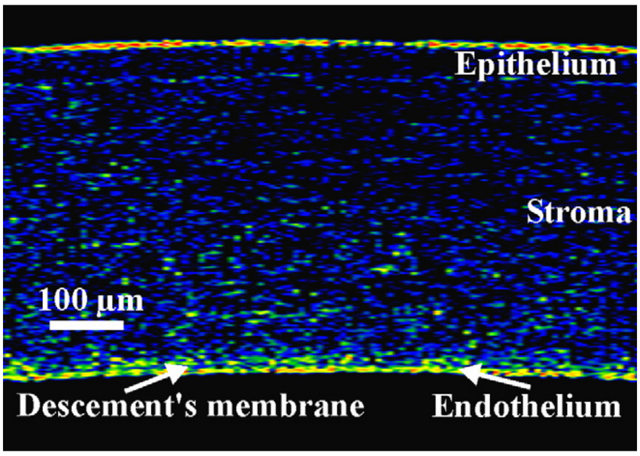


Figure 21: High resolution OCT picture of an *ex vivo* rabbit cornea

The damage observed is due to micro-structural changes in the cornea in direct relation with molecular chemical interactions.

All these changes are the origin of the loss of transparency that has been macroscopically observed. Because of its high accuracy, this method is naturally adapted to the comparison of efficacy of various ocular decontaminating solutions.

To obtain an ocular burn by HF, 25µl of 2.5 % (1.25 mol/L) solution soaking a 10 mm diameter filter paper is kept in contact with a cornea for 20 seconds. Then, the rinsing started 25 seconds after the burn. One group of corneas was kept unwashed, one was rinsed with tap water, a third one with 1% calcium gluconate and a last one rinsed with Hexafluorine®. The washing lasted for 15 min at a 66.7 ml/min flow rate, using 1000 ml of each solution.

Results

HF penetrates into the whole of the cornea within 240 seconds (Fig. 22).

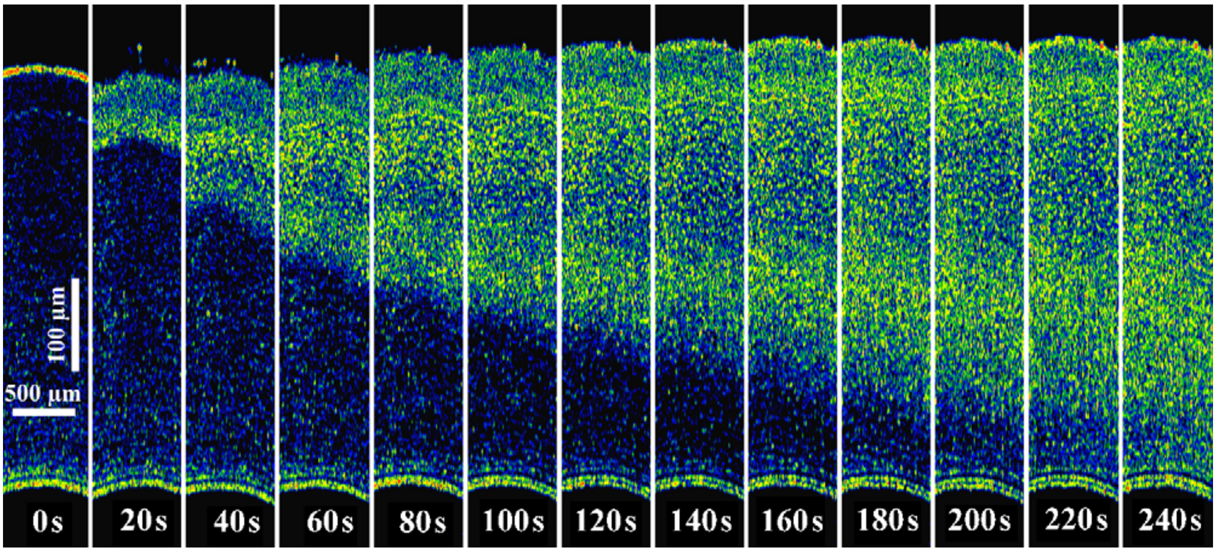


Figure 22: Sequence of OCT-HR pictures showing the 2.5 % HF penetration into the cornea

Initially transparent, the cornea becomes opaque.

Opacification of cornea has appeared in all the following groups, which signifes a developing burn:

- exposed to HF and not treated,
- exposed to HF and then rinsed with water,
- exposed to HF and then washed with 1 % calcium gluconate.

With Hexafluorine®, the cornea remains transparent. Thus, the experiment clearly shows the action of Hexafluorine® on the ocular decontamination of HF, in comparison with the other rinsing solutions.

This conclusion (Fig. 23) is corroborated by the data about the diminution of the corneal thickness after Hexafluorine® washing. Not observed with the other tested solutions, this result shows the action of the hypertonicity of Hexafluorine® and its faculty of decontaminating from the inside towards the outside of tissues.

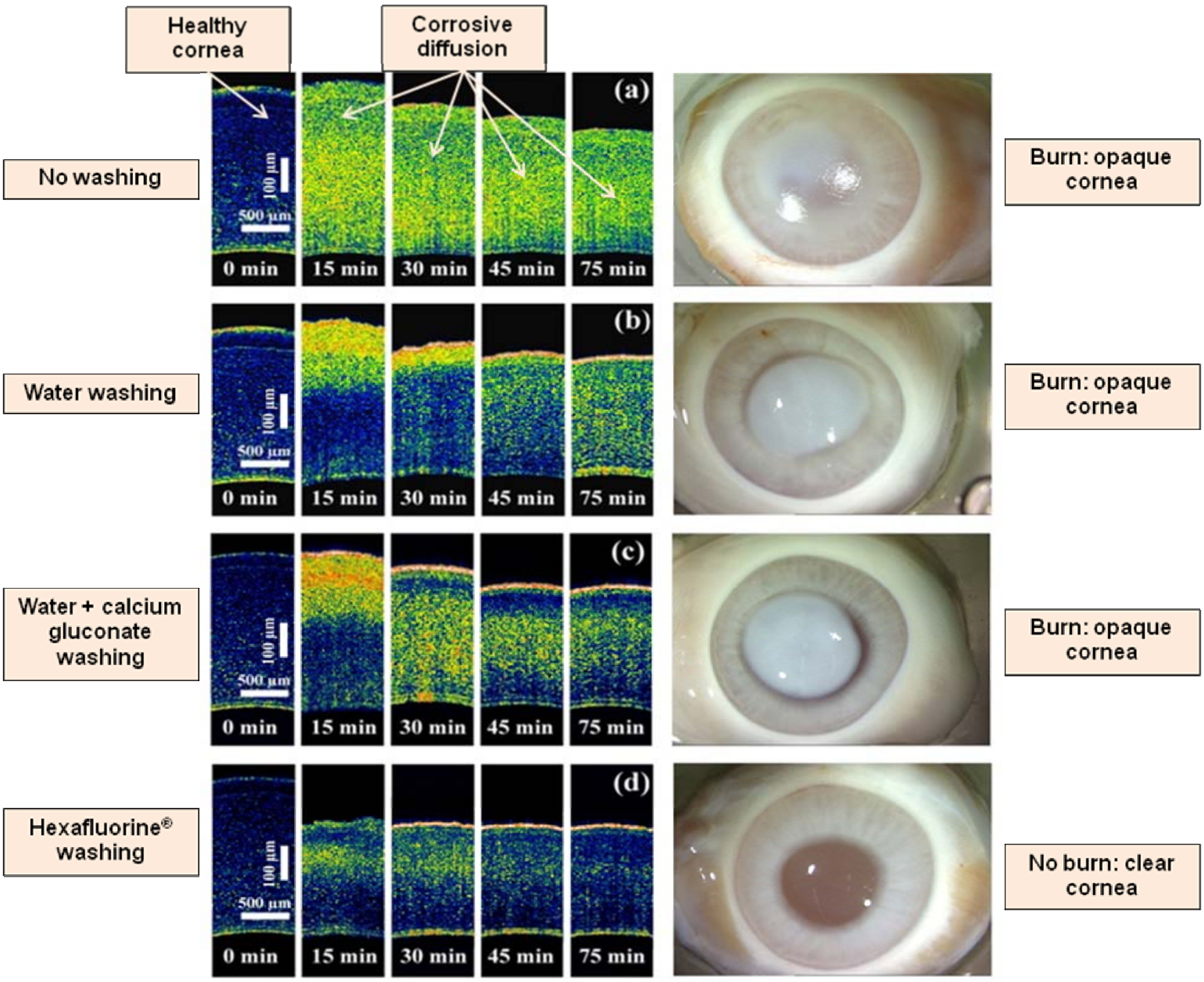


Figure 23 : Influence of various rinsing solutions onto the diffusion of hydrofluoric acid into cornea on an *ex vivo* model of rabbit eye, 20 second contact with 25 µl 2.5 % HF, 15 minute washing.

2.1.2.2 Experimental method for cutaneous burns

Considering how difficult it is to extrapolate animal studies onto human standards, working on human explants of skin is a first step ahead. Experimental conditions are:

- Concentrated 70 % hydrofluoric acid, in order to simulate a situation representing the most serious industrial exposures,
- A 20 seconds contact time with soaked filter paper
- A 30 µL on a surface of 1 cm diameter quantity in order to get a sufficient burn, though maintaining the whole structure of tissues in order to realize a valuable comparison of various after-burn washing solutions,
- A histological analysis in order to observe the progression of tissular lesions from the most superficial layer of epidermis to the deep layer of dermis,
- Experimentation in parallel on three samples in order to guarantee the reproductibility of experiment.
- Quantity of 30 µL on a surface of a centimeter in diameter. These quantitative data were chosen to reproduce the concentrations observed for a splash on the skin. It was indeed measured experimentally during an immersion in water of a whole human body (2 m^2), it remains on the surface of the skin, the maximum quantity of 250 ml of liquid.

Results

Non decontaminated burned explants show an attack of the epidermis and dermis within five minutes, as mentioned in paragraph 1.1.1. The lesions increase until complete necrosis during the 24th hour. The examination of the progression of cellular damages during the 5 first minutes:

- no lesion after a 20 seconds contact,
- alterations of the superficial layers of epidermis start within the 1st minute,
- basal layer of epidermis is attacked within the 3rd minute,
- most superficial layer of dermis (papillary dermis) is attacked within the 4th minute and
- deep reticular dermis is injured within the 5th minute.

The following table sums up the chronology of the lesions (Fig. 24):

Time of exposure	Microscopical lesions
1 min	Start of penetration within the superficial layer of epidermis.
2 min	Attack of the basal layer (the deepest layer) of epidermis.
3 min	Epidermis completely damaged. Apparition of the first lesions in papillary dermis (the most superficial layer of dermis).
4 min	Epidermis completely damaged. The papillary dermis is severely attacked.
5 min	Epidermis completely damaged. Attack of the reticular dermis begins (the deepest layer of dermis).

Figure 24: Chronology of lesions on human skin during a 70 % HF burn

With this model of human skin explants, after the validation of the experimental burn, the challenge was to compare various methods for washing HF burns. We selected two of them: water washing followed by the application of a 2.5 % calcium gluconate (CaG) cutaneous gel *versus* Hexafluorine® as a specific washing solution, which, due to its anti-acid and fluoride ion chelating properties, matches the two properties of HF : corrosion and toxicity.

The explants burned by 30 µl 70 % HF for 20 seconds, with water washing for 15 minutes followed by superficial application of 2.5 % CaG show:

- A delay of the apparition of lesions until the 15th minute in comparison with non-washed explants. As for the exposed and non-washed sample, epidermal cells have relatively pyknotic nuclei with slightly acidophilic cytoplasms whereas this aspect is more remarkable in the two sub-layers of dermis.
- After 30 minutes, some necrotic cells appear in the epidermis whereas the whole dermis recovers a normal aspect.
- When controlling after one and two hours, epidermis and dermis are normal.
- Within the 4th hour, epidermis modifies again but lesions do not have the same shape as initially because the aspect of epidermal cells is now slightly edematous with a breaking up of cellular junctions (acantholysis). In this stage, dermis remains normal.
- During the last series of sampling after 24 hours, the epidermal edema has clearly increased. Pyknotic nuclei and acidophilic cytoplasms reappear clearly in papillary dermis and more slightly in reticular dermis.

Finally, with CaG, the burn is initially delayed, then starts after 15 minutes and declines completely afterwards, until it reappears secondarily under the shape of edematous lesions, before generating later a pre-necrosis aspect. A unique superficial CaG application can stop the corrosive and toxic potential of HF temporarily. But its action does not last. In these specific experimental conditions, it stops after the 4th hour when the process of burn starts again under an edematous form and then a pre-necrotic form after 24 hours.

Several applications of calcium gluconate with massage compared to an only one should have given better results.

The above observations and comments highlight the benefit of the usual recommendations about protocols using water and local CaG applications:

- intervene as early as possible after the splash,
- make the calcium gluconate penetrate as deep as possible by massaging the area in order to improve its efficacy,
- repeat local applications of gluconate calcium as many times as required (usually when pain reappears).

Burned in the same conditions, the explants washed with Hexafluorine® showed no lesion at all, whatever the time of observation, from 1 minute to 24 hours.

In a schematic way, the following table sums up the comparative results of decontamination methods in the experimental conditions described above (Fig. 25).

Time of exposure and skin layers		T (Non treated control sample) 20 explants	F (HF with no washing) 18 explants	FWCaG (HF + water washing + calcium gluconate) 16 explants	FHexa (HF + 400 ml Hexafluorine®) 16 explants
T0	Epidermis	Good morphology	Good morphology	Good morphology	Good morphology
	Papillary dermis				
	Reticular dermis				
20 s	Epidermis				
	Papillary dermis				
	Reticular dermis				
5 min	Epidermis		PN + AC*		
	Papillary dermis				
	Reticular dermis		PN + AC* relatively		
10 min	Epidermis		PN = Pyknotic nuclei AC = Acidophilic Cytoplasms		
	Papillary dermis				
	Reticular dermis				
15 min	Epidermis			PN + AC* Relatively	
	Papillary dermis			PN + AC*	
	Reticular dermis				
30 min	Epidermis			Some necrotic cells	
	Papillary dermis			Good morphology	
	Reticular dermis				
1 h	Epidermis				
	Papillary dermis				
	Reticular dermis				
2 h	Epidermis				
	Papillary dermis				
	Reticular dermis				
4 h	Epidermis			Slightly edematous cells with relative acanthosis	
	Papillary dermis			Good morphology	
	Reticular dermis				
24 h	Epidermis		Complete necrosis	Very edematous cells with very clear cytoplasm	
	Papillary dermis		PN + AC*	PN + AC*	
	Reticular dermis			Lesser damages	

* GM = good morphology; PN=Pyknotic nuclei; AC=Acidophilic Cytoplasms

Figure 25 : Schematic sum up of the results of comparative decontamination of experimental burns by 70 % HF on human skin explants

This experiment also shows that an active washing solution such as Hexafluorine® can simplify the decontamination procedure. Compared to the protocol water followed by calcium gluconate, which needs several prolonged topical applications, the use of Hexafluorine®, by non medical personnel, only requires a single initial action of decontamination.

