Prism Inter Africa
CHEMICAL SAFETY

Diphoterine® solution Hexafluorine® solution Trivorex® neutralizing absorbent

EMERGENCY FIRST AID FOR CHEMICAL SPLASHES TO THE EYES AND SKIN

INFORMATION BOOKLET CONTAINING PRODUCT INFORMATION, SCIENTIFIC CASE STUDIES AND RELATED PUBLICATIONS

CONTACT: MANDY WESSELS (CELL) 084 412 5839

PATRICK ELLIS (CELL) 083 251 3359

HEAD OFFICE: DEBBIE BOYD / LESLEY KRETZMANN (021)823 6809

A member of:

SAMED
south african medical device industry association
advancing innovation responsibly

COMPANY PROFILE

We at Prism Inter Africa represent Prevor, a French laboratory specialising in toxicology and the development and manufacture of emergency first aid medical devices for the decontamination of chemical splashes to the eyes and skin. These products come in the form of dedicated eyewashes and aerosol sprays for the skin.

Diphoterine® solution is highly effective in minimising the potential damage caused by acids, bases, oxidising agents, reducing agents, chelating agents and solvents. This is achieved by the combination of three main actions:

- The mechanical effect of washing
- The absorption effect of the molecule stopping the aggressive process of the chemical.
- The hypertonicity of the solution which prevents the penetration of the chemical into the tissues.

Diphoterine® solution has limited effect in neutralising the harmful effects of hydrofluoric acid. To minimise risk in this regard Hexafluorine® solution has proved highly effective.

Calcium gluconate is a recommended treatment when injury caused by hydrofluoric acid has progressed by treating the hypocalcaemia thereby avoiding the systemic effects of the fluoride (toxic) ions.

SITE TECHNICAL SURVEYS AND TRAINING

We are happy to arrange site surveys of your chemical risk zones and to provide on-site staff product training and certification. We have a 'DropBox' link taking customers to our refresher training DVD. All relevant literature and site-posters are also provided. We pride ourselves in offering full support to our clients and we manage their product renewals and maintenance from the onset of our chemical safety relationship.

UNIVERSITY OF CAPE TOWN

POISONS INFORMATION CENTRE
SCHOOL OF CHILD & ADOLESCENT HEALTH
RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL
KLIPFONTEIN ROAD
RONDEBOSCH
7700

TEL: +27 21 658 5308
FAX: +27 21 650 4492
Email: poisonsinformation@uct.ac.za
www.afritox.co.za

To whom it may concern

This serves to confirm that the product Diphoterine® has been listed on AfriTox® poisons information database.

AfriTox® is a computerised database which is widely available at emergency units and paediatric treatment facilities throughout South Africa. It is available on a subscription basis for medical practitioners.

Sincerely

Linda Curling
Pharmacist

Prism Inter Africa
CHEMICAL SAFETY

PRODUCT GUIDE

2016

EMERGENCY FIRST AID DEVICES FOR CHEMICAL SPLASHES TO THE EYES AND SKIN

IMAGE	STOCK CODE	DESCRIPTION
	LMPE.DAS	DIPHOTERINE® SOLUTION WALL MOUNTED STATION. • 2X500ML EYEWASH • 1X200ML AFTERWASH • 1X200ML MINI DAP SPRAY
	LMPE.DAS.TXP	DIPHOTERINE® SOLUTION WALL MOUNTED STATION. • 2X500ML EYEWASH • 1X200ML AFTERWASH • 1X200ML MINI DAP SPRAY WITH TRIVOREX® NEUTRALIZING ABSORBENT
	LMPE.DA2S	DIPHOTERINE® SOLUTION WALL MOUNTED STATION • 2X500ML EYEWASH • 1X200ML AFTERWASH • 2X200ML MINI DAP SPRAY
 NEW FOR 2016	"Clean Room" Wall Mounted Station	This cabinet is available empty or fitted with DIPHOTERINE® SOLUTION • 2X500ML EYEWASH • 1X200ML AFTERWASH • 2X200ML MINI DAP SPRAY Size: 360 x 270 x 130 mm Weight: 6.2 kg (empty) Material: Stainless steel 304

	LPMD6	DIPHOTERINE® SOLUTION EYEWASH • PACK SIZE (6X500ML)
	LOA6	AFTERWASH II®SOLUTION • PACK SIZE: (6X200ML)
	LIS	DIPHOTERINE® SOLUTION SINGLE INDIVIDUAL EYEWASH • PACK SIZE: (10X50ML)
	MINI	DIPHOTERINE® SOLUTION MINI DAP SPRAY • PACK SIZE: (6X200ML)

	MICRO	DIPHOTERINE® SOLUTION MICRO DAP SPRAY • PACK SIZE: (12X100ML)
	DAPD	DIPHOTERINE® SOLUTION 5L PORTABLE SHOWER DAP WITH BOX
	CICH.D	DIPHOTERINE® SOLUTION WALL MOUNTED STATION AND 5L DAP • 2X500ML EYEWASH • 1X200ML AFTERWASH • 1X200ML MINI DAP SPRAY • 5L PORTABLE SHOWER DAP WITH BOX • COMPLETE WITH STEEL TROLLEY
	CI.D	DIPHOTERINE® SOLUTION WALL MOUNTED STATION AND 5L DAP • 2X500ML EYEWASH • 1X200ML AFTERWASH • 1X200ML MINI DAP SPRAY • 5L PORTABLE SHOWER DAP WITH BOX

	LMPE.FA	HEXAFLOURINE® SOLUTION WALL MOUNTED STATION • 2X500ML EYEWASH, • 1X200ML AFTERWASH
	LMPE.FACA.TXP	HEXAFLUORINE® SOLUTION WALL MOUNTED STATION WITH TRIVOREX® NEUTRALIZING ABSORBENT WITH CALCIUM GLUCONATE • 2X500ML EYEWASH • 1 X 200ML AFTERWASH • 1X700G TRIVOREX • 1X40G TUBE CALCIUM GLUCONATE
	LPMF6	HEXAFLUORINE® SOLUTION EYEWASH • PACK SIZE: (6X500ML)
	DAPF	HEXAFLUORINE® SOLUTION 5L PORTABLE SHOWER DAP WITH PROTECTIVE BOX

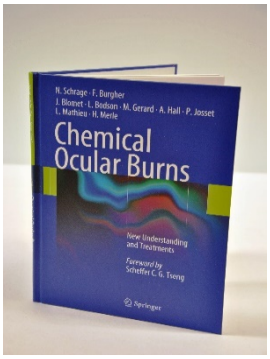
	CI.FC	HEXAFLUORINE® SOLUTION WALL MOUNTED STATION AND 5L DAP • 2X500ML EYEWASH, • 1X200ML AFTERWASH • 5L PORTABLE SHOWER DAP WITH BOX
	CI.CH.FC	HEXAFLUORINE® SOLUTION WALL MOUNTED STATION AND 5L DAP • 2X500ML EYEWASH, • 1X200ML AFTERWASH • 5L PORTABLE SHOWER DAP WITH BOX • COMPLETE WITH STEEL TROLLEY
	KCAGLU12	CALCIUM GLUCONATE GEL • PACK SIZE: (12X40G TUBES)
	DAPBOX	PROTECTIVE BOX ONLY

TACTICAL HALF VELCRO 	BELTWHV	WEB BELT HALF VELCRO • (PER ONE)
WEB BELT PLASTIC BUCKLE 	BELTW	WEB BELT • (PER ONE)
	ETMICT	BELT HOLSTER FOR MICRO DAP SPRAY • PACK SIZE: (12)
	ETLIST	BELT HOLSTER FOR LIS • PACK SIZE: (10)

	ETMICTRP	PLASTIC HOLSTER FOR MICRO DAP SPRAY • PACK SIZE: (12)
	ETLISRP	PLASTIC HOLSTER FOR LIS • PACK SIZE: (10)
	TXP4	TRIVOREX® NEUTRALIZING ABSORBENT • 4 X 700G DISPENSERS
	TXP10	TRIVOREX® NEUTRALIZING ABSORBENT • 10 X 700G DISPENSERS

	TXS10	TRIVOREX® NEUTRALIZING ABSORBENT • 10KG BUCKET
	P4.AC	ACICAPTAL® ABSORBENT • 4 X 600G
	P10.AC	ACICAPTAL® ABSORBENT • 10 X 600G
	S.AC	ACICAPTAL® ABSORBENT • 9KG BUCKET

	P4.BC	BASICAPTAL® ABSORBENT • 4 X 500G
	P10.BC	BASICAPTAL®ABSORBENT • 10 X 500G
	S.BC	BASICAPTAL®ABSORBENT • 9KG BUCKET
	S.PC	POLYCAPTOR® ABSORBENT • 4KG BUCKET
	P4.OC	PETROCAPTOR® ABSORBENT • 4 X 400G

	P10.OC	PETROCAPTOR® ABSORBENT • 10 X 400G
	S.OC	PETROCAPTOR® ABSORBENT • 6KG BUCKET
	LIVCOB	CHEMICAL OCULAR BURNS BOOK
	TRAIN	PRODUCT TRAINING COMPLETE WITH CERTIFICATION

Lonza

Diphoterine® was introduced at the Lonza Slough UK sites in 2002 because we use corrosive, acid and irritant chemicals on a daily basis.

Whilst Lonza prides itself on developing safe processes and Lonza personnel have a huge respect for chemicals and the potential hazards when handling them, accidents can still happen, equipment can fail or storage containment can be breached resulting in the unexpected release of a hazardous substance.

Lonza personnel have used Diphoterine® over the last 10 years as a first aid response when their skin or eyes have come into contact with a chemical. This has meant that since the introduction of Diphoterine®, no member of staff working for Lonza has been left with any lasting effects from chemical contact – an amazing result.

Regards,

Paul McCarroll

EHS Specialist.
Lonza Biologics

Lonza Biologics plc
228 Bath Road
Slough, Berkshire SL1 4DX, UK
Tel +44 (0)1753 777000
Fax +44 (0)1753 777001
www.lonza.com

Testamonial for Prevor Product - Diphoterine skin and eyewash

I was employed as the Occupational Health Nurse Practitioner at the University of KwaZulu Natal – Pietermaritzburg Campus from January 2009 until February 2011.

This university, like most such institutions, have a large number of teaching and research laboratories. Students, technicians and academic staff make use of a large number of different types and classes of chemicals on a daily basis. As in any laboratory, there is always the risk of a splash to the skin or the eye regardless of the safety mechanisms in place. Many post graduate students and researchers work after hours and weekends when there are few first aiders and no medical staff on campus.

Having worked as a nurse practitioner in a chemical manufacturing plant for the four years previous to the University, I was highly sensitised to the importance of the reaction time in the emergency 1st aid of such accidental injuries, the possible long term effects on the injured person both from a medical and an cosmetic point of view and as well as the lost time and financial burden of such injuries on the industry/institution.

During the latter part of 2009 I was invited to a presentation by AHN Pharma, where the use of Diphoterine was demonstrated as the first aid of chemical splashes to the skin and eyes. I transferred this information to the relevant Safety Committee Chairpersons and the University Safety Manager. A demonstration was arranged at the University by AHN Pharma and a very good attendance by academics, technicians and students was recorded. Many questions where tossed back and forth and the University Health and Safety Department decided to purchase the product in the 200ml Mini Dap format for 1st aid of skin splashes, and, in the 50ml format (Standard individual eyewash) for the emergency 1st aid of eye splashes.

The relevant training of all technicians and first aiders whom work in the laboratories was conducted and the product was placed in designated first aid boxes. The emergency bag which is carried by the Campus Medical staff was also stocked with the product.

The first call came in early 2010 when a student accidently spilt Phenol on the palm of her hand and between her fingers. She immediately placed her hand under running water and a few minutes later her hand was washed with the Diphoterine. The affected skin remained sensitive for a few days but only a very superficial skin loss occurred. No blistering or deep injury or scarring occurred.

A student splashed a small amount of 98% sulphuric acid onto her chest area (in the V area not covered by the lab coat). The area was washed with Diphoterine and no blistering took place, thus no pain or scarring occurred. When the student came to see me the following day there was no evidence that acid had in fact fallen on her skin!

A student was working with heated Naphthalene and sustained a splash on the face and a few drops splashed her in the one eye. The first aider had washed her eye with water, when I reached her (about 5 mins) after the splash I used the diphoterine eye wash. She explained the pain relief of the eye as being immediate. The skin did not blister either despite the fact that the chemical was

heated. She saw me the following morning and no redness and swelling of the eye or skin was evident and her visual acuity was not affected.

These are just three examples of how this product proved effective as an emergency 1st aid in our institution. Granted, the splashes were not on the scale which occur in industry such as a pipe or valve failure resulting deluges of chemicals, consequently resulting in much larger and therefore more serious chemical burns. The three cases as described did not result in the injured person requiring intervention at an emergency facility or needing to leave the practical or work they were busy with at the time of the accident.

As an Occupational Health Practitioner I found this product provided me with an advantage in the emergency 1st aid of chemical burns and that extra little peace of mind when students and researchers were working after hours!

Written by Sandra Koekemoer OHNP at University of KwaZulu Natal – Pietermaritzburg Campus Jan 2009 to Feb 2011

The initial management of ocular chemical burns in an academic hospital

Bayanda N Mbambisa and Trevor R Carmichael, Division: Ophthalmology, Department of Neurosciences, University of the Witwatersrand

Corresponding author: Dr BN Mbambisa, Registrar, Division: Ophthalmology, Department of Neurosciences, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand.

E-mail: bayanda@iburst.co.za

Abstract

Purpose: **To report the clinical findingsofacaseofocularchemicalburnsfollowingcement alkali burn to both eyes to illustrate the importance of using protective eye wear and the need for immediate treatment following chemical injury to the eyes.**

Methods: **Case report.**

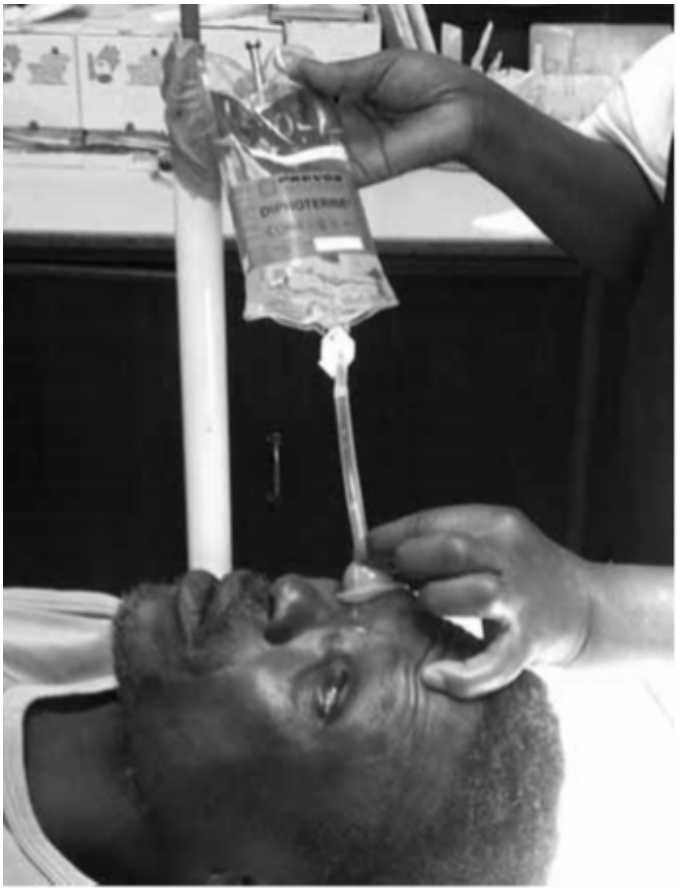
Results: **A 31-year-old man had a delayed presentation with an occupational injury due to cement in both eyes. He had a Grade 3 chemical burn in his right eye and Grade 1 burn in his left eye. Immediate irrigation was done but his right eye required surgical debridement.**

Conclusions: **This case illustrates the consequences of not using protective eye wear when working with chemical substances and the need for immediate and effective irrigation following chemical injury to the eyes.**

Key words: chemical burns, irrigation, occupational injury

Introduction

Chemical burns of the eye are an ophthalmological emergency and prompt and appropriate management is important to prevent the potentially visually disabling complications of this ocular injury. The purpose of this case study is to illustrate the consequences of not using protective eye wear when working with chemical substances and the need for immediate and effective irrigation following chemical injury to the eyes.



Irrigation of the eye.

Case study

A 31-year-old male patient presented to Chris Hani Baragwanath Hospital with a history of cement burns to both eyes. He was working as a casual labourer on a building site and while mixing cement some of the cement powder entered his eyes. He immediately put his head into a bucket fi lled with tap water to wash out the cement. He still had remnants of the cement in his eyes and when he went home and he washed his eyes with sugar water. He presented to hospital 23 hours after the initial injury.

On initial assessment, the pH of the conjunctiva in the inferior fornix was 9 in both eyes. Both eyes were irrigated with 500 ml Diphoterine®, a fi rst aid eye wash, and residual cement particles were removed from both conjunctivae. Most of the cement particles from his right eye were removed and the pH was 7 after irrigation. We were unable to remove all the cement particles in his left eye as they were embedded in the conjunctiva and his pH remained 9 after irrigation. Further irrigation was withheld as the patient needed surgi-cal debridement.

On subsequent examination, his visual acuity in the right eye was hand movements and 6/12 in his left eye which improved to 6/6 with pinhole occluder. His lids on the right eye were swollen but he had no burns of the skin. Both con-junctivae were injected and his right eye had cement particles adherent to the conjunctiva under his upper lid. He had four clock hours of limbal ischaemia superonasally in his right eye and no limbal ischaemia in his left eye. His entire right cornea had stromal haze with iris details poorly visible through the cornea. His left cornea was clear with an epithelial defect

of a quarter of the corneal area inferonasally. The anterior chamber of the right eye could not be assessed due to the corneal haze but the anterior chamber in his left eye had no signs of infl ammation. The intraocular pressure in his right eye was 18 mm Hg and 10 mm Hg in his left eye. His hazy cornea prevented a view of the lens, vitreous and fundus of his right eye. The media were clear in his left eye and fundoscopy was normal. His injuries were graded according to severity.[1] His right eye had a Grade 3 burn, which indicates three to six clock hours of limbal involvement and 30-50% conjunctival involvement. His left eye had a Grade 1 burn, which has the best prognosis with only corneal involvement and no limbal or conjunctival involvement. He was started on prednisolone acetate 1% drops 4 times a day, atropine sulphate 1% twice a day and chloromycetin ointment 1% three times a day in both eyes. In addition he received oral doxycycline 100 mg twice a day and oral ascorbic acid 2 g four times a day. Due to the residual cement remnants in his right eye medical therapy alone was insuffi cient and he was taken to theatre for surgical debridement of the remaining cement particles.

Discussion

Chemical burns of the eye form a small fraction of ocular trauma.[2] The majority of injuries are occupational injuries and, because of their more frequent presence in household clean-ing agents and industrial and building materials, alkali injuries are more common than acid injuries.[3,4] The injuries caused by chemical burns to the eye can range from mild unilateral conjunctival or corneal epithelial damage to sight threatening bilateral burns. The severity of the injury is related to the surface area of contact, the degree of penetration and the concentra-tion and nature of the agent involved.[5] Injuries caused by alkalis are usually more severe as they penetrate the cornea more effectively than acids. Immediate and thorough irriga-tion is the most important intervention affecting the prognosis and outcome of ocular chemical burns.[3,6,7] Water or saline is commonly the initial irrigating fl uid used but it may not be the most effective fl uid to use as large quantities are required to dilute the chemical.[8] New agents, such as Diphoterine®, have been developed which effectively remove the chemical from the eye and neutralise both the acid and alkali.[3,7-9]

Conclusion

Prevention of ocular injury is important when working with chemicals and protective eye wear should always be used. In the occupational setting, factories and building sites should have eye wash solutions readily available. In the event of an injury to the eye/s, immediate and prolonged irrigation of the eye/s should be undertaken. Patients should be taken to their nearest hospital as soon as possible to ascertain the degree of injury. With early treatment some of the blinding complications can be prevented.

Ethics

Ethics approval was obtained from the University of the Witwatersrand Human Research Ethics Committee. The patient signed informed consent after the initial irrigation was performed, having been given an information sheet and an opportunity to ask questions.

"Chemical burns of the eye are an ophthalmological emergency and prompt and appropriate management is important . . ."

Lessons learned

1. The severity of the injury is related to the surface area of contact, the degree of penetration and the concentration and nature of the agent involved.
2. Alkali injuries are more common than acid injuries, and are usually more severe as they penetrate the cornea more effectively than acids.
3. Immediate and prolonged irrigation is the most important intervention.
4. Water or saline is commonly the initial irrigating fl uid used but new agents may be more effective.
5. Patients should be taken to their nearest hospital as soon as possible to ascertain the degree of injury.

References

1. Dua HS, King AJ, Joseph A. A new classifi cation of ocular surface burns. Br J Ophthalmol. 2001;85(11):1379-1383.
2. Adepoju FG, Adeboye A, Adigun IA. Chemical eye injuries: presen-tation and management diffi culties. Ann Afr Med. 2007;6(1):7-11.
3. Kuckelkorn R, Schrage N, Keller G, Redbrake C. Emergency treatment of chemical and thermal eye burns. Acta Ophthalmol Scand. 2002;80(1):4-10.
4. Wagoner MD. Chemical injuries of the eye: current concepts in pathophysiology and therapy. Surv Ophthalmol. 1997;41(4):275-313.
5. Merle H, Donnio A, Ayeboua L, Michel F, Thomas F, Ketterle J. et al. Alkali ocular burns in Martinique (French West Indies) Evaluation of the use of an amphoteric solution as the rinsing product. Burns. 2005;31(2):205-211.
6. Rihawi S, Frentz M, Becker J, Reim M, Schrage NF. The consequences of delayed intervention when treating chemical eye burns. Graefes Arch Clin Exp Ophthalmol. 2007;245(10):1507-1513.
7. Schrage NF, Langefeld S, Zschocke J, Kuckelkorn R, Redbrake C, Reim M. Eye burns: an emergency and continuing problem. Burns. 2000;26(8):689-699.
8. Rihawi S, Frentz M, Schrage NF. Emergency treatment of eye burns: which rinsing solution should we choose? Graefes Arch Clin Exp Ophthalmol. 2006;244(7):845-854.
9. Schrage NF, Kompa S, Haller W, Langefeld S. Use of an amphoteric lavage solution for emergency treatment of eye burns. First animal type experimental clinical considerations. Burns. 2002;28(8):782-786.

