PREVOR Symposium

Chemical Burns

EBA Budapest September 2007

What is Prevor Laboratory?

- PREVOR was created **in 1958 in France**
- and **is managed** by **medical doctors**
- **In different fields**
  - Eye
  - Skin
  - Digestive / inhalation
- Our main target is now **chemical burns**

Chemical Burns, but what ?

- We perform **researches** in order to **understand** the **mechanism** of **chemical burns**

- We have created **solutions** for **an active decontamination** of **chemical burns**
  - a **polyvalent solution, Diphoterine®**
  - a **specific solution, Hexafluorine®** against **hydrofluoric acid**

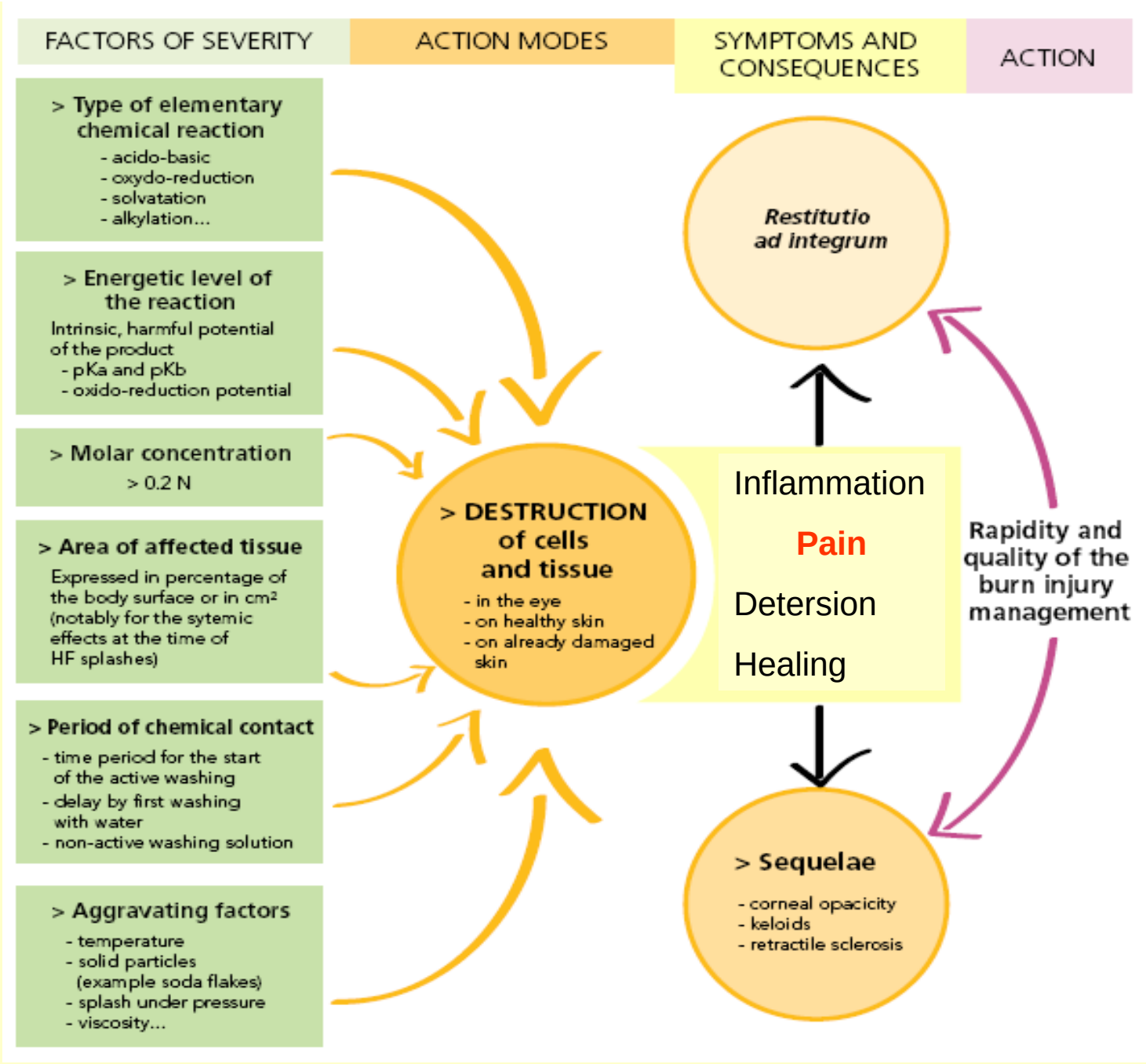
- We work on the improvement of the emergency care and the management of chemicals burns

What is the scientific Program ?