2.1.3 *In vivo* experimentation

2.1.3.1 Skin burn with 70% HF

An initial experiment[62] was performed on rabbits in order to observe burn lesions in histological sections, comparing water washing, water washing followed by a local application of 2.5 % calcium gluconate gel and washing with Hexafluorine®.

120 rabbits, type New Zealander hybrid Albinos «Blanc du Bouscat», were divided into 6 groups. For the three washing methods, we have studied two groups, each one constituted of 20 rabbits. With three deaths not due to the experiment, 117 observations were carried out.

The cutaneous burn was caused by the application of a 1 cm diameter filter paper soaked into 70 % HF. This is a burn of less than 1 % of the complete body surface of an animal. In order to keep its properties, the HF reserve was renewed every 10 minutes. Animals were shaved in order to maintain the properties of skin. The HF soaked filter paper was applied for 20 seconds then the various washing methods were applied:

- water washing only with a 10 liters/minute flow for 5 minutes,
- water washing only with a 10 liters/minute flow for 3 minutes followed by a 5 minute massage with 2.5 % calcium gluconate gel,
- washing with Hexafluorine® for 3 minutes (500 ml).

Complete observation lasted 6 days. The consequences of burns wer manifested as as irritations or edemas. The selected classification for the valuation of the intensity of reactions was set up according to Draize scale (no lesion, visible, extended or severe lesion). The following table (Fig. 26) shows the results:

Draize scale (score)	Lesions	Burn intensity
0-1	Erythema or edema	No mark
2-3		Visible lesion
4		Extended lesion
> 4	Out of Draize scale	Severe lesion

Figure 26: Results of the animal experiment, 70 % HF burn, with comparison of washing media

Given the specificity of evolution of HF burns (color, depth) and because it can reach stages of severity beyond those usually observed with other chemicals, we have decided to provide a description beyond Draize's scale.

The main observations about the stage of burn after washing are summed up as follows (Fig. 27):

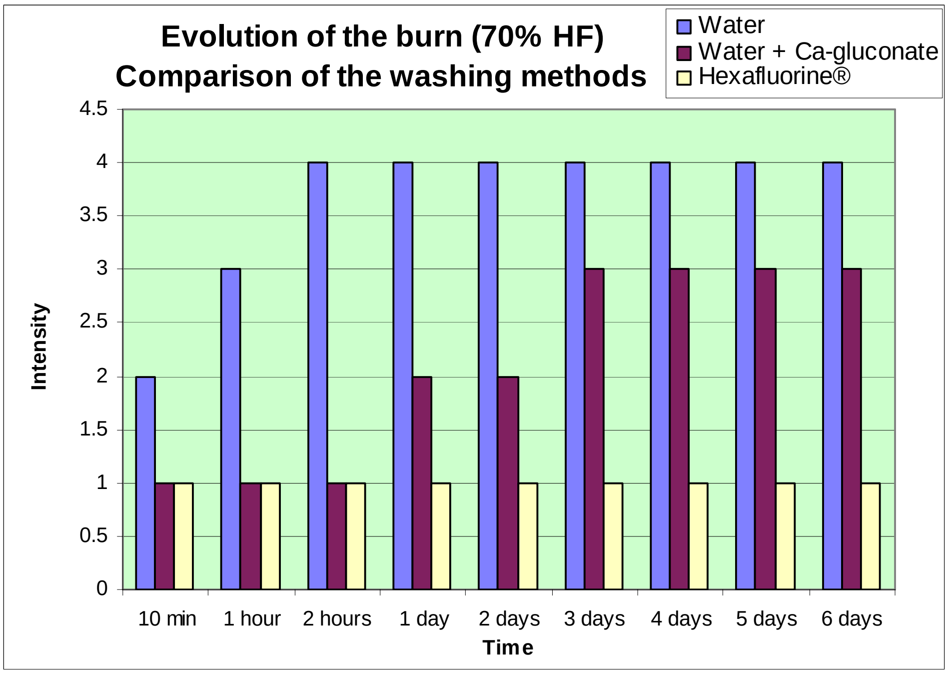


Figure 27: Comparison of the effects of the washing methods onto the evolution of a HF burn in rabbits

Conclusion

- Washing with water drags the HF to the surface but it does not react with it and, therefore not efficient enough for stopping the evolution of a burn, which becomes a severe burn.

- After washing with water, the secondary use of calcium gluconate prevents the appearance of a burn, at least during the first 24 hours, but a unique application is not sufficient for the complete elimination of all fluoride ions. When treatment stops, a burn reappears because the residual rate of released fluoride ions is still above the non-toxicity limit.

- The immediate use of an active solution specific to HF, such as Hexafluorine®, suppresses the action of hydrofluoric acid and does not give the F^- ions the opportunity to bond with calcium in tissues. The 6 days observation of the animals showed no sequelae after a unique wash with Hexafluorine® whereas, after washing with water, a secondary therapeutic management is required and whereas, to be efficient, calcium gluconate requires repeated applications and / or sub-cutaneous or intra-vascular injections.

2.1.3.2 Evolution of serum calcium during a 70% hydrofluoric acid burn

A study has focused on the evolution of calcemia[62] in the blood, in 62 Wistar male rats, 50 g each, that have been contaminated with 70 % hydrofluoric acid. Rats were classified into 4 study groups and 2 control groups.

Observations were scheduled after 10 minutes, 1 hour, 4 hours, 24 hours and 5 days. Rats were divided into 4 groups depending on the washing method used:

- water washing: 10 liters/minute for 5 minutes,
- washing with water and calcium gluconate: 10 liters/minute for 3 minutes then massage with 2.5 % calcium gluconate for 5 minutes,
- washing with water and calcium chloride ($CaCl_2$): 10 liters/minute water flow for 3 minutes then 10 % $CaCl_2$ 0.2 liter/minute flow for 3 minutes,
- washing with Hexafluorine® for 3 minutes (500 ml).

The burn is due to the 20 seconds application of a 1 cm side square filter paper soaked in 70 % HF (supplied by Atochem). It represents 0.6 % of the body surface of an animal. The rat is thoroughly shaved in order not to change the superficial properties of skin.

The supervision of calcemia (calcium concentration into the circulating blood) was made on 60 rats, divided in 4 series. Every series was made of 5 groups of 3 rats each. With 7 deaths not due to the experiment, 53 observations were performed. The research was made on blood samples (Fig. 28) then, after slaughtering, on the anatomopathological exam of liver and kidneys. Observations were scheduled after 10 minutes, 1 hour, 4 hours, 24 hours and on 5^{th} day.

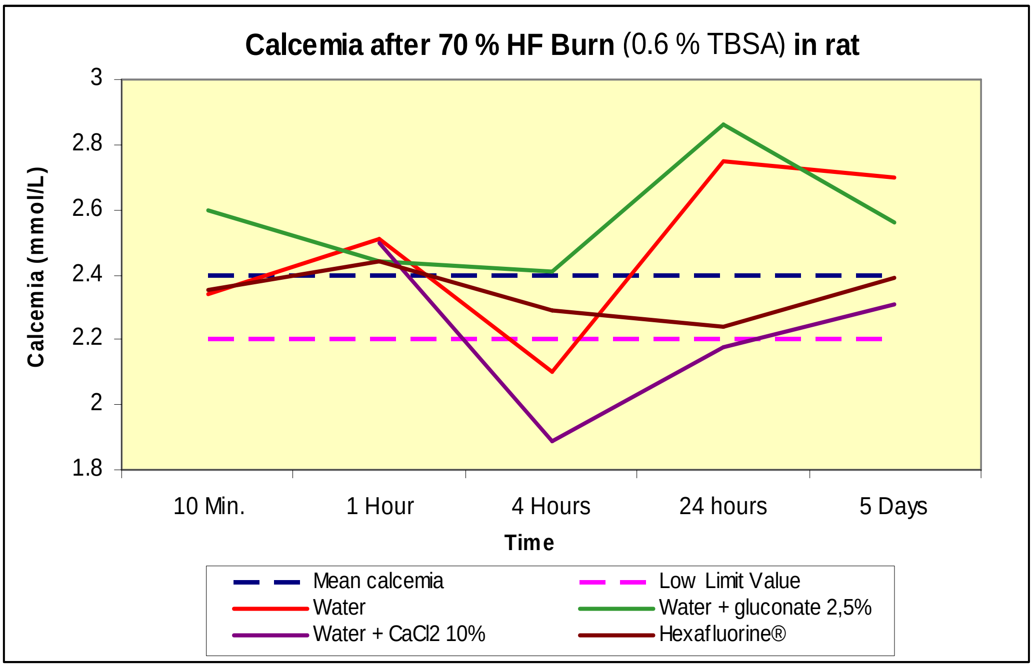


Figure 28: Evolution of calcemia, during a 70 % HF burn, in rats

The analysis shows that all the washing methods produce similar results after 1 hour. After 4 hours, a clear hypocalcemia can be observed for water and water + $CaCl_2$ washing methods. Then an improvement is observed after 24 hours.

In opposition, results clearly show that serum calcium remains constant after washing with Hexafluorine®.

By optical microscopy, the histological study of liver and kidneys showed no significant lesions.

2.1.3.3 Experimental study with a 50% HF skin burn during 3 min + 30s delay

The study was performed as a blind controlled experimental study on Sprague Dawley rats which were anesthetised and shaved on their back. The burn was performed by applying 50% HF during 3 minutes followed by a 30 second delay before decontamination.

4 groups were created depending on the washing method used:

- no washing as a control group,
- water washing, 500 mL during 3 minutes (group W),
- water washing, 500 mL during 3 minutes followed by a single application of 2.5% calcium gluconate (CaGlu) (group Ca),
- Hexafluorine®, 500 mL during 3 minutes (group H).

2.1.3.3.1 Evaluation of the burn following a modified Draize scale

Four filter papers (10 mm in diameter) were soaked in 50% hydrofluoric acid and applied on the shaved back of each rat for 3 minutes. A modified Draize scale (Fig. 30) was used to analyse the results[66].

Score	Observations
0	No visible injury
1	Diffuse erythema
2	Distinct erythema
3	Distinct erythema plus wounds or discolored spots
4	Distinct erythema plus wounds or discolored areas covering > 50% of the burn
5	A necrotic wound covering the whole burn

Figure 30: Modified Draize Scale

Results: The severity of the burn was significantly different between Hexafluorine® and water + CaGlu at day 2 and 3 (in favour of the latter group), but this was not observed at day 4 and 5 (Figure 31).

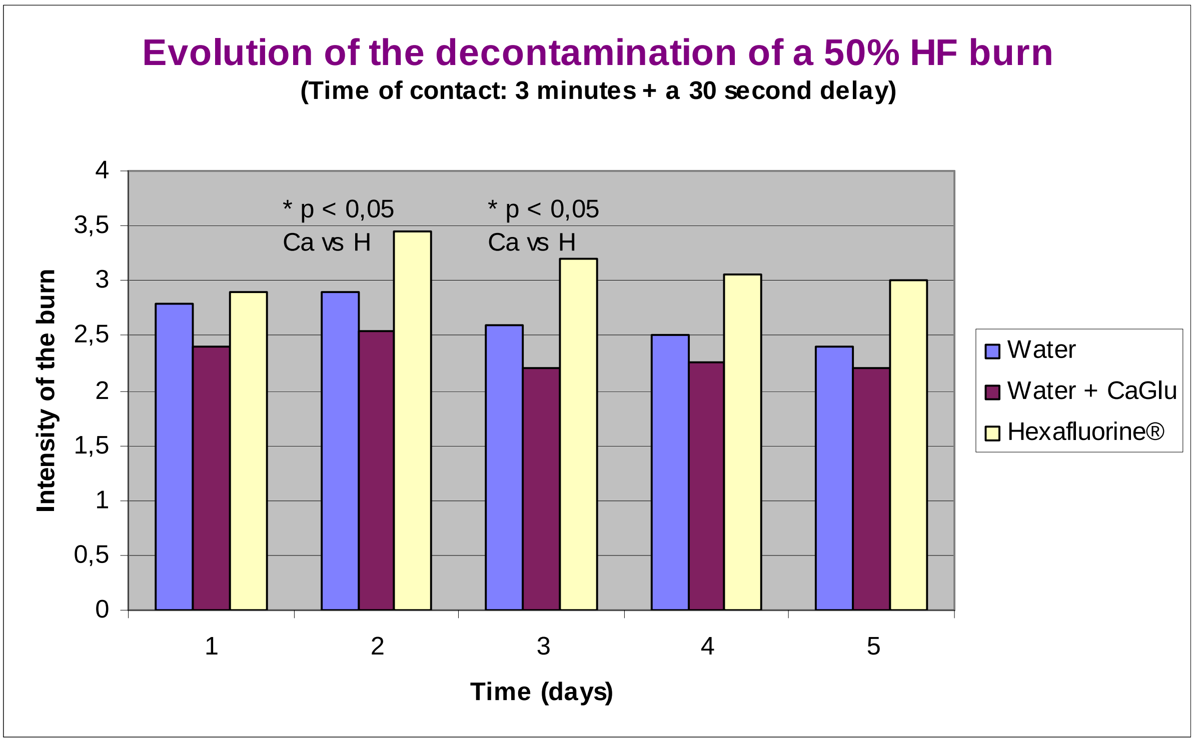


Figure 31: Evolution of the decontamination of a 50% HF burn

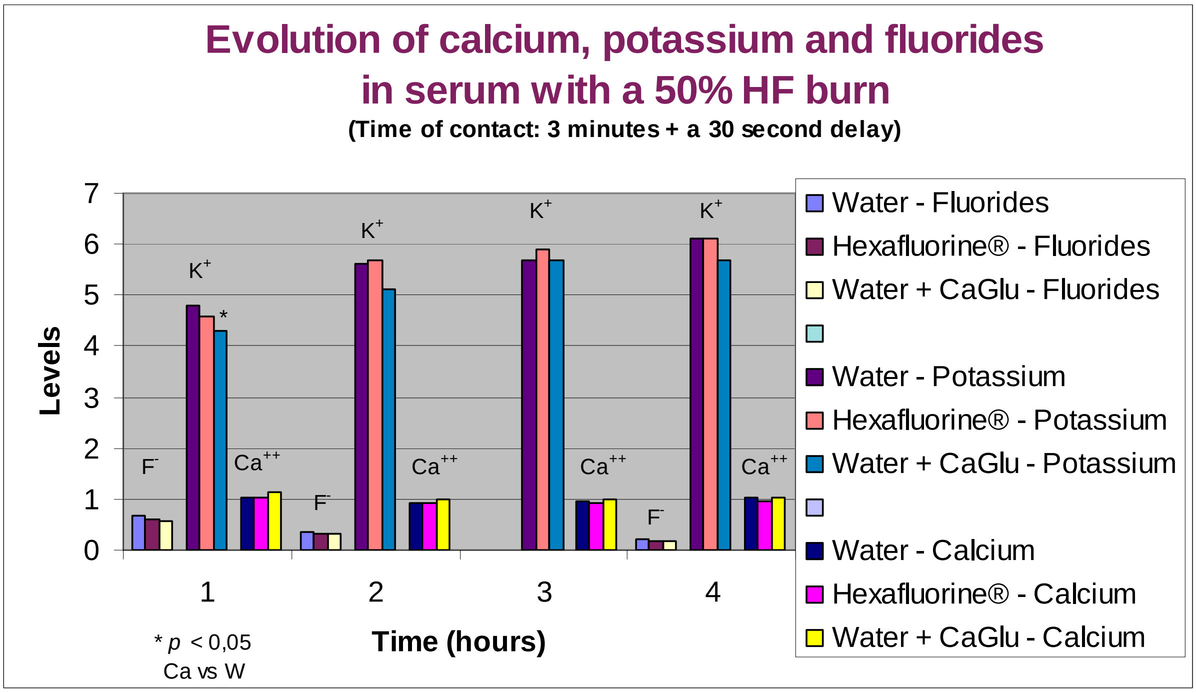
Conclusion: The authors conclude that water rinsing followed by topical calcium should remain the standard first aid treatment for skin exposure to hydrofluoric acid even at day 4 and 5, all three decontamination protocols gave the same results without any significant difference[67, 68].