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Complex chemical burns following a mass casualty chemical plant incident: How optimal planning and organisation can make a difference

Tomás B. O'Neill *, *Jeremy Rawlins*, *Suzanne Rea*, *Fiona Wood*

Burns Service of Western Australia, Royal Perth Hospital, Perth, Western Australia, Australia

ARTICLE INFO

Article history:
Accepted 10 December 2011

Keywords:
Mass casualty
Chemical burns
Disaster management
Communication
Planning

ABSTRACT

Introduction: Four employees at a chemical plant sustained extensive chemical burns following the explosion of a pipeline containing 100% sulphuric acid. We describe the management of these patients from the initial ED triage through to discharge from hospital in life and limb threatening chemical burns.

Methods: Four patients who sustained chemical burns to the torso and extremities are reviewed. Data was retrieved from patient case notes and operating theatre logbooks.

Results: Four patients sustained chemical burns during the blast and were immediately transferred to a local ED where a prompt referral was made to the burns service. All patients were male aged 25–59 years (mean 46.5). Burn size was 2–50% BSA (mean 22.5). Following RFDS transfer to the state burns service two patients required immediate excisional surgery. In these patients the chemical burn involved full thickness skin loss with extensive underlying muscle and neurovascular damage. One patient required immediate above knee amputation of one leg and fascial burn excision of the other. The other patient required fascial burn excision of both legs followed by Integra placement 24 h later. Both patients had prolonged hospital stays due to the complex nature of their injuries requiring multiple trips to theatre and lengthy rehabilitation. The two patients with smaller burns had straightforward surgery and an unremarkable recovery.

Conclusion: Early communication following this mass casualty incident allowed for organisation of tertiary services and early radical surgery which was life saving. Management lessons were learnt following this mass casualty chemical burn incident.

1. Introduction

Mass burn casualty management, has been extensively examined in the international literature since 1964 [1]. Many lessons were learned following the September 11th attack in New York, 2001 [2,3], the Bali Bombings in Kuta, 2002 [4–6], and the Madrid train bombings, 2004 [7], where large numbers of burn-casualties were generated from terrorist attacks. The Bali bombings alone culminated in a rapid influx of 62 burn-casualties to Australia, which resulted in every adult burn bed on the continent being occupied [4]. Unforeseen surges in patient numbers can cripple a unit, which occur in the context of normal routine daily operations and standard burns admissions. In reality however the number of casualties required to stretch a burns unit to its resource limit, is far less than those generated by terrorist attacks or natural disasters.

* *Corresponding author*. Tel.: +61 404103366.
E-mail address: tomasoneill@gmail.com (T.B. O'Neill).
0305-4179/$36.00
doi:10.1016/j.burns.2011.12.010

We describe a four-victim mass burn-casualty incident in which our hospital was placed on code 'brown', anticipating mass casualties for an external event. We describe the timeline of events and communication, which resulted optimal resuscitation, triage, transport and intervention for the chemical burn casualties, and almost certainly contributed to two casualties surviving what were undoubtedly life-threatening injuries. We also discuss the health and safety implications that this incident had on the chemical manufacturing industry worldwide.

2. Methods

Data pertaining to the four casualties from an industrial chemical plant incident were retrieved and examined. Information from the patient's individual medical notes and theatre logbooks were cross-referenced. Senior burns team members were asked to document and recall the events as they unfolded. Finally, health and safety experts were consulted in collaboration with the chemical plant owner/operators.

3. Incident

On February 25, 2010 at 11.00 h, the director of the Burns Service of Western Australia (BSWA), based in Perth, received a direct phone call from the Emergency Department (ED) consultant in Bunbury Hospital (180 km away), informing her of a mass casualty incident at an industrial chemical plant, which had resulted in four burns casualties. Digital photographs illustrating the injuries were emailed from Bunbury ED to the Director of the BSWA clarifying the natureof the injuries. A pipe containing 100% sulphuric acid had burst in the plant and had showered four workers with the concentrated acid. The four workers were immediately taken to safety showers, however the lower garments of clothing were not removed. The closest safety shower was still in the zone of the spraying acid and therefore the workers had to move across the plant to another shower to escape the continuing acid flow. Thinking that the call for help had not yet been made, one of the victims left the emergency shower to raise the alarm.

Whilst the patients continued to be stabilised in Bunbury ED pending transfer, a code 'brown' call was instigated at Royal Perth Hospital (RPH) at 11.25 h. A code brown call corresponds to an external event, and the RPH ED, State Trauma Unit, and Intensive Care Unit (ICU) were placed on alert.

The burns unit, ICU, State Trauma Unit and Operating Theatre (OT) staff, were all aware of the code brown call and immediately prepared for incoming casualties. The Director of the BSWA along with senior and experienced members of the burns team including medical, anaesthetic and nursing staff convened, discussed the injuries and prepared for urgent and radical debridement in multiple simultaneous theatres. The resuscitation bay in the ED was prepared and two burns theatres were warmed. All necessary equipment and staff for radical and simultaneous debridement were prepared. Our Burns ICU was informed of the anticipated need for two beds and extra staff were allocated. The agreed plan was for the Burns and Anaesthetic teams to review the casualties in the ED and transfer straight to the OT suite once satisfactorily stabilised.

The Royal Flying Doctors Service (RFDS) transported all four victims to Perth via fixed wing aircraft. The first two casualties arrived at RPH ED at 14.00 h, only two and a half hours after the initial referral.

The four victims were all male aged 59, 54, 48 and 25 years (Table 1).

The first patient was a 59-year-old male. He received 45% TBSA burns to his bilateral lower limbs, hands and back. His lower limb burns were extensive and deep and had penetrated the fascia and underlying muscle on the left leg (Fig. 1). The burns on his right leg were also extensive and full thickness for the most part (Fig. 2). He was transferred directly from the ET to the OT at 14:30 h. An above knee amputation was performed on the left leg and a fascial excision of the burns to his right leg were performed (Fig. 3). Both legs were dressed with Jelonet (Smith and Nephew, Hull, UK) and betadine soaked gauze and he was transferred to the Intensive Care Unit (ICU) where he remained intubated and ventilated overnight. The following morning a V.A.C.® dressing was applied to the left AKA stump. Split thickness skin grafts (SSG) were meshed 1:3 and applied to his right lower limb. In addition ReCell® non-cultured autologous cells were sprayed over the right leg to augment wound healing. ReCell® was also used to treat his burns to the upper extremities and to the skin graft donor sites. He required ICU support for 8 days and subsequent trips to the OT for VAC

Table 1 – Summary of the casualties and their injuries.

Patient No.	Age	TBSA%	Body site	Timing of surgery	Initial procedure	LoS	Total no. Sx's	Subsequent procedures	LoS per % TBSA
1	59	45	Bilateral legs and hands. Back	Immediate	Left AKA fascial excision burns right leg	114	2	SSG and ReCell® to right leg. ReCell® to upper limb VAC to AKA stump.	2.5
2	54	1	Bilateral legs	Delayed	None	4	1	SSg and ReCell®	4
3	48	2.5	Right flank	Delayed (6 days)	None	11	1	SSG and ReCell® to right flank	4.4
4	25	38	Bilateral legs and hands	Immediate	Fascial excision of bilateral lower limb burns	79	2	Integra to lower limbs @ 24 h. SSG and ReCell® to upper limbs	2

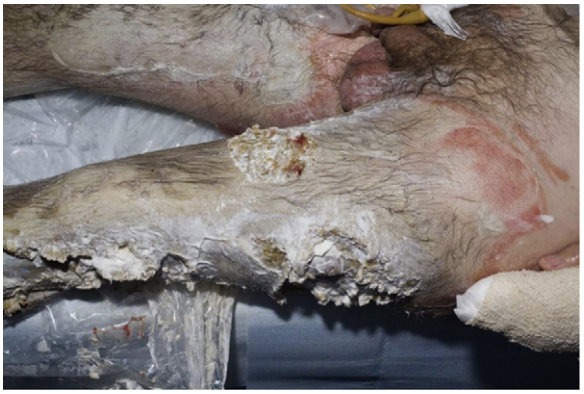


Fig. 1 – Left lower limb chemical burn necessitating amputation.

changes and further skin grafting to achieve wound closure. The remainder of his inpatient stay was complicated by intermittent atrial fibrillation and sepsis. He was discharged on day 114, and continues to receive rehabilitation (Fig. 4).

The second patient was a 54-year-old male. He received small burns to his bilateral lower limbs totalling 1% TBSA. He did not require immediate surgery for his burns but was admitted to the burns unit for analgesia, dressings and psychosocial care. He was discharged 4 days following his admission. After 12 days of conservative management his wounds had failed to close satisfactorily and he was re-admitted for SSG and ReCell® application. He was subsequently discharged following an unremarkable post-operative recovery (Fig. 5).

The third patient was a 48-year-old male with a 2.5% TBSA burn to his right flank. He underwent surgery (SSG and ReCell®) on day 6 of his admission, had a satisfactory post-operative recovery and was subsequently discharged 11 days following his admission (Fig. 6).

The final patient was a 25-year-old male. He had full-thickness burns to both lower limbs and deep dermal injuries to both his hands totalling 38% TBSA. (Fig. 7.) He was taken to the OT following stabilisation in the ED (approximately 30 min following patient 1). He underwent fascial excision to both

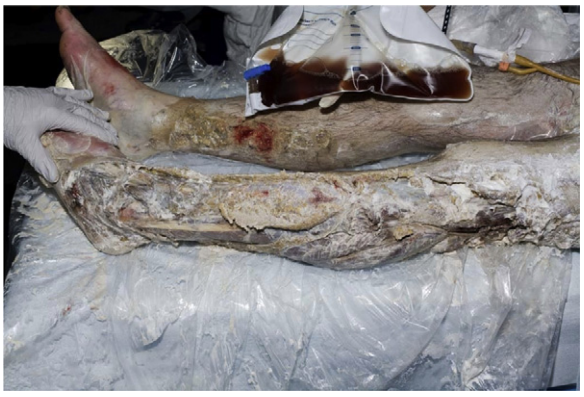


Fig. 2 – Bilateral lower limbs demonstrating extent of injuries. Note myoglobinuria in catheter bag from extensive myonecrosis.

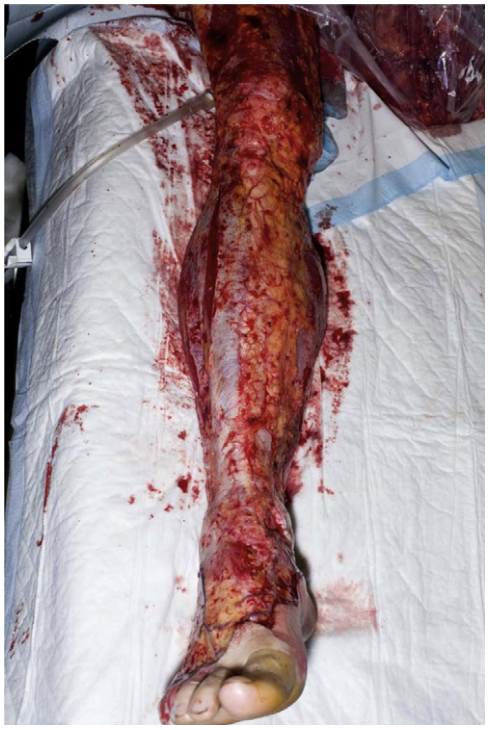


Fig. 3 – Left AKA and fascial excision of right lower limb burns.

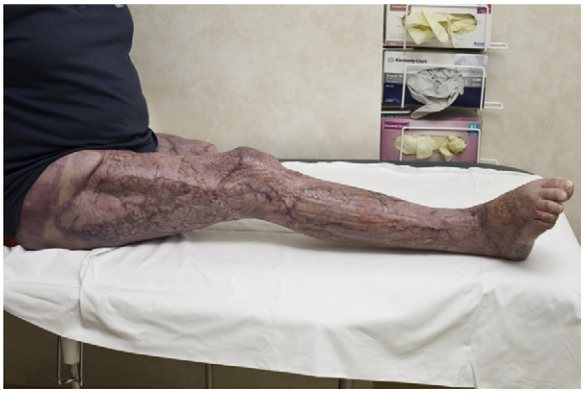


Fig. 4 – Patient 1 in OPD following discharge.

lower limbs and dermabrasion of his hand burns and application of ReCell®. The common peroneal nerve of his left leg was noted at surgery to be partially burnt but was preserved to act as a conduit to facilitate nerve growth (Fig. 8). His legs were dressed with Jelonet and betadine soaked gauze. The following day he was returned to the OT. Minimal further debridement was required and Integra® was applied to both lower limbs (Fig. 9). His post-operative recovery was hampered by an episode of sepsis and partial loss of the Integra (30% lost) and a profound depressive illness. He subsequently had SSG and ReCell® applied to the vascularised Integra over three further trips to the OT. He continues to attend for rehabilitation and scar management (Fig. 9).

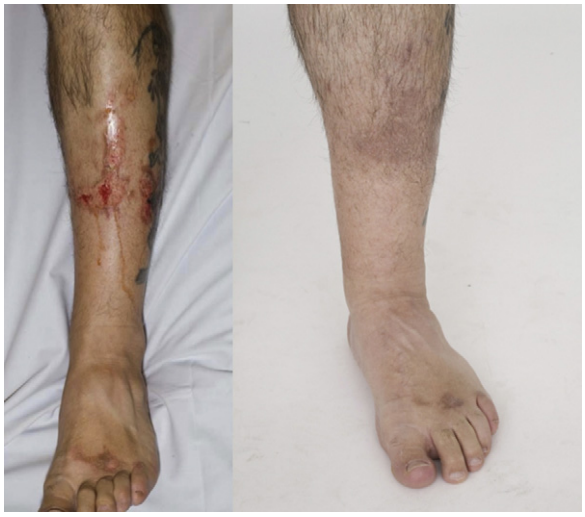


Fig. 5 – Patient 2 pre-op and 6 months post-operatively.

4. Discussion

A well-devised and communicated management plan, instigated for as few as four burn casualties, can result in optimal intervention and ensure adequate and necessary care delivery. The burns service of Western Australia has been called-upon to treat several mass-casualty burns in the past. In the senior authors 20 years experience of providing this service, there have been at least 14 mass casualty incidents. In 2002 for example, it responded to the Bali bombings by accepting 28 of the patients into the burns unit at Royal Perth Hospital [4]. More recently in 2009, 23 patients were transferred to Perth following a fire onboard a vessel off the coast of Ashmore Reef in the Indian Ocean [8]. On both of these occasions the burns service of Western Australia responded appropriately by

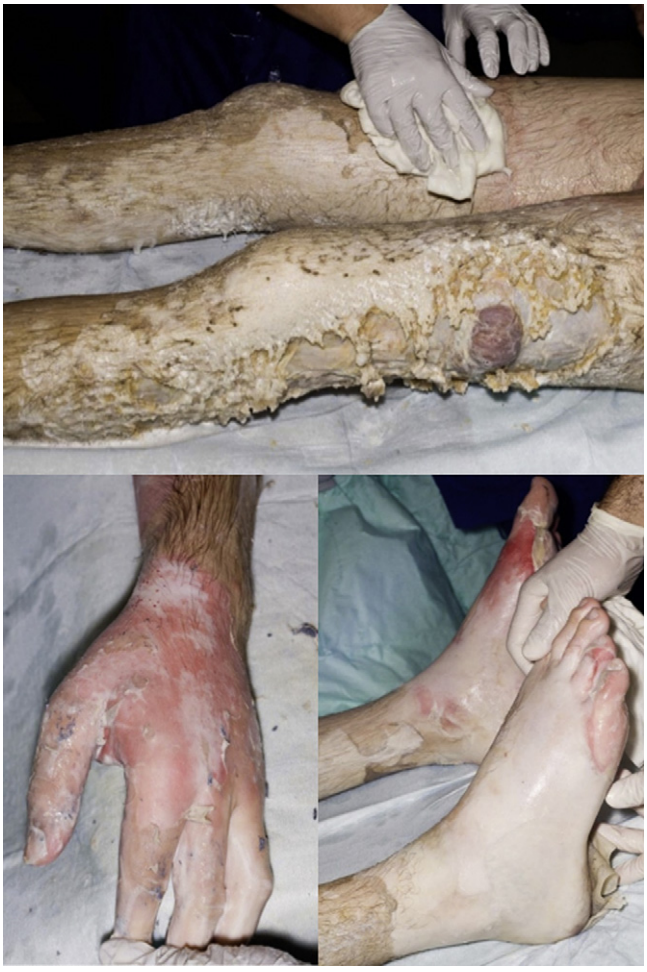


Fig. 7 – Bilateral lower limb and hand burns in the fourth patient, a 25-year-old male.

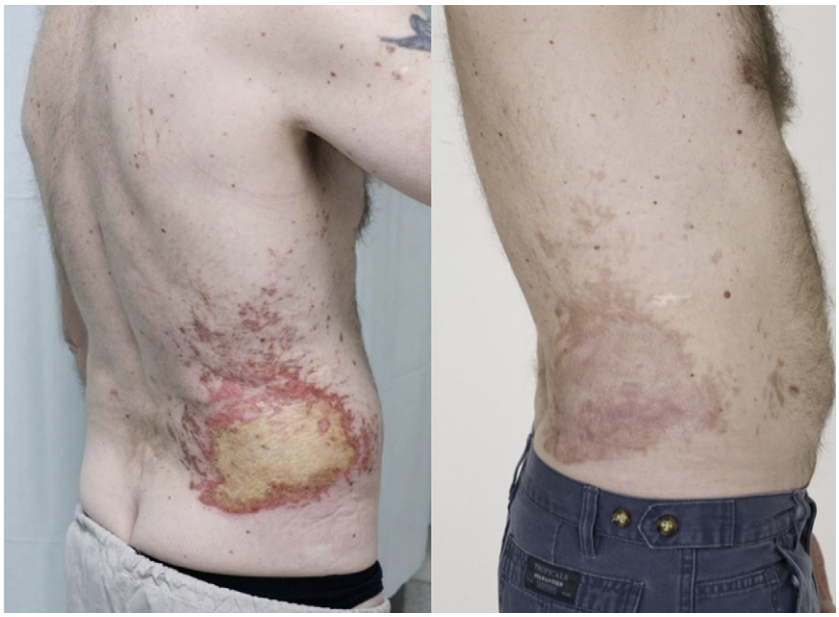


Fig. 6 – Patient 3 pre-op and 6 months post-operatively.

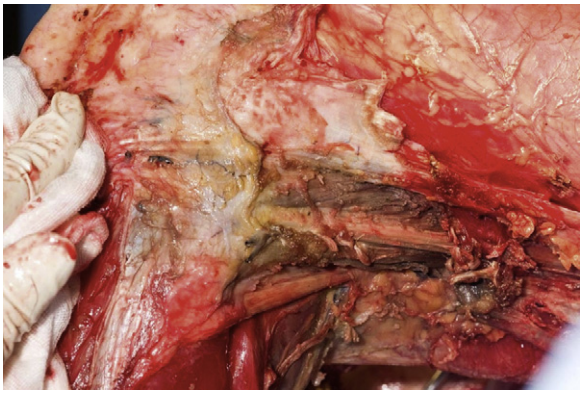


Fig. 8 – Fascial excision of burn revealing involved common peroneal nerve (preserved).

increasing bed capacity on the burns unit, calling-up additional nursing and medical staff, and rostering theatre personnel to allow multiple surgeries simultaneously. Good communication and meticulous planning was paramount to successful operations in both 2002 and 2009, and such was the case following this chemical plant incident. The initial call to the burns service was between the receiving emergency consultant and the director of the burns service on-call for burns admissions that day. This direct communication avoided a lot of unnecessary passing things 'up and down the line' and ensured a prompt response. Following the Bali bombs and Ashmore reef we had 24–48 h to prepare for patients arriving into Perth; on this occasion we had just 3 h.

Technology certainly expedited our response on this occasion. Digital photographs of the patients taken in the admitting emergency department were emailed directly to the on-call burns consultant in Perth before the patients had left the department. This detailed information clarified the extent of the injuries, allowing us to prepare two operating theatres for radical surgery involving amputation and fascial burn excision.

Large body surface area deep chemical injuries require early (and aggressive) surgery to save life [9]. With deep structures involved amputation and fascial excision is lifesaving and certainly proved to be the case in this situation. Whilst some of the Integra was lost due to infection the fact that the majority was salvaged suggests that it was worth doing and that the benefits of using the dermal matrix will be evident for many years. Integra was not used in the patient requiring the amputation for the main reason that we felt any additional sepsis (from the Integra) would not be tolerated by the older patient with medical co-morbidities.

Much was learnt from the management of these complex chemical burn patients – not only at the burns unit. Immediately following the incident the chemical plant halted operations (for approximately 1 week) to allow a full investigation of the event to be carried out. Prior to this event the plant (and indeed the company managing the plant) had not recorded an injury since 2007, and no lost work days since 2003 [10]. The investigation reported that it was a combination of factors that led to such deep injuries to the legs including the employees being too close to the malfunctioning pipes and valve, and a failure to remove the acid soaked lower garments and boots prior to entering the safety shower. The injuries may have been less severe had the employees showered their burns with the neutralising agent Diphoterine® immediately following the incident [12]. Diphoterine® is an amphoteric and chelating solution that can be applied to a chemical burn to help stop the irritating and corrosive actions on the skin. Compared to water it is thought to have an improved rinsing effect and reduces the penetration of tissues due to its hypertonicity [11]. Following on from this incident, all employees at Cristal Global chemical manufacturing plants (including the plant where this incident occurred) now have access to Diphoterine® for use following a chemical burn.

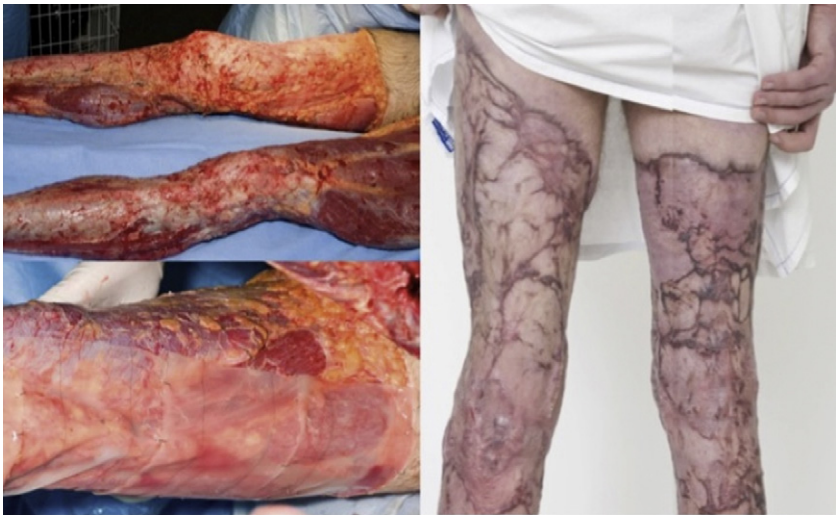


Fig. 9 – Patient 4, 24 h following fascial excision of bilateral lower limb burns and 6 months post-op. Integra was applied to both lower limbs.