- **Laurence Mathieu, PhD, Scientific maganement, PREVOR**
  - An update about Diphoterine® and Hexafluorine®
- **Pr M Cavallini, Plastic surgeon, Galeazzi Hospital, Milan, Italy**
  - An update about Skin burns knowledege and management
- **Dr Lucien Bodson, Intensive care, Liege Hopital, Belgium**
  - An update about digestive burns

Knowledge and evolution of chemical burn decontamination

- Knowledge
  - **Chemical burns** represent about **5-10% of the burns**
  - There are more than **32 millions of molecules** registered by the Chemical Abstract Society
  - Chemical burns are generally due to **acids**, **bases**, **oxidising** and **reducing** agents, **chelating** or **alkylating** agents, and **solvents**
  - About 25.000 have been identified as irritant or corrosive



Mathieu L et al Journal of Chemical Health and Safety 2007, 14, 4, 32-39

Caustic sodium hydroxide effect

on L929 murine fibroblast cell culture

Schrage NF et al, Klin Monatsbl Augenheilkd. 2004, 221, 253-261

Evolution of the chemical burn decontamination

- **Water** was the **first improvement** for **emergency care**
  - **Water** has only a **mechanical effect** at the surface of the tissue
    - **Advantages**:
      - it was the obvious **universal** means of decontamination,
      - and was a great advance for **limiting the severity** of **chemical burns**
    - There was **two limiting factors** with water:
    - the time to intervene is only a few seconds,
    - There are non reproductible results with **concentrated products**,
    - **Water is Hypoosmolar**: it creates a flux from the outside to the inside

Evolution of the chemical burn decontamination

- How could we improve water washing?
  - **Two interests and ways**:
    - **To avoid the diffusion of chemical agents** into the tissues with **hyperosmolar solutions**
    - **To « neutralise » the irritant or corrosive** properties of the chemical agent with **amphoteric compounds**

What is Diphoterine®?

- An aqueous solution containing the fundamental properties of water

⇒ the effect of pulling the chemical agressor away from the surface of the tissues

- An amphoteric solution

⇒ acts on acids as well as bases, and rapidly restores the eye and/or skin's physiological pH

- An hypertonic solution

⇒ stops the penetration of corrosive chemicals into the tissues creating a flux from the inside to the outside of the tissues

A medical device CE 0459, class IIa

Diphoterine®: Innocuousness and properties

- **Non irritating** to the eyes or skin (pH = 7.4)
- **Non cytotoxic** (keratinocytes, fibroblasts)
- **Non anti-inflammatory**
- **non toxic** (acute oral, dermal LD_{50} > 2000 mg/kg)
- Rinsing **residues non irritating** (for acids and bases)
- **Non sensitising, non mutagenic** (Ames test)
- **No side effects** have been reported in workplace use
- **Immediate decrease in pain**

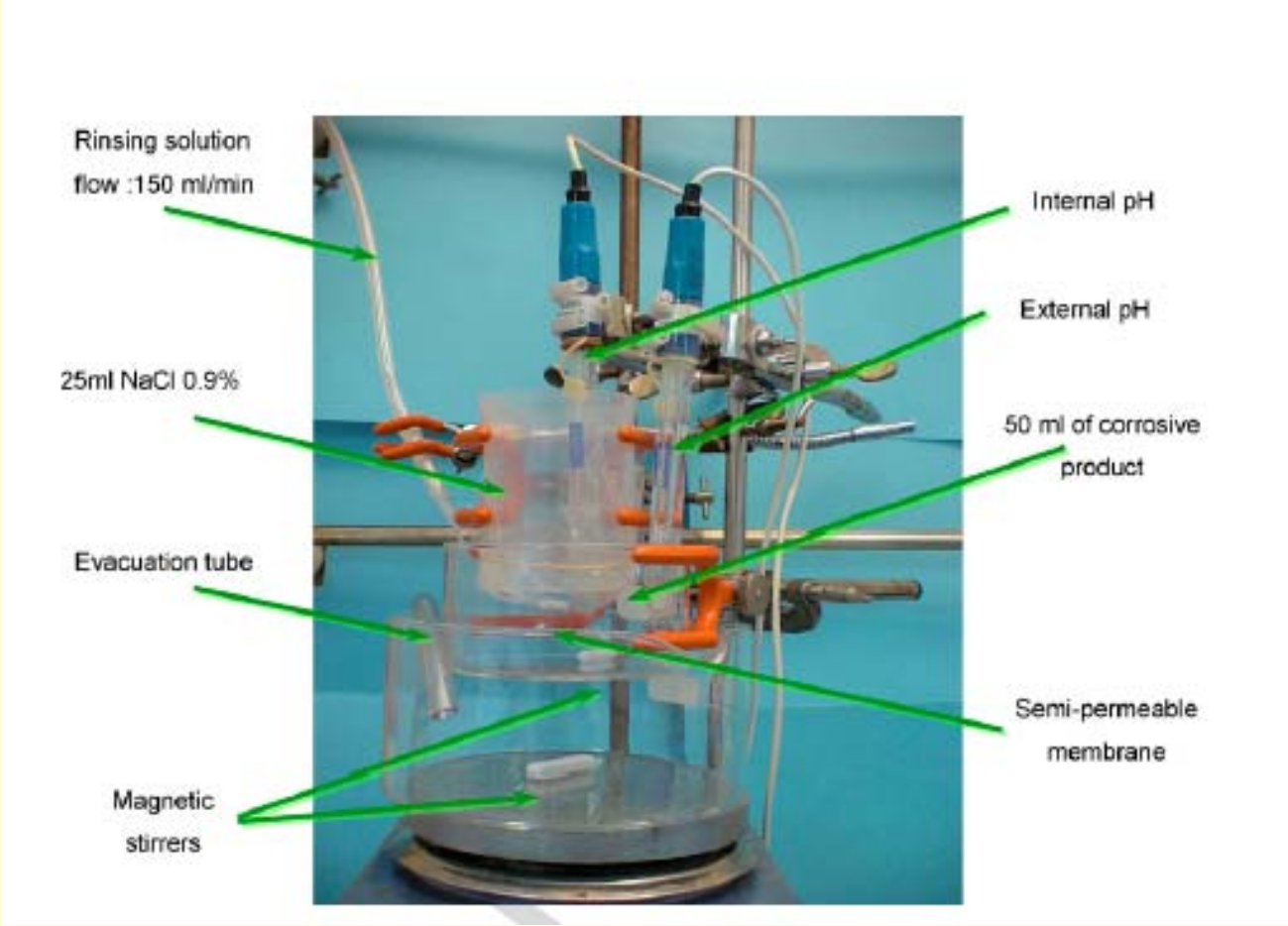
Mathieu L, Burgher F, Hall AH Cutan Ocul Toxicol. 2007;26(3):181-187