2.1.3.3.2 Systemic toxicity

A filter paper (3.5 x 6 cm) was soaked in 50% HF and applied on the back of each rat for 3 minutes. Blood samples[69] were taken and analysed for ionized calcium and potassium (before injury and after injury at 1, 2, 3, 4 hours after) and also fluoride (1, 2, 3, 4 hours after injury).

Results:

- The untreated animals exposed to HF developed hypocalcemia, hyperkalemia, and hyperfluoridemia.
- The only significant difference was observed in serum potassium at 1 hour between the group water + calcium gluconate and the group water alone.



*No data about fluoride in serum were given at 3 hours.

Figure 32: Evolution of calcium, potassium and fluoride in serum

Conclusion: The authors conclude that there is no difference between water alone and Hexafluorine®. However, considering that there is no significant difference excepting the value between water and water + CaGlu at one hour for potassium level (4.8 vs. 4.3 mmol/l), it can be concluded that there is no significative difference in the three groups.

Conclusion of these two studies: There is no significant difference of efficacy between the three groups of decontamination at the end of each study. This can be explained because the burn model was too strong; it did not allow observing decontamination in good conditions. The burn is severe and painful, 3 minutes of contact with 50% HF + 30 seconds delay which is not representative of the accidental situation. If the burn has already appeared, decontamination with Hexafluorine® must be followed by a specific treatment against toxic fluoride ions such as calcium gluconate. May be adding a fourth group in this study, such as Hexafluorine® followed by calcium gluconate, could have made the difference.

2.2 References in industry

2.2.1 Isolated cases with early management (Woeste, Krupp, Alcan, Arques International)

These cases are gathered in a recapitulative edition[70]. On the PREVOR website, www.prevor.com, you will find other cases and testimonials.

Described below, the cases from Woeste, Krupp and Alcan have recently been published[71].

2.2.1.1 A case in WOESTE, Verbert, Germany, 1997

A worker fell into a bath made of 1505 liters of water, 30 liters of 31/33 % hydrochloric acid and 233 liters of 59 % hydrofluoric acid. He was completely immersed. Due to the immediate action of his colleagues, his body was quickly washed with Hexafluorine®, his eyes were rinsed with an ocular water shower. On the body, the worker only had slight burns on his abdomen and back. However, he developed a severe burn of the left eye.

Finally, the victim only suffered of a severe burn of the left eye, probably due to an unsufficient decontamination, whereas, given the extreme aggressiveness of the mixture involved and the attack of 100 % body surface, this case might have been lethal (as shown in Fig. 4, paragraph 1.1).

2.2.1.2 A case in Krupp, Werdohl, Germany, 1996

While he was filling a bath with hydrofluoric acid and nitric acid, a worker was the victim of an ocular 38 % hydrofluoric acid splash. He immediately washed his eye with Hexafluorine® and suffered no damage. He was back to work on the next day.

2.2.1.3 A case in Alcan, Göttingen, Germany, 1993

Two workers were splashed by 5 % hydrofluoric acid. Both were rapidly decontaminated with Hexafluorine®. The workers went back to hospital for evaluation the day after. They did not have any lost work time.

2.2.1.4 A case of facial splash of 70 % hydrofluoric acid vapours, Cristalleries d'Arques, Arques, France, 1996

Since 1993, in order to improve the management of victims of hydrofluoric acid splash, instead of using water, the medical and the safety services of the company have chosen to use Hexafluorine® for the emergency washing of any hydrofluoric acid splash. The use of calcium gluconate is maintained but only as a secondary treatment if required.

A 35 year old technician, with 12 years of seniority in the company, was splashed onto the right cheek by 70 % HF vapours when opening a gate in the hydrofluoric acid circuit[72]. He immediately felt pain in the splashed area. Because he was wearing impermeable protective glasses, his eyes were not splashed. He immediately headed for a DAP (autonomous portable shower). He pulled out the pin and started the decontamination with the Hexafluorine® DAP directing it towards the painful area. He felt a cooling sensation and mentioned the immediate and complete disappearance of pain. In accordance with the protocol for use of to which he had been trained on site, he used the whole 5 liter contents which accounts for the 6 minutes of washing. He then went to the infirmary.

After medical examination, no particular sign was observed, except a slight painless erythema. The technician did not require any sick days, so there was no lost work time.

The next day, the erythema has almost disappeared, the patient did not feel any pain, but, as a precaution, calcium gluconate gel was applied. The following week, the patient underwent a medical examination, in which no squelae were observed. One month after the accident, another medical examination lead to the same conclusion. Then, it was decided to stop any further medical management.

2.2.2 Isolated case with delayed management

In Sao Paulo, Brazil[73], a worker was the victim of a 70 % HF splash onto about 10 % body surface (left cheek, external side of the left arm and thigh, external and anterior sides of the same leg).

The victim was immediately showered for « some minutes », then his clothes were removed and the victim was showered for the second time. Then some blisters appeared under the surface of face and leg.

The initial treatment of the lesions combined compresses soaked in a magnesium oxide solution (Fig. 33) and the IV injection of analgesics.

At this stage, clinically, the decontamination with water was not sufficient, the burn had already occurred and the pain was persistent.

Transferred to hospital, the victim was **secondarily decontaminated with Hexafluorine® 3 hours after the accident** (Fig. 34). The spraying of a 5 liter DAP (Portable Autonomous Shower) (Fig. 34) for 5 to 6 minutes **decreased the pain and gave a feeling of coolness of the burn lesions**, clinically estimated between first and third grade. **The redness of the affected zones which, initially, were simply erythemic, quickly disappeared.**

In addition to cutaneous decontamination, the treatment included:

- IV injection of 40 mL 10 % calcium gluconate in 500 mL sterile isotonic glucose solution
- inhalation of 5 mL isotonic solution enriched with 3.5 mL 3.5 % calcium gluconate
- sub-cutaneous injection into the area around the lesions of 40 mL 10 % calcium gluconate (Fig. 35), coupled with
- the application of 2.5 % calcium gluconate gel by massaging the affected area (Fig. 36).

Figure 33: After washing with water and application of magnesium oxide

Figure 34: Secondary and late washing with Hexafluorine®

Figure 35: Sub-cutaneous injections of calcium gluconate

Figure 36: Application of CaG gel

Figure 37: Final condition of victim, after skin grafts, 90 days later

The whole initial therapeutic management took 5 hours. There was only slight respiratory discomfort, but no systemic symptoms appeared, and specifically no sign of cardiac complication shows on monitoring. On the biological level, there was a slight decrease to 1.4 (normal: 1.9-2.5) of circulating magnesium on same day. The day after, there was a small decrease of serum calcium 7.9 (normal: 8.5-10.5).

The patient left the intensive care section at the 48th hour. By the 4th day, the patient felt no more pain. Grafts proved secondarily necessary.

The pictures (Fig.37) showing complete healing were taken 90 days after the splash.

After three hours of contact, the decontamination with Hexafluorine® seems to bring an improvement in stopping the progression of HF burn, even late. If this accident is compared to a similar one (paragraph 1.1.1), the use of water followed by late use of Hexafluorine® versus water allows to decrease the sequelae. This shows that it remains some hydrofluoric acid to neutralize after a long time of contact and that Hexafluorine® is able to neutralize it. However, Hexafluorine® is not intended to treat a burn. It is specifically designed to decontaminate HFsplahes as early as possible, ideally within the minute following the splash.

2.2.3 Testimonials

2.2.3.1 Panasonic, Matsuhita Electronics, Germany

Testimonial from Panasonic, Matsuhita Electronics GmbH, Esslingen, Germany (1996-1998). This company uses hydrofluoric acid for glass cleaning. HF comes in 40 % hydrofluoric acid barrels and is diluted to 12 % HF. Matsuhita Electronics has used Hexafluorine® for more than two years to wash HF splashes. Staff training made the protocol of first aid washing with Hexafluorine® operational and effective. Since implementing Hexafluorine®, this company has reported no situation requiring secondary treatment due to hazardous splashes (testimonial letter).

2.2.3.2 Sobodec, France

Summary of the oral presentation, extract from « Chemical splashes: prevention, first aid actions and management », presented in the convention « Quality on work premises » organized by CRAM Aquitaine in November 2000 in Bordeaux (complete French version on www.preventica.com).

SOBODEC is a glass decorating company, whose activities include grinding glass (chemical attack of glass in a bath comprising hydrofluoric acid). A chemical splash can happen:

- during handling of the products,
- during preparation and renewing of bath with transfer pumps,
- during maintenance on machines or transfer pumps.

The exposed staff members are employees that prepare the bath and the maintenance team. To prevent chemical splashes, the following is required:

- wearing of individual protections such as gloves, masks, boots, aprons, overalls, glasses or eyeshades
- good ventilation before baths,
- presence of a Hexafluorine® DAP safety shower and of a Hexafluorine® Eyewash (eye washing device),
- training of staff on chemical risks and washing protocols.

Two kinds of accidents may happen:

- Either splashes of concentrated corrosive product,
- Or the penetration of a much diluted product during a long exposure time.

In the first case, the victim immediately feels a burn and must wash as soon as possible with Hexafluorine®. M. Sajous, safety manager at SOBODEC, reports an accident in which the victim could not wash early because of the first-aid post being too far away. Taken to hospital and with secondary treatment, the victim was given sick leave but with no sequelae. From then on, M. Sajous advises –with good reason - to install the washing devices close to the work position. Conversely, water washing has proved much less effective.

When HF is diluted and washing was not early, pain appears lately, up until 24 hours for an extended contact (as explained in paragraph 1.1.1). In such cases of late management, the protocol must be different because the product has already penetrated into the tissues. Then, the cutaneous application of calcium gluconate or injections under medical control may be necessary.

Finally, when treatment is performed by external rescue services (firefighters, medical rescue teams, hospital staff) a file containing the medical safety data sheets (MSDS) of the chemicals used at the work position and the details of the Hexafluorine® washing protocol must be given to the victim to enable better analysis and coordination of the secondary management.

2.2.4 Series of splashes in the industrial environment

2.2.4.1 Eleven cases in Mannesmann, Remscheid, Germany

From 1994 to 1998, eleven cases using Hexafluorine® have been referenced in Mannesmann, Remscheid, Germany. This study has been published in the international journal, *Veterinary and Human Toxicology*[74].

Over a period of four years, 11 splashes of hydrofluoric acid occurred (Fig.38 and Fig.39):

- 6 by a mixture 6 % HF / 15 % HNO_3
- 5 by 40 % HF splashes.

- HF splashes have hit men, age 35 $\pm$ 11 years.
- One 40 % HF splash has hit both eye and skin.
- One splash by the mixture 6 % HF / 15 % HNO_3 was only ocular (Fig. 38).
- Cutaneous splashes have hit 0.2 % (1 finger) to 16.5 % body surface (Fig. 39), among which 6 splashes have hit 4 % or more.
- One splash by the mixture 6 % HF / 15 % HNO_3 and one splash by 40 % HF have attacked more than 10 % body surface, respectively 10.5 % and 16.5 %.

Splashes have mostly attacked hands, limbs (superior or inferior), face and eyes, as well as the thorax.

All hydrofluoric acid splashes, whether pure or in a mixture, have been washed within the first two minutes (between 30 and 120 seconds) after the splash, on the accident scene, while clothes of the victim were removed in the case of a cutaneous splash. Washing with Hexafluorine® was performed by the victim or by a witness. For every HF splash, a secondary wash with Hexafluorine® was performed in the infirmary. The patient was given clean clothes.

No sequelae were observed for all the splashes washed with Hexafluorine® as first aid.

No secondary treatment required and no lost work time.

Ocular Splashes	40 % HF	40 % HF + 15 % HNO_3
Number	1	1
Area	1 eye	1 eye
Primary washing	Hexafluorine®	Hexafluorine®
Secondary washing	Hexafluorine®	Hexafluorine®
Secondary treatment	0	0
Sequelae	0	0
Lost work time	0	0

Figure 38: First aid washing of ocular HF splashes using Hexafluorine®

Cutaneous Splashes	40 % HF	40 % HF + 15 % HNO_3
Number	5	5
% body surface	0.2 % 1 % 4.5 % 4.5 % 16.5 %	0.2 % 2.25 % 4 % 4.5 % 10.5 %
Primary washing	Hexafluorine®	Hexafluorine®
Secondary washing	Hexafluorine®	Hexafluorine®
Secondary treatment	0	0
Sequelae	0	0
Lost work time	0	0

Figure 39: First aid washing of cutaneous HFsplashes using Hexafluorine®

2.2.4.2 Sixteen cases in Outokumpu (Avesta) Sweden

16 cases have been referenced in the series from Avesta Welding, Sweden. This study is published in the journal *Veterinary and Human Toxicology*[75].