5. Conclusion

Mass casualty incidents involving burns can very rapidly overwhelm a burns service. With early involvement of senior clinicians, rapid assessment of the injuries, and prompt communication across health networks, even the most devastating of injuries may be salvaged and lives saved. The use of digital photography was certainly an advantage in this case, and proved an efficient and accurate method of communicating the extent and severity of the injuries. With the help of the multidisciplinary burn care team all of our patients (including the two men who underwent radical excision/amputation were rehabilitated back to their homes and to work. Key to any incident such as this, lessons must be learnt. It is hoped that now employees have access to Diphoterine® on site, any further chemical incidents will result in far less serious injuries requiring far less mutilating surgery.

Conflict of interest statement

The authors have no conflict of interest to declare.

REFERENCES

[1] Pessereau G, Monteil R, Morvan R. Treatment of mass burn casualities. Gaz Med Fr 1964;71:2237–50.

[2] Jordan MH, Hollowed KA, Turner DG, Wang DS, Jeng JC. The Pentagon attack of September 11, 2001: a burn center's experience. J Burn Care Rehabil 2005;26:109–16.

[3] Yurt RW, Bessey PQ, Alden NE, Meisels D, Delaney JJ, Rabbitts A, et al. Burn-injured patients in a disaster: September 11th revisited. J Burn Care Res 2006;27:635–41.

[4] Edgar D, Wood F, Goodwin-Walters A. Maintaining physical therapy standards in an emergency situation: solutions after the Bali bombing disaster. Burns 2005;31:555–7.

[5] Fisher D, Burrow J. The Bali bombings of 12 October, 2002: lessons in disaster management for physicians. Intern Med J 2003;33:125–6.

[6] Palmer DJ, Stephens D, Fisher DA, Spain B, Read DJ, Notaras L. The Bali bombing: the Royal Darwin Hospital response. Med J Aust 2003;179:358–61.

[7] Carresi AL. The 2004 Madrid train bombings: an analysis of pre-hospital management. Disasters 2008;32:41–65.

[8] Satterthwaite PS, Atkinson CJ. Using 'reverse triage' to create hospital surge capacity: Royal Darwin Hospital's response to the Ashmore Reef disaster. Emerg Med J 2010.

[9] Sanford A. Chemical burns. In: Herndon D, editor. 2nd ed., Total burn care, London: Saunders; 2002.

[10] Cristalglobal. Bunbury operations [online]; 2009, Available: www.cristalglobal.com/AboutCristalGlobal_Resources/Bunbury_6_15.pdf [accessed 17.04.11].

[11] Cavallini M, Casati A. A prospective, randomized, blind comparison between saline, calcium gluconate and diphoterine for washing skin acid injuries in rats: effects on substance P and beta-endorphin release. Eur J Anaesthesiol 2004;21:389–92.

[12] Mathieu L, Burgher F, Blomet J. Comparative evaluation 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. J Chem Health Safety 2007.

Report

Diphoterine for alkali chemical splashes to the skin at alumina refineries

A. Michael Donoghue MBChB, MMedSc, PhD

Alcoa of Australia, Perth, WA, Australia

Correspondence
A Michael Donoghue MBChB, MMedSc, PhD
Chief Medical Officer
Alcoa of Australia
Corner of Davy and Marmion Streets
Booragoon
WA 6154
Australia
E-mail:
michael.donoghue@alcoa.com.au

Funding
The implementation and evaluation of Diphoterine described in this paper was funded by Alcoa of Australia.

Conflicts of interest
Dr Donoghue is the Chief Medical Officer of Alcoa of Australia, which operates the refineries at which Diphoterine was implemented, but he has no affiliation or financial involvement with Prevor, the manufacturer of Diphoterine.

Abstract

Background Diphoterine is a commercially available amphoteric, hypertonic, chelating solution used to decontaminate and irrigate chemical splashes. The aim of this study was to evaluate the implementation of Diphoterine at three alumina refineries. This is the largest case series reported to date.

Methods One hundred eighty cases of alkali splashes to the skin were evaluated clinically. Two groups were compared; those who had applied Diphoterine first and those who had applied water first.

Results There were no signs of chemical burn in 52.9% of the group who applied Diphoterine first compared with 21.4% of the group who applied water first. Only 7.9% of the group who applied Diphoterine first had blisters or more severe signs compared with 23.8% of the group who applied water first. The differences were statistically significant ($P < 0.001$). After implementation of Diphoterine the "first aid" injury rate for chemical burns fell 24.7% (95% CI 0.5–43.0%).

Conclusions Applying Diphoterine first was associated with significantly better outcomes following alkali skin splashes than applying water first.

Introduction

Diphoterine is an amphoteric hypertonic chelating solution used to decontaminate and irrigate chemical splashes of the skin and eyes.[1] It was developed in France and is manufactured by Prevor.[2] It has very low toxicity with oral and dermal rat LD_{50}s greater than 2000 mg/kg.[1] It has been shown to have low irritancy and has not caused sensitization in experimental animal studies.[1,3] Diphoterine has been shown in vitro to neutralize acids and bases.[1] It is water soluble.[1]

Diphoterine irrigation of experimental hydrochloric acid skin splashes in rats resulted in better wound outcomes at 7 d compared with irrigation with normal saline or calcium gluconate. Serum concentrations of substance P were lower at 6 and 48 h for rats irrigated with Diphoterine compared with rats irrigated with normal saline or calcium gluconate.[4]

Diphoterine has been reported as giving prompt relief from the eye and skin symptoms induced by CS "Tear gas" in volunteer French Gendarmes.[5]

A case series of 24 workers treated with Diphoterine shortly after chemical splash in a German metallurgical plant reported no sequelae and no further treatment required. There were 11 cases of acid splash to the eyes, 8 cases of acid splash to the skin, 4 cases of alkali splash to the eyes and 1 case of alkali splash to the skin.[6]

A case series of 66 patients presenting to a hospital with alkali splash to the eyes found that Diphoterine treatment resulted in a shorter time to corneal re-epithelialization than did treatment with "physiological solution."[7]

Diphoterine irrigation following alkali application to *ex vivo* rabbit eyes resulted in a greater decline in pH within the anterior chamber than was achieved by irrigation with water, normal saline, or phosphate buffer solution.[8]

Alcoa of Australia operates three alumina refineries in Western Australia at Kwinana, Pinjarra, and Wagerup. These three refineries employ about 3000 people and produce about 13% of the world's alumina. Much of the Bayer alumina refining process involves strong alkali solutions (primarily sodium hydroxide), which have the potential to

cause chemical burns if the skin is splashed. There are many engineering and administrative controls to reduce the likelihood of splashes occurring, but the possibility still exists that they will occur. Therefore, it is important to provide the best first aid available for chemical splashes. Traditionally, this has involved deployment of emergency showers and emergency eyewash stations in close proximity to any areas of risk. Employees and contractors have been trained for many years to respond to skin splashes by immediately removing contaminated clothing and showering for 20 min. All cases are required to report to the onsite medical centers for assessment. All reported skin splashes are logged in Alcoa's Environment Health and Safety Incident Management System (EHSIMS), which triggers a safety investigation and corrective actions. Employees and contractors have been trained to call the plant emergency number for emergency medical response by onsite ambulance if they sustain or witness a large skin splash.

Following review of the published reports in 2003 and discussion with occupational health and safety staff from alumina refineries in the United States and South America, Alcoa of Australia sought approval of Diphoterine by the Therapeutics Goods Administration of the Australian Government. This was granted in December 2005 and the product was imported in 2006. Alcoa of Australia then decided to implement Diphoterine at its three alumina refineries in Western Australia. To evaluate the effectiveness of the program, a clinical case series was undertaken and injury data were interrogated. The objective of the clinical case series was to determine if the clinical severity of chemical burns were any different when Diphoterine was applied first following chemical splash, compared to when water was applied first. This comparison was made possible when the Diphoterine program was introduced because some employees chose to use Diphoterine first, whilst others chose to apply water first. This is the largest clinical case series reported to date. The objective of the injury rate analysis was to determine if there were any differences in the injury rates for chemical burns before and after the introduction of Diphoterine.

Materials and methods

Diphoterine was first applied in Australia for a chemical splash at the Pinjarra alumina refinery on May 11, 2006. Over the ensuing 8 months, all employees and contractors working in the operational areas of all three refineries were trained in the use of Diphoterine and issued with a 100 ml personal aerosol can, belt, and carrying pouch. Employees and contractors were trained to respond to skin splashes by immediately removing contaminated clothing and applying Diphoterine from their personal can. They were instructed to discharge the entire contents of the can and to seek assistance from nearby colleagues if necessary to spray larger splashes with multiple cans. They were specifically advised that there was no need to shower before applying Diphoterine and that they had to shower only if they did not have access to enough Diphoterine to cover the affected skin promptly. The instruction to call the plant emergency number for emergency medical response by onsite ambulance if they sustained or witnessed a large skin splash remained unchanged. The ambulances and medical centers were equipped with 5 l canisters of Diphoterine and a large supply of 100 ml cans. The program became mandatory on February 01, 2007. The clinical case series began on October 01, 2006, and ended on February 29, 2008.

All injuries and specifically any chemical splashes (whether injury occurs or not) are required to be reported to the onsite medical centers and logged in Alcoa's EHSIMS.

Clincal case series

During the clinical case series, all cases reporting the use of Diphoterine for chemical splashes were assessed using a standardized one page form and received conventional treatment for any injury. The assessments were made by emergency response officers, occupational health nurses, or plant physicians in the onsite medical centers. Assessments were made 24 h per day, 7 d per week. For each case, the following data were obtained: date and time of clinical assessment, date and time of chemical splash, name of the chemical and estimated time elapsed before the first application of Diphoterine. The subject was asked if water was also used for irrigation and if so whether this was before or after applying Diphoterine. The person undertaking the clinical assessment was asked to draw on a body surface area diagram, the area of skin that was splashed by the chemical. He/she was also asked to answer yes or no to the following questions:

1 Is there any redness (erythema) of the skin where the chemical splash occurred?
2 Is there any blistering of the skin where the chemical splash occurred?
3 Are there any signs of more severe burns?

The answers to these questions were used to assess the severity of the outcome. Severity was graded 1–4 where 1 indicated no signs of a burn, 2 indicated erythema only, 3 indicated blisters were the most serious sign, and 4 indicated signs of more severe burns.

All of these case details were entered into an Excel file spreadsheet. Where the clinical assessments listed a range for the "Estimated time elapsed before the first application of Diphoterine" the upper bound of the range was selected. For example, if "2–3 min" was stated, a value of 3 min was entered into the spreadsheet. Where "a few minutes" was stated, a value of 5 min was entered into the spreadsheet. When analyzing the data two groups were formed, those who had applied Diphoterine first and those who had applied water first,

before using Diphoterine. The ''Diphoterine first'' group comprised those who had applied water after Diphoterine and those who had said they had not applied water – just Diphoterine. The percentage of body surface area skin splashed by a chemical was estimated visually from the shaded areas on the body surface area diagram. Where a cross was used instead of a shaded area, it was assumed this was a small area and a value of 0.25% body surface area was entered.

Normal clinical follow-up of cases took place depending on the severity of the burns. The study did not attempt to evaluate any possible delayed responses and does not present any clinical assessment data beyond 24 h from the time of the splash.

Environment Health and Safety Incident Management System was interrogated to determine the number of cases reported during the clinical case series timeframe that were potentially eligible to have been studied.

This involved downloading cases using two strategies:

1 All cases with a ''Nature of Injury'' recorded as ''Burn (Chemical)'' that occurred during the timeframe at any of the three refineries were downloaded from EHSIMS into an Excel file. This spreadsheet was then restricted to cases which did not list ''Eye'' as the ''Body part'', and further restricted by deleting ''Deactivated'' cases (i.e., cases not substantiated following investigation). Two cases were removed because the ''Contact Agent'' was acid, not alkali.
2 All cases that occurred during the timeframe at any of the three refineries were downloaded from EHSIMS into an Excel file. This spreadsheet was then restricted to cases which did not list ''Eye'' as the ''Body part'', and further restricted to cases which listed the ''Contact Agent'' as ''Caustic…'' or ''Liquor'' and further restricted to cases which did not list ''Burn (Chemical)'' as the ''Nature of Injury''. This spreadsheet was then reviewed and further restricted to cases which gave a history of a chemical splash to the skin of an employee or contractor in the ''What Occurred'' narrative. There were no deactivated cases to remove from this file.

The two spreadsheets therefore contained any cases that involved employees or contractors in a ''Burn (Chemical)'' to the skin because of an alkali contact agent, or a splash to the skin of any material with the word ''Caustic'' included in the ''Contact Agent'' description or a splash to the skin of ''Liquor''. There was no duplication of cases in these two files.

Injury rate analysis

Environment Health and Safety Incident Management System was also interrogated to establish data for two timeframes, one prior to and one after implementation of Diphoterine. The two timeframes were:

Before: May 01, 2005 to April 30, 2006 inclusive.

After: May 01, 2007 to April 30, 2008 inclusive.

Seasonal effects were controlled by selecting the same dates for different years.

For each of these two timeframes, cases were downloaded from EHSIMS using two strategies similar to those listed above. Specifically:

1 All cases with a ''Nature of Injury'' recorded as ''Burn (Chemical)'' that occurred during the relevant timeframe at any of the three refineries were downloaded from EHSIMS into an Excel file. This spreadsheet was then restricted to cases which did not list ''Eye'' as the ''Body part'', and further restricted to cases involving employees not contractors, and further restricted by deleting ''Deactivated'' cases (i.e., cases not substantiated following investigation).
2 All cases that occurred during the relevant timeframe at any of the three refineries were downloaded from EHSIMS into an Excel file. This spreadsheet was then restricted to cases which did not list ''Eye'' as the ''Body part'', and further restricted to cases involving employees not contractors, and further restricted to cases which listed the ''Contact Agent'' as ''Caustic…'' or ''Liquor'' and further restricted to cases which did not list ''Burn (Chemical)'' as the ''Nature of Injury''. This spreadsheet was then reviewed and further restricted to cases which gave a history of a chemical splash to the skin of an employee in the ''What Occurred'' narrative. There were no deactivated cases to remove from this file.

The two spreadsheets therefore contained any cases that involved employees (not contractors) in a ''Burn (Chemical)'' to the skin because of any contact agent (acid or alkali), or a splash to the skin of any material with the word ''Caustic'' included in the ''Contact Agent'' description or a splash to the skin of ''Liquor.'' There was no duplication of cases in these files. The case data for the before and after analyses came from administrative data and were not derived from the clinical assessments.

Environment Health and Safety Incident Management System was also interrogated to determine the number of hours worked by employees (not contractors) at the three refineries during the relevant timeframes. Contractors were not included in the injury rates analysis because the Alcoa EHSIMS database does not record worker-hours for contractors, only for employees. This lack of ''denominator'' data for contractors meant that it was not possible to calculate injury rates for contractors.

All EHSIMS case types are classified according to the criteria of the US Occupational Safety and Health Administration (OSHA).

Statistical methods

Histograms of the following variables were positively skewed, necessitating the use of nonparametric methods:

1 Time elapsed from the chemical splash to the clinical assessment.
2 Time elapsed from the chemical splash to the application of Diphoterine.

3 Percentage of body surface area splashed by chemical.

For each of these variables the differences between the two groups ("Diphoterine first" and "water first") were assessed by the Mann–Whitney *U* test.

Cross-tabulation of outcome severity by group ("Diphoterine first" and "water first") was undertaken. The difference in the outcome severity categorization by group was assessed using the Chi Square test. Because more than 20% of the cells had expected counts less than 5, severity categories 3 and 4 were amalgamated to resolve this issue.

Injury rate ratios were generated from injury rates calculated for the periods before and after implementation of Diphoterine.

The 95% confidence intervals for the injury rate ratios were derived using the equations of Kirkwood and Sterne.[9] All other statistical analyses were undertaken using SPSS 14.0 (SPSS Inc, Chicago, Illinois, USA).

Results

Clinical case series

In total, 197 cases were studied in the clinical case series. However, 11 cases were removed because the clinical assessment occurred more than 24 h after the chemical splash. In addition, two cases were removed because the chemical was acid not alkali and another three cases were removed because the chemical type was not stated. One case was removed because there was no record of the effects on the skin. Therefore, a total of 17 cases were removed leaving 180.

In total, there were 318 cases that were potentially eligible to have been studied during the clinical case series timeframe of October 01, 2006 to February 29, 2008. These comprised 1 "Lost Work Day" case (LWD), 7 "Restricted Work Day" cases (RWD), 9 "Medical Treatment" cases (MT), 207 "First Aid" cases (FA) and 94 "Injury Free Event" cases (IFE).

Therefore, the clinical case series included 180 out of 318 (56.6%) potentially eligible cases. Figure 1 shows the derivation of the clinical case series study population. It is important to note that potentially eligible cases did not necessarily apply Diphoterine, especially in the first 4 months of the 17 month clinical series when it was not yet mandatory. Consequently, the proportion of eligible cases is probably higher than 56.6%.

Table 1 lists results for the following variables:

1. Time elapsed from the chemical splash to the clinical assessment.
2. Time elapsed from the chemical splash to the application of Diphoterine.
3. Percentage of body surface area splashed by chemical.

The results are listed for the two groups – those who applied Diphoterine first and those who applied water first. There were no statistically significant differences between the groups for time elapsed from the chemical splash to the clinical assessment ($P = 0.496$) or for body surface area splashed by the chemical ($P = 0.233$). As expected, there was a statistically significant difference between the groups for time elapsed from the chemical splash to the application of Diphoterine ($P < 0.001$). More time elapsed for the water first group, because they were, by definition, applying water first. The Diphoterine first group applied Diphoterine within a median time of 1 minute from the time of the chemical splash, whereas the water first group applied Diphoterine within a median time of 5 min from the time of the chemical splash. It is likely that both groups initiated first aid treatment in a similar timeframe, be that Diphoterine first, or water first, because there was a high spatial density of emergency showers throughout the refineries. It is therefore unlikely that there was a meaningful difference between the groups in terms of the length of time that alkali was on the surface of the skin. The median size of chemical splashes was fairly small at about 1%, but some large skin splashes did occur, up to a maximum of 38%.

Table 2 gives the number and percentage of cases in each severity group. There were no signs of a chemical burn in 52.9% of the group who applied Diphoterine first. There were no signs of a chemical burn in only 21.4% of the group who applied water first. Only 7.9% of the group who applied Diphoterine first had blisters or more severe signs. However, 23.8% of the group who applied water first had blisters or more severe signs. The difference in the outcome severity categorization by group was statistically significant ($P < 0.001$).

Injury rate analysis

In the period before implementation of Diphoterine (May 01, 2005 to April 30, 2006 inclusive), there were a total of 140 cases amongst employees (not contractors) comprising 1 MT case, 112 FA cases, and 27 IFE cases. During this period, employees worked 5 944 593 h. Therefore, the total case rate was 4.71 per 200 000 h worked.

In the period after implementation of Diphoterine (May 01, 2007 to April 30, 2008 inclusive), there were a total of 126 cases amongst employees (not contractors) comprising 1 RWD case, 4 MT cases, 88 FA cases, and 33 IFE cases. During this period, employees worked 6 202 230 h. Therefore, the total case rate was 4.06 per 200 000 h worked.

There was therefore a 13.7% reduction in total cases after the implementation of Diphoterine. However, this was not statistically significant. The rate ratio was 0.863 (95% CI 0.678–1.098).

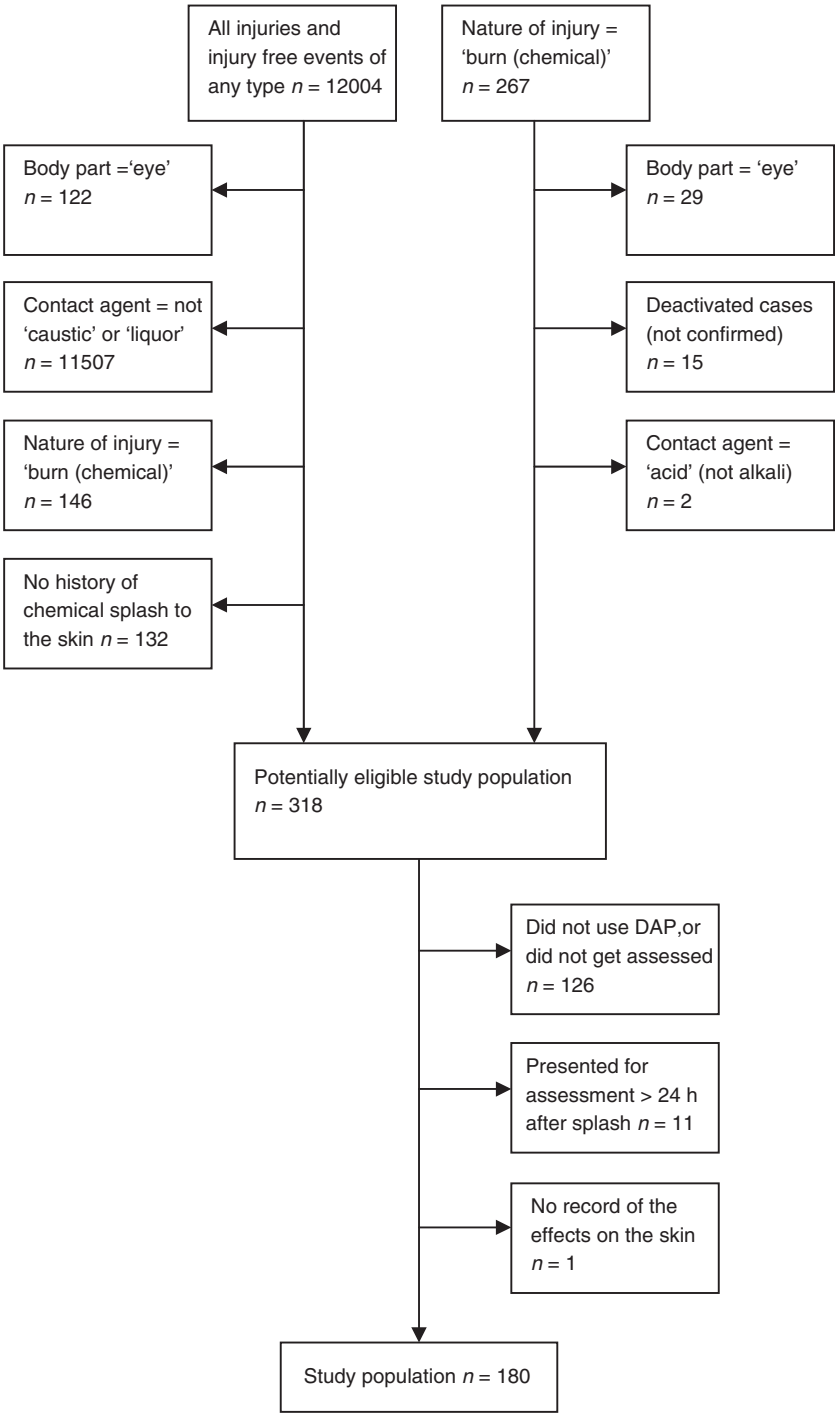


Figure 1 Derivation of clinical case series study population: in the period October 01, 2006 to February 29, 2008. DAP, diphoterine

Table 3 gives the rates and rate ratios for IFE cases, FA cases, and all injuries combined (FA + MT + RWD + LWD). The IFE rate ratio was 1.172 (95% CI 0.706–1.947), indicating a nonstatistically significant increase in IFE cases following implementation of Diphoterine. The FA rate ratio was 0.753 (95% CI 0.570–0.995), indicating a statistically significant decrease in FA cases following implementation of Diphoterine. The all injury rate ratio was 0.789 (95% CI 0.600–1.038), indicating a nonstatistically significant decrease in all injury cases following implementation of Diphoterine. The numbers of MT and RWD cases were too small to calculate confidence intervals. There were no LWD cases.