Diphoterine®:
New proofs in innocuity, 2007

- ***Cutaneous local tolerance on healthy or scarified skin in the rabbit***
  - **No dermal irritation was observed as well as no toxic effect**
- ***Clinical evaluation of cutaneous tolerance after a unique application with occlusive bandage during 48 hours (55 patients)***
  - **Diphotérine® was not irritant for an occlusive application**

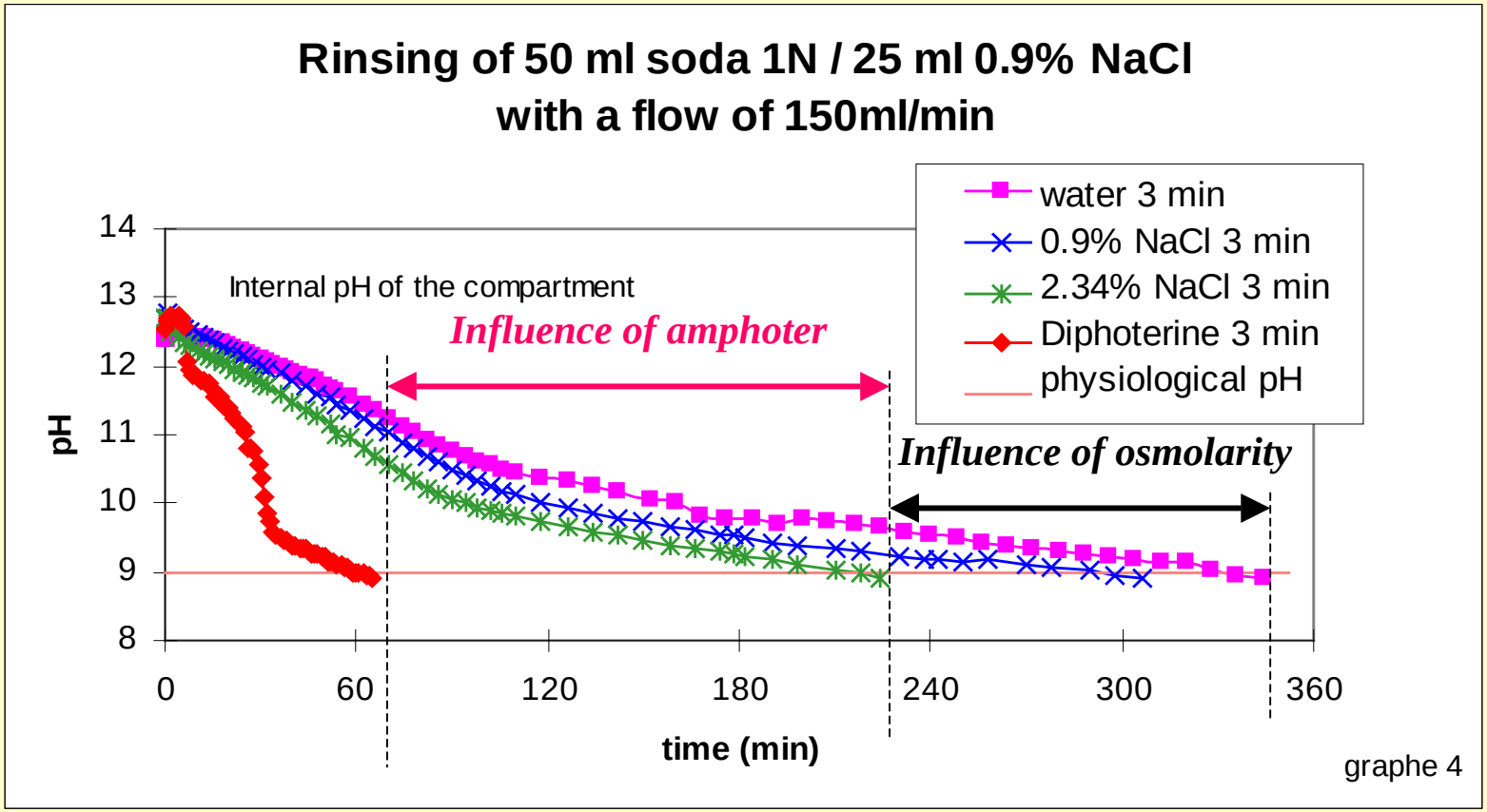
Mathieu L et al, accepted for poster presentation at EUROTOX 2007, to be published