Between 1998 and 1999, 16 cases of ocular or cutaneous splashes by hydrofluoric acid occured in the AVESTA plant in Sweden. 80 % of exposed workers are men and the average age of victims was 39 ± 11 years; One third of the victims were external workers.

There were two cases of splash by 70 % hydrofluoric acid. The others were due to a mixture of hydrofluoric acid and nitric acid (HNO_3) with pH = 1. Another splash was containing, in addition to the HF/HNO_3 mixture, some sulfuric acid, still with pH = 1. This projection hit both face and eyes. Two cutaneous splashes happened at hot temperatures (about 45 °C) with stripping acid (HF/HNO_3). All the splashes were washed with Hexafluorine® as a primary action within the first minute in 75 % cases. Three splashes with the diluted HF/HNO_3 mixture were washed after one hour.

All the victims reported an immediate cessation of pain during or just after washing with Hexafluorine®. More than 60 % workers were taken to hospital for a control medical examination. No sequelae were observed. The victim of the ocular splash of hydrofluoric acid, with an unknown concentration, developed signs of secondary irritation several hours after accident. This irritation may be due to the use of calcium gluconate to do an "aggressive wash" in hospital. The victim of a facial and buccal hot splash presented a few phlyctenae on the eyelid the day after accident.

The next table (Fig. 40) shows the various cases of splashes in Avesta in Sweden:

Number of cases	Corrosive product	Hit area	Contact time	Sick leave (days)
2	70 % HF	Left forearm + mouth	< 1 min	0-1
1	HF (unknown concentration)	One eye	< 1 min	0
2	HF + HNO_3 pH=1	One eye	< 1 min	0-0
1	HF + HNO_3 pH=1*	One eye	3-5 min	3
1	HF + HNO_3 pH=1	Two eyes	< 1 min	0
1	HF + HNO_3 pH=1	One thigh	< 1 min	0
2	HF + HNO_3 pH=1	Two thighs	1h - 1h30	2 –2
1	HF + HNO_3 pH=1*	Face	3-5 min	3
2	HF + HNO_3 pH=1	Face + mouth + forehead	< 1 min	1-1
3	HF + HNO_3 pH=1	Forearms + arms + hand + elbows	< 1 min	0-0-1
1	HF + HNO_3 pH=1	Wrist	2 h	0

Figure 40: Series of cases of HF burns in Avesta Sweden

*Sixteen total patients but one with both eye/skin splash.

*HF + HNO_3 + H_2SO_4 pH = 1 was involved in one cutaneous and one ocular splash.

Results

Globally 32 detailed cases have been reported.
In all cases, there was a complete and extremely fast relief of pain, whereas, in the development of burns, it is well known that:

- pain may be remarkably intense,
- pain is relative to the chemical reactivity of fluoride ions as mentioned in paragraph 1.1,
- pain is a characteristic element which shows the evolution of lesions and the efficacy of decontamination.

No actual burn has developed after washing with Hexafluorine®. No secondary treatment has been necessary in more than 75 % treated cases, including the two cases of splashes by very concentrated 70 % HF. There were no death, while in 5 out of 32 cases, the combination of the penetration route, the HF concentration and the percentage of attacked body surface might have put the vital prognosis at stake, according to the criteria developed above in figure 4, paragraph 1.1.

On average, victims only had one day of lost work time (σ = 1.1).

Furthermore, even in cases of secondary decontamination and delayed management, Hexafluorine® still seems to have proved beneficial.

2.2.5 Institutional recommendations

- INRS[76] (Institut National de la Recherche Scientifique), in its brochure Aide Mémoire Technique ED953, « Manipulations in chemistry laboratories: Hazards and prevention », advises the following protocol in case of chemical burns: *« As soon as possible, wash with clean water for 15 minutes, removing clothes and accessories soaked by the chemical; follow the instructions given by the company doctor or the medical officer and contact a medical service. If another method is advised, follow the userguide and the instructions given by the company doctor or the medical officer»*.

- CNAM[77] (Caisse Régionale d'Assurance Maladie) in its R442 Recommendation R 442 (signed by the national technical committee of metalworks industry on November 13th, 2008) from the series "Prevention of chemical risks : activities of surface treatment " gives exactly the same advice as the ones recommended in the INRS ED953 brochure and adds : in the part of the paragraph dealing with collective prevention in surface treatment using HF : *Hexafluorine® showers and ocular fountains in the chapter about hydrofluoric acid* (Fig.41a and 41b).

Décapage, dérochage	Acide fluorhydrique	Très toxique et corrosif par contact, inhalation et ingestion : irritations, brûlures, lésions, ulcérations (peau, voies respiratoires, yeux, tube digestif). Sensation de brûlure retardée. Provoque des hypocalcémies, des nécroses des tissus et des os. Tableau MP 32.	***Collective*** Couvrir les bains. Captage des vapeurs et des aérosols par aspiration au niveau de la cuve. Douche de sécurité et fontaine oculaire à l'hexafluorine. ***Individuelle*** Gants (butyle, néoprène), écrans de protection, masque équipé de filtre BEP3, vêtements anti-acides et bottes anti-acides Prévoir la trousse de secours³ notamment les produits spécifiques (gluconate de calcium en solutions injectable et buvable, comprimés de calcium, crème au gluconate de calcium) en cas d'accident.

Figure 41a: Institutional recommendation by CNAM, French original version

Etching, metal cleaning	Hydrofluoric acid	Very toxic and corrosive by contact, inhalation and ingestion: irritation, burns, lesions, ulcerations (skin, respiratory tract, eyes, gastrointestinal tract). Delayed burning sensation. Causes hypocalcemia and necrosis of the tissues and the bones. Table MP 32	**Group Protection.** Cover vats. Capture vapors and aerosols by exhaust ventilation near tanks. Hexafluorine safety shower and eyewash. **Individual Protection.** Gloves (butyl, neoprene) , protective screens, mask equipped with BEP_3 filters, acid-resistant clothing, acid-resistant boots. Prepare a first-aid kit, notably with specific products (calcium gluconate in injectable and orally-administered forms, calcium tablets, calcium gluconate cream) in case of accident.

Figure 41b: Institutional recommendation by CNAM, translated from the above original French version

- INRS[78] again, in its brochure concerning laboratories involved in the teaching of chemistry (reference ED 1506) advises: « *the installation of eye washing devices in every laboratory is also recommended*». *Specific products designed for first aid treatment of ocular or other chemical burns can complete the display and improve the efficacy of washing with water, which must immediately follow. Such products can be delivered by autonomous portable showers and should only be used under the agreement of the medical service and should be renewed regularly* ».

2.3 Physical-chemical data about Hexafluorine®

- Clear and colorless liquid
- pH between 7.2 and 7.7
- Density : 1.047
- Osmotic pressure: 1030 mosmoles.

2.4 Evidence of Hexafluorine® innocuousness

The tests of inocuity performed on Hexafluorine® are summed up in the following table (Fig. 42):

Type of test	Animal	Realized by	Test number	Result
Ocular irritation	Rabbit	Safepharm Laboratories UK	133/8	**Non irritant** (indice 1.3)
Cutaneous irritation	Rabbit	Safepharm Laboratories UK	133/7	**Non irritant** (indice 0.0)
Inocuity by oral route of a 2000 mg/Kg dose	Rat	CERB France	990553 ST	**Non toxic** > 2000 mg/kg
Sensitization using Magnusson Kligman method	Guinea pig	CERB France	20030418 ST	**Non sensibilizing**
Cytotoxicity	Fibroblast culture	Integra Italy	REL/622A/07 /IRRC/ELB, ISO 13995-3 standard	**Non cytotoxic**

Figure 42: Evidence of Hexafluorine® inocuity

2.5 Hexafluorine® classified as a medical device

Hexafluorine® has been classified as a medical device (MD) by the competent authorities according to the European Directive 93/42 because it is used preventively without any pharmacological effects. It may be used on damaged skin, is classified IIa, CE 0459, and is sterile.

3 General conclusion

Technical prevention and first aid care on work premises allow the control of the frequency and the severity of accidents by chemical splash and, particularly, those due to hydrofluoric acid. The severity of burns by hydrofluoric acid depends on (Fig. 43):

- time of contact of HF with skin or eye surface,
- concentration of HF
- its temperature, as well as
- the extent of the affected surface[79].

Ccontact route with HF	Affected surface	Concentration of HF
Cutaneous	1 %	Anhydrous
	5 %	> 70 %
	7 %	50 à 70 %
	10 %	20 à 50 %
	20 %	< 20 %
Ingestion Inhalation		> 5 %

Figure 43: Lethal risk of burns by HF

When applying the Dünzer table mentioned above to the situation, among the 32 cases of accidental burns by HF reported in chapter 3.2 (references of cases that occurred in industry with early washing with Hexafluorine®), 5 victims incurred a lethal risk. However, there has been no death and even no systemic effects have been observed after decontamination with Hexafluorine® used immediately, whether followed or not by a complementary application of calcium gluconate, when necessary. In the case report decontaminated with Hexafluorine® after water washing and a 3 hours delay, no systemic effet was observed, even if the affected area was 10% of the total body surface area.

Therefore, it is crucial to wash hydrofluoric acid splashes as soon as possible, and to display first aid washing devices close to exposed staff[80]. It is also important to offer exposed workers as well as safety and medical personnel in charge of chemical decontamination, a quick simple and secured decontamination protocol, whatever the concentrations and the affected surface area.

The classic washing protocols including washing with water only and washing with water followed by application or injection of calcium gluconate, have not always given any evidence of their optimal efficacy in the most serious situations. The international literature indeed reports some tragic cases for which heavy secondary therapeutic managements are crucial with no guarantee of avoiding a lethal outcome[81, 82, 83, 84, 85]. Some disabling sequelae have been described. All of such accidents are particularly accidents involving high concentrations of HF.

Hexafluorine® is a washing solution specific to ocular and cutaneous splashes by hydrofluoric acid, and has been developed by Prevor Laboratory in order to realize an optimal decontamination. The present dossier gives answers to the questions concerning its efficacy:

The *in vitro* experiments show the double effectiveness of Hexafluorine® on corrosivity (pH measurement) and toxicity (pF measurement), whereas calcium gluconate acts only on toxicity but has little effectivness on acidity. Water only dilutes hydrofluoric acid and does not act on either of those two hazards.

The use of ex vivo human skin explant model, shows that, an active solution such as Hexafluorine® can significantly simplify the decontamination procedure, compared to the water followed by calcium gluconate protocol which requires several prolonged topcal applications.Even with additive intra-vascular injections, the use of Hexafluorine® by a non medical personnel, only requires an initial single washing.

Hexafluorine® has enabled the apparition of the *ex vivo, in vivo* burn by 70 % hydrofluoric acid to be avoided and to maintain a constant calcemia concentration. Other tested solutions do not have such effects.

The success of the clinical cases of use of Hexafluorine®, presented in this dossier, comes both from its intrinsic optimal efficacy which is due to acid ion absorption and fluoride ion chelation. In cases of delayed use of Hexafluorine ®, the burn appears. Decontamination is then necessary but not sufficient and a secondary treatment with the gluconate of calcium is required. In cases of delayed use of Hexafluorine®, after 1 minute, prolong the washing with Hexafluorine® following the recommended protocol and apply calcium gluconate if needed.

It is thus imperative to decrease the contact time and to wash as soon as possible to optimize the effectiveness of Hexafluorine®.

Within companies, chemical risk awareness and training of employees exposed to chemicals, as well as health and safety personnel, will make it possible to minimize the risk of chemical splashes and, if need be, to effectively decontaminate oneself in emergency situations.

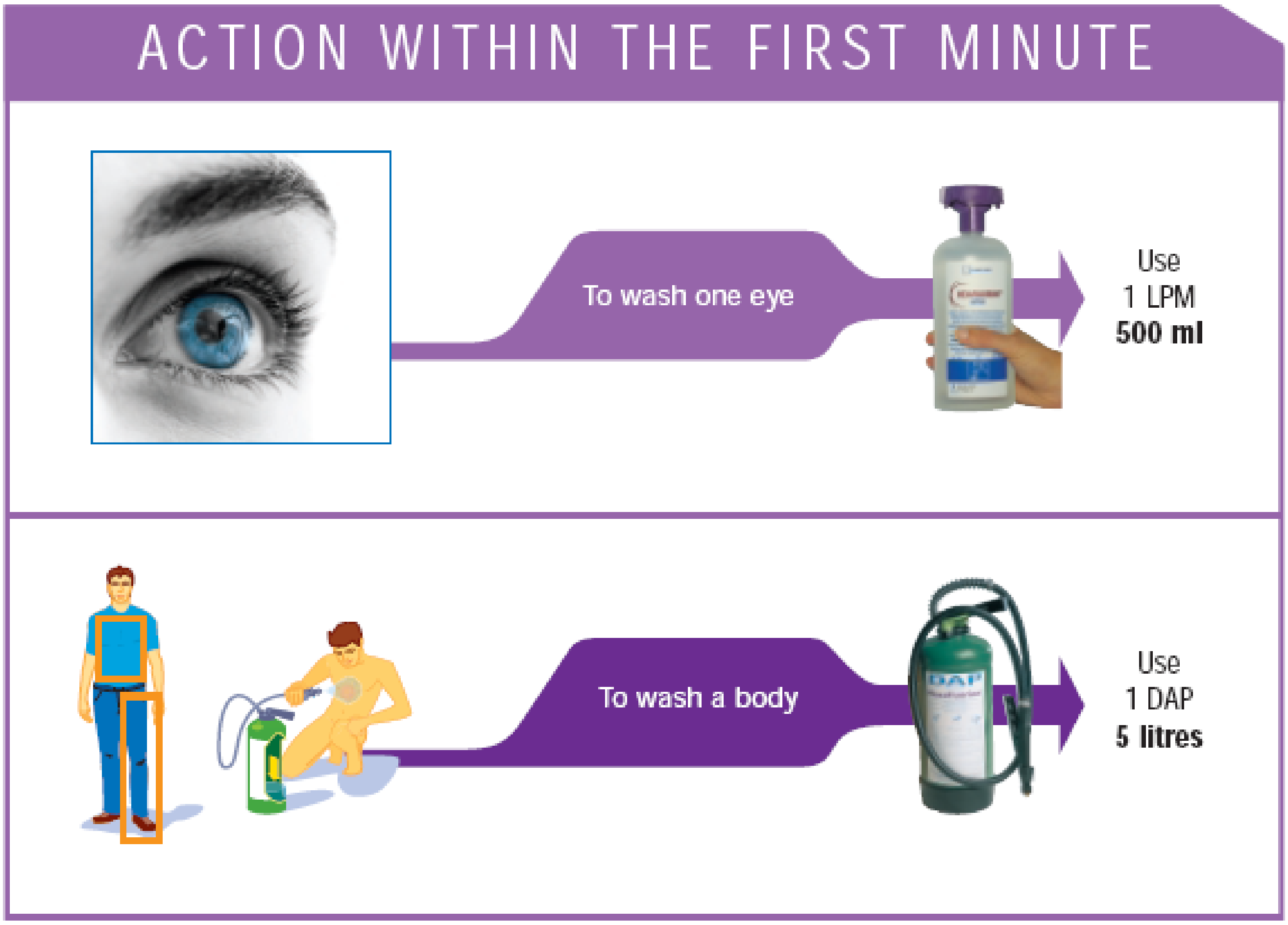
The next chapter suggests technical tools to improve the management of victims of HF splashes.