Table 1 Clinical case variables – for the group that applied DAP first and for the group that applied water first

	Time splash to assessment (min)		Time splash to DAP (min)		Body surface area (%)	
	DAP first	Water first	DAP first	Water first	DAP first	Water first
n	135	41	135	42	138	42
Median	25	30	1.0	5.0	0.75	1.0
Mean	89	66	2.9	11	1.6	2.9
95% CI	45–134	0–135	1.7–4.1	7.0–15	1.1–2.0	0.98–4.8
SD	260	220	6.9	13	2.7	6.2
Range	0–1410	0–1430	0.0–60	0.0–45	0.10–18	0.10–38
P-value	0.496		<0.001		0.233	

DAP, diphoterine.

Table 2 Number of cases (%) in each severity category – for the group that applied DAP first and for the group that applied water first

Severity (associated signs)	DAP first	Water first
1 (no signs)	73 (52.9%)	9 (21.4%)
2 (erythema)	54 (39.1%)	23 (54.8%)
3 (blisters)	10 (7.2%)	8 (19.0%)
4 (more severe)	1 (0.7%)	2 (4.8%)
Total	138 (100%)	42 (100%)

$P < 0.001$ when severity categories 3 and 4 are combined.
DAP, diphoterine.

Comment

The use of Diphoterine first was associated with significantly better outcomes following alkali skin splashes than the use of water first. There were no signs of chemical burn in 52.9% of the group who applied Diphoterine first when compared with 21.4% of the group who applied water first. Only 7.9% of the group who applied Diphoterine first had blisters or more severe signs when compared with 23.8% of the group who applied water first. The difference in the outcome severity categorization by group was statistically significant ($P < 0.001$). It was possible that people confronted with a larger, potentially more serious splash might have tended to use water first, trusting what they were familiar with. However, the difference between the two groups in median percentage body surface area splashed by alkali was small and not statistically significant, making this unlikely. It was also possible that there might have been a difference between the two groups in the time elapsed from the splashes occurring to the clinical assessments being undertaken. This might have resulted in a difference in the observed severity of the burns, with for example; erythema resolving in cases taking longer to present for clinical assessment. However, the difference between the two groups in the time elapsed between the splashes occurring and the clinical assessments being undertaken was small and not statistically significant, making this unlikely. It is important to note that the staff undertaking the clinical assessments were not blinded to the nature of the chemical exposure, or to whether Diphoterine had been used first. This could potentially have introduced bias, although it seems unlikely that this would have resulted in the magnitude of differences in severity outcomes that were observed between the two groups.

Following implementation of Diphoterine, there was a 21.1% decrease in the injury rate from chemical splashes and a 17.2% increase in the IFE rate – for cases where there were no signs of skin damage observed. These changes in rates did not reach statistical significance, however, the 24.7% decrease in the FA rate was statistically significant. These observations are consistent with the better clinical outcomes observed using Diphoterine. It seems most likely that implementing Diphoterine has reduced the severity of chemical burns and has resulted in more cases being registered as IFE cases – where there has been no harm carried out at all. Another possibility is that the renewed focus on chemical burns resulting from

Table 3 Chemical burn injury rates before and after implementation of diphoterine

	IFE		FA		FA + MT + RWD + LWD	
	Before	After	Before	After	Before	After
n	27	33	112	88	113	93
Person-hours	5 944 593	6 202 230	5 944 593	6 202 230	5 944 593	6 202 230
Rate	0.91	1.06	3.77	2.84	3.80	3.00
Rate ratio (95% CI)						
	1.172 (0.706–1.947)		0.753 (0.570–0.995)		0.789 (0.600–1.038)	

IFE, injury free event cases; FA, first aid cases; MT, medical treatment cases; RWD, restricted work day cases; LWD, lost work day cases.

the implementation of Diphoterine has improved behavioral safety, with a reduction in the underlying frequency and severity of splashes. This may have contributed, but the improved clinical outcomes observed in the clinical series are likely to have been an important contributor – and perhaps the main reason for the improvement in injury rate. The possibility that changes in personnel might have affected the injury rates for chemical burns, perhaps because of a lack of experience in the job, is unlikely, given that the percentage of employee turnover during the study period was quite low and stable: 5% in 2005, 6% in 2006, and 7% in 2007 and 2008. There were no significant changes in the refineries processes or work procedures during the study period, which could have affected the injury rates for chemical burns.

There was only one RWD case and no LWD cases in the before and after analyses – showing that although there has been further improvement, there was already effective first aid management in place with no serious cases of skin burn.

The improved outcomes seen with the use of Diphoterine first, suggest we had to reinforce the message to the workforce about the efficacy of Diphoterine and encourage people to have confidence in using Diphoterine first. After decades of using water for irrigation of alkali splashes, it is understandable that some people are reluctant to change.

Acknowledgment

Many thanks to Professor Fiona Wood and Joy Fong of the Burn Service of Western Australia at Royal Perth Hospital for reviewing the clinical assessment form used in this study.

References

1 Hall AH, Blomet J, Mathieu L. Diphoterine for emergent eye/skin chemical splash decontamination: a review. *Vet Hum Toxicol* 2002; **44**: 228–231.
2 Prevor. *France: Chemical Burns - Diphoterine*. Valmondois, France, Prevor. http://www.prevor.com/EN/sante/RisqueChimique/diphoterine/00_diphoterine.php.
3 Mathieu L, Burgher F, Hall AH. Diphoterine chemical splash decontamination solution: skin sensitization study in the guinea pig. *Cutan Ocul Toxicol* 2007; **26**: 181–187.
4 Cavallini M, Casati A. A prospective, randomized, blind comparison between saline, calcium gluconate and diphoterine for washing skin acid injuries in rats: effects on substance P and beta-endorphin release. *Eur J Anaesthesiol* 2004; **21**: 389–392.
5 Viala B, Blomet J, Mathieu L, Hall AH. Prevention of CS "tear gas" eye and skin effects and active decontamination with Diphoterine: preliminary studies in 5 French Gendarmes. *J Emerg Med* 2005; **29**: 5–8.
6 Nehles J, Hall AH, Blomet J, *et al.* Diphoterine for emergent decontamination of skin/eye chemical splashes: 24 cases. *Cutan Ocul Toxicol* 2006; **25**: 249–258.
7 Merle H, Donnio A, Ayeboua L, *et al.* Alkali ocular burns in Martinique (French West Indies) evaluation of the use of an amphoteric solution as the rinsing product. *Burns* 2005; **31**: 205–211.
8 Rihawi S, Frentz M, Schrage NF. Emergency treatment of eye burns: which rinsing solution should we choose? *Graefes Arch Clin Exp Ophthalmol* 2006; **244**: 845–854.
9 Kirkwood BR, Sterne JAC. *Essential Medical Statistics*, 2nd edn. Oxford: Blackwell, 2003: 241–243.

ELSEVIER

Burns 31 (2005) 205–211

BURNS

www.elsevier.com/locate/burns

Alkali ocular burns in Martinique (French West Indies) Evaluation of the use of an amphoteric solution as the rinsing product

Harold Merle[a,*], Angélique Donnio[a], Lucas Ayeboua[a], Franck Michel[b], Félix Thomas[c], Jeannine Ketterle[d], Christian Leonard[d], Patrice Josset[e], Max Gerard[f]

[a]*Service d'Ophtalmologie, Centre Hospitalier Universitaire de Fort de France, Hôpital Pierre Zobda Quitman, BP 632, 97261 Fort de France Cedex, Martinique - France (French West Indies)*

[b]*Pharmacie, Centre Hospitalier Universitaire de Fort de France, Hôpital Pierre Zobda Quitman, BP 632, 97261 Fort de France Cedex, Martinique - France (French West Indies)*

[c]*Sapeurs Pompiers de la Martinique*

[d]*Service des Urgences, Centre Hospitalier Universitaire de Fort de France, Hôpital Pierre Zobda Quitman, BP 632, 97261 Fort de France Cedex, Martinique - France (French West Indies)*

[e]*Laboratoire d'Anatomie Pathologique, Hôpital Armand Trousseau (Assistance Publique/Hôpitaux de Paris), 26 avenue Arnold Netter, 75571 Paris Cedex 12, France*

[f]*Service d'Ophtalmologie, Centre Hospitalier de Cayenne, Rue des Flamboyants, 97300 Cayenne, Guyane Française - France*

Accepted 7 September 2004

Abstract

Precis: During the 4 years of this study, we noted 66 cases of alkali ocular burns, or approximately 16 cases per year, nearly half (45.5%) of which are due to an assault. For grade 1 and 2 burns the time elapsed to reepithelialization appears to be shorter when rinsed with Diphoterine* versus physiological solution.

Purpose: Comparison of the effectiveness of two rinsing solutions for emergency use: a physiological solution and an amphoteric solution (Diphoterine*, Laboratories Prevor, Valmondois, France). Description of the clinical and progressive characteristics of alkali burns treated at the University Hospital Center of Fort de France in Martinique (French West Indies).

Design: Prospective consecutive observational case series and nonrandomized comparative study.

Participants: Sixty-six patients were included. The total number of burned eyes is 104. Forty-eight eyes (46%) were rinsed with physiological solution and 56 eyes (54%) with Diphoterine*.

Methods: All patients benefited from an ocular rinse with 500 ml of physiological solution or Diphoterine*, followed by a complete ophthalmologic exam. The ocular injuries were classified according to the Roper-Hall modification of the Hughes classification system. The same standardized therapeutic protocol was applied and adapted to the seriousness of the burn.

Main outcome measures: Demographic data, time to corneal reepithelialization, final best corrected visual acuity and complications were analysed.

Results: Twenty-eight (42.4%) patients have a unilateral burn and 38 (57.6%) patients have bilateral burns. In decreasing order of frequency, the circumstances surrounding the injury are: assaults in 45.5% of cases ($n = 30$), work-related accidents in 32% of cases ($n = 31$), and domestic accidents in 23% of cases ($n = 15$). For grade 1 and 2 burns the time elapsed to reepithelialization appears to be shorter when rinsed with Diphoterine* versus physiological solution (respectively): 1.9 ± 1 days versus 11.1 ± 1.4 days ($p = 10^{-7}$) and 5.6 ± 4.9 days versus 10 ± 9.2 days ($p = 0.02$). For grade 3 and 4 burns, there are complications in 11 cases (11.6%): 8 corneal opacities and 3 perforations.

* Corresponding author. Tel.: +33 596 55 22 51; fax: +33 596 75 84 47.
E-mail address: harold.merle@chu-fortdefrance.fr (H. Merle).

doi:10.1016/j.burns.2004.09.001

Conclusions: This study is the first conducted in humans that takes into account the type of ocular rinse product used in the progressive follow-up study of injuries. The time elapsed to reepithelialization is shorter with Diphoterine* for grade 1 and 2 burns. There are not enough cases of grade 3 and 4 burns to make a conclusion. Diphoterine* seems very effective in terms of its mechanism of action and the experimental and clinical results.

1. Introduction

Chemical burns represent 7.7–18% of ocular traumas [1,2]. Alkali burns are responsible for serious injuries to the stroma and to the corneal endothelium, iris, and ciliary body. Bases cause the death of epithelial cells through saponification of fatty acids in the cell membrane and also facilitate the penetration of the product into the eye. The most severe injuries are associated with the destruction of limbal stem cells and result in recurring epithelial ulcerations, chronic stromal ulcers, profound stromal neovascularization, conjunctival covering or even corneal perforation [3]. The prognosis of chemical burns depends on the extent of the ocular surface damaged, the degree of intraocular penetration, and the concentration and nature of the agent involved.

Situated in the middle of the arch of the Lesser Antilles at a latitude of 14°36 north and a longitude of 62°34 west, Martinique is an island in the French West Indies. Alkali ocular burns are common among the 381,500 inhabitants of Martinique and are distinct because of the large proportion of assaults and the use of ammonia. Their social and sometimes legal consequences are serious [4]. Medical or surgical treatment of ocular burns are well-documented, but few studies have focused on the comparison between different solutions of ocular rinse in humans. The principal objective of our study is the comparison of the effectiveness of the emergency use of two rinsing solutions: physiological solution and an amphoteric solution, Diphoterine* (Laboratories Prevor, Valmondois, France). The secondary objective is the description of the clinical and progressive characteristics of alkali burns treated at the University Hospital Center of Fort de France in Martinique.

2. Patients and methods

This study was conducted in a prospective manner from January 1, 1998 to December 31, 2001, at the University Hospital Center of Fort de France in Martinique. This public hospital is the largest on the island and receives all of the ophthalmologic emergencies in Martinique. This study obtained a favorable recommendation from the Consultative Committee for the Protection of Persons in Biomedical Research authorized by the French Health Ministry. Patient consent was obtained in writing for each observation. The population studied includes all of the patients who came to the hospital emergency room, either on their own or transported by the emergency services (firemen ...) for an alkali ocular burn. Other etiologies of burns (acids, thermal, plants ...) were excluded. For each patient, we noted the exact nature of the product causing the burn, the circumstances, and the delay between the accident and the first ocular irrigation performed by the victim or by a third party. The delay between the accident and the first action taken at the hospital, which is immediate ocular irrigation, was noted. From January 1, 1998 to December 31, 1999, the immediate ocular irrigation was performed after the instillation of anesthetic eye drops with 500 ml of physiological solution, and from January 1, 2000 to December 31, 2001, with 500 ml of Diphoterine*. Then, a complete ophthalmologic exam was performed and the ocular injuries were classified according to the Roper-Hall modification of the Hughes classification system [5–7] (Table 1). This classification, which includes 4 stages, establishes a prognosis from the initial phase. It is based on the extent of the stromal opacity and possible limbal ischemia. We noted the existence of possible associated palpebral injuries. The time elapsed to corneal reepithelialization was specified, as well as the final best corrected visual acuity and the incidence of complications if applicable. Whichever rinse product used (physiological solution or Diphoterine*) the same therapeutic protocol was applied. For the grade 1 and 2 burns: immediate ocular irrigation, verification of anti-tetanus vaccination, rifamycin drops six times/day, 2% ascorbic acid drops six times/day and tropicamide drops six times/day. The follow-up care for burns of grades 1 and 2 was performed in an outpatient setting. For the grade 3 and 4 burns: immediate ocular irrigation, verification of anti-tetanus vaccination, rifamycin drops six times/day, 2% ascorbic acid drops six times/day, dexamethasone-neomycin drops six times/day for 7 days, 1% atropine drops three times/day, 1 g of oral ascorbic acid three times/day and placement of an antisymblepharon ring. The patients with grade 3 and 4 burns are hospitalized for the follow-up care. The treatment is continued until complete corneal reepithelialization is achieved. When

Table 1
Classification of chemical burns

Grade	Clinical findings
1	Corneal epithelial damage; no ischemia
2	Cornea hazy: iris details visible; ischemia less than one-third at limbus
3	Total loss of corneal epithelium; stromal haze obscures iris details; ischemia of one-third to one-half at limbus
4	Cornea opaque; iris and pupil obscured; ischemia affects more that one-half at limbus

necessary, an analgesic treatment (paracetamol) is prescribed. The progression of the injuries was not carried out blindly and the patient was informed of the nature of the ocular rinse product used. The exploitation of data is carried out in a strictly anonymous, computerized manner. The statistical tests used are: chi-square for the comparison of frequencies, Fisher's exact test (chi-square with Yates correction for small sample size), and Student *t*-test for the comparison of means.

3. Results

Between January 1, 1998 and December 31, 2001, 66 patients were treated in the Ophthalmology Department of the University Hospital Center of Fort de France for alkali ocular burns. Twenty-eight (42.4%) patients have a unilateral burn and 38 (57.6%) patients have bilateral burns. The total number of eyes burned is 104. Table 2 shows the demographic characteristics and the nature of the burn. There are two times as many men as women (45/21). The average age is 38.2 ± 14.8 years. In decreasing order of frequency, the circumstances surrounding the burn are: assaults in 45.5% of cases ($n = 30$), work-related accidents in 32% of cases ($n = 21$) and domestic accidents in 23% of cases ($n = 15$). We note that the number of assaults differs between the first 2 years of the study, with 22 assaults (73% of cases), and the two following years, with 8 assaults (22% of cases). Alkali* is the most commonly used product: 32 cases (48.5%). Alkali* contains 15.3% ammonia and has a pH of 12.8. Javel* is the product in 10 cases (15.1%). Javel* contains 6.8% sodium hypochlorite and has a pH of 11.5. Included in the category of ''others'' are: soda-based cleansers and detergents, lime, and cement. Table 3 displays the overall characteristics of the burns. Forty-eight eyes (46%) were rinsed with physiological solution and 56 eyes (54%) with Diphoterine*. The grade 1 and 2 burns, with 84 cases, represent more than 80% of the cases. Palpebral injuries generally accompany the most serious burns. The grade 3 and 4 burns, 15 eyes (31.3%) are primarily in the group rinsed with physiological solution. The group rinsed with Diphoterine* includes 51 eyes (91%) with grade 1 and 2 burns. In every case, the first ocular irrigation was carried out by the victim with tap water or mineral water. The average delay of this first irrigation is 1 h. The second irrigation performed at the hospital occurs 5 h after the accident. The average time elapsed to corneal reepithelialization is 9 ± 14.2 days. The final visual acuity is on average $20/22 \pm 20/70$. The total number of complications is 12 cases (11.6%): 9 corneal opacities and 3 perforations. Three cases of ocular hypertonicity observed from grade 3 burns were treated by hypotonic eye drops and oral acetazolamide. We did not observe symblepharon, ectropion, or entropion. Table 4 displays the results of the comparison between victims of an assault and victims of a work-related or domestic accidents. In the case of an assault, the victims are most often men, the lesions are bilateral in 22 cases (73.3%), and the product used is Alkali* in 26 cases (86.7%). We find the majority of the most severe burns of grade 3 and 4 in this group of burns by assault: 17 cases (32.7%) compared to only 3 cases (5.8%) of grade 3 burns in the group of work-related or domestic accidents. The time elapsed to reepithelialization is greatest and the final visual acuity lower. The delays between the first rinse and the hospital treatment (second rinse) are longer. Among the 12 complications, 11 cases (21.1%) belong to this group. One case of corneal opacity was observed in the group of work-related or domestic accidents. Table 5 compares the progress of the burns according to product used for the second rinse. For the grade 1 burns: the delays of irrigation differ by 30 min for the first rinse and 1 h for the second. The time elapsed to reepithelialization appears shorter when the second rinse was carried out with Diphoterine*: 1.9 ± 1 days versus 11.1 ± 1.4 days ($p = 10^{-7}$). No complications were observed in the grade 1 burns. For the grade 2 burns, the time elapsed to reepithelialization is also shorter with Diphoterine*: 5.6 ± 4.9 days versus 10 ± 9.2 days ($p = 0.02$). The delay of the first irrigation is practically identical in the two groups but in the Diphoterine* group, the burns were rinsed later ($p = 0.57$ NS). One case of corneal

Table 2
Demographic characteristics and the nature of the burn

	Total ($n = 66$)	Physiological solution ($n = 30$)	Diphoterine* ($n = 36$)	p-value
Male:female ratio	45/21	24/6	21/15	0.06 NS
Mean age (years)	38.2 ± 14.8	37.9 ± 14.7	38.5 ± 15.1	0.87 NS
Bilateral burn	38 (57.6%)	18 (60%)	20 (55.5%)	0.7 NS
Circumstances of the accident				
Assault	30 (45.5%)	22 (73.4%)	8 (22.2%)	0.0001
Work accident	21 (31.8%)	5 (16.6%)	16 (44.4%)	
Domestic accident	15 (22.7%)	3 (10%)	12 (33.4%)	
Nature of the product				
Alkali*	32 (48.5%)	23 (76.7%)	9 (25%)	0.0001
Javel*	10 (15.1%)	3 (10%)	7 (19.4%)	
Autres	24 (36.4%)	4 (13.3%)	20 (55.6%)	

n: number of patients, NS: no significant.