In vitro model for evaluation of irritant and corrosive potential and effectiveness of decontamination



Mathieu L et al Journal of Chemical Health and Safety 2007, 14, 4, 32-39

Result and interest of this *in vitro* model?



Time is won by the use of an active solution with a quick return to a physiological state

Mathieu L et al Journal of Chemical Health and Safety 2007, 14, 4, 32-39

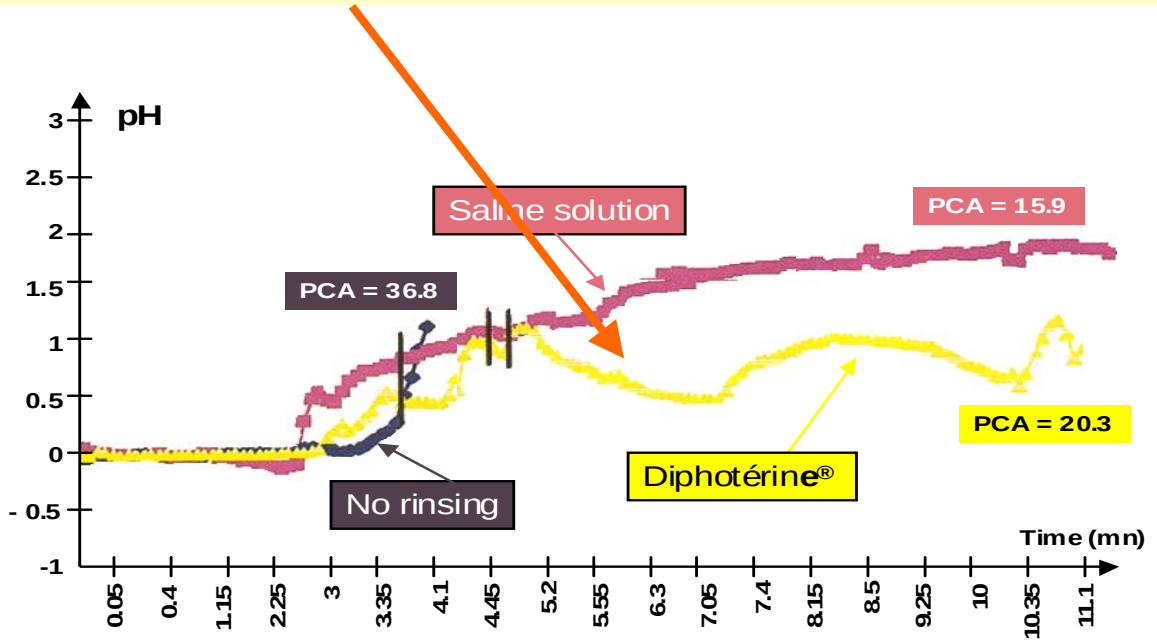
Ocular study in rabbits (concentrated ammonia burn) Saline solution versus Diphoterine®

- 18 **rabbit eyes**
- Anaesthesia: intramuscular injection in each leg of Flunitrazepam (Narcosep®)
- Ocular burn with 0.01 ml of **15.3 % ammonia** during 1 min of contact
- pH 15.3% ammonia = 12.8
- **Blind washing** with 250 ml of **saline solution** vs. **Diphotérine®**
- pHmeter probe in the anterior chamber
- **pH measurements** of aqueous humor every 5 seconds
- **Histology** of the cornea