4 Improvement of management of victims of chemical splashes due to Hexafluorine®

4.1 Protocol for use of Hexafluorine®

Protocol for Hexafluorine® use

In cases of hydrofluoric acid splashes or its derivatives in an acidic medium*



WASHING PROTOCOL WITH HEXAFLUORINE®*

Start washing within the first minute following the splash, beginning **with uncovered areas**.

Remove clothing and/or contact lenses.

Continue washing the unclothed areas as quickly as possible. Never put back on clothes stained with washing residue or chemicals.

Consult a specialist.

GENERAL INSTRUCTIONS

Never delay washing.

For optimal effectiveness use Hexafluorine® **as the primary action**. If there is no available Hexafluorine®, use water and then wash with Hexafluorine® as soon as possible.

Use the entire contents of the container.

For a contact time **greater than 1 minute**, prolong the washing with Hexafluorine® and if needed, continue the washing for **3 to 5 times the duration of the contact time**. In case of an ocular splash, it is not necessary to continue washing for more than 15 minutes.

Depending on the company's recommended medical protocol, apply locally a specific antidote such as **calcium gluconate.**

Then immediately seek medical advice.

After an active washing of the eye, the use of **Afterwashll®** is recommended to facilitate a quicker return to a physiological state.

If **oral mucosa** is affected by the splash, rinse the mouth with Hexafluorine® and then spit it out.

If the **ear canal** is affected, wash as rapidly as possible with Hexafluorine® by instilling 500ml inside the canal, leaning the head to one side, in order to allow the liquid to flow out of the ear.

As in any case of unilateral rinsing of one ear with a liquid at room temperature, a dizzy feeling, with no serious consequences, can occur. It will spontaneously stop after a few minutes.

Container	Average diffusion time
LPM (500 ml)	3 minutes
DAP (5 l)	5 minutes

** Limited efficacy on alkaline chemicals. Diphoterine® is better adapted for this use.*

PREVOR
ANTICIPATE AND SAVE
Toxicology Laboratory & Chemical Risk Management

4.2 Activity spectrum

Hexafluorine® can be used on:

- hydrofluoric acid, whatever its concentration,
- HF mixed with other acids,
- fluorides in an acidic medium,
- simple acids (H^+ ion),
- Lewis acids such as BF_3,
- organofluorine compounds with fluoride ions that can be released into tissues.

On basic fluorides, Hexafluorine® has a limited efficacy. On non fluoride alkali, its efficacy is limited to the simple efficacy of a mechanical and hypertonic wash. In such a case, the use of Diphotérine® is advised.

Below is the list of products tested with Hexafluorine® (Fig. 44) on user's requirements. This list is updated and available in the PREVOR website following address:

http://www.prevor.com/FR/sante/RisqueChimique/produits_testes/produitsTestesV2.php

HYDROFUORIC ACID	7664-39-3	TOXIC/CORROSIVE
HYDROFLUORIC ACID / AMMONIUM FLUORIDE		TOXIC/CORROSIVE
37 % HYDROFLUORIC ACID	73602-61-6	TOXIC/CORROSIVE
HYDROFLUORIC ACID / NITRIC ACID		TOXIC/CORROSIVE
FLUOROSILICIC ACID	16961-83-4	CORROSIVE
HEXAFLUOROPHOSPHORIC ACID	16940-81-1	TOXIC/CORROSIVE
TETRAFLUOROBORIC ACID	16872-11-0	TOXIC/CORROSIVE
ACTIVATOR N°2		CORROSIVE
ALODINE 1200		TOXIC/CORROSIVE
ALODINE 4780		TOXIC/CORROSIVE
AMMONIUM FLUORIDE ETCHANT AF 87,5-12,5 VLSI SELECTIPUR		
AQUAREX 2290		NOXIOUS
AUROCA STAINLESS STEEL RENOVATOR		TOXIC/CORROSIVE
BHF 39/1		
POTASSIUM BIFLUORIDE	7789-29-9	TOXIC/CORROSIVE
AMMONIUM BIFLUORIDE	1341-49-7	TOXIC/CORROSIVE
BULCOAT 33	17439-11-1	TOXIC/CORROSIVE
CDR 1045		TOXIC/CORROSIVE
CERAMEX		
CUPOSIT ACCELERATOR 19H		IRRITANT
DEOXIDINE SC 56 CF		TOXIC/CORROSIVE
DIFLUOR	7782-41-4	TOXIC/CORROSIVE
MAGNESIUM FLUOROSILICATE	16949-65-8	TOXIC
PEXTER FLUORIDE (II)	7783-47-3	NOXIOUS/IRRITANT
FORAPERLE 321		TOXIC/IRRITANT
HCR 840LIQUID (500)		VERY TOXIC/CMR/CORROSIVE
AMMONIUM HYDROGENODIFLUORIDE	1341-49-7	TOXIC/CORROSIVE
15 % NITRIC ACID AND 3 % HYDROFLUORIC ACID MIXTURE		TOXIC/CORROSIVE
MIXED ACID ETCH 10:1:4:1		TOXIC/CORROSIVE
MIXED ACID ETCH 3:1:1		TOXIC/CORROSIVE
MIXED ACID ETCHANT 4:2:2		TOXIC/CORROSIVE

NETTOR AL 12 (HF/H2SO4)		TOXIC/CORROSIVE
NITRIC ACID ETCHANT SF 68-01 VLSI SELECTIPUR		
STRIPPING PASTE PX 100		TOXIC/CORROSIVE
PROCAP AV		TOXIC/CORROSIVE
PRÜFLÖSUNG 10	7789-23-3	TOXIQUE
STRIP ISO-VERRE NORMAL		TOXIC/CORROSIVE
SYSTOCHROMAT 1653/1		TOXIC/CORROSIVE
SILICIUM TETRAFLUORIDE	7783-61-1	TOXIC/CORROSIVE
BORE TETRAFLUORIDE IN ACETIC ACID	373-61-5	CORROSIVE/NOXIOUS
ANHYDROUS BORE TRIFLUORIDE	7637-07-2	TOXIC/CORROSIVE/REACTING WITH WATER
DIHYDRATED BORE TRIFLUORIDE	13319-75-0	TOXIC/CORROSIVE
ETHYLETHERATE BORE TRIFLUORIDE	109-63-7	CORROSIVE/FLAMMABLE/REACTING WITH WATER
METHYLETHERATE BORE TRIFLUORIDE	353-42-4]	CORROSIVE/FLAMMABLE/REACTING WITH WATER
PHOSPHORE TRIFLUORIDE	7783-55-3	TOXIC/CORROSIVE
TURCO ALUMIGOLD FLUSSIG		TOXIC/CORROSIVE
TURCO LIQUID SMUT-GO NC		TOXIC/CORROSIVE
TURCO SMUT-GO#4		TOXIC/CORROSIVE
UNICHROME CR 842		VERY TOXIC/CMR/COROOSIVE
WELD-GUARD STAINLESS STEEL PICKLING GEL		TOXIC/CORROSIVE

Figure 44: List of products tested with Hexafluorine® washing

4.3 Washing time

Washing time with Hexafluorine® does not depend on the concentration of hydrofluoric acid causing the accident. Washing must be performed as a primary action, as early as possible, in the first minute after the splash whether it is ocular or cutaneous. The later the washing, the longer the time of contact between hydrofluoric acid and skin cells, the more the burn risk increases and the more the time of washing must be extended.

In case of first aid washing (within 1 minute), the contents must be completely used. Given our current knowledge, for washing in different conditions as those recommended by the protocol, we consider that the washing time must correspond to 3 to 5 times the time between splash and start of washing. The longer the time of contact is, the more significant the lesions are. Once more, **staff must be sensibilized to the hazards of handling HF and decontamination devices must be installed closed to accident sources in order to shorten the time of decontamination after contact. This can be vital in numerous cases.**

The efficacy of washing with Hexafluorine® is limited when washing with water as a primary action. Because of its hypotonicity, water creates an osmotic flow from the outside towards the inside of tissues and, doing so, progressively leaches a part of substances from the contact surface towards the deep layers of skin or eye. Therefore it is easy to understand why Hexafluorine® must be directly available on sites with HF splash hazards, in order to start washing as early as possible after a splash. Obviously, washing initially with water is better than doing nothing.

Decontamination with Hexafluorine® may be followed by secondary applications of calcium gluconate, depending on the protocol set up under the responsibility of the medical authority. PREVOR distributes 2.5 % calcium gluconate tubes, content 28 g, manufactured by KAYS. CaG is classified as a medical device (MD) type IIa, CE0120.

In any case, a splash by hydrofluoric acid remains a serious accident. It is always recommended to have a medical evaluation performed in order to decide on a potential secondary management.

Remember !

The victim's clothes must be removed. The victim must be washed with Hexafluorine®, as a primary action, within the first minute after a hydrofluoric acid splash. Then ask advice from a specialist.

4.4 Packaging

The following table (Fig. 45) displays all the available packaging:

	Wall Mounted Eyewash (500 ml)	Portable Eyewash (500 ml)	Autonomous Portable Shower (5 l)
Use	Ocular use	Ocular use	Use on body
Intervention time for optimal efficacy	**< 1 min**		
Shelf-Life	**2 years**		
Content	2 bottles of 500 ml Hexafluorine® + 1 bottle of 200 ml of Afterwash®	500 ml Hexafluorine®	5 liters
Total time of utilization of packaging	**500 ml Hexafluorine®: 3 minutes of washing**		**6 minutes**

Figure 45: Types of Hexafluorine® packaging

500 ml Hexafluorine® packagings (glass bottles or soft plastic pouches) are sterilized by autoclave. Their shelf-life is 2 years when sealed and 6 months when ready to use. The 500 ml eyewas of the wall mounted station is directly ready to use and has a shelf-life of 2 years. When started, the autonomous portable shower (DAP) must be immediately and completely used. Every packaging is for a unique utilization. After each use, make sure that the washing solution is set back into working order, meaning either replaced or changed, so that the first aid material is always ready to use.

Presentation of the different types of packaging of Hexafluorine® (Fig. 46, 47, 49) and calcium gluconate (Fig. 48).

Figure 46: 500 ml portable Eyewash
(for complete washing of one eye)

Figure 47: Wall mounted Eyewash
(2 bottles of 500 ml for complete washing of two eyes)

KAYS 28 g GCaG tubes are supplied with a wall mounted display or as 10 tube refills.

Figure 48: KAYS Medical 2.5 % CaG tubes

Figure 49: Autonomous portable shower (DAP) 5 l
to wash complete body

Figure 50: Protection box for DAP with antifreeze system

5 Material safety data sheet of Hexafluorine®

The Material Safety Data Sheet of Hexafluorine® is available on the PREVOR web site (www.prevor.com).

6 Technical data sheet of hydrofluoric acid

6.1 Physical-chemical data

- **Formula :** HF, may partly dissociate into H^+ and F^- in water (pK_a = 3,2)
- **Chemical name** : hydrofluoric acid, hydrogen fluoride
- **Class:** Weak Mineral Acid
- **CAS number**: 7664-39-3
- **EINECS Number: 231-634-8**
- **EC index**: anhydrous HF 009-002-00-6, aqueous solutions of HF 009-003-00-1
- **Physical, chemical properties and specificities** [86] **:**
  - Molar mass: 20 g/mol
  - Colorless liquid for temperatures below 20 ° C, very volatile,
  - Boiling point 19.4°C (in atmospheric pressure),
  - 0°C Density: 1.002
  - Vapour density (air = 1) : 0.7
  - Vapour tension: 13.3 kPa at –28.2°C, 53.3 kPa at 2.5°C et 150 kPa at 30°C
  - Produces irritant and corrosive white vapours when in contact with water,
  - Miscible with water in any proportion and thus great faculty to be concentrated,
  - When very concentrated, remarkably volatile,
  - Unlike other acids, it attacks glass. Aqueous solutions of HF attack most metals. It does not attack platine, gold, silver and mercury.
  - HF reacts violently with anhydrous alkali or bases in concentrated solutions.
  - Its corrosive action and penetrating potential cause deep tissular destruction.

Hydrofluoric acid (HF) is the smallest mineral acid. It can be indefinitely concentrated, first as a HF monomer then as a dimer or polymer $(HF)_n$. In water, it only dissociates a little (its dissociation constant pk_a= 3,2, meaning about one molecule out of 1000 = $1/10^{-3.2}$). Thus, hydrofluoric acid can appear under three forms in water: H^+, F^-, HF.

Therefore, one must be careful with pH measurement because, for HF, it does not represent all the acid potential. This is very different from strong acids which completely dissociate in water.

For instance, hydrochloric acid, HCl, is to be found in water completely in the form of H^+ and Cl^-. pH measurement which only takes the H^+ ions concentration in account is not a real parameter indicating the danger of HF.

With equal pH, for instance when pH=0, the HF concentration is 1000 times higher than the concentration in HCl.

6.2 Storage

Solutions with a HF concentration above 70 % or anhydrous HF must be stored in stainless steel barrels. More diluted HF solutions may be stored in containers made of aluminium bronze, lead or synthetic resin materials.