Table 3
Overall characteristics of ocular burns

	Total ($n = 104$)	Physiological solution ($n = 48$)	Diphoterine* ($n = 56$)	p-value
Grade 1	52 (50%)	17 (35.4%)	35 (62.5%)	0.002
Grade 2	32 (30.8%)	16 (33.3%)	16 (28.6%)	
Grade 3	12 (11.5%)	7 (14.6%)	5 (8.9%)	
Grade 4	8 (7.7%)	8 (16.7%)	0	
Eyelid burns	44 (42.3%)	29 (60.4%)	15 (26.8%)	0.0005
Delay of first irrigation (min)	53 ± 142	76.3 ± 177	33 ± 100	0.009
Delay of second irrigation (h)	4.7 ± 7.3	3.5 ± 4.7	5.8 ± 8.9	0.57 NS
Time elapsed to reepithelialization (days)	9 ± 14.2	16.3 ± 18.8	3.7 ± 5	10^{-7}
Final visual acuity	20/22 ± 20/70	20/25 ± 20/70	20/20 ± 20/200	0.01
Complications				
Corneal opacity	9 (8.7%)	7 (14.5%)	2 (3.5%)	0.03
Perforation	3 (2.9%)	2 (4.1%)	1 (1.8%)	

n: number of eyes, NS: no significant.

opacity was observed among the burns rinsed with the physiological solution. For the grade 3 burns, the time elapsed to reepithelialization is also shorter: 20 ± 14.1 days versus 45.2 ± 23 days ($p = 0.21$ NS). Three of the 4 complications appear in the Diphoterine* group. They correspond to three grade 3 burns for which the second rinse was delayed: the 2 opacities of the cornea were rinsed 9 h after the accident and the perforation 12 h after the accident. All the injured eyes of grade 4 burns were rinsed with the physiological solution. The delay of the first irrigation is 263 ± 287 min, the delay of the second irrigation is 5.1 ± 4.3 h, the time elapsed to corneal reepithelialization is 27 days for the uncomplicated case, and the final visual acuity is 2.2 ± 3.1. The number of complications is 7 (87.5%): 5 opacities and 2 perforations of the cornea. In general, the delay of the first rinse carried out by the victim increases according to the seriousness of the burn. It is 18 min for the grade 1 burns and exceeds 4.5 h for the grade 4 burns.

4. Discussion

During the 4 years of this study, we noted 66 cases of alkali ocular burns, or approximately 16 cases per year, nearly half (45.5%) of which are due to an assault. Chemical burns occur for the most part in the context of industrial or domestic accidents. In Germany, 73% of burns are related to occupational accidents and are divided equally between agriculture, chemical, and mechanical industry [8]. In Melbourne, Australia, 71% of accidents are work-related, 23% are domestic accidents, and 2.5% are assaults [9]. The low level of industrialization in Martinique partly explains why only 30% of our observations are related to a workplace accident. Our proportion of assaults is significant and unusual. However, since 1976, Klein, then Beare in 1990, show the predominance of ocular burns by assault within certain socioeconomic settings. As in our study, the victim is most often a man, the assailant a woman, and the assault takes place in the home of the victim during a domestic

Table 4
Comparison of burns by assault and by occupational or domestic accidents

	Assault (30 patients)	Occupational and domestic accidents (36 patients)	p-value
Male:female ratio	4/26	19/17	0.003
Mean age (years)	37.6 ± 15	38.8 ± 14.7	0.7 NS
Bilateral burn	22 (73.3%)	16 (44.4%)	0.02
Alkali*	26 (86.7%)	6 (16.6%)	10^{-7}
Javel*	1 (3.3%)	9 (25%)	
Others	3 (10%)	21 (58.4%)	
	Assault (52 eyes)	Occupational and domestic accidents (52 eyes)	p-value
Grade 1	17 (32.7%)	35 (67.3%)	0.00005
Grade 2	18 (34.6%)	14 (26.9%)	
Grade 3	9 (17.3%)	3 (5.8%)	
Grade 4	8 (15.4%)	0	
Delay of first irrigation (min)	97.8 ± 189	8.2 ± 25	10^{-6}
Delay of second irrigation (h)	5.6 ± 7.4	3.9 ± 7.3	0.01
Time elapsed to reepithelialization (days)	11.7 ± 15.8	6.9 ± 12.5	0.0003
Final visual acuity	20/25 ± 20/70	20/22 ± 20/125	0.003
Corneal opacity	8 (15.4%)	1 (1.9%)	0.009
Perforation	3 (5.7%)	0	

NS: no significant.

Table 5
Characteristics of grade 1, 2 and 3 burns

	Total ($n = 52$)	Physiological solution ($n = 17$)	Diphoterine* ($n = 35$)	p-value
Grade 1				
Delay of first irrigation (min)	18.5 ± 51	25.6 ± 58	15 ± 48	0.49 NS
Delay of second irrigation (h)	3.2 ± 6	2.6 ± 3.6	3.4 ± 6.9	0.85 NS
Time elapsed to reepithelialization (days)	4.9 ± 9	11.1 ± 1.4	1.9 ± 1	10^{-7}
Final visual acuity	20/20 ± 20/200	20/20 ± 20/100	20/20 ± 20/250	0.74 NS
Corneal opacity	0	0	0	–
Perforation	0	0	0	–
	Total ($n = 32$)	Physiological solution ($n = 16$)	Diphoterine* ($n = 16$)	
Grade 2				
Delay of first irrigation (min)	19.8 ± 52	17.3 ± 45	22.2 ± 60	0.79 NS
Delay of second irrigation (h)	6.9 ± 9.9	3.6 ± 6.1	10.2 ± 11.9	0.57 NS
Time elapsed to reepithelialization (days)	7.7 ± 7.5	10 ± 9.2	5.6 ± 4.9	0.02
Final visual acuity	20/22 ± 20/100	20/22 ± 20/80	20/20 ± 20/200	0.83 NS
Corneal opacity	1 (3.1%)	1 (6.2%)	0	0.5 NS
Perforation	0	0	0	–
	Total ($n = 12$)	Physiological solution ($n = 7$)	Diphoterine* ($n = 5$)	
Grade 3				
Delay of first irrigation (min)	150 ± 254	120 ± 264	193 ± 262	0.64 NS
Delay of second irrigation (h)	5.5 ± 4.9	3.1 ± 4.1	8.8 ± 4.1	0.04
Time elapsed to reepithelialization (days)	38.9 ± 23	45.2 ± 23	20 ± 14.1	0.21 NS
Final visual acuity	20/28 ± 20/70	20/28 ± 20/50	20/28 ± 20/70	0.8 NS
Corneal opacity	3 (25%)	1 (14.3%)	2 (40%)	0.21 NS
Perforation	1 (8.3%)	0	1 (20%)	

n: number of eyes, NS: no significant.

dispute [10,11]. In Jamaica, a neighboring island of Martinique, between 1981 and 1990, 562 chemical burns were treated in the hospitals: 13.3% were related to an assault. This proportion exceeds two-thirds in certain urban areas with a significant population density and a low social and economic status. The burns are mainly located at the level of the face; the eyes and the eyelids are injured in 19% of cases. In Jamaica, as in Hong Kong, the intention of the assailant is to disfigure his victim [12,13]. In Martinique, the product used by the assailant is Alkali* sold in a plastic bottle containing 15.3% ammonia and a pH of 12.8. The bottle is compressible, easy to open, and lacking a safety device. Alkali* is used as both a household cleaning product and as a purifier: when one takes possession of a house or when chasing bad spirits from the victim. Ammonia is also used in Africa. Ukponmwan reports 12 cases of ocular burns in Benin City, Nigeria, which has similar demographic characteristics to ours: all the victims are men, 10 cases result from an assault, and the number of complications appears more significant taking into account the delay of medical treatment [14]. One-fourth of the burns by work-related or domestic accidents are related to the handling of Javel*. This product is sold in a completely deformable soft plastic carton, without a security system for opening. This type of packaging is not absolutely adapted to the danger of the contents as Pouliquen had already shown in 1972 [15].

Three cases of corneal perforations were noted. The incidence of this complication is probably related to the quantity of the product exposed to the eye but also with the duration of contact between the product and the ocular surface; actually the first rinse was carried out at 5 min, 3 h, and 12 h, and the second rinse, respectively at: 12 h with physiological solution, 3 h with physiological solution, and 12 h with Diphoterine*. Local corticoids could also be incriminated because their use in the treatment of chemical burns is controversial. In decreasing the keratocyte migration, they inhibit collagen synthesis and delay scarring. However, they decrease stromal invasion by polynuclear neutrophils, possess an anti-collagenase action and limit the accumulation of stromal edema [16–18]. Donshik showed in the rabbit that the intensive use of local corticoids in the first week after the burn does not lead to a greater risk of corneal perforation [19]. In association with local and oral ascorbic acid, Davis suggests that local corticoids can be prescribed beyond the 8 days with a beneficial effect [20]. Corticoids favor infections, but we did not observe any infection during the use of treatment.

Diphoterine* is an external rinse solution of the skin and eye. It is a medical device under the European directive 93/42CEE, with the marking CE obtained on September 30, 1996. It has been used for several years in industry and by the Paris fire department. In the event of an accident, it has proven to be very effective in reducing the number of work days missed [21,22]. This is the first human study that takes into account the type of ocular rinse product in the progressive follow-up study of injuries. Forty-eight eyes were rinsed with physiological solution and 56 eyes with Diphoterine*. The time elapsed to reepithelialization is

shorter with Diphoterine* than with physiological solution: for grade 1 burns: 1.9 ± 1 day versus 11.1 ± 1.4 days, for grade 2 burns: 5.6 ± 4.9 days versus 10 ± 9.2 days and for grade 3 burns: 20 ± 14.1 days versus 45.2 ± 23 days. These results obtained with Diphoterine* are similar to those noted by Brodovsky in a retrospective study that included 177 burned eyes: from 2.5 to 4 days for grade 1 burns, from 5.4 to 7.7 for grade 2 burns, and from 10 to 19 days for grade 3 burns. In this study, a proportion of the patients benefited from a standardized therapeutic protocol including local corticoids, antibiotics, ascorbate and citrate, but the nature of the rinse liquid used for the medical treatment was not specified [9]. Diphoterine* is a solution containing a molecule that is multisite, amphoteric, and chelatic. Amphoteres, like ethylene-diamine-tetraacetate (EDTA), act by the capture of ions and neutralization by an amphophilic reaction. They can bind with acids or bases without altering the pH of the environment and without undergoing exothermic reaction. Diphoterine* possesses sites of chelation for acids with a pK_1 of 5.1 and for bases with a pK_2 of 9.3, its pH is 7.4, and its osmolarity 820 mosm/l. Diphoterine* is hypertonic and creates a movement of water from the hypotonic anterior chamber towards the surface of the hypertonic cornea. The OH^- ions migrate to the exterior of the ocular globe by this movement [21]. Several studies carried out in animals have compared Diphoterine* to the physiological solution as a rinse product in alkali burns. A rinse with Diphoterine* leads to a quicker return to normal extra-ocular pH, a lesser ascension as well as a slight drop, and faster and steeper descent of the intraocular pH curve. Epithelial necrosis was observed for all the burns; on the other hand, the stromal edema is much less significant with Diphoterine*. This edema is related to an impairment of endothelial cells. They are destroyed or greatly altered by the physiological solution, but only present a few morphologic variations with Diphoterine* [21,23–27]. Initial stromal edema is a pejorative factor: Kubota showed that its extent would actually correlate to the size of the consequently scarred corneal opacity [28]. In the observation of a grade 4 alkali burn reported by Gerard, irrigation with Diphoterine* would immediately manifest as a reduction of the corneal edema, objectified by an increase in the visual acuity [16]. In the course of all these studies, no harmful effects of Diphoterine* have been shown. A serious chemical burn often leads to a functional or even anatomical loss of the eye. The emergency treatment proposed long ago is to rinse by water or better yet by isotonic solutions of physiological solution with the goal of eliminating a maximum amount of the toxic agent but without any demonstration of intrinsic pharmacologic effectiveness. Diphoterine* seems very effective in terms of its mechanism of action and the experimental results obtained. Compared to the physiological solution, the healing time of corneal scarring from grade 1 and 2 burns is shorter with Diphoterine*. For grade 3 and 4 burns, there are not enough cases to judge the effectiveness of rinse with Diphoterine*. Our study shows that the longer the delay between the accident and the rinse, the more serious the burn. The establishment of a standardized protocol in advising the susceptible workforce to seek treatment in emergencies of chemical ocular burns will contribute to reduce this delay.

References

[1] Pfister RR. Chemical injuries of the eye. Ophthalmology 1983;90:1246–53.
[2] Liggett P. Ocular trauma in an urban population. Ophthalmology 1989;97:581–4.
[3] Tseng SC. Concepts and application of limbal stem cells. Eye 1989;3:141–57.
[4] Gérard M, Merle H, Ayéboua L, Richer R. Etude prospective sur les brûlures par bases au CHU de Fort de France. J Fr Ophtalmol 1999;22:834–47.
[5] Hughes WF. Alkali burns of the cornea. I. Rewiew of the literature and summary of present knowledge. Arch Ophthalmol 1946;35:423–36.
[6] Hughes WF. Alkali burns of the cornea. II. Clinical and pathologic course. Arch Ophthalmol 1946;36:189–214.
[7] Roper-Hall MJ. Thermal and chemical burns of the eye. Trans Ophthalmol Soc UK 1965;85:631–46.
[8] Kuckelkorn R, Makropoulos W, Kottek A, Reim M. Retrospektive betrachtung von schweren alkaliverätzungen der Augen. Klin Monatsbl Augenheilkd 1993;203:397–402.
[9] Brodovsky SC, McCarty CA, Snibson G, Loughnan M, Sullivan L, Daniell M, et al. Management of alkali burns. An 11-year retrospective review. Ophthalmology 2000;107:1829–35.
[10] Klein R, Lobes LA. Ocular alkali burns in a large urban area. Ann Ophthalmol 1976;8:1185–9.
[11] Beare JDL. Eye injuries from assault with chemicals. Br J Ophthalmol 1990;74:514–8.
[12] Branday J, Arscott GDL. Smoot EC, Williams GD, Fletcher PR. Chemical burns as assault injuries in Jamaica. Burns 1996;22:154–5.
[13] Young RC, Ho WS, Burd YA. Chemical assaults in Hong Kong: a 10-year review. Burns 2002;28:651–3.
[14] Ukponmwan CU. Chemical injuries to the eye in Benin City, Nigeria. W Afr J Med 2000;19:71–6.
[15] Pouliquen Y. Les brûlures de la cornée. Clin Ophtalmol 1972;5:21.
[16] Gérard M, Merle H, Chiambaretta F, Rigal D, Schrage N. An amphoteric rince used in the emergency treatment of a serious ocular burn. Burns 2002;7:670–3.
[17] Brent BD, Karcioglu ZA. Effect of topical corticosteroids on goblet-cell density in an alkali-burn model. Ann Ophthalmol 1991;23:221–3.
[18] Chung JH, Kang YG, Kim HJ. Effects of 0.1% dexamethasone on epithelial healing in experimental corneal alkali wounds: morphological changes during the repair process. Graefes Arch Clin Exp Ophthalmol 1998;236:537–45.
[19] Donshik PC, Berman MB, Dohlman CH, Gage J, Rose J. Effect of topical corticosteroids on ulceration in alkali-burned corneas. Arch Ophthalmol 1978;96:117–21.
[20] Davis AR, Ali QH, Aclimandos WA, Hunter PA. Topical steroid use in treatment of ocular alkali burns. Br J Ophthalmol 1997;81:732–4.
[21] Hall AH, Blomet J, Mathieu L. Diphotérine for emergent eye/skin chemical splash decontamination:a review. Vet Human Toxicol 2002;44:228–31.
[22] Falcy M, Blomet J. Evaluation de l'efficacité des premiers soins lors de projections de produits chimiques. Institut national de Recherche et de Sécurité. Documents pour la Médecine du Travail 1993;53:137–46.
[23] Gérard M, Josset P, Louis V, Ménérath JM, Blomet J, Merle H. Existe-il un délai pour le lavage oculaire externe dans le traitement d'une brûlure oculaire par l'ammoniaque? Comparaison de deux solutions

de lavage:sérum physiologique et Diphotérine* J Fr Ophtalmol 2000;5:449–58.

[24] Josset P, Pelosse B, Blomet J, Saraux H. Intérêt d'une solution isotonique amphotère dans le traitement précoce des brûlures chimiques basiques cornéo-conjonctivales. Bull Soc Ophthalmol Fr 1986;6–7:765–9.

[25] Kompa S, Schareck B, Tympner J, Wüstemeyer H, Schrage NF. Comparison of emergency eye-wash products in burned porcine eyes. Graefe's Arch Clin Exp Ophthalmol 2002;240:308–13.

[26] Kuckelkorn R, Schrage NF, Keller G, Redbrake C. Emergency treatment of chemical and thermal eye burns. Acta Ophthalmol Scand 2002;80:4–10.

[27] Schrage NF, Kompa S, Haller W, Langefeld S. Use of an amphoteric lavage solution for emergency treatment of eye burns. First animal type experimental clinical considerations. Burns 2002;28:782–6.

[28] Kubota M, Fagerholm P. Corneal alkali burn in the rabbit. Water-balance, healing and transparency. Acta Ophthalmol Scand 1991;69:635–40.

ELSEVIER

Burns 28 (2002) 670–673

BURNS

www.elsevier.com/locate/burns

An amphoteric rinse used in the emergency treatment of a serious ocular burn

Max Gerard [a,*], Harold Merle [b,1], Frédérick Chiambaretta [c,2], Danièle Rigal [c,3], Norbert Schrage [d]

[a] *Service d'Ophtalmologie, Centre Hospitalier de Cayenne, Rue des Flamboyants, 97300 Cayenne, Guyane Française, France*
[b] *Service d'Ophtalmologie, Centre Hospitalier Universitaire de Fort de France, Hôpital Pierre Zobda Quitman, BP 632, 97261 Fort de France Cedex, France*
[c] *Service d'Ophtalmologie, Centre Hospitalier Universitaire de Clermont Ferrand, Hôpital Gabriel Montpied, Rue Montalembert, BP 69, 63003 Clermont Ferrand Cedex, France*
[d] *Labor der Augenklinik RWTH, PauwelsstraBe 30, D-52057 Aachen, France*

1. Introduction

Serious eyes burns represent extreme problems in the treatment and rehabilitation of victims. Although progress has been made in the general understanding of eye burns [1], the inflammatory response to eye injury [2], electrolyte shifts [3], understanding neurobiological mechanisms [4] and major improvements in treatment by the use of limbal grafts [5], the best treatment of eye burns is to avoid progression of the damage. Experimental research has shown the correlation between the concentration, time and the type of chemical exposure, and the clinical prognosis, in rela-tion to parameters such as rate of change in intraocular pH [6–12]. This gives a rough estimate of the seriousness of the burn. In contrast to these results clinical experience shows that delay in treatment of eye burns carries serious prognostic implications. This report is part of our prospective study in Martinique [13] that shows that in the eyes burnt with ammonia (Alcali®: ammonia 15.3%, pH: 12.8) a delay of more than 30 min before treatment will result in a serious eye burn. Early rinsing is essential to limit to a considerable extent the severity of eye burns.

The development of a new external rinsing solution using an amphoteric agent such as Diphoterine® which can capture both base and acid in contrast to conventional buffers or electrolytic solutions, has potential to improve the clinical outcombe of eye burns. Diphoterine® has been shown to be effective in vitro and in vivo experiments [10–12] and in occupational medicine [13], where the time to rinsing was shorter than 10 min. Nevertheless, our own experimental work has presented histological evidence of the reduction of corneal edema even after a delayed rins-ing with Diphoterine® up to 30 min following the accident [10]. This corneal stromal edema is highly correlated with the development of corneal scars [14]. In this to report we present a case of serious eye burns (grade IV of Ropper Hall's classification) healed by a simple conservative therapeutic regimen, preceded by an initial rinsing with 1 l of Diphoterine®, 1 h after the accident.

2. Case report

A 49-year-old woman, social assistant, was attacked with a chemical product which was thrown onto her face and eyes on 19 August 1999. She was driven to the Ophthalmolog-ical Service. The immediate eye examination showed a se-rious burn to the right eye. The visual acuity was 2/20, the cornea was opaque. As a consequence, the iris was hardly distinguishable. The limbus showed a conjuctival and lim-bal ischemia throughout 360°, with scleral necrosis on the infero-nasal region. The corneal epithelium was completely removed. An immediate eye rinse was started 1 h after the accident. One liter of Diphoterine® was used. The rinsing was enhanced by instillation of local anaesthesia with oxy-buprocaïne eye drops. Further treatment consisted of instil-lation of two drops of a combination of dexamethasone and neomycin. An immediate anterior chamber puncture was made following the rinse and the lacrymal duct was cleaned by a direct rinsing. The eye was examined a second time. An eye burn grade IV of Roper Hall's classification was con-firmed (Figs. 1 and 2). A slight decrease of the corneal edema

* Corresponding author. Tel.: +33-594-39-53-32; fax: +33-594-30-52-50.
[1] Tel.: +33-596-55-22-57.
[2] Tel.: +33-473-62-57-16.
[3] Tel.: +33-473-62-57-16.