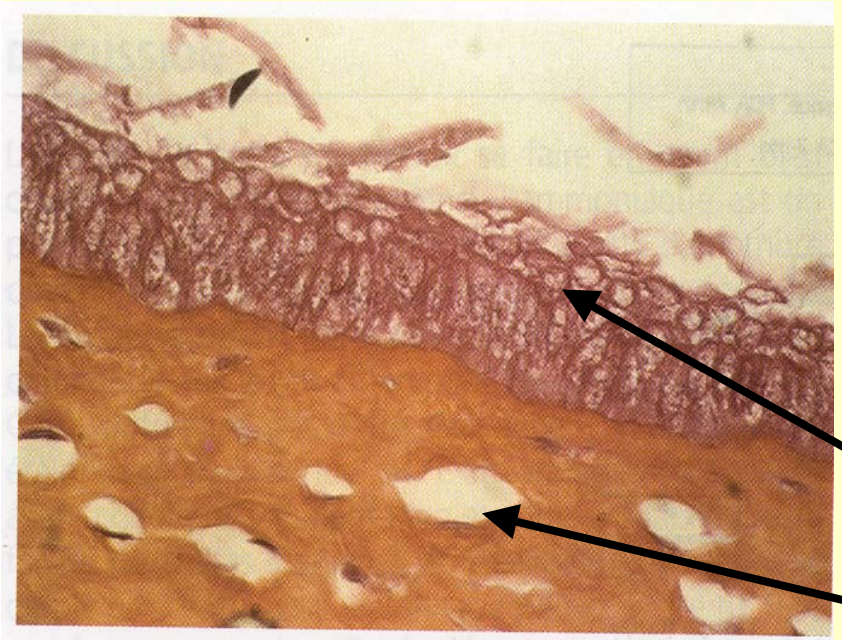
Gérard M, Josset P, Louis V, Ménérath JM, Blomet J, Merle H. J Fr Ophtalmol 2000 ; 5 : 449-458.

Ocular study in rabbits (concentrated ammonia burn) Saline solution versus Diphoterine®

- **Diphotérine®: inflexion of pH curve = decrease of pH**



Washing at 3 min

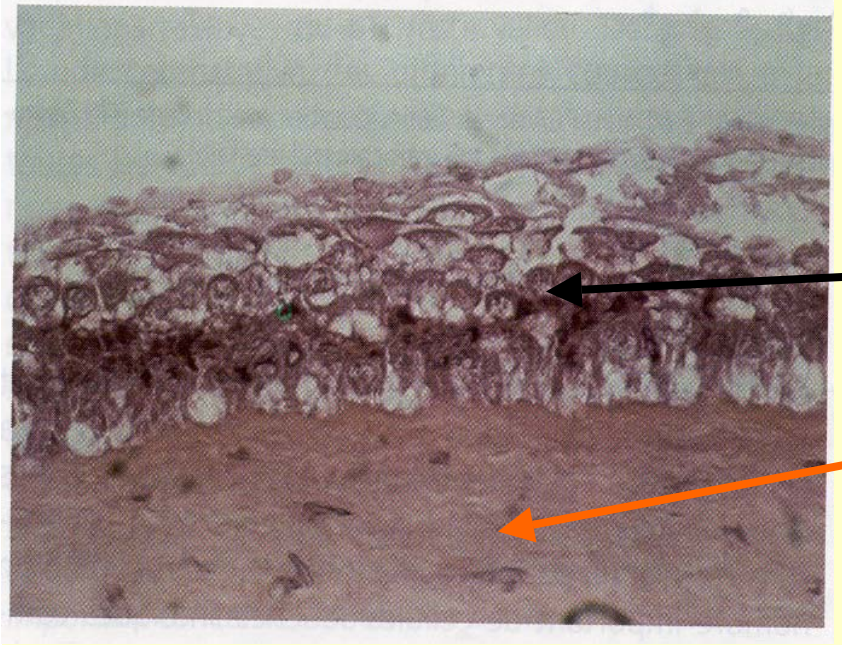


Cornea burnt by ammonia

washing after 3 min of contact

By saline solution:

- Coagulated epithelium,
- edematous stroma



By Diphotérine® :

- Vacuolisated and coagulated epithelium,
- Normal stroma

Diphotérine ® efficacy for human eye/skin chemical splashes

- **Results in occupational medicine in Europa**
  - **Decrease of the pain sensation** after the washing with Diphotérine®
  - **Decrease or lack of sequelae**,
  - **Decrease** of the need of **secondary care**,
  - **Decrease** of **loss of work**.
- **Results of its use for a delayed eye washing at the hospital**

Clinical study: - Diphotérine® vs. Saline solution
followed by the same therapeutical protocol

- Significant Quicker **reepithelialisation**

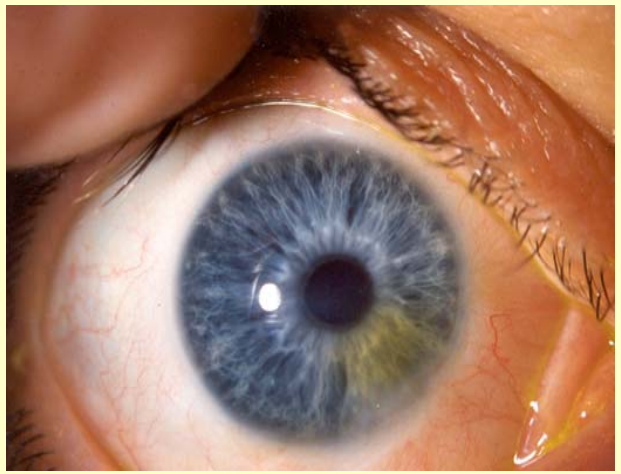
- **Result for a delayed and repeated skin washing at the hospital**
  - Case reports with a **good** and **quick wound healing**