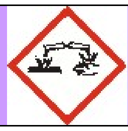
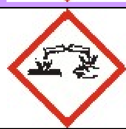
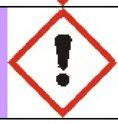
6.3 Labeling

According to the labeling rules from appendix 1 of the modified EC directive 67/548/CEE, the HF labeling is the following (Fig. 51):

HF Concentration Insertion in 19th ATP, modification in 26th ATP	**Class**	**Pictogram**	**Risk comments**
≥ 7 %	**Very toxic** **Corrosive**	 	**R26/27/28**: Very toxic by inhalation, skin contact and ingestion, **R35**: Causes severe burns
1 to 7 > %	**Toxic**	 	**R23/24/25**: Toxic by inhalation, skin contact and ingestion, **R34** : causes burns
0.1 to 1 %	**Noxious**		**R20/21/22:** Noxious by inhalation, skin contact and ingestion, **R36/37/38**: Irritant for eyes, respiratory ways and skin

Figure 51: European labeling before GHS

With the application of the new labeling rules according to the Global Harmonized System, since January 2009, it has been possible the new labeling according to the EC regulation CLP 1272/2008, therefore the labeling of HF becomes (Fig. 52):

Product	Danger	Caution	Danger class	Pictogram	H comments
Hydogen fluoride	Acute toxicity	Danger	2*		**H330**: causes severe skin burns and ocular lesions.
	Acute toxicity	Danger	1		**H310**: causes severe skin burns and ocular lesions.
	Acute toxicity	Danger	2*	Danger	**H300**: causes severe skin burns and ocular lesions.
	Cutaneous corrosivity	Danger	1A		**H314**: causes severe skin burns and ocular lesions.
Hydrofluoric acid** … %***	Acute toxicity	Danger	2*		**H330**: causes severe skin burns and ocular lesions.
	Acute toxicity	Danger	1	Danger	**H310**: causes severe skin burns and ocular lesions.
	Acute toxicity	Danger	2*		**H300**: causes severe skin burns and ocular lesions.
	Cutaneous corrosivity	Danger	1A ou 1B**		**H314**: causes severe skin burns and ocular lesions.
	Ocular irritation	Attention	2**		**H319**: causes a severe irritation of eyes.

* The reference (*) is also present in the column of specific concentrations limits and M factors, where it shows that the involved entry is restrained by specific concentrations limits for acute toxicity according to the EC directive 67/548/CEE. When there is the reference (*), the claasification of this entry as acute toxicity must be the object of a specific attention.

** Corrosive for skin class 1A for concentrations ≥ 7 %

Corrosive for skin class 1B for concentrations between 1 and 7 %

Irritant for eyes class 2 for concentrations between 0.1 and 1 %, with in this case H319 comment: « Causes a severe irritation of eyes ».

*** Some substances (acids, bases…) are sold and circulate in aqueous solutions with diverse concentrations. Then these solutions require a different labeling, because their potential dangers depend on the concentration.

Figure 52: European labeling according to the CLP

In addition to the above table, are the C comments of caution. For class 1 and 2 of acute toxicity, the C comments are (Fig. 53):

Type of CA (Caution Advice)	Number	Comment
Prevention CA (Toxicity by oral way)	P264 P270	Wash… thoroughly after handling. Do not drink, eat or smoke when handling this product.
Intervention CA (Toxicity by oral way)	P301 + P310 P321 P330	IN CASE OF INGESTION: call an ANTIPOISON CENTER or a doctor immediately. Specific treatment (ckeck label). Rinse mouth.
Storage CA (Toxicity by oral way)	P405	Keep locked.
Elimination CA (Toxicity by oral way)	P501	Empty content/container into
Prevention CA (Toxicity by cutaneous way)	P262 P264 P270 P280	Avoid contact with eyes, skin or clothes. Wash… thoroughly after handling. Do not drink, eat or smoke when handling this product. Wear protective clothes and gloves, protective gear for eyes and face.
Intervention CA (Toxicity by cutaneous way)	P302 + P350 P310 P322 P361 P363	IN CASE OF CONTACT WITH SKIN: wash thoroughly with water and soap. Call an ANTIPOISON CENTER or a doctor immediately. Specific measures (ckeck label). Immediatley remove contaminated clothes. Wash contaminated clothes before use.
Storage CA (Toxicity by cutaneous way)	P405	Keep locked.
Elimination CA (Toxicity by cutaneous way)	P501	Empty content/container into
Prevention CA (Toxicity by inhalation)	P260 P271 P284	Do not breathe dust/fumes/gaz/fog/vapours/sprays. Only use in wide or space or well ventilated place. Wear breathing protective gear.
Intervention CA (Toxicity by inhalation)	P304 + P340 P310 P320	IN CASE OF INHALATION: take victim outside and keep resting in a position of easy breathing.. Call an ANTIPOISON CENTER or a doctor immediately. Specific treatment is urgent (check label).
Storage CA (Toxicity by inhalation)	P403 + P233 P405	Store in a well ventilated place. Keep container sealed and airtight. Keep locked.
Elimination CA (Toxicity by inhalation)	P501	Empty content/container into

Figure 53: Risk comments for class 1 and 2 of "Acute toxicity" danger

For class 1A or 1B, skin corrosive/irritant agents, the P phrases are (Fig.54):

Caution Advice Prevention	**P260:** Do not breathe dust/fumes/gaz/fog/vapours/sprays. **P264:** Wash thoroughly after handling. **P280:** Wear protective clothes and gloves, protective gear for eyes and face.
Caution Advice Intervention	**P301 + P330 +P331:** IN ACSE OF INGESTION: rinse mouth. DO NOT purge. **P303 +P361 +P353:** IN CASE OF CONTACT WITH SKIN (or hair): remove contaminated clothes immediately. Rinse skin with water/ shower. **P363:** wash contaminated clothes before use. **P304 + P340:** IN CASE OF INHALATION: take victim outside and keep resting in a position where breathing is easy. **P310:** Call an ANTIPOISON CENTER or a doctor immediately. **P321:** Specific treatment (check label). **P305 + P351 + P338:** IN CASE OF CONTACT WITH EYES: rinse thoroughly with water for several minutes. If victim wear contact lenses, remove them when easy to remove. Keep on rinsing.
Caution Advice Storage	**P405:** Keep locked.
Caution Advice Elimination	**P501:** Empty content/container into

Figure 54: Risk comments for class 1A and 1B of cutaneous corrosion/irritation » danger

7 Glossary

Acantholysis

Dislocation of the cells of the medium layer of epidermis, due to the diminution of their reciprocal adherence, causing the formation of cavities into the epidermis.

Calcemia

Medical name for the concentration of calcium in blood. Normal rate for an adult between 2.2 and 2.6 mmol/L

Cation

Name of the positive ions (such as: Ca^{2+}, Mg^{2+}, K^{+}, Na^{+})

Caustic

Every chemical substance that destroys tissues. Regulations more often use « corrosive » which is the modern word for caustic.

Chelation

Physical-chemical process of complexation of multivalent positive ions (calcium, copper, lead, mercury, iron, chromium) by some particular bodies. The chelating agent associates with the positive ion, which the body wants to release, a complex compound (the chelate) which Is soluble, steady, non ionized, non toxic and quickly eliminated by kidneys.

Coagulation

Transformation of a liquid organic substance into a solid or semi-solid mass, of more or less gelatinous consistency.

- **Collagen**: Fibrous glycoprotein with a function comparable to a framework. It is the most common protein of the body, representing ¼ of all proteins. Collagen is secreted by the cells of the conjuctival tissues. Its molecular weight is 300 kDa. Collagen is a protein made of three associated polypeptidic chains (illustration Fig. 55).

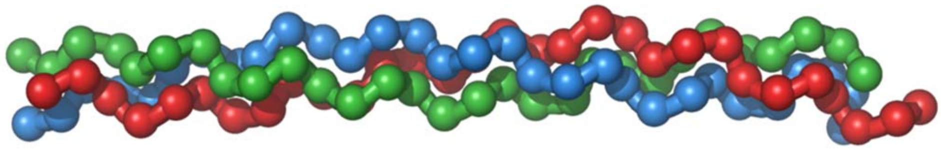


Figure 55: The three chains constituting collagen

As those three chains can combine in different ways, we should deal with collagens and not only collagen. Everey type of collagen has got its own structure and is to be found in specific organs. For instance, collagen of type I acts in the formation of skin, and particularly during the process of cicatrization. Unlike elastine which is also present in conjunctival tissues, collagen is unextensible and has a good resistance to traction. The degradation of collagen is difficult and requires specific enzymes, the collagenases (family of matricial metalloproteinases).

Conjunctiva

Conjunctiva is a smooth, bright and transparent thin mucous membrane. It covers the deep face of eyelids (palpebral conjunctiva) and reflects, thus forming an irregular cul-de-sac (fornix), to cover the anterior face of the eyeglobe (bulbar conjunctiva). This membrane produces the mucus which spreads onto and lubricates the eye surface.

Corrosive

A substance attacking violently a material and causing its corrosion.

Dermis

Dermis is the medium layer of skin, between the epidermis above and the hypodermis below. Made of conjunctival tissue, the dermis is subdivided in two (Fig. 56):

- The papillary dermis, which is the most superficial, is constituted of columns rich in blood vessels and cells. It “fits” into the deep projections of the epidermis at the level of the dermis-epidermis junction.
- The reticular dermis is more fibrous and thicker. It is sub-jacent to the papillary dermis.

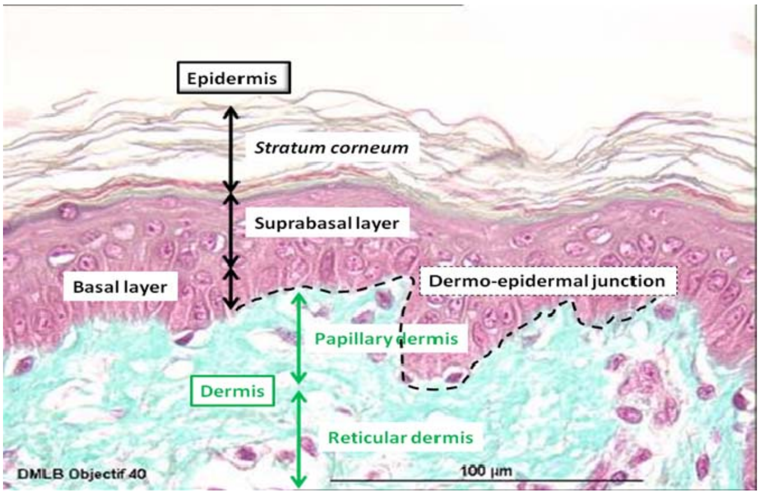


Figure 56: Different skin layers

Electrolyte

Body that can dissociate when in a solution. An electrolyte may be made of ions (for instance, sodium chloride) or molecules. An electrolyte is called strong when all its constituents ionize in a solution. This applies to salts, strong acids and alkali. An electrolyte is called weak if only a part of its constituents dissociate in a solution.

Epidermis

Epidermis is the most superficial layer of skin. It is made of 5 sub-layers of cells (Fig.57). The epidermis is only about one millimeter or even less thick. Its thickness depends on the groups under consideration and on the parts of the body. For instance, in humans, the epidermis is thicker on the palm of the hand and on the sole of the foot (because of the thickening of the corneal layer).

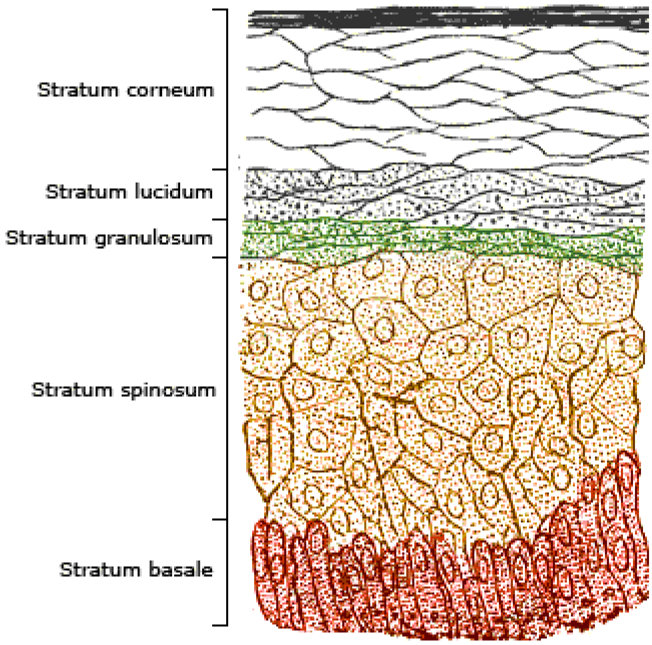


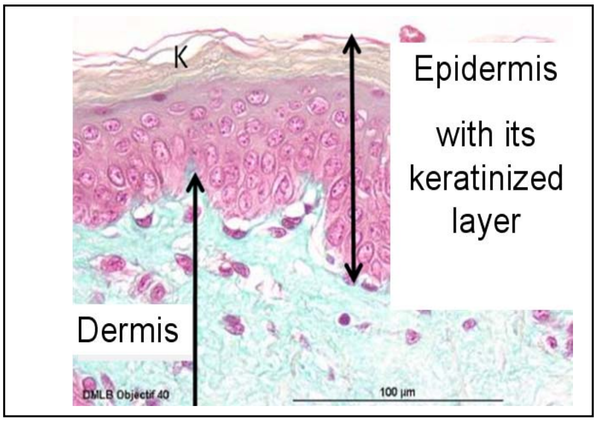
Figure 57: the sub-layers constituting the epidermis

Epithelial

Adjective relating to the epithelium

Epithelium

Tissue with the function of coating external parts and internal cavities of the body, made of tightly juxtaposed cells, with no interposition of fiber or fundamental substance (which makes them different from conjunctival tissues).There are several types of epithelium depending on the shape, the function and the number of layers of constituting cells. The epithelium of skin (Fig. 58) is multilayer like the epithelium of cornea. The epithelium of skin is keratinized, whereas the epithelium of eye is not (Fig. 59).



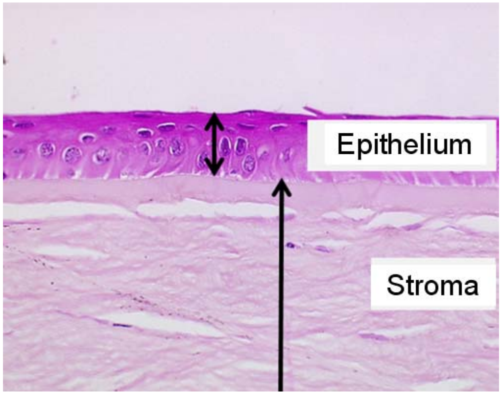


Figure 58:
Epidermis = epithelium covering the surface of skin

Figure 59: epithelium of cornea

Erythema

Generic name of cutaneous alterations having a more or less intense redness of the integuments (covering tissue, skin) as a common clinic character. It disappears with pressure (Fig. 60). Sunburns are good illustrations of eythematous reactions.

Figure 60: Local cutaneous erythema (irritation by contact)

Histology

Science and techniques studying the structure of organic tissues. In the old days, they were referred to as « microscopic astronomy ».

Histological

Adjective relating to histology.

Hypercalcemia

Calcium concentration in the blood higher than normal rate.

Hypertonicity

State of a liquid or a solution with an osmotic tension higher than that of another liquid, in the presence of which it is put and which is used as a reference.

Hypocalcemia

Calcium concentration in the blood lower than normal.

Hypothermia

Decrease of body temperature below 35 °C.

Hypotonicity

State of a liquid or solution with an osmotic pressure lower than that of the reference milieu.