PII: S0305-4179(02)00094-3

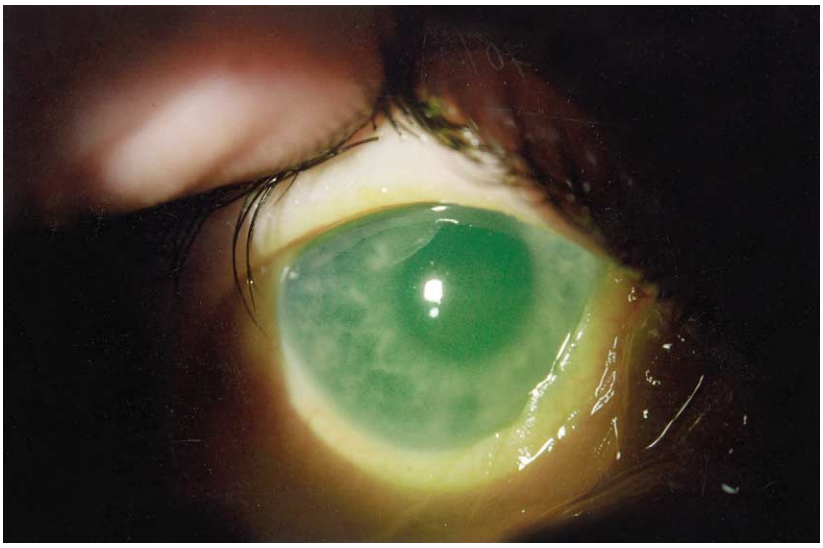


Fig. 1. Initial examination of the right eye after the rinsing by Diphoterine® (1 h after accident): importance of stromal oedema.

was noticed. The visual acuity was then 0.3. We continued with dexamethasone–neomycin eye drops every 20 min during 3 h more. The subsequent therapy regimen consisted of dexamethasone–neomycin eye drops, indomethacin 0.01%, rifamycin, gentamycin and ascorbate eye drops six times per day. This medication was complemented with high doses of oral ascorbate (3 g per day). To obtain cycloplegia, we administered atropine 1%, two drops a day. An antisymblepharon ring was placed immediately. Progression to healing with a progressive re-epithelialization took place within 21 days. The corneal surface was irregular and showed a punctuate keratopathy pattern. An infero-nasal stromal edema persisted. The visual acuity obtained was 4/20. We stopped the local antibiotic and removed the antisymblepharon ring. Tear substitutes with carbomere and vitamin A ointment and drops were used. On day 35, we noticed a corneal infero-nasal ulcer. The local corticosteroid was stopped and antibiotic treatment with rifamycin restarted. After this 5% acetyl cysteine eye drops were used. The ulcer increased its size and the stroma edema enlarged. New vessels appeared on this site. At this point, local corticosteroid administration was started again using fluorometholone six times a day. On day 42, we noticed a decrease of the stromal edema and ulcer size. On day 56, the rifamycin eye drops were stopped when an orange impregnation of the corneal stroma was seen. Tobramycin was substituted in place of the rifamycin. Vitamin C eye drops were stopped when the patient complained about pain due to there use. The cornea was fluorescein stain

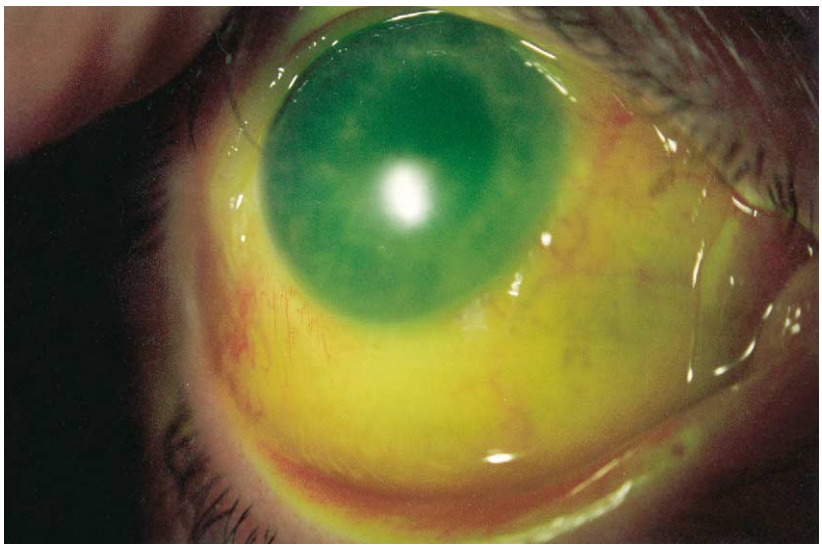


Fig. 2. Initial examination of the right eye after the rinsing by Diphoterine® (1 h after accident): conjunctival and limbal ischemia 360°; scleral necrosis on the infero-nasal region.

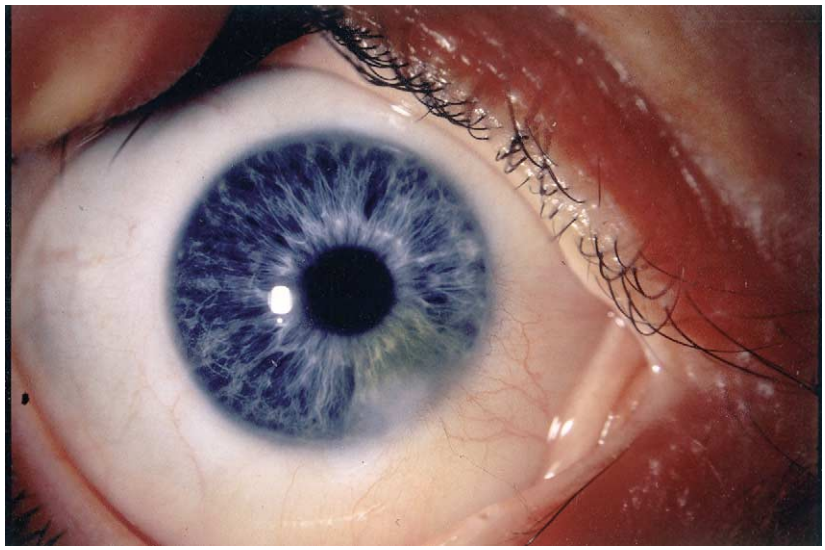


Fig. 3. Final examination of the right eye: total re-epithelialization of the cornea; stable neovascularization in the infero-nasal region; visual acuity: 14/20.

negative and non-edematous since day 97. The visual acuity obtained was 20/40. Topical corticoids were discontinued and local tear substitutes and vitamin A oinment were prescribed. In the infero-nasal region, the neovascularisation was replaced by a conjunctivalization which progressed to day 180, and is now stable (Fig. 3). The visual acuity is currently 14/20. The other eye had a less serious burns with a punctuate keratopathy within the interpalpebral region.

3. Discussion

This report presents a clinical case of a serious chemi-cal ocular burn which healed with conservative treatment. Among the numerous factors involved in this healing, its seems important for us to underline the initial ocular external rinsing with Diphoterine®. In fact, it is quite unusual for such serious burns to heal, and in extremely serious cases, the healing is generally associated with sequelae. The treatment may involve several surgical procedures. The relevance of the rinsing with Diphoterine® was proved by in vitro and in vivo experiments [10–12], which showed a return to a physiological pH a few minutes after its use. Clinical human data [13] obtained on workers in the chemical industry also showed the relevance of ocular rinsing in the first minutes following the chemical splashes: the losses of days of work is diminished thanks to use of Diphoterine® [13].

Diphoterine® is an amphoteric solution, hypertonic to the anterior chamber of the eye. An amphoteric molecule is a molecule which is able to bind a base as well as an acid. So, Diphoterine® can bind both acids and bases and, thanks to its hypertonicity, it can create a flow of water from the hypotonic anterior chamber to the external surface of the hypertonic cornea. This flow of liquid induces the outflow of the H^+ and OH^- ions. The, Diphoterine® will bind H^+ and OH^- ions. This is a very simple approach to the mechanism explaining the efficacy of Diphoterine®. Other mechanisms, which will be evaluated in further experiments, seem to play a role to explain especially its capacity to remove H^+ and OH^- ions from the anterior chamber. But from an experimental point of view, the return to a physiological pH, proof of the ocular extraction of the chemical product, occurs only if the rinsing is made in the first minutes following the chemical splash. Our experimental study showed interesting anatomopathological results [10]. So, the presence of a stromal oedema in the experiments without rinsing or with a rinsing by a 0.9% saline solution is quite remarkable as no edema was observed after rinsing with Diphoterine®. We can note that for our patient, the corneal oedema decreased after rinsing with Diphotérine®. Stromal oedema is a negative factor as Kubota and Fagerholm [14] showed that the degree of this initial oedema is correlated with intensity of the resultant leucoma, responsible for the decrease of the visual acuity. These authors explain that the stromal blank thus created by the odema will be colonized by keratinocytes. These cells will then form an anarchic net of collagen fibers which are responsible for the decrease of the transparency of the cornea.

After the decrease of the amount of the chemical prod-uct in the eye, the second important factor in the treatment of a chemical burn is the fight against stromal invasion by inflammatory cells. Stromal invasion by polymorphonuclear cells (neutrophils) was observed experimentally 2 h after the chemical splash. Two peaks of invasion were seen: the first peak occurred after 12–24 h, while a second peak occurred around day 21 with a beginning on day 12 [15]. For this reason strong doses of dexamethasone were given topically to continue to counteract the stromal oedema. The use of topical corticoids on an ulcer was discussed as they could slow down the wound healing. But experimental studies

[16] and then clinical studies [17] demonstrated the lack of deleterious effects in this pathology. Finally, it is neces-sary to give to the cornea the possibility to heal. This heal-ing progresses through re-epithelialization of the cornea, as shown in our case report. Two factors are fundamental in this re-epithelialization: a good quality of stroma to act as a framework and a proliferative capacity in the epithelium. The first point is fundamental, so it is necessary to counter-act stromal oedema, which is why corticoids are relevant, even if used at a certain time after from the burn, as shown in our case. It is also necessary to give strong doses of vitamin C because of its assisting role in collagen synthesis [18–20]. The other factors involve the limbal stem cells and a partic-ularly important influences is the density of the stem cells found in each unit of the corneal circumference. The recur-rent inferior nasal ulcer seen in our case can be explained by the fact that the burn, more serious on this level, induced necrosis of the large part of these limbal stem cells. Wound healing in this area will involve only a moderate conjuncti-valization. It is also necessary to help this epithelialization providing lachrymal substitutes (the victim of this type of burn develops a lachrymal deficiency) and vitamin A eye lotion. Finally, our case report demonstrates the interest of placing anti-symblepharon rings to prevent or decrease the importance of the symblepharon which usually happens af-ter such a serious burn.

4. Conclusion

Our clinical case demonstrates that a well-conducted ther-apeutical protocol can sometimes heal a serious ocular chem-ical burn. Nevertheless, the prognosis for such burns remains dependent on the delay before intervention and more par-ticularly on the rapidity and efficiencies of the external oc-ular rinse. Among the different rinsing solutions available, Diphoterine® seems to be valuable even after a longer delay of more than 10 min.

Acknowledgements

Conflict of interest: no financial support for this case study was received for any source.

References

[1] Burns FR, Paterson CA. Chemical injuries: mechanisms of corneal damage and repair. In: Beuerman RW, Crosson CE, Kaufman HE, editors. Healing processes in the cornea. Advances in applied biotechnology series, vol. 1. Houston: Gulf Publishing Co., 1989. p. 45–58.

[2] Grant WM. Experimental investigation of parenthesis in the treatment of ocular ammonia burns. Arch Ophthalmol 1950;44:399–404.

[3] Siegrist A. Konzentrierte Alkali und Säurewirkung auf Auge. Ztschr F Augenh 1920;43:176–94.

[4] Paterson CA, Pfister RR, Levinson RA. Aqueous humor pH changes after experimental alkali burns. Am J Ophtalmol 1975;79:414–9.

[5] Tseng SCG, Tsai JF. Limbal transplantation for ocular surface reconstruction. A review. Fortschr Ophthalmol 1991;88:236–42.

[6] Hugues Jr WF. Alkali burn of the eye. Clinical and pathological course. Arch Ophthalmol 1946;36:189–214.

[7] Hugues Jr WF. Alkali burns of the eye. Review of literature and summary of present knowledge. Arch Ophthalmol 1946;35:423–49.

[8] Gérard M, Louis V, Merle H, Josset P, Menerath JM, Blomet J. Etude expérimentale sur la pénétration intra-oculaire de l'ammoniaque. J Fr Ophtalmol 1999;22(10):1047–53.

[9] Gérard M, Merle H, Ayeboua L, Richer R. Etude prospective des brûlures oculaires par bases au CHU de Fort de France. J Fr Ophthalmol 1999;22(8):834–47.

[10] Gérard M, Josset P, Louis V, Menerath JM, Blomet J, Merle H. Existe-il un délai pour le lavage oculaire externe dans le traitement d'une brûlure oculaire par l'ammoniaque? Comparaison de deux solutions de lavage: sérum physiologique et Diphotérine®. J Fr Ophtalmol 2000;23(5):449–58.

[11] Schrage N, Flick S, Aschrenbrenner W, Reim A, et al. Rinsing therapy in severe alkali burns of rabbit eye. Vision Res 1996;(Suppl 1).

[12] Josset P, Pelosse B, Saraux H. Intérêt d'une solution isotonique amphotère dans le traitement précoce des brûlures chimiques basiques cornéosclérales. Bull Soc Ophtalmol Fr 1986;6/7:765.

[13] Falcy M, Blomet J. Evaluation de l'efficacité des premiers soins lors de projections de produits chimiques, Document pour le médecin du travail. INRS 70:2.

[14] Kubota M, Fagerholm P. Corneal alkali burn in the rabbit. Waterbalance healing, and transparency. Acta Ophthalmol 1991;69: 635–40.

[15] Paterson CA, Williams RN, Parker AV. Characteristics of poly-morphonuclear leukocyte infiltration into the alkali burned eye and the influence of sodium citrate. Exp Eye Res 1984;39:701–8.

[16] Donshik PC, Berman MB, Dohlman Ch, Gage J, Rose J. Effect of topical corticosteoïds on ulceration in alkali burned cornea. Arch Ophthalmol 1978;96:117–21.

[17] Davis AR, Ali QK, Aclimandos WA, Hunter PA. Topical steroïd use in treatment ocular alkali burns. Br J Ophthalmol 1997;81(9):732–4.

[18] Levinson R, Paterson CA, Pfister RR. Ascorbic acid prevents corneal ulceration and perforation following experimental alkali-burns. Invest Ophthalmol 1976;15:986–93.

[19] Petroutsos G, Pouliquen Y. Effet de l'acide ascorbique sur l'ulcération dans les brûlures alcalines de la cornée. Ophthalmic Res 1984:185–9.

[20] Pfister RR, Paterson CA. Additional clinical and morphological observations on the favorable effect of ascorbate in experimental ocular burns. Invest Ophthalmol Vision Sci 1977;16:478–87.

AN IMPROVED METHOD FOR EMERGENT DECONTAMINATION OF OCULAR AND DERMAL HYDROFLUORIC ACID SPLASHES

K SODERBERG, P KUUSINEN, L MATHIEU, AH HALL

Reprinted from **Veterinary and Human Toxicology**, Vol. 46, No. 4, August 2004, pp. 216-218

An Improved Method for Emergent Decontamination of Ocular and Dermal Hydrofluoric Acid Splashes*

Kjell Soderberg MD
Medical Service, Avesta Polarit, Torshalla, Sweden

Petri Kuusinen
Health and Safety Group, Avesta Polarit, Torshalla, Sweden

Laurence Mathieu PhD
Laboratoire PREVOR, Moulin de Verville, F95760, Valmondois, France

Alan H Hall MD
Toxicology Consulting and Medical Translating Services, Elk Mountain, Wyoming 82324

ABSTRACT. Accidental hydrofluoric acid (HF) splashes often occur in industrial settings. HF easily penetrates into tissues by initial acid action allowing fluoride ions to penetrate deeply, chelating calcium and magnesium. Resultant hypocalcemia and hypomagnesemia can be fatal. This report describes the utilization of Hexafluorine® — a hypertonic, amphoteric, chelating decontamination solution — in workplaces where water decontamination followed by calcium gluconate inunction failed to prevent HF burns and systemic toxicity. Between 1998 and 1999, 16 cases of ocular and dermal HF splashes with either 70% HF or 6% HF/15% nitric acid (HNO_3) were decontaminated with Hexafluorine® at the worksite. HF burns did not develop and medical treatment other than initial decontamination was not required in 12/16 (75%). In 7/16 (44%) cases, lost work time corresponded to duration of hospital observation (mean < 1 d).

Hydrofluoric acid (HF) is a weak acid (pK = 3.2) widely utilized in industrial settings in areas such as metallurgy, paper production, ceramics, microelectronics, glass cutting and etching. Workers can be exposed in such operations as metal stripping and polishing, decanting or maintenance. Risks of HF splashes include the development of severe burns, as well as systemic intoxication that is sometimes fatal with exposure to high concentrations. Decontamination with water followed by inunction of calcium gluconate gel has been relatively efficacious for skin splashes with low concentrations of HF, but is not capable of preventing either burns or systemic toxicity with exposure to high concentrations. This report describes the results of an improved protocol using Hexafluorine® for decontamination of HF splashes in a Swedish metallurgy facility.

METHODS

Avesta Polarit Group is a company working with stainless steel, including pickling operations. In different workplaces, HF is utilized as a 70% concentrate or a dilute mixture of 6% HF/ 15% HNO_3. Splashes with either concentrated HF or the dilute HF/HNO_3 mixture occurred mainly during repair or maintenance operations.

Prior to 1998, an HF splash protocol of initial water decontamination followed by inunction of calcium gluconate gel used in this facility did not produce satisfactory results (see following Case Report). The facility first made an inventory and minimized the risks, and where a risk of HF splashes persisted, evaluated where it was necessary to pre-position first aid devices containing Hexafluorine® HF and acid decontamination solution.

As a second step, the facility established a major education campaign for personnel with potential HF exposure which included the importance of using adequate personal protective equipment and the immediate and delayed effects of HF exposure, depending on the concentration.

A new decontamination protocol was then put into effect: initial decontamination of all ocular or dermal HF splashes should consist of Hexafluorine® lavage within 1 min of exposure. In the absence of Hexafluorine® in close proximity to the accident site, initial decontamination with water should be done. Following all HF splashes decontaminated with Hexafluorine®, the victim should also have a consultation with a hospital-based medical specialist.

An internal maintenance program was established for safety equipment and particularly for the Hexafluorine® DAPs (stand-alone portable showers) to guarantee proper functioning in an emergency. A tracking system for accidents and their outcomes was also established.

CASE REPORT

In August 1996, while checking a leaking valve, an operator received a splash with concentrated 70% HF in his face and on his throat, one arm and the abdomen. There was an immediate sensation of pain. The victim was immediately undressed and lavaged with water for 15 min. The worker was transported to the hospital, arriving about 30 min after the accident. Bandages where then immediately soaked with a calcium chloride solution (20 g/2 L of water) and placed on the burned areas of the

* Presented at the XXXVII European Congress of Toxicology (Eurotox-2000), London, UK, September 17-20, 2000. Funding for this translation from the French and editing for publication in English was provided by Laboratoire PREVOR, Moulin de Verville, F95760, Valmondois, France.

skin. Subcutaneous injections of calcium gluconate (0.5 ml/cm^2) at a concentration of 9 mg of Ca^{2+}/ml were given, followed by calcium gluconate via an iv infusion with 30 ml/2 h in 1,000 ml of Ringers lactate. The ionized serum calcium was 0.67 mmol/L (laboratory normals = 0.9–1.32 mmol/L). Topical application of 2.5% calcium gluconate gel was also done.

About 4 h after exposure, ventricular fibrillation developed that responded to defibrillation, but recurred 4 times over the following 2 h, each time requiring defibrillation. The patient was anesthetized and intubated, the vital signs were stabilized, and hemodialysis was done. Serum levels of calcium and magnesium were then normal. The concentration of fluoride in the urine was 5800 mmol/L before starting hemodialysis, and was 3800 mmol/L following hemodialysis (reference range < 105 mmol/L). The following day, the patient was transferred to the Burn Center at the Karolinska Hospital in Stockholm for treatment of deep dermal burns, where skin grafting was done. The patient was released in mid-September 1996. In August 1997, 1 y after the accident, the patient returned to work.

RESULTS

During 1998-1999, there were 16 HF ocular and dermal splashes at the Avesta Polarit plants. Victims were aged 39 ± 11 y and 80% were males. One-third of exposed workers were external workers. Two dermal chemical splashes involved 70% HF, and 1 ocular splash involved an unknown HF concentration (Table 1). Twelve splashes were with the 6% HF/15% HNO_3 mixture, pH = 1 (Table 2). One exposure was to a mixture of 6% HF/15% HNO_3 that also included an unknown concentration of sulfuric acid, pH = 1 and involved both 1 eye and facial skin (Table 2). In 2 dermal splashes involving the hand and arm or the face and oral cavity, exposure was to the 6% HF/15% HNO_3 pickling acid mixture that had been heated to 45 C (Table 2).

All workers with HF or mixed acid exposure were initially decontaminated with Hexafluorine® which began within 1 min of the splash in 12/16 (75%) of cases. In 3 cases involving the dilute 6% HF/15% HNO_3 mixture, decontamination began 1 h after exposure.

All HF-exposed workers reported immediate pain relief during or after Hexafluorine® decontamination. More than 60% of exposed workers were transported to the hospital for medical examination, but no systemic toxicity was noted.

The worker with an ocular splash with an unknown concentration of HF developed some delayed irritation several hours after the accident that proved an allergic reaction to an instilled topical medication. A small corneal lesion was treated with topical cortisone. In the worker with facial and oral cavity exposure to 6% HF/15% HNO_3, some blistering on the outside of the eyelid was noted 1 d following the accident.

Table 1. Results from chemical splashes with hydrofluoric acid (HF).

Cases	Body surface area	Time until decontamination	Lost work time (d)
Splashes with 70% HF			
1	Left forearm	< 1 min	0
1	Oral cavity	< 1 min	1
Splashes with an unknown concentration of HF			
1	One eye	< 1 min	0

Table 2. Splashes with a mixture of 6% HF/15% HNO_3

Cases	Body surface area	Time until decontamination	Lost work time (d)
2	One eye	< 1 min	0-0
1*	Face and one eye	3-5 min	3
1	Both eyes	< 1 min	0
1	One thigh	< 1 min	0
2	Both thighs	1 h-1 1/2 h	2-2
2	Face + oral cavity, forehead	< 1 min	1-1
3	Forearm, arm + hand, right and left arm folds	< 1 min	0-0-1
1	Wrist	2 h	0

* Mixture also included an unknown concentration of sulfuric acid ($H2SO_4$).

No permanent sequelae or severe burns were observed in any of these 16 HF-exposed workers. In 12/16 (75%) of cases including the 2 workers with 70% HF splashes, there was no requirement for further treatment following initial Hexafluorine® decontamination. The mean lost work time was < 1 d (0.69 ± 0.95 d).

DISCUSSION

The severity of HF burns is due to its "double danger". The acid portion (due to the H^+ ion) is responsible for superficial tissue necrosis. This superficial acid injury allows the fluoride (F^-) ion to penetrate deeply into the tissues and to chelate calcium (Ca^{2+}) as calcium fluoride (CaF_2) (1). Calcium depletion can induce physiological perturbations, such as non-perfusing cardiac arrhythmias, cardiac conduction defects, and hypotensive shock. There is also liberation of potassium ions (K^+) which may be responsible in part for the sensation of intense pain with HF burns (2). The higher the HF concentration, the faster the onset and greater the severity of pain (3). With exposure to HF concentrations > 50%, onset of pain is nearly immediate, and tissue necrosis and depletion of serum Ca^{2+} and magnesium ions plus release of K^+ may occur. These electrolyte abnormalities can lead to cardiac arrest and death. With exposure to HF concentrations less than 20%, pain onset and tissue necrosis are delayed.

The problem of decontamination of HF eye and skin splashes is not simple. The development of water plus topical calcium gluconate decontamination/treatment protocols has allowed a decrease in the sequelae of HF splashes, but has not allowed prevention of burns (4-6).

The first emergency actions following a chemical splash are removing contaminated clothing as well as lavage. The quality and rapidity of the initial lavage following an HF splash determine whether or not burns and/or deleterious sequelae will develop (7).