Hall AH, Blomet J, Mathieu L Vet Hum Toxicology 2002, 44, 4, 228-231

Merle H et coll. Burns 2005, 31 205-211

A case report of a severe Grade 4 burn
before the beginning of the clinical study

- Woman, 49 years old, assaulted at work place
- Grade 4 right eye
- Visual acuity < 1/10
- Limbic ischemia on 360°
- Scleral necrosis
- Diphotérine® : 1 hour after the splash
- Decrease of stromal edema (AV 0.3)
- Application of an adapted treatment



Gérard M, Merle H, Chiambaretta F, Rigal D, Schrage N. Burns, 2002, 28, 670-673

A case report of a cutaneous acid splash

Medical summary of the accident 28 of July, 2005

- A tube worker, was victim of a chemical burn on his face, neck and right ear, due to 98% sulfuric acid, while opening a badly purged pipe.
- **First aid** with **water** after **5 min** of **exposure,**
  - appearance of a **severe burn**
- **Secondary rinsing** and **care** with **Diphoterine®, 15 min after,** by the nurse
  - Induces an immediate antalgic effect
  - allows an important decrease of the seriouness of the burn.
- The employee is sent to an emergency department.

Dr Berengere BELLIARD, MD

Evolution of the lesions

- 24 h after the accident, the victim always presented severe burn, an important edema has appeared.
- The use of Diphoterine® is followed up 24h.

At 72 h : The edematous stage has entirely regressed.

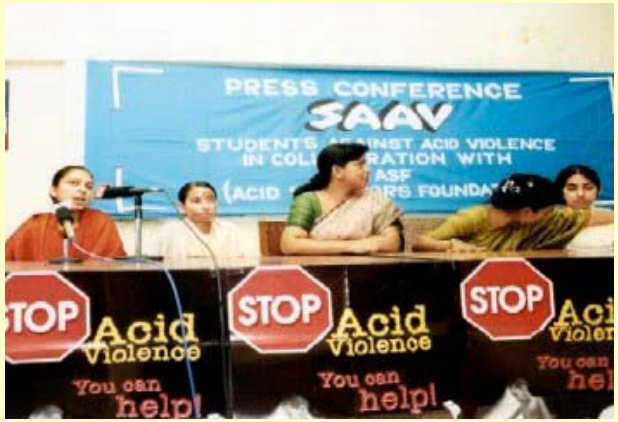
Only the auditory duct is exsudative.

The severe lesions are no more visible.

- 29 days after the accident, the wound healing is almost complete.
- The employee will work at an adapted place in a clean area during all the time of cares.

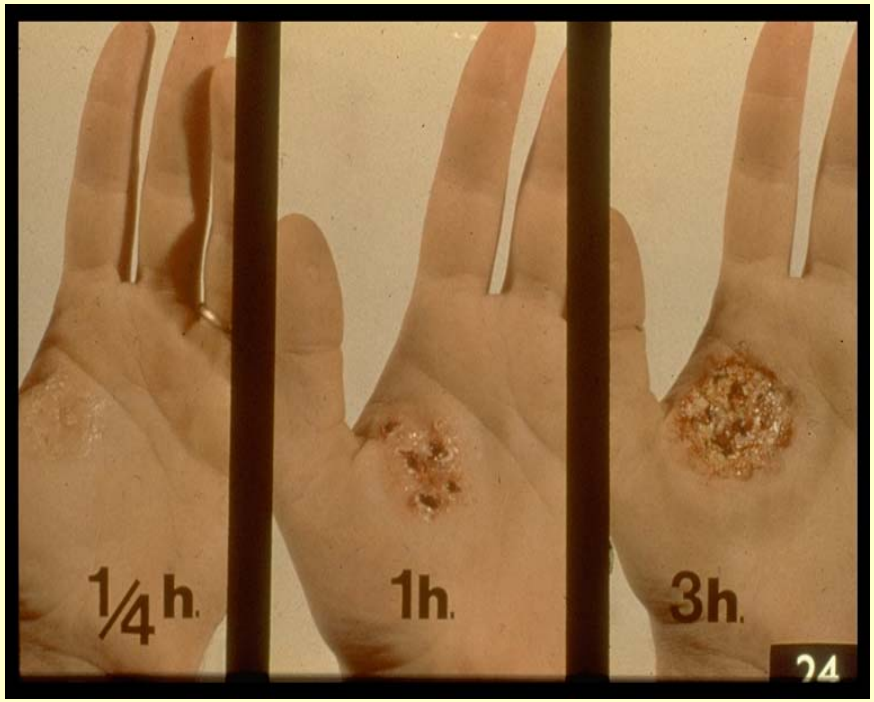
Perpestives of studies

•Clinical study in Bangladesh with the Acid Survivors Foundation, ***www.acidsurvivors.org***



Hydrofluoric acid (HF)
A small and weak acid but a double danger

- a corrosive attack
- due to H^+ ion
- penetration of F^- ion:
  - systemic toxic action