Inocuity

Quality of anything without danger.

Ischemia

Ischemia is a slow down or a temporary stop of the vascularization of a zone of the body. Myocardial infarction is an illustration of ischemia.

Keloids

Object in the shape of a scar, resulting from a growth of the dermis at the level of a cured wound. It is made of lesions of firm consistency, which are unsteadily raised and slowly extensive in a more or less radicular way, and harden all along their evolution. They can also be nodular. It is of fibrous nature. It is mostly constituted of collagen, excessively synthetized by fibroblasts during the cicatricial stage of reconstruction. Its extension spreads beyond the initial zone of trauma, which makes the difference between a keloid scar and an "only" hypertrophic scar. Its color varies from pink to dark brown (for black skins). A keloid scar is a minor scar but may look really bad, and sometimes be painful and/or itching.

Normality

The normality of an acid solution corresponds to the number of moles of H^+ ions that may be released per liter of this solution. For a monoacid such as HF, a solution containing one mole per liter is called one time molar 1M or one time normal 1N. For a diacid such as H_2SO_4 which delivers two H^+ ions for one mole of acid, a molar solution will be two times normal or 2 N.

- **Necrosis**: this word is used for a wide range of morphological changes, which follow the definitive pathological stoppage of the vital process of the cells constituting the living tissues. The nuclei of necrotic cells may become *pyknotic* (definition below).
  Histologically (check *histological*), there are two types of necrosis:

Coagulative necrosis

It implies the preservation of the contours of coagulated cells (check coagulation). Appearance of ghost cells (Fig. 61). It is thought that the increase of intracellular acidity does not only damage structure proteins but also enzymatic proteins, and thus stops proteolysis. The cytoplasm looks uniformly pink with an acidophilic tinctorial character. Finally, the process of coagulative necrosis protects the general architecture of tissues. This aspect is typical of a death of cells due to oxygen deprivation (hypoxia).

The myocardial infarction is an excellent illustration, in which acidophilic and coagulated anucleate cells (the nucleus of which is no longer visible) can survive in situ for several weeks.

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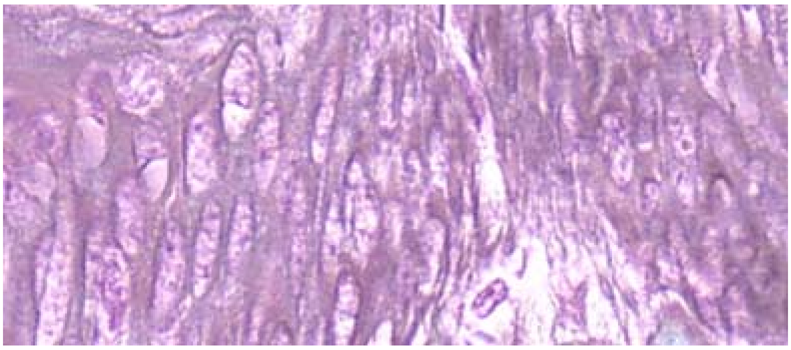

Figure 61: Ghostly aspect of epidermal cells during a liquefactive necrosis

Liquefactive necrosis

Conversely, liquefactive necrosis results from the progressive action of degradation enzymes inside cells lethally attacked by an external cause (thermal burn, chemical corrosion or toxicity, microbial agents…). The morphological appearance of liquefactive necrosis results from the denaturation of intracellular proteins by enzymatic digestion. The cytolasmic content (internal milieu of cells) turns into a viscous liquid mass. Necrotic cells cannot maintain the integrity of their cytoplasmic membrane and they release their contents and thus an inflammatory reaction of the surrounding tissue is started. The necrotic tissue loses its architecture (Fig. 62). The process of necrosis takes several hours to become visible. A common example: the formation of yellowish pus mostly made of leukocytes suffering from liquefactive necrosis due to an acute inflammatory response which settles in response to a bacterial infection.

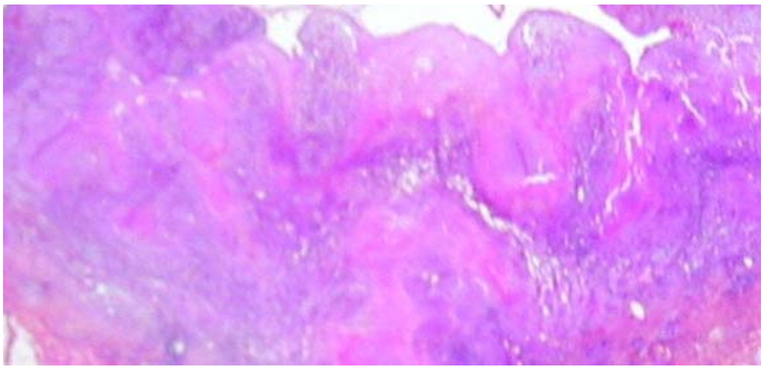

Figure 62: Liquefactive necrosis

Edematous

Suffering from edema

Edema

Serious infiltration of different tissues and specifically of the conjunctival tissue covering skin or mucus. Concerning the skin, the edema appears as a painless swelling without redness, on which a fingerprint may be visible for a little time.

Osmolarity

Osmolarity is equivalent to the number of osmotically active particles per liter of solution and permits the measurement of osmotic pressure.

Osmotic

Osmotic pressure or tension = force applied by two liquids, of different concentrations in dissolved molecules or electrolytes, onto both sides of the semipermeable membrane that separates them. The word « osmosis » was created by the Scottish chemist Thomas Graham from the Greek word ?σμός, meaning "thrust", to name the force that tends to balance molecular concentrations. Osmosis is therefore defined, through its experimental highlighting, as the phenomenon of diffusion of solvent molecules (in general, water) through a semipermeable membrane that separates two liquids with different concentrations of solute. The migration of solvent from one side to the other creates a difference of hydrostatic pressure which compensates exactly for the difference of osmotic pressure (Fig. 63).

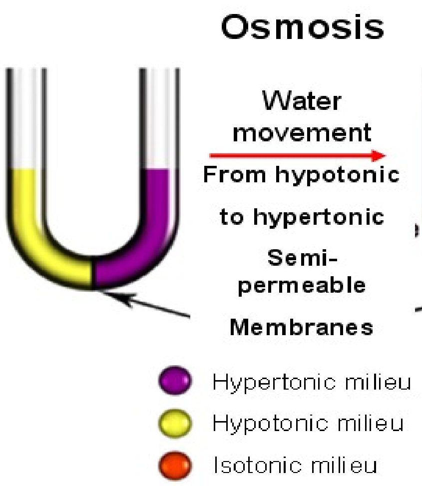

Figure 63: Principle of osmosis

pF

Opposite of the logarithm of the concentration in free fluoride ions. The more the pF rises, the lower the concentration in free fluoride ions is. And the smaller the pF is, the higher the concentration of free fluoride ions is.

« Physiological » pF

Zone of non-danger for a given range of concentration in free fluoride ions.

pH

Opposite of the logarithm of the concentration in proton (H^+). The more the pH increases, the lower the concentration in acid is. And the smaller the pH is, the higher the concentration in H+ is.

« Physiological » pH

Zone of non-danger for a given range of concentration of H^+ and OH^- ions, between acidic and basic milieu.

pK_a

Dissociation constant relating to an acid.

Phlyctena

A cutaneous phlyctena (blister, vesicle) is a circumscribed rise of the cutaneous epidermis, due to a collection of clear liquid into a newly formed cavity resulting from the detachment of the epidermal lamina. This word applies to both vesicle and blister.

Pyknotic

Typical aspect of the nuclei of necrotizing cells. It is a condensation of DNA, the main constituent of nuclei, which is responsible for their morphological modification. The nuclei appear as a compact and basophilic (affinity of basic colourings) solid mass (Fig. 64).

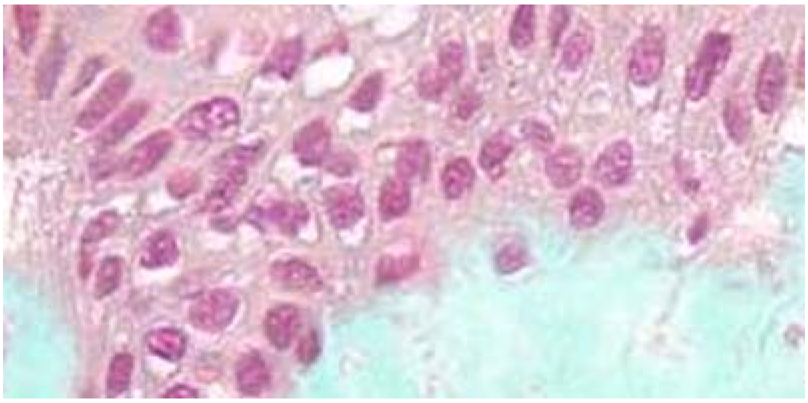

Figure 64: Pyknotic aspect of the nuclei of epidermal cells necrotized by penetration of 70 % HF

Proton

Positive ion which is the entity H^+.

Stroma

Layer formed by an extracellular matrix constituted of collagen lamellae and few cells (mostly keratocytes). All those elements sit in some fundamental substance, constituted of glycorpoteins and proteoglycans. The stroma accounts for 90 % of the complete thickness of human cornea.

Stromal

Relating to the stroma (layer of the cornea at the level of eyes).

8 Hexafluorine® bibliography

The bibliography about Hexafluorine® is available on the web site of PREVOR (www.prevor.com).

9 Bibliography of the dossier

[1] Thomas D., Jaeger U., Sagoschen I., Lamberti C., Wilhelm K.
Intra-arterial calcium gluconate treatment after hydrofluoric acid burn of the hand.
Cardiovasc Intervent Radiol. 2009, Jan,32(1), 155-8.

[2] McCulley JP.
Ocular hydrofluoric Acid Burns : animal model, mechanism of Injury and Therapy.
Tr Am Ophth. 1990, 88, 649-84.

[3] Herbert K., Lawrence JC.
Chemical Burns.
Burns. 1989, dec, 15(6), 381-4.

[4] Peletier A .
Cahier de Notes documentaires- Hygiène et sécurité du Travail 2000. 178, 37-41, références INRS ND 2122
Use of hydrofluoric acid in the laboratories of Chemistry [French] Utilisation de l'acide fluorhydrique dans les laboratoires de Chimie.

[5] Aubertin G., Schorsch F.
Acute toxicity of hydrofluoric acid [French] Toxicité aiguë de l'acide fluorhydrique.
INERIS, Mars 1999, rapport final du Ministère de l'aménagement et du territoire et de l'Environnement.

[6] Marquis RE., Clock SA., Mota-Meira M.
Fluoride and organic weak acids as modulators of microbial physiology.
FEMS Microbiol Rev. 2003, Jan, 26(5), 493-510.

[7] McCulley JP., Whiting DW., Petitt MG., Lauber SE.
Hydrofluoric acid burns of the eye.
J Occup Med. 1983, 25, 447-50.

[8] Dibbell DG., Iverson RE., Jones W., Laub DR., Madison MS.
Hydrofluoric acid burns of the hand.
J Bone Joint Surg Am. 1970, Jul, 52(5), 931-6.

[9] Boink ABTJ., Meulenbelt J.
Systemic fluoride poisoning following dermal hydrofluoric acid exposure: development of an intravenous sodium fluoride infusion model in rats.
J Toxicol Cut and Ocular Toxicol. 1995, 14, 2, 75-87.

[10] Yoshida Y., Watanabe M., Shimada M., Kurimoto K.
Effect of hydrofluoric-acid burn on glucose metabolism.
Nippon Eiseigaku Zasshi. 1975, Apr, 30(1), 145.

[11] Yoshida Y., Watanabe M., Watanabe M., Shimada M., Kurimoto K.
Effect of hydrofluoric acid burn on glucose metabolism (author's transl)
Nippon Eiseigaku Zasshi. 1975, Aug, 30(3), 404-10.

[12] Kono K., Yoshida Y., Harada A., Watanabe M., Hirota T., Tanimura Y., Shibuya Y.
An experimental study on the biochemical consequences of hydrofluoric acid burns.
Bull Osaka Med Sch. 1982, Oct, 28(2), 124-33.

[13] Matsuno K.
Department of Environmental Health, School of Medicine, University of Occupational and Environmental Health, Japan.
The treatment of hydrofluoric acid burns.
Occup Med (Lond). 1996 Aug, 46(4), 313-7.

[14] Anderson W.J., Anderson J.R.
Hydrofluoric acid burns of the hand : mechanism of injury and treatment.
Journal of Hand surgery. 1988,13A,52-7.

[15] Klauder J.V., Shelanski L., Gabriel K.
Industrial uses of compounds of fluorine and oxalic acid; cutaneous reaction and calcium therapy.
AMA Arch Ind Health. 1955, Oct, 12(4), 412-9.

[16] Upfal M., Doyle C.
Department of Family Medicine, Wayne State University, Detroit, MI 48201.
Medical management of hydrofluoric acid exposure.
J Occup Med. 1990, Aug, 32(8), 726-31.

[17] Quevautilier A., N'Guyen V.
Etude expérimentale des brûlures par l'acide fluorhydrique et de leur traitement.
Thérapie. 1976 31-3 4007-411, 413-420.

[18] Division of Industrial Hygiene, National Institute of Health,
Hydrofluoric Acid burns.
Industrial Medecine. 1943, 634.

[19] Rusch G., Mathieu L., Hall AH., MacKinnon M., Padgett E.
Skin decontamination of 49 % and 60 % HF: relation between burn model and decontamination in an immature domestic pig.
EAPCCT XXIV International Congress, May 2004, Strasbourg France.

[20] Mathieu L., Lati E., Burgher F., Gasser P., Hall AH., Peno-Marzzarinon L., Maibach HI., Blomet J.
Comparative experimental decontamination of concentrated hydrofluoric acid in an ex vivo skin model
ISBI, Montreal, Quebec, September 2008.
Submitted for publication, presented at the EAPCCT congress, may 2009, Stockholm, Sweden.

[21] Mathieu L., Lati E., Burgher F., Gasser P., Hall AH., Peno-Marzzarinon L., Maibach HI., Blomet J.
Valuation of lesions caused by hydrofluoric acid on ex vivo human skin and decontamination with tap water + calcium gluconate or Hexafluorine.
Medichem, Amterdam, Netherland, September 2008
Submitted for publication, presented at the EAPCCT congress, may 2009, Stockholm, Sweden.

[22] Camarasa J.
A propos de 3 brûlures cutanées graves dues à l'acide fluorhydrique.
Archives de maladies professionnelles. 1983, 422-5.

[23] McCulley J.P., Whiting D.W., Petit M.G., Lauber SE.
Hydrofluoric acid burns of the eye.
J Occup Med. 1983, 25, 447-50.