Water decontamination has only the effects of mechanical rinsing and dilution of the chemical product on the surface of the exposed tissue. Being hypotonic, water may actually favor the penetration of the toxicant into the tissues. Water decontamination is therefore not optimal.

The use of water lavage followed by topical calcium gluconate has in general allowed a decrease in the severity of HF burns. However, with exposure to high concentrations of HF, despite treatment with water decontamination plus Ca^{2+} (even with iv injection of calcium gluconate or calcium chloride), the outcome can be fatal (8-10).

The case reported here of a 70% HF splash on the arms and abdomen clearly demonstrates that initial water decontamination followed by treatment with topical, sc and iv calcium preparations is not optimal. Cardiac arrest was only avoided by repeated defibrillations, intubation and other intensive care measures. Deep burns also developed which required skin grafting, and the victim lost 1 y of work as well as functional and psychological sequelae.

While the protocol of water + topical calcium gluconate has been used for dermal splashes, it is controversial for HF ocular splashes (11). The interest of an efficacious and single-agent emergent decontamination protocol that can be used regardless of the HF concentration, mixture with other acids, and tissue involved remains significant (12).

Hexafluorine® is an emergent lavage solution specifically designed for decontamination of eye and skin HF splashes. Because it is hypertonic, it prevents HF tissue penetration and establishes an osmotic gradient that can leach out some HF that has penetrated into the tissues but not yet bound to tissue receptors. Moreover, its strong affinity for both H^+ and F^- ions allows it to bind them both at the same time and prevents the development of deleterious sequelae. Hexafluorine®'s chemical reactions with these ions is not exothermic (does not release heat which could itself damage tissues).

The efficacy of Hexafluorine® has been previously demonstrated in vitro (3) and in the industrial setting (13, 14). In the 16 cases reported, initial Hexafluorine® decontamination was of interest regardless of the concentration of HF (alone or mixed with strong acids) or the location and extent of the splash. There were no sequelae or severe burns. In 12/16 cases (75%), there was no requirement for treatment other than initial Hexafluorine® decontamination, and the mean lost work time was < 1 d (due to the duration of hospital observation).

This study also demonstrates the interest of developing a policy of prevention for chemical splash risks and a systematic method of response. In the involved workplace, there was a hospital consultation in more than 60% of HF splash cases and in 75% of cases active decontamination began within 1 min. Decontaimination was delayed in 3 cases. These involved exposure to the dilute 6% HF/15% HNO_3 mixture, which likely explains the delayed decontamination as the sensation of pain was probably delayed in onset. Exposure to such dilute HF preparations, which are decontaminated only after a delay, can lead to development of burns and complications (15,16).

The dilute HF involved in the present study was mixed with nitric acid, a strong corrosive that can cause superficial tissue injury and increase the penetration of toxic fluoride ions. In 3 cases of exposure to dilute HF reported here, even delayed decontamination with Hexafluorine® allowed prevention of chemical burns.

Two workers splashed with 70% HF were efficaciously decontaminated with Hexafluorine®. The risks of systemic toxicity and prolonged further treatment were avoided. Burns did not develop, in contrast to the 70% HF exposure case reported here when treatment was with initial water decontamination followed by topical, sc and iv calcium salts.

The combination of establishing an effective chemical safety policy and the utilization of the active HF and other acids lavage solution, Hexafluorine®, has allowed maximal decontamination of HF splashes and avoidance of HF burns in the Avesta Polarit Group.

REFERENCES

1. McCulley JP: Ocular hydrofluoric acid burns: animal model mechanism of injury and therapy. Trans Am Ophth Soc 88: 649-684, 1990.
2. Klauder JV, Shelanksi L, Gabriel K: Industrial uses of compounds of fluorine and oxalic acid. Arch Ind Health 12: 412-419, 1955.
3. Anderson WJ, Anderson JR: Hydrofluoric acid burns of the hand: Mechanism of injury and treatment. J Hand Surg 13A: 52-56, 1988.
4. Greco RJ, Hartford CE, Haith LR et al: Hydrofluoric acid-induced hypocalcemia. J Trauma 28: 1593-1596, 1988.
5. Dunn BJ, MacKinnon MA, Knowlden NF et al: Topical treatments for hydrofluoric acid burns. J Occup Environ Med 38: 507-514, 1996.
6. Kono K, Watanabe T, Dote T et al: Successful treatment of lung injury and skin burn due to hydrofluoric acid exposure. Int Arch Occup Environ Health 73: S93-S97, 2000.
7. Peletier A: Utilisation de l'acid fluorhydrique dans les laboratories de chimie (French). [Utilization of hydrofluoric acid in chemical laboratories]. INRS CDN-Hygiene et Securite du Travail 178: 37-41, 2000.
8. Sheridan RL, Ryan CM, Quinby WC et al: Emergency management of major hydrofluoric acid exposures. Burns 21: 62-64, 1995.
9. Chataigner D, Garnier R, Bonnin C et al: Brulures et intoxication systemique mortelle secondaires a une projection d'acide fluorhydrique (French). [Burns and fatal systemic poisoning secondary to an hydrofluorhydric acid splash]. Arch Mal Prof 53: 13-29, 1992.
10. Mullett T, Zoeller T, Bingham H et al: Fatal hydrofluoric acid cutaneous exposure with refractory ventricular fibrillation. J Burn Care Rehabil 8: 216-219, 1987.
11. Beiran I, Miller B, Bentur Y: The efficacy of calcium gluconate in ocular hydrofluoric acid burns. Human Exp Toxicol 16: 223-228, 1997.
12. Segal EB: First aid for a unique acid, HF: A sequel. Chemical Health and Safety of the American Chemical Society January/February: 18-23, 2000.
13. Hall AH, Blomet J, Gross M et al: Hexafluorine for emergent decontamination of hydrofluoric acid (HF) eye/skin splashes. Semiconductor Safety Assoc J 14: 30-33, 2000.
14. Mathieu L, Nehles J, Blomet J et al: Efficacy of Hexafluorine for emergent decontamination of hydrofluoric acid eye and skin splashes. Vet Human Toxicol 43: 263-265, 2001.
15. Stenal JR, Tobin JS: Hydrofluoric acid burn: latent period was key factor. Am Ind Hyg Assoc J 48: A451-A452, 1987.
16. Barbier F, Bonnet P, Julie R et al: Brulures cutanees par acide fluorhydrique. A propos de 32 cas. (French) [Skin burns with hydrofluoric acid . 32 cases]. Arch Mal Prof Apr: 400-402, 1987.

·Informatics Research·

Treatment of hydrofluoric acid exposure to the eye

Katherine Atley, Edward Ridyard

Oxford University Hospital NHS Trust, Headley way, Headington, Oxford OX3 9DU, UK

Correspondence to: Katherine Atley. 11 Birch Lea, Walkington, Beverley, East Yorkshire HU17 8TH, UK. Katherine.atley@doctors.org.uk

Received: 2014-03-26 Accepted: 2014-09-05

Abstract

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

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

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

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

• KEYWORDS: hydrofluoric acid; cornea; ocular; injury

DOI:10.3980/j.issn.2222-3959.2015.01.28

Atley K, Ridyard E. Treatment of hydrofluoric acid exposure to the eye. *Int J Ophthalmol* 2015;8(1):157-161

INTRODUCTION

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

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

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

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

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

HYDROFLUORIC ACID

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

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

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

Table 1 Ocular chemical burn classification (Roper-Hall) (Adapted from[7])

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

OCULAR EXPOSURE

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

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

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

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

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

Various treatments have been used since the early 20th century for ocular HF burns; however, nowadays these are rarely used in modern practice. Magnesium oxide (MgO) and the quaternary ammonium compounds; Zephiran (Benzalkonium Chloride) and Hyamine (Benzethonium chloride) were once recommended, but have since been found to be too toxic to the eye causing additional ocular damage [13-16]. It has also been established through studies that the irrigation with calcium chloride ($CaCl_2$) increases the frequency of corneal ulceration [8,15]. Magnesium chloride ($MgCl_2$) is occasionally still used as it has been shown to be effective for ocular HF burns; however, compared to the other newer treatments it is less effective[8,15,16].

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

METHODOLOGY

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

1) Medline 1946-06/2012 using the OVID interface. Searched using the standard Boolean system linking-Searched-{(HF OR HF burn OR HF) AND (eye OR ocular) AND (calcium gluconate).mp.} LIMIT (English)

15 papers found of which 4 are relevant (Table 2).

Searched-{(HF OR HF burn OR HF) AND (eye OR ocular) AND (Hexafluorine).mp.} LIMIT (English)

Six papers found of which three are relevant (Table 2).

2) Embase search from 1974-06/2012 using the OVID interface.

Searched-{(HF OR HF burn OR HF) AND (eye OR ocular) AND (calcium gluconate).mp.} LIMIT (English)

Sixteen papers found of which the same three are relevant (Table 2).

Searched-{(HF OR HF burn OR HF) AND (eye OR ocular) AND (Hexafluorine).mp.} LIMIT (English)

Nine papers found of which the same three are relevant (Table 2).

3) The Cochrane Library search

Searched-(HF) AND (calcium gluconate)

No papers found.

Searched-(HF) AND (Hexafluorine)

No papers found.

Four papers which are relevant were found in references (Table 2).

Table 2 Comparing calcium gluconate, water irrigation and Hexafluorine

No.	Title and author of paper	Study type	Conclusion
1	Ocular hydrofluoric burns: animal model, mechanism of injury and therapy (McCulley 1990)[16]	Experimental study	Immediate single irrigation with H_2O, NaCl or $MgCl_2$ solution was most effective. Other therapeutic agents commonly used in HF skin burn therapy were either too toxic in normal eyes or caused additive damage to burned eyes.
2	The efficacy of calcium gluconate in ocular hydrofluoric acid burns (Beiran *et al* 1997)[9]	Experimental study	HF ocular injury 1% calcium gluconate did not have any significant advantage over saline irrigation. Given subconjunctivally, 1% calcium gluconate may be toxic and worsens clinical outcome.
3	Hydrofluoric acid burns to the eye (McCulley *et al* 1983)[15]	Case report and experimental study	Immediate single irrigation with water, normal saline or isotonic magnesium chloride solution is the most effective therapy for ocular HF burns. Extrapolation of other skin burn treatments to use in the eye is unacceptable due to the toxicity of these agents in normal eyes and the additive damage caused in burned eyes.
4	The role of calcium gluconate in the treatment of hydrofluoric acid eye burn (Bentur *et al* 1993)[11]	Case report	The quick and uneventful recovery in this patient suggests that repeated instillation of 1% calcium gluconate eye drops may be efficacious in treating HF burn of the eye. They suggest that this mode of administration allows more calcium ions to reach the free fluoride ions not removed or bound by initial irrigation. However, more data are needed before recommending this procedure.
5	Ocular hydrofluoric acid burns (Rubinfeld *et al* 1992)[17]	Case reports	Patients that received immediate calcium gluconate lavage were still needed to be transferred to the burn unit for specialised monitoring. It concludes that, if an ophthalmologist is the first to treat a patient with chemical exposure, the history of HF exposure must be obtained, and the burn team and other medical specialists must be quickly consulted to avoid potentially fatal complications.
6	Hydrofluoric acid burns of the eye: report of possible delayed toxicity (Hatai *et al* 1986)[1]	Case report	Copious irrigation with water or normal saline is simple and the most effective treatment in HF ocular burns. The possible use of lactated Ringer's solution and milk as irrigants of the eye has been raised, but studies are needed to determine their practicality and effectiveness in the treatment of ocular HF exposure.
7	Analysis of hydrofluoric acid penetration and decontamination of the eye by means of time-resolved optical coherencetomography (Spöler *et al* 2008)[18]	Experimental study	Tap water and 1% calcium gluconate managed to slow the acid but couldn't prevent full penetration; however Hexafluorine stopped the acid penetration. Tap water and 1% calcium gluconate increased cornea opacification whereas the cornea remained clear after rinsing with Hexafluorine.
8	Hexafluorine for emergent decontamination of hydrofluoric acid eye/skin splashes (Hall *et al* 2000)[19]	Case report and experimental study	Hexafluorine solution has been compared with water and calcium gluconate decontamination in rabbits and rats, and was more efficacious. It worked best on the pH and pF and therefore is the best alternative for decontamination of HF eye splashes.
9	An improved method for emergent decontamination of ocular and dermal hydrofluoric acid splashes (Soderberg *et al* 2004)[20]	Series of cases and a case report	During 1998-1999 in a Swedish factory 16 cases of HF eye exposure were described. All had immediate decontamination with Hexafluorine. No damage observed in any of these patients. Mean lost work time was <1d.
10	Efficacy of hexafluorine for emergent decontamination of hydrofluoric acid eye and skin splashes (Mathieu *et al* 2001)[21]	Series of cases	During 1994-1998 PubMed in a German metallurgy factory-11 cases, with 2 cases of ocular exposure. Immediate decontamination with Hexafluorine. No eye injuries and no lost work time.

RESULTS

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

DISCUSSION

The current recommended treatment for eye exposure to HF, water or 0.9% saline decontamination, works by mechanically rinsing the HF off the corneas surface. It also permits the dilution of the HF attempting to restore the pH back to safe limits [22]. However, as water has no chemical action, it cannot control the corrosive and toxic potential of HF. Furthermore, as HF is highly permeable to the corneal surface, it is imperative that the mechanical rinsing with water is done immediately to have effect, otherwise the acid penetrates deeper and it is too late to prevent further damage. In fact, as water is hypotonic, it has been suggested it may actually favour the penetration of the acid into the tissue [20]. While it is presently the recommended treatment, the

Table 3 Emergency decontamination of 40% HF or 6% HF/15% HNO_3 eye splashes with Hexafluorine (Adapted from[21])

Exposure	Splash area involved	Initial decontamination	Second decontamination	Sequelae	Requirement for further treatment	Lost work time
40% HF	Eye	Hexafluorine	Hexafluorine	None	None	None
6% HF/15% HNO_3	Eye	Hexafluorine	Hexafluorine	None	None	None

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

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

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

Additionally, various experiments testing the efficacy of subconjunctival injections of 1% and 10% calcium gluconate have found that they are too toxic to the eye, causing additional damage and worsening the clinical outcome[9,15,16]. This is reported in a clinical case where the patient after being splashed with HF in the eyes, was given 0.5 mL 10% calcium gluconate subconjunctival injections in both eyes. Four years post-injury, vision remained significantly impaired and he continues to suffer from rare spontaneous corneal epithelial erosions[15].

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

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

Hexafluorine is safe to use in the eyes, is non-toxic and non-sensitising [8]. It is already widely used in France and Germany, and gaining popularity in Italy, Ireland and Sweden[4].

Several clinical cases have been reported regarding the efficacy of Hexafluorine. In 1995, whilst working in a stainless steel factory, a patient accidently splashed 38% HF into his eye. He rinsed the eye immediately with Hexafluorine and fortunately didn't sustain any eye injuries and was able to return to work the next day[19,23]. Moreover, in a German metallurgy facility between 1994 and 1998, any HF exposure was to be decontaminated with Hexafluorine. During this period, two workers sustained eye splashes and after immediately rinsing with Hexafluorine solution, no burns or sequelae were observed and neither lost any work time (Table 3)[21].

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

LIMITATIONS OF STUDY

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

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

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

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

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

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

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

ACKNOWLEDGEMENTS

The authors would like to thank the allied healthcare professionals and nursing team for their unwavering cooperation and assistance to facilitate the preparation of this manuscript.

Conflicts of Interest: Atley K, None; **Ridyard E,** None.

REFERENCES

1 Hatai JK, Weber JN, Doizaki K. Hydrofluoric acid burns of the eye: report of possible delayed toxicity. *Cutaneous and Ocular Toxicology* 1986;5(3):179-184

2 TOXBASE. The primary clinical toxicology database of the National Poisons Information Service. http://www.toxbase.org/Poisons-Index-A-Z/H-Products/Hydrofluoric-Acid/ (Accessed June 2012)

3 Makarovsky I, Markel G, Dushnitsky T, Eisenkraft A. Hydrogen fluoride-the protoplasmic poison. *Isr Med Assoc J* 2008;10(5):381-385

4 Segal EB. First aid for a unique acid, HF: a sequel. *J Chem Health Saf* 2000;7(1):18-23

5 Burgher F, Mathieu L, Lati E, Gasser P, Peno-Mazzarino L, Blomet J, Hall AH, Maibach HI. Part 2. Comparison of emergency washing solutions in 70% hydrofluoric acid-burned human skin in an established *ex vivo* explants model. *Cutan Ocul Toxicol* 2011;30(2):108-115

6 Chapa L, Surani S, Varon J. Management of hydrofluoric acid injury in the Emergency Department and Critical Care Units. *Crit Care Shock* 2009;12:117-119

7 Mathieu L, Burgher F, Blomet J. Comparative evaluation 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. *J Chem Health Saf* 2007;14(4):32-39

8 Upfal M, Doyle C. Medical management of hydrofluoric acid exposure. *J Occup Med* 1990;32(8):726-731

9 Beiran I, Miller B, Bentur Y. The efficacy of calcium gluconate in ocular hydrofluoricacid burns. *Hum Exp Toxicol* 1997;16(4):223-228

10 Harun S, Srinivasan S, Hollingworth K, Batterbury M, Kaye S. Modification of classification of ocular chemical injuries. *Br J Ophthalmol* 2004;88(10):1353-1354

11 Bentur Y, Tannenbaum S, Yaffe Y, Halpert M. The role of calcium gluconate in the treatment of hydrofluoric acid eye burn. *Ann Emerg Med* 1993;22(9):1488-1490

12 Matsuno K. The treatment of hydrofluoric acid burns. *Occup Med (Lond)* 1996;46(4):313-317

13 Grant WM. *Toxicology of the eye.* 2nd Ed. Springfield, Illinois. Thomas CC, 1974

14 DeTreville RTP. *Hydrofluoric acid burn management.* Medical Series Bulletin No.17-70, Industrial Hygiene Foundation of America, 1970

15 McCulley JP, Whiting DW, Petitt MG, Lauber SE. Hydrofluoric acids burns of the eye. *J Occup Med* 1983;25(6):447-450

16 McCulley JP. Ocular hydrofluoric acid burns: animal model, mechanism of injury and therapy. *Trans Am Ophthalmol Soc* 1990;88:649-684

17 Rubinfeld RS, Silbert DI, Arentsen JJ, Laibson PR. Ocular hydrofluoric acid burns. *Am J Ophthalmol* 1992;114(4):420-423

18 Spoler F, Frentz M, Forst M, Kurz H, Schrage NF. Analysis of hydrofluoric acid penetration and decontamination of the eye by means of time-resolved optical coherence tomography. *Burns* 2008;34(4):549-555

19 Hall AH, Blomet J, Gross M, Nehles J. Hexafluorine solution for emergent decontamination of hydrofluoric acid eye/skin splashes. *Semiconductor Safety Assoc J* 2000;14:30-33

20 Soderberg K, Kuusinen P, Mathieu L, Hall AH. An improved method for emergent decontamination of ocular and dermal hydrofluoric acid splashes. *Vet Hum Toxicol* 2004;46(4):216-218

21 Mathieu L, Nehles J, Blomet J, Hall AH. Efficacy of hexafluorine for emergent decontamination of hydrofluoric acid eye and skin splashes. *Vet Hum Toxicol* 2001;43(5):263-265

22 Hall A, Maibach H. Water decontamination of chemical skin/eye splashes: a critical review. *Cutan Ocul Toxicol* 2006;25(2):67-83

23 Siewel CL, Nehles J, Blomet J, Gross M. A review of the taking up of hydrofluoric acid burns: two cases reported. XVII International Congress of the European Association of Poisons Centres and Clinical Toxicologies. Zurich 24-28 March, 1998

CHEMICALS REACTING WITH WATER: RESPONSIBLE OF CHEMICAL AND THERMAL BURNS? PRELIMINARY *IN VITRO* RESULTS AND EVALUATION OF THEIR DECONTAMINATION

Fosse C, Lutz F, Coudouel H, Duhamel R, Mathieu L

PREVOR, Valmondois, France

14th European Burns Association congress, 14-17 September 2011, The Hague, The Netherlands

RATIONALE

Chemicals reacting violently with water can be responsible of severe chemical injuries. They are identified in the new European Classification CLP by:

- The hazard class WATER-REACT. (categories 1, 2 and 3)
- The corresponding hazard statement:
  - H260 - In contact with water releases flammable gases which may ignite spontaneously.
  - H261 - In contact with water releases flammable gases.
- The supplement hazard statement for chemicals releasing gases not flammable but that can be corrosive or even toxic:
  - EUH14 - Reacts violently with water

Their reaction with water can be exothermic (heat release) and hazardous chemical can be released, leading to chemical and sometimes thermal burns. Intoxication for both the patient and the responders can be associated[a].

Some of them are worldwide used in enough quantity to ask the following question: if they violently react with water, how deal with the first aid washing protocol? How washing with an amphoteric compound brings advantages compared to tap water washing?

LIST OF CLASSIFIED CHEMICALS

SUBSTANCE NAME	INDEX #	GAS RELEASE
aluminium lithium hydride	001-002-00-4	H_2
sodium hydride	001-003-00-X	H_2
calcium hydride	001-004-00-5	H_2
lithium	003-001-00-4	H_2
sodium	011-001-00-0	H_2
magnesium powder (pyrophoric)	012-001-00-3	H_2
potassium	019-001-00-2	H_2
zinc powder - zinc dust (pyrophoric)	030-001-00-1	H_2
magnesium, powder or turnings	1012-002-00-9	H_2
aluminium powder (pyrophoric)	2013-001-00-6	H_2
calcium	4020-001-00-X	H_2
calcium phosphide, tricalcium diphosphide	015-003-00-2	PH_3
aluminium phosphide	015-004-00-8	PH_3
magnesium phosphide, trimagnesium diphosphide	015-005-00-3	PH_3
trizinc diphosphide, zinc phosphide	015-006-00-9	PH_3
tetraphosphorus trisulphide, phosphorus sesquisulphid	015-012-00-1	PH_3
diphosphorus pentasulphide, phosphorus pentasulphide	015-104-00-1	PH_3
n-hexyllithium	003-002-00-X	n-hexane
(2-methylpropyl)lithium, isobutyllithium	003-003-00-5	isobuthane
magnesium alkyls	012-003-00-4	alkane
aluminium alkyls	013-004-00-2	alkane
sodium((n-butyl)x(ethyl)y-1,5-dihydro)aluminate)	013-009-00-X	ethane, butane
ethyl propoxy aluminium chloride	017-020-00-0	HCl, ethane
dimethylzinc [1]	030-004-00-8	methane
diethylzinc [2]		ethane
trichlorosilane	014-001-00-9	HCl
phosphorustribromide	015-103-00-6	H_3PO_3, HBr
boron trifluoride	005-001-00-X	HF
borontrichloride	005-002-00-5	HCl
borontribromide	005-003-00-0	HBr
phosphorus trichloride	015-007-00-4	H_3PO_3, HCl
disulphurdichloride; sulfurmonochloride	016-012-00-4	SO_2, HCl, S_8 (sulfur)
sulphurdichloride	016-013-00-X	HCl
thionyldichloride; thionylchloride	016-015-00-0	HCl
chlorosulphonic acid	016-017-00-1	HCl
oleum...%SO_3	016-019-00-2	H_2SO_4
titaniumtetrachloride	022-001-00-5	HCl, $TiCl_4$
acetylchloride	607-011-00-5	CH_3COOH, HCl
chloroacetyl chloride	607-080-00-1	HCl
propionylchloride	607-093-00-2	propionic acid
2,4,6-trichloro-1,3,5-triazine;	613-009-00-5	HCl
morpholine-4-carbonylchloride	613-041-00-X	HCl
calcium carbide	006-004-00-9	acetylene
sodium methanolate	603-040-00-2	methanol
4-isocyanatosulphonyltoluene; tosylisocyanate	615-012-00-7	CO_2, urea
methyl3-isocyanatosulfonyl-2-thiophene-carboxylate	615-022-00-1	CO_2, urea

Chemicals which react with water can be classify by chemical family: alkali metal, hydride metal, alkyl metal, acid chloride, phosphorus metal, chlorosilanes, sulfonyle isocyanates etc.