50% of the severe burns are due to HF

Effects due to HF burns

- Concentration > 50% :
  Immediate pain and rapid necrosis

- Concentration 20%-50% :
  Delayed burn from 1 to 8 hours

- Concentration < 20% :
  Delayed pain and necrosis until 24 hours

📖 *Segal EB Chemical Health and Safety, 2000, 18-23*

HF burns with a lethal risk

Penetration	% affected surface	HF Concentration
Burn due to contact	1	anhydrous
Burn due to contact	5	> 70%
Burn due to contact	7	50-70%
Burn due to contact	10	20-50%
Burn due to contact	20	< 20%
Prolonged exposure or long delay before treatment	Minor burns	
HF Ingestion		>5%
HF Inhalation		>5%

Dunser MW, Burns, 2004, 391-398

Photo 1 : Cas n°1 - Acide fluorhydrique 70% Initial

Photo 2 : Cas n°1 - Acide fluorhydrique 70% à J+4 après excision et décharges

Photos 3 et 4 : Cas n°1 - Acide fluorhydrique 70% à 1 an

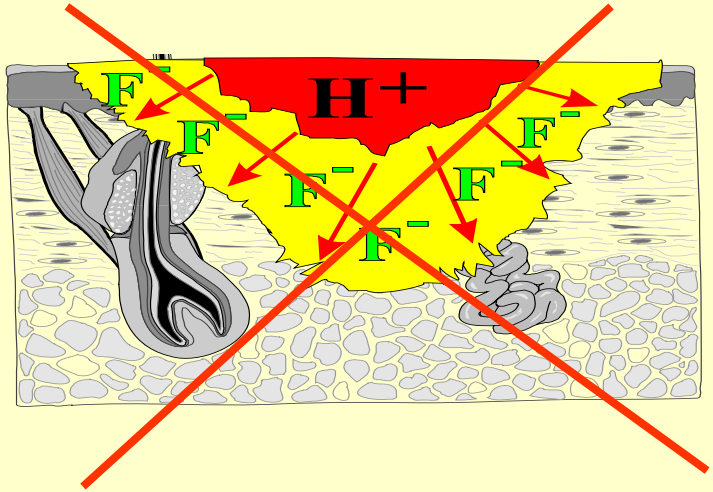
A case report
with water + Calcium gluconate

- a 45 years old worker
- 70% HF
- Checking of a valve
- immediate rinsing with water (15 min) then saline solution during transport
- hospital : IV injection of Ca and Mg + Ca Glu gel

➢ 1 year lost from work

Hexafluorine®

- Emergency rinsing solution of ocular or cutaneous HF splashes (neutralising, chelating and hypertonic)
  - deactivates H^+ ions
  - deactivates F^- ions
  - Quick return to physiological status



Hexafluorine®

- Innocuity and properties
  - **Non irritant** for eye/skin
  - **Non toxic** (LD_{50} > 200 mg/kg)
  - **Non sensitising**
  - **No side effects** detected after its use in industries
  - **Immediate relief** of **pain**

A medical device CE 0459, class IIa

Hexafluorine ® efficacy for human eye/skin chemical splashes

- **Results in occupational medicine in Europa**
  - **32 cases with exposure to 5-70% hydrofluoric acid**
  - **5 of the 32 cases could have present a lethal risk**
  - **Decrease of the pain sensation** after the washing with Hexafluorine®
  - **Decrease or lack of sequelae**,
  - **Decrease** of the need of **secondary care**,
  - **Decrease** of **loss of work**

- **Results of its use for a delayed eye washing at the hospital**
  - **No clinical case report**

Hall AH et al, SSA J, 2000, 14, 30-33

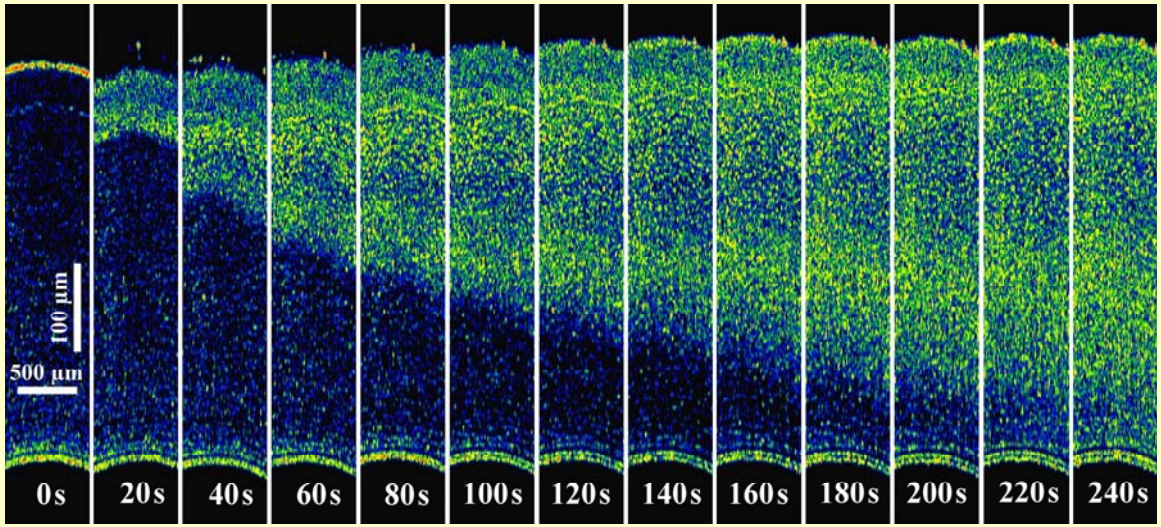
Mathieu L et al, Vet Hum toxicol 2001, 43(5), 263-265