[24] Hatai J.K., Weber J.N., Doizakik K.

Hydrofluoric acid burns of the eye report of possible delayed toxicity.
J Toxicol-Cut Ocular Toxicol. 1986, 5, 179-84.

[25] Gérard M., Josset P., Louis V., Menerath J.M., Blomet J., Merle H.
Existe-t-il un délai pour le lavage oculaire externe dans le traitement d'une brûlure oculaire par l'ammoniaque? Comparaison de deux solutions de lavages : sérum physiologique et Diphotérine® ?
J Fr Ophtalmol. 2000, 23, 5, 449-58.

[26] Rubinfeld R.S., Silbert D.I., Arentsen J.J., Laibson P.R.
Ocular hydrofluoric acid burns.
American Journal of Ophtalmology 1992, 114, 420-3.

[27] Chan K.M., Svancarek W.P., Creer M.
Fatality due to acute hydrofluoric acid exposure.
Clinical Toxicology. 1987, 25(4), 333-9.

[28] Dünser M.W., Ohlbauer M., Rieder J., Zimmermann I., Ruatti H., Schwabegger A.H., Bodrogi F., Huemer G.M., Friesenecker B.E., Mayr A.J., Lirk P.
Critical care management of major hydrofluoric acid burns: a case report, review of the literature, and recommendations for therapy.
Burns. 2004 Jun;30(4):391-8. Review.

[29] Markovsky I., Markel G.
Hydrogen Fluoride – The Protoplasmic Poison.
IMAJ 2008: 10: 381-5.

[30] Sheridan R.L., Ryan C.M., Quinby W.C., Blair J., Tompkins R.G.
Emergency management of major hydrofluoric acid exposures.
Burns. 1995, 21, 62-4.

[31] Muriale L., Lee E., Genovese J., Trend S.
Fatality due to fluoride poisoning following dermal contact with hydrofluoric acid in a palynology laboratory.
Ann. Occup. Hyg. 1996, 40, 705-10.

[32] Schrage N.F., Rihawi R., Frentz M., Reim M.
Acute therapy for eye burns
Klin Monatsbl Augenheilkd. 2004 Apr;221(4):253-61.

[33] Gérard M., Louis V., Merle H., Josset P., Menerath J.M., Blomet J.
Experimental study about intra-ocular penetration of ammonia
J Fr Ophtalmol. 1999 Dec;22(10):1047-53.

[34] Kubota M., Fagerholm P.
Corneal alkali burn in the rabbit. Water balance, healing and transparency.
Acta Ophthalmologica, 1991, 69, 635-40.

[35] Paterson C.A., Williams R.N., Parker A.U.
Characteristics of polymorphonuclear leukocyte infiltration into the alkali burned eye and the influence of sodium citrate. Exp. Eye Res. 1984, 39, 701-8.

[36] Paterson C.A., Pfister R.R., Levinson R.A.
Aqueous humour pH changes after experiment alkali burns.
Am. J. Ophtalmol. 1975, 79, 414-9.

[37] Dunn B.J., MacKinnon M.A., Knowlden N.F. et al.
Topical treatments for hydrofluoric acid dermal burns.
J Occup Env Medecine. 1996, 38, 507-14.

[38] Seyb S.T., Noordhock L.N., Botens S. et al.
A study to determine the efficacy of treatments for hydrofluoric acid burns.

J Burn Care Rehabil. 1995, 16, 253-7.

[39] Boink A.B. T. J., Meulenbelt J., Wemer J. et al.
Systemic fluoride poisoning following dermal hydrofluoric acid exposure : development of an intravenous sodium fluoride infusion model in rats.
J Toxicol-cut and ocular toxicology. 1995, 14, 75-87

[40] Cox R.D., Osgood K.A.
Valuation of intravenous magnesium sulfate for the treatment of hydrofluoric acid burns.
Clinical Toxicology 1994, 32, 123-36.

[41] Dowback G., Rose K., Rohich R.J.
A biochemical and histologic rationale for the treatment of hydrofluoric acid burns with calcium gluconate
J Burn care Rehabil. 1994, 15, 323-7.

[42] Kono K., Yoshida Y., Harada et al.
An experimental study on the biochemical consequences of hydrofluoric acid burns.
Bull of the Osaka Med School. 1982, 28, 124-3.

[43] Cartotto R.C., Peters W.J., Neligan P.C. et al.
Chemical burns.
CJS. 1996, 39, 205-11.

[44] Kirkpatrick J.J.R., Burd D.A.R.
An algorithmic approach to the treatment of hydrofluoric acid burns.
Burns. 1995, 21, 495-9.

[45] Kirkpatrick J.J.R, Enion D.S., Burd D.A.R.
Hydrofluoric acid burns : a review.
Burns. 1995, 21, 483-93.

[46] Perrotte M.C., Caubet A., Paysant F. et al.
Hydrofluoric acid : Management of the risk through an example [French] Acide fluorhydrique : Maîtrise du risque à partir d'un exemple.
Arch Mal prof. 1993, 541-3.

[47] Kono K., Yoshida Y., Watanabe M., Tanioka Y., Dote T., Orita Y., Bessho Y., Yoshida J., Sumi Y., Umebayashi K.
An experimental study on the treatment of hydrofluoric acid burns.
Arch Environ Contam Toxicol. 1992, 22, 414-8.

[48] Barbier F., Bonnet P., Julie R., Lambert J., Loriot J., Pointeau G.
Brûlures cutanées par acide fluorhydrique. A propos de 32 cas.
Archives de maladies professionnelles. 1987, 400-2.

[49] Beaudoin L., Le Trionnaire C., Nail J.P.
Accidents du travail dus à l'utilisation de l'acide fluorhydrique ou des fluorures alcalins en milieu acide.
Archives de maladies professionnelles. 1989, 403-5.

[50] Lheureux P., Goldschmidt D., Hossey D., Berre J., Askenasi R.
Brûlures digitales par l'acide fluorhydrique.
Réan. Soins intens. Méd. Urg. 1991, 7, 4, 227-30.

[51] Henry J.A., Hla K.K.
Intravenous regional calcium gluconate perfusion for hydrofluoric acid burns.
Clinical Toxicology. 1992, 30, 203-7.

[52] Mayer T.G., Gross P.L.
Fatal systemic fluorosis due to hydrofluoric acid burns.

Ann Emerg Med. 1985, 149-53.

[53] Mullett T., Zoeller T., Bingham H., et al.
Fatal hydrofluoric acid cutaneous exposure with refractory ventricular fibrillation.
J Burn Care Rehabil. 1987 ; 8, 216-9.

[54] Teppermann P.B.
Fatality due to acute systemic fluoride poisoning following an hydrofluoric acid skin burn.
J Occup Med. 1980 ; 22 ; 691-2.

[55] Rubinfeld R.S., Silvert D.I., Arentsen J.J., Laibson P.R.
Ocular hydrofluoric acid burns.
American Journal of Ophthalmology. 1992, 114, 420-3.

[56] Chataigner D., Garnier R., Bonnin C., Arnoult F., Fraisse F., Efthymiou M.L.
Cutaneous burns and systemic lethal intoxication due to hydrofluoric acid splash [French] Brûlures cutanées et intoxication systémique mortelle secondaires à une projection d'acide fluorhydrique.
Archives de Maladies Professionnelles. 1992, 53,13-14

[57] Bentur Y., Tannenbaum S., Yaffe Y., Halpert M.
The role of Calcium Gluconate in the treatment of Hydrofluoric Acid Eye Burn.
Annals of Emergency Medecine.1993, 22, 9, 161-3.

[58] Carney S.A., Hall M., Lawrence J.C., Ricketts C.R.
Rationale of the treatment of hydrofluoric acid burns.
Br J Ind Med. 1974 Oct;31(4):317-21.

[59] Bentur Y., Tannenbaum S., Yaffe Y., Halpert M.
The role of Calcium Gluconate in the treatment of Hydrofluoric Acid Eye Burn.
Annals of Emergency Medecine.1993, 22, 9, 161-163

[60] Beiran I, Miller B, Bentur Y.
The efficacy of calcium gluconate in ocular hydrofluoric acid burns.
Human and experimental Toxicology. 1997, 16, 223-8.

[61] Dunn B.J., MacKinnon M.A., Knowlden N.F., Billmaier D.J., Derelanko M.J., Rush G.M., Naas D.J., Dahlgren R.R.
Hydrofluoric acid dermal burns : An Assesment of Treatment efficacy using an experimental pig model.
JOM, 1992, 34, 9, 902-909

[62] Hall A.H., Blomet J., Gross M., Nehles J.
Hexafluorine for emergent decontamination of hydrofluoric acid eye/skin splashes.
Semiconductor and Safety Association Journal. 2000, summer, 14, 30-3.

[63] Spöler F., Frentz M., Först M., Kurz H., Schrage N.F.
Analysis of hydrofluoric acid penetration and decontamination of the eye by means of time-resolved optical coherence tomography.
Burns. 2008 Jun;34(4):549-55.

[64] Frentz M., Goss M., Reim M., Schrage N.F.
Repeated exposure to benzalkonium chloride in the Ex Vivo Eye Irritation Test (EVEIT): observation of isolated corneal damage and healing.
Altern Lab Anim. 2008 Feb;36(1):25-32.

[65] Spöler F., Först M., Kurz H., Frentz M., Schrage N.
Dynamic analysis of chemical eye burns using high resolution optical coherence tomograpohy
Journal of Biomedical Optics. 2007, 12(4), 041203.

[66] Höjer J., Personne M., Hultén P., Ludwigs U.
Topical treatment for hydrofluoric acid burns: A blind controlled expériemental study.

Journal of Toxicology Clinical toxicology. 2002, 40(7), 861-6.

[67] Hall A.H., Blomet J., Mathieu L.
Topical treatment for hydrofluoric acid burns: A blind controlled expériemental study.
Journal of Toxicology Clinical toxicology. Letter to the editor. 2003, 41(7), 1031-2.

[68] Höjer J., Personne M., Hultén P., Ludwigs U.
Existing evidence does not support the use of Hexafluorine.
Journal of toxicology clinical toxicology. 2003, 41(7), 1033-4.

[69] Hultén P., Höjer J., Ludwigs U., Janson A.
Hexafluorine vs. Standard decontamination to reduce systemic toxicity after dermal exposure to hydrofluoric acid.
Journal of toxicology clinical toxicology. 2004, 42(4), 355-61.

[70] Mathieu L., Burgher F., Blomet J.
Comparative valuation of the active eye and skin chemical splash decontamination solutions Diphoterine® and Hexafluorine® with water and other rinsing solutions: Effects on burn severity and healing.
Journal of Chemical Health & Safety. July/August 2007, 14(4), 32-9.

[71] Hall A.H., Blomet J., GrossM., Nehles J.
Hexafluorine for emergent decontamination of hydrofluoric acid eye/skin splashes.
Semiconductor and Safety Association Journal 2000, summer, 14, 30-3.

[72] Siéwé C.L., Barbe J.M., Blomet J.
Point sur la prise en charge de brûlures par l'acide fluorhydrique (HF). Observation à propos d'un accident par l'HF 70% : intérêt du lavage à l'Hexafluorine®.
1er congrès international sur l'évolution des connaissances sur les brûlures chimiques. La Baule, Oct 1997

[73] Yoshimura C.A., Mathieu L., Hall A.H.
70% Hydrofluoric Acid (HF) Burns: Delayed Skin Decontamination with Hexafluorine® Plus Calcium Gluconate: Case Report.
Soumis pour publication.

[74] Mathieu L., Nehles J., Blomet J., Hall A.H.
Efficacy of Hexafluorine® for emergent decontamination of hydrofluoric acid eye and skin splashes,
Veterinary and Human Toxicology , 2001, 43(5), 263-5.

[75] Soderberg K., Kuusinen P., Mathieu L., Hall A.H.,
An improved method for emergent decontamination of ocular and dermal hydrofluoric acid splashes.
Vet Hum Toxicol 2004, 46(4), 216-8.

[76] INRS Institut National de Recherche et de Sécurité. France
Aide Mémoire Technique ed953, « Manipulations dans les laboratoires de chimie : Risques et prévention » 2005. http://www.inrs.fr/htm/manipulations_dans_laboratoires_chimie_risque.html

[77] CNAM Caisse Nationale d'Assurance Maladie. France.
Recommandation R 442 (adoptée par le Comité technique national des industries de la métallurgie le 13 novembre 2008). Série Prévention du risque chimique : « Les activités de traitement de surface ». 2009
http://www.risquesprofessionnels.ameli.fr/media/R%20442%20WEB.pdf

[78] INRS Institut National de Recherche et de Sécurité. France
« Laboratoires d'enseignement de la chimie : salles de travaux pratiques et laboratoires de recherche » : référence ED 1506
http://www.inrs.fr/inrs-pub/inrs01.nsf/intranetobject-accesparreference/ED%201506/$file/ed1506.pdf

[79] Dünser M.W., Ohlbauer M., Rieder J., Zimmermann I., Ruatti H., Schwabegger A.H., Bodrogi F., Huemer G.M., Friesenecker B.E., Mayr A.J., Lirk P.

Critical care management of major hydrofluoric acid burns: a case report, review of the literature, and recommendations for therapy.
Burns. 2004 Jun;30(4):391-8. Review.

[80] Segal B.E.
First aid for a unique acid, HF: A sequel.
Journal of Chemical Health and Safety. 2000 jan-feb, 18-23.

[81] Takase I., Kono K., Tamura A., Nishio H., Dote T., Suzuki K.
Fatality due to acute fluoride poisoning in the workplace.
Leg Med (Tokyo). 2004 Jul;6(3):197-200.

[82] Blodgett D.W., Suruda A.J., Crouch B.I.
Fatal unintentional occupational poisonings by hydrofluoric acid in the U.S.
Am J Ind Med. 2001 Aug;40(2):215-20.

[83] Gubbay A.D., Fitzpatrick R.I.
Dermal hydrofluoric acid burns resulting in death.
Aust N Z J Surg. 1997 May;67(5):304-6.

[84] Ohtani M., Nishida N., Chiba T., Muto H., Yoshioka N.
Pathological demonstration of rapid involvement into the subcutaneous tissue in a case of fatal hydrofluoric acid burns.
Forensic Science International 2007, 167(1), 49-52.

[85] Takase I., Kono K., Tamura A., Nishio H., Dote T., Suzuki K.
Fatality due to acute fluoride poisoning in the workplace.
Legal Medicine 2004, 6(3), 197-200.

[86] Bonnard N., Brondeau M.T., Falcy M., Jargot M., Schneider O.
Hydrogen fluoride and aqueous solutions [French] Fluorure d’hydrogène et solutions aqueuses.
INRS. 2006, Fiche Toxicologique n°6, éd.

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