Or, depending on the gases released during the reaction with water:

- Flammable gases can be released - Dihydrogen (H_2) or alkanes (methane, ethane etc...)
- Corrosive acids can be released - Hydrochloric or hydrobromic acids (HCl, HBr), sulphuric acid (H_2SO_4), propionic acid, phosphorus acid (H_3PO_3), etc...
- Toxic gases, such as carbon dioxyde (CO_2), dihydrogen sulfur (H_2S), methanol, phosphine (PH_3) or hydrofluoric acid (HF)

IN VITRO ASSAY OR HOW TO DEAL WITH WATER-REACTANT CHEMICALS?

Heat will be released during the reaction of these chemicals with water.

Theoritically:

$$TiCl_{4(l)} + 4\,H_2O_{(l)} \rightarrow TiO_{2(s)} + 4\,HCl_{(aq)}$$

ΔH = -237 kJ/mol

Enthalpy indicates the chemical reaction exothermy. In the case of titanium tetrachloride $TiCl_4$, the released heat is significant.
In cases of ocular or cutaneous splashes, question can be asked how first aid washing can avoid or limit the injury.

The hydrolysis of 1 molecule of $TiCl_4$ produces 4 molecules of hydrochloric acid (HCl) and 1 solid particule of titanium dioxide (TiO_2). HCl is responsible of the solution acidity and therefore its corrosivity (pH<0). This chemical reaction is exothermic in a beaker (Fig. 1).

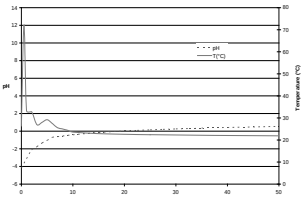


FIGURE 1 - Hydrolysis of 1ml $TiCl_4$ in a beaker (passive washing)

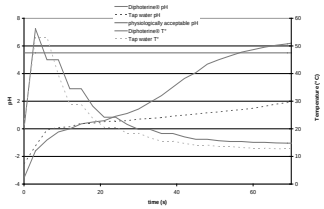


FIGURE 2 - Active washing simulation of 1ml $TiCl_4$ by tap water or by Diphoterine®, an amphoteric molecule

The comparison of these 2 graphs shows that the exothermy of the titanium tetrachloride hydrolysis is decreased by the mechanical effect of washing (from 55°C to 30°C in 20 sec.) for both washing solution. Diphoterine® washing helps to recover a pH physiologically acceptable more rapidly than with tap water washing (Fig. 2).

Hydrolysis of boron tribromide in water does not correspond to temperature increase superior to 40°C during washing.

$$BBr_3 + 3H_2O \rightarrow H_3BO_3 + 3HBr$$

Boric acid and hydrogen bromide generated during hydrolysis are responsible of the corrosivity.

Washing with the amphoteric compound restores the pH to a physiologically acceptable value faster than washing with water.

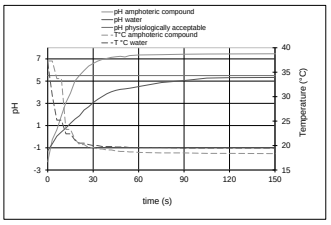


FIGURE 3 - pH evolution of 1ml Boron tribromide after tap water or Diphoterine® washing (active washing)

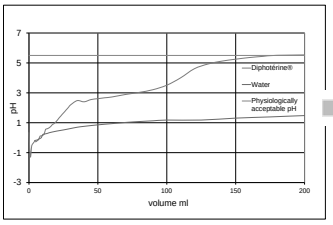


FIGURE 4 - pH evolution of 1ml 98% trichloromethylsilane after tap water or Diphoterine® washing in a beaker

Trichloromethylsilane CH_3SiCl_3 is also classify as a chemical reacting violently with water (EUH014).

Hydrolysis reaction:

$$CH_3SiCl_3 + 3\,H_2O \rightarrow CH_3Si(OH)_3 + 3\,HCl$$

Releasing HCl is clearly corrosive. Less amount of amphoteric compound solution is needed to restore the pH at a physiologically acceptable value compared to water.

CONCLUSION

Even with chemicals reacting violently with water, first aid washing must begin the earliest possible. Prolonged flushing must be done, in order to limit heat release and temperature increasing. An amphoteric washing, which also acts directly on the released corrosive chemicals, appears more effective than a tap water washing.

Reference:

[a] Lazzeri D., & al., Silane coupling agent chemical burns: a risk for medical personnel too, Burns 35 (2009) 600-605

Active or Passive Washing

There are more than 25,000 chemicals likely to cause **cutaneous or ocular lesions and burns** (after a single or repeated contact), such as acids, bases, oxidizers, reducing agents, and solvents.

The Benefits and the Limitations of Rinsing with Water

After receiving **a chemical splash**, the victim must be undressed and the affected tissues must be rinsed as quickly as possible. **Rinsing with water was the first protocol used for chemical decontamination** and this dogma persists on the basis of arguments which are more practical than scientific, because of its general-purpose and non-toxic character, and of its availability. It allows the chemical agent at the surface of the affected tissues to be carried away by a mechanical effect, independent of its nature and concentration.

However, there are limits to water rinsing:

- it does not act on the potentially **irritating or corrosive nature of the chemical agent**,
- there is no rapid return to a physiological state (the effect of carrying the chemical agent away is limited to the surface tissue and has no in-depth effect),
- water favours the chemical agent's penetration of the tissue (Professor Schrage) (link with the publication Schrage, Klin Monastbl Augenheilkd, 2004),
- in order to obtain optimal results, it is necessary to intervene very quickly (10 seconds according to the ANSI standard) after the splash. However, there is sometimes only partial effectiveness, in particular on major corrosive agents.
- Observations of significant after-effects, secondary care and surgical interventions resulting in permanent disability, and even fatalities are regularly reported in the scientific literature[2,3].
- Recently, comparative studies have shown the possibility of improving on rinsing with water[4].

Increasing the Chances of Being Saved

Improving on rinsing with water consists of finding other solutions without these limitations in order to increase the chances of the victim both being saved and experiencing a minimum of after-effects.

In order to accomplish this, Diphoterine®, an amphoteric and chelating molecule was introduced in the form of an aqueous solution. The aim of the resulting solution is **to prevent chemical burns** or to lessen their seriousness.

The improvements brought by the Diphoterine® solution to chemical decontamination are as follows:

- it stops the irritating and corrosive agent's actions on the eye and skin, thanks to its **amphoteric and chelating properties**,
- it stops the chemical agent's penetration of the tissues and carries the chemical away from the interior to the exterior of the tissue, thanks to its **hypertonicity**,
- it allows a rapid return to a **pH level between 5.5 and 9**, without any danger of a burn,
- it has a prolonged intervention time compared to water (in the minute following the chemical splash) with improved rinsing effectiveness: **absence of after-effects**, little need or no need for secondary care, and no or little loss of work.

The Diphoterine® solution has been classified as a medical device according to the 93/42 CEE Directive. It claims to act on the chemical agent in order to stop or to minimize the development of chemical burns. It is classified IIa because it can be used on injured skin.(Dr Cavallini) (link with the publications: Cavallini, Annals of Burns and Fire disasters 2004, vol XVII-2, 84-87 and Cavallini, European Journal of Anaesthesiology 2004, 21, 389-392).

Since the Diphoterine® solution does not act on the human organism and its action on the chemical agent is not obtained neither by pharmaceutical, immunological or by metabolism means, it has not been classified as a drug.

Analysis of the Scientific Data

The analysis of the clinical and experimental data of **chemical decontamination with the Diphoterine® solution** is based on three levels of scientific evidence.

Convergent clinical data:

In spite of the difficulties of performing studies on first aid in the workplace and the inevitable limitations related to the interpretation of the results, much of the data collected on human subjects provides convergent elements.

Many accounts of the Diphoterine® solution use (Hall Vet Hum Toxicol 2002, 44, 4, 228-231) have been provided by companies. Generally transmitted by occupational health doctors, the reports can be criticized one by one, either for a problem of methodology or interpretation, but when all of these several hundreds cases of the Diphoterine® solution uses are combined, the coherence of the whole reveals some certainties about its effectivenes:

- no noxious effects,
- lessens pain,
- no after-effects,
- absence of or only a small amount of secondary care,
- absence of or a few days of work loss.

The INRS (National Institute of Research and Safety) decided to independently verify the effectiveness of **the various chemical splash decontamination methods**, including the Diphoterine® solution. For that purpose, an investigation was carried out with the help of occupaitonal health doctors (link with the paper: Falcy, DMT 53, 1er quarter 1993) in France. 73 companies and more than 60 accidents were taken into consideration. This study shows Diphoterine® action on a varied sample of chemicals, and indicates that the Diphoterine® solution, when used according to the recommended protocol, is always at least as effective as water. The continuation of this investigation (link with the publication Falcy DMT 70, 2nd quarter 1997) showed that the results, for a total of 145 chemical splash cases studied, were superior on concentrated bases. This was confirmed by the study carried out by Martinswerk (link with the publication: Hall Vet Hum Toxicol 2002, 44, 4, 228-231), which made it possible to confirm the superiority of the Diphoterine® rinsing on bases, both in terms of effectiveness and rinsing safety, despite the small size of the statistical series:

Rinsing solution	**the Diphoterine® solution**	**Acetic Acid**	**Water**
No secondary care	100 % +/- 15 %	0 % +/- 15 %	0 % +/- 15 %
Simple secondary care	0 % +/- 15 %	80 % +/- 15 %	25 % +/- 15 %
Medicalized secondary care	0 % +/- 15 %	20 % +/- 15 %	75 % +/- 15 %
Number of days of work loss	0.18 +/- 0.4	2.91 +/- 4.3	8 +/- 8.12

For isolated reported cases, the examples are also very significant. Take the case of 2 large **cutaneous splashes of concentrated sulfuric acid** with equal concentrations (95%): the one rinsed with water lead to serious after-effects, and six months of work loss, and the other rinsed with the Diphoterine® solution resulted in neither after-effects nor work loss. (link with the letter from Quinoléine. Translation into English).

Experimental data in vivo which confirm the clinical results:

When the chemical burn does occur, its development is determined by two phenomena:

- the cleaning phase (inflammation, destruction), which is increased in cases of **chemical burns**,
- the reparing phase (healing), which is decreased.

The in vivo experiments have confirmed that when the development of the chemical burn is stopped, the healing of the injured tissues is carried out in optimal conditions. Dr Cavallini (lien Cavallini European Journal of Anaesthesiology, 2004, 21, 389-392) compared the effectiveness of rinsing with the Diphoterine® solution to rinsing with saline solution on a **concentrated cutaneous hydrochloric acid burn** in rats. The concentrated Diphoterine® solution stopped **the development of the chemical burn**, which had the following consequences:

1. **better healing of the skin** (size of the lesion at 7 days : the Diphoterine® solution 4 mm versus saline solution 6 mm), see also another publication by the same (link with Cavallini Annals of Burns and Fire Disasters, vol XVII, 2004)
2. **a significant reduction of pain** (Substance P in the first 48 hours, $p < 0.05$; beta-endorphine after 7 days, $p < 0.05$),
3. **a reduction of inflammation** (IL-6 to 48h, $p < 0.01$; at 7 days, $p < 0.05$).

Doctor Gérard studied a 15.3% amonia occular burn in rabbits (link with the study J Fr Ophtalmol 1999;22, 10, 1047-1053). This study has allowed an understanding of the chemical burn mechanism and has showed the relevance of delayed treatment of such a burn. This experimental burn model was then tested in order to compare the **effectiveness of the Diphoterine® solution versus saline solution**.(link with Gérard, J Fr Ophtalmol, 2000, 23,5,449-458).

After rinsing with the Diphoterine® solution, there is:

- **an absence of a stromal edema,** while it has been observed after rinsing with saline solution or when there is no rinsing,
- **an inflexion of the pH,** which has not been observed after rinsing with saline solution or when there is no rinsing.

The presence of a stromal edema, resulting from inflammation due to the **burn and the hypotonic effect of rinsing**, is known to be an aggravating factor in the development of chemical burns[5].

Experimental data ex vivo/in vitro which explain the clinical results:

These studies have allowed us to understand and confirm the clinical results obtained. Professor Schrage (link with Klin Monatsbl Augenheilkd, 2004) compares the effectiveness of different rinsing solutions by dosage of 5ml of 0.5 M caustic soda or hydrochloric acid and shows **the limitations of water rinsing on corrosives**. Despite adding an amount of water which represented 50 times the amount of caustic soda or of hydrochloric acid contamination, water did not bring the pH level back to physiological values:

chemical	**Added water (250 ml)**	**Added Diphoterine (Previn) (100ml)**
0.5M Caustic Soda	11.8	<9
0.5M Hydrochloric Acid	2	6.3

Physiological Zone (no burn): 5.5 < pH < 9

An experiment on enucleated pig eyes measured the effect of rinsing on the development of the intra-ocular pH according to whether it was early or delayed: **only rinsing with the Diphoterine® solution showed an improvement of the intra-ocular pH, even if the rinsing was delayed**.

In this same publication, the physical limits of water rinsing on fibroblast cultures is shown. Water is hypotonic. When there is a chemical burn, the osmotic pressure of the cornea increases up to 1280 mosmoles/kg. Rinsing with a hypotonic solution (such as water) can cause an osmotic shock and a cellular cytolysis (destruction of cells after swelling). See also the following publication (link with Kompa, Graefe's Arch Clin Exp Ophthalmol, 2002) on the direct effect of a rinsing solution's osmolarity on the cornea's osmolarity.

The following table clearly shows the advantages of using the Diphoterine® solution

WATER		**DIPHOTERINE®**	
Advantages	**Limitations**	**Advantages**	**Limitations**
Chemical agent at the surface of the affected tissues carried away		Chemical agent at the surface of the affected tissues carried away	
Dilution		Dilution	
Polyvalent		Polyvalent	Polyvalent: Theoretical effectiveness proven on major chemical groups Should be verified case by case for specific chemical agents
	Hypotonic, Favors a part of the chemical agent's penetration of the tissue, especially in eyes	Hypertonic, Stops the chemical agent's penetration of the tissue and carries the chemical away from the interior to the exterior of the tissue	
	No action on corrosives or irritants Development of the chemical burn	"Neutralizing" action on the potentially irritating or corrosive nature of the chemical agent Stops the development of the burn	
		Amphoteric, Allows a rapid return to a physiological pH	
	Intervention time: the first 10 seconds	Intervention time: the first minute	
	Possibility of serious physical after-effects, which may even be fatal	Decrease or absence of after-effects Prevents chemical burns	
	In certain cases, complex secondary treatment with reconstructive surge	Decrease or absence of secondary treatments Prevents chemical burns	A medical consultation is necessary in every case
		Decreases in work loss	
Non toxique		Non toxic, sterile	Expiration date must be observed

The latest study published by Dr. Merle (link with publication Burns 31 (2005) 205-211) shows **the importance of using the Diphoterine® solution in the first hours following an accident**. The study compares, for the equivalent stages of burns, the differences which occur after rinsing with the Diphoterine® solution versus rinsing with water before treatment of a basic burn . This study shows a significant reduction in the amount of time needed for the reepithelialisation of the eye:

Reepithelialisation time in days	**the Diphoterine® solution**	**Sérum physiologique**	**Value of p**
Stade I	1.9 +/- 1	11.1 +/- 1.4	$p < 10^{-7}$
Stade II	5.6 +/- 4.9	10 +/- 9.2	p <0.02
Stade III	20 +/- 14.1	45.2 +/- 23	0.21 NS

Absence of ocular Stage IV with the Diphoterine® solution

Dr Max Gérard has published a case of a severe ocular chemical burn (stage IV) which shows the advantages of delayed rinsing with the Diphoterine® solution and describes the associated secondary treatment, principally aimed at **reducing inflammation**, as well as infection and pain. No surgical act was necessary in this case.

What is important to remember

First-aid rinsing with water was the first decisive improvement in the decontamination of chemical splashes; But water rinsing has limits that have been improved on with the Diphoterine® solution.
The Diphoterine® solution can be used according to two protocols:

1. either as a first-aid treatment in emergency situations, in the workplace, (at the scene of the accident), in order to avoid any after-effects when used in the first minute after the splash has occurred,
2. or with a delayed usage, in the case of treatment before or after hospitalization, where **the Diphoterine® solution stops the develpment of chemical burns** and allows **a rapid return to a physiological state**. It is a treatment adapted to the seriousness of the burn which can then be applied in optimal conditions.

If the chemical is corrosive, or if there is a risk that the splash will not be handled in the first seconds, the water protocol represents a missed opportunity when compared to the Diphoterine® solution protocol.

Access to more detailed publications

****

(*)Additional Information

Diphoterine® is an active molecule which permits the rapid and effective rinsing of chemical agents.

Its effectiveness has been proved on more than 600 chemical agents representing the majority of major chemical groups.

The Diphoterine® solution, thanks to its amphoteric characteristics can never be dangerous.

The Diphoterine® solution, even if it has no chemical activity on a compound, is always more effective when compared to an isotonic solution, and even more when compared to water.

If their is any doubt regarding new chemicals, the Diphoterine® solution's effectiveness must always be evaluated.

We remain at you disposition to perform this evaluation.

****
****

- [1] Liao CC, Rossignol AM Landmarks in burn prevention. Burns 2000 ; 26 : 422-434
- [2] Sykes RA, Mani MM, Hiebert JH Chemical burns : retrospective review. J Burn Care Rehabil 1986 ; 7 : 343-347
- [3] Bromberg BE, Song IC, Walden RH : Hydrotherapy of chemical burns. Plastic Reconstr Surg 1965 ; 35 : 85-95
- [4] Andrews K, Mowlavi A, Milner S The treatment of alkaline burns of the skin by neutralization. Plastic Reconstr Surg 2003 ; 111 : 1918-1921
- [5] Kubota M, Fagerholm P. Corneal alkali burn in the rabbit. Water-balance, healing and transparency. Acta Ophthalmol Scand 1991 ; 69 : 635-640

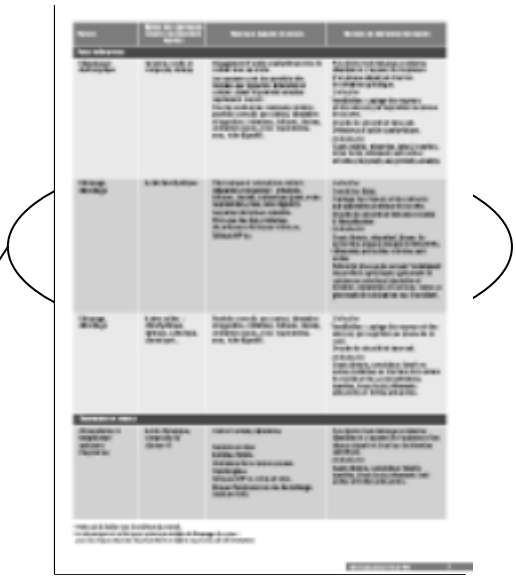
PREVOR - Moulin de Verville - 95760 Valmondois cedex - FRANCE - Tel : +33 (0)1 30 34 76 76 - Fax : +33 (0)1 30 34 76 70 - export@prevor.com

CNAMTS
French National Insurance for Employees

" THE ACTIVITIES FOR SURFACE TREATMENT
Prevention of Chemical Risk"

This document here below is the recommendation adopted by the National Technical Committee of Metallurgy Industries in collaboration with the CNAMTS, dated from November 2008, and dealing with prevention of chemical risk in the surface treatment field.

On page n°3, for the process involving the use of hydrofluoric acid, one of the recommended preventive measures is to "use the Hexafluorine showers and eyewash.



Stripping	Hydrofluoric acid	Very toxic and corrosive by contact, inhalation and ingestion: irritations, burns, lesions, ulcerations (skin, airway, eyes ,alimentary canal). Delayed burning feeling. Causes hypocalcemia, tissues and bone necrosis. 32MP Table.	***Collective*** Cover baths. Channelling of vapors and aerosols by aspiration at the tank's level. HEXAFLUORINE safety shower and eyewash. ***Individual*** Gloves (butyl, neoprene), protective screens, mask with BEP3 filter, anti-acid clothing and anti-acid boots. Plan to have the rescue kit, in particular specific products (injectable and drinkable calcium gluconate solution, calcium tablets, calcium gluconate cream) in case of accidents.

Translation of Medical intervention sheet « hydrofluoric acid » from Fedichem Wallonie, 2001

Contact with the eyes

- Rinse the eyes with temperate water during 15 minutes, maintaining the eyelids largely opened
- If available immediately, rinsing with HEXAFLUORINE® provides better results, especially if followed by a rinsing with physiologic solution
- Rapidly consult a specialist

Contact with the skin

- Remove the clothes (! Source of secondary contamination!)
- Give an abundant shower if possible during the removal of the clothes
- Wash the touched area with temperate water
- If immediately available, a rinsing with HEXAFLUORINE® provides better results
- Avoid the cooling – give cleaned clothes
- Medical care (if needed) in a specialized burn treatment center.

Fedichem
WALLONIE