Soderberg K et al, Vet Hum toxicol 2004, 46(4), 216-218

Hexafluorine® : Last results

An ex vivo study (EVEIT model) about HF diffusion and decontamination in the cornea

Diffusion of 2.5% of hydrofluoric acid in the rabbit cornea



With the use of OCT Optical coherence tomography

The diffusion of HF through the cornea is achieved within 4 minutes

Schrage F, Frentz M, Spöler F, Först M, Kurz H. Accepted for publication in Burns

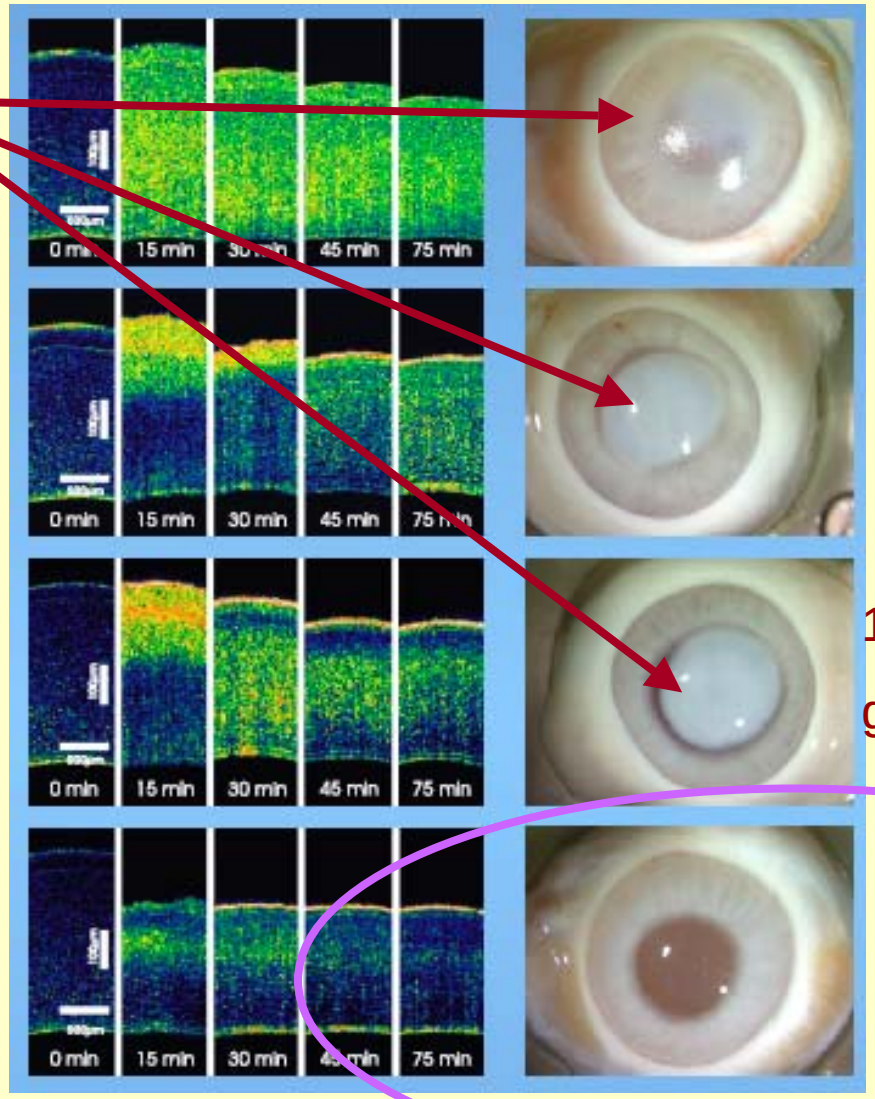
Hexafluorine® : Ex vivo study

Burn =

Cornea opacification

Influence of different washing solutions on HF penetration through the cornea

- 20s of contact,
- 25µl of 2.5% HF,
- 15 minutes of washing



Schrage F, Frentz M, Spöler F, Först M, Kurz H. Accepted for publication in Burns

EBA Budapest September 2007

Conclusion :
How to treat a chemical burn?

- **Never delay a washing**
  - If possible, use an active solution (such as Diphotérine® or Hexafluorine®)
  - If not, use water

- **Protocol of washing in a firm**
  - Wash as soon as possible and the needed time
  - while undressing or taking off contact lenses
  - consult a specialist

- **Protocol of washing at the hospital**
- Wash at the arrival at the hospital
  - Apply a treatment to decrease inflammation/ infection