Chemical Ocular Burns

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New Understanding and Treatments

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Foreword

Despite rapid advances made in a number of medical fields for the last decades, chemical burns to the eye remain one of the most challenging ocular emergencies that eye doctors face today. Literature testifies that both the victim and the treating doctor have been plagued with frustration and disappointment even when a colossal of corrective measures have been taken during acute and chronic phases. This is because the outcome of chemical ocular burns is judged not solely by the completion of wound healing, a gold standard used in other medical subspecialties, but also by the recovery of normal vision. Inasmuch as successful wound healing is a desirable endpoint for emergency management of chemical ocular burns, the vision continues to be threatened and impeded by the resultant scarring.

Thus, it is exciting to witness the publication of a scientific book solely dedicated to such an important subject. In this book, Professor Norbert Scharge has assembled a group of experts specialized in chemistry, biochemistry, biology, epidemiology, emergency care, eye diseases, and surgical reconstruction to compile clinically useful and up-to-date knowledge related to chemical ocular burns. The contents are laid in a logical fashion and comprehensively and succinctly structured so that this book can be used as a handy reference for any acute care physician or eye doctor to gain an in-depth review before or during the management of such an eye emergency.

The book starts with a retrospective review of the history illustrating how chemical ocular burns had been managed in the past. The evolution of various treatment concepts and modalities discloses both human desperation and ingenuity. Intuitionally, the first goal of managing chemical ocular burns is to mitigate the extent of damage by instant elimination of the offending chemical (usually by irrigation with clean water or saline) so as to shorten its exposure. For the first time, this book makes a unique attempt to bridge the gap between basic chemistry and molecular pathogenesis by providing the scientific basis of how an exogenous chemical may alter biological materials at cellular and subcellular levels. Such information may allow researchers to uncover new therapeutic strategies not only to further negate but also to prophylactically avert the damaging effect. The latter notion is highly relevant in the wake of a future chemical warfare.

Upon halting the ongoing insult generated by exogenous chemicals, the conventional management has focused on ways to speed up wound healing so as to fend off potential infections. As eluded above, completion of wound healing often results in sight-threatening scar. To restore a useful vision, a number of surgical techniques including transplantation of limbal epithelial stem cells have been developed. These reconstructive surgeries have indeed brought back useful vision in a significant number of patients if an autologous source of limbal stem cells is employed. Nevertheless,

the overall success is hampered if an allogeneic source is chosen for burns affecting both eyes unless a more vigorous systemic immunosuppression is instituted.

Therefore, pursuits should be continued to identify promising therapies to prevent cicatricial complications that inflict patients at the chronic phase. Emerging knowledge has told us that the wound healing is triggered by inflammation activated via innate immunity. Although the pathogenic basis remains elusive, all cicatricial complications due to chemical ocular burns are characterized by protracted and relentless inflammation. Several chapters of this book are devoted to providing enlightening glimpse into the mechanism thereby acute inflammation evolves into a chronic one. Such information has been useful for researchers to devise a new measure to abolish the progression of inflammation. One such potential therapy that has been put forth is transplantation of amniotic membrane as a biological bandage. When applied at the acute phase, i.e., within two weeks of burns, some moderately damaged eyes exhibit a remarkable recovery with rapid cessation of inflammation and few cicatricial complications. We begin realized that there is a golden window in which inflammation caused by chemical burns can be downregulated. Because such a novel intervention has resulted in notable tissue regeneration, chemical ocular burns may well be the ideal clinical arena where regenerative medicine can be practiced in the future.

Miami, Florida, USA Scheffer C. G. Tseng

Preface

Whatever the origin of chemical burn lesions (i.e., whether resulting from a domestic accident, a chemical assault, or an industrial accident), such injuries can often result in serious functional visual injuries and significant physical and psychological consequences for the victims.

Nine authors of various disciplines and experiences have joined together to produce this book whose aim is to collectively present the most current and relevant data for each specific topic addressed.

As an introduction to the field of chemical ocular burn lesions, an historical and epidemiological perspective has been reviewed by an historian, an ophthalmologist, and a medical toxicologist. Next, a section is presented covering an expanded review of the mechanisms of action and reactivity of chemicals which can cause ocular injuries, prepared by a group of chemists and physicians.

A practicing ophthalmologist with additional experience in ocular physiology and histology then addresses fundamental and newly-developed methods for assessing ocular chemical burn injuries, particularly of the cornea, thus completing the discussion of the various mechanistic and pathophysiological aspects of ocular chemical burn lesions. Various methods for ocular chemical splash decontamination and the desirability of an efficacious active decontamination with the goal of preventing or minimizing ocular chemical burn injuries are discussed.

Following this are two sections prepared by practicing ophthalmologists which discuss clinical evaluation and current surgical treatment of ocular chemical burn injuries.

The book concludes with a section prepared by a chemist/physicist who conceived the innovative possibility of an active decontamination solution for ocular chemical splashes and an emergency physician who discuss specific decontamination measures and the emergent care of patients with ocular chemical burn injuries.

This work will prove useful for medical students, physicians-in-training, occupational medicine physicians and nurses, and private practice or hospital-based ophthalmologists, as well as for occupational health and safety personnel who deal with prevention and first aid measures for ocular chemical splashes, and who wish to supplement or update their understanding of ocular chemical burn injuries.

Gathering together all this technical knowledge introduces a new philosophy in the approach to chemical ocular burn lesions, in particular at the initial stage of victim management with increased practicality, specificity, and efficacy.

The multidisciplinary approach developed in this book also allows us, from the fundamental knowledge base, to envision other more diversified research on chemical burns in general.

The authors' goal is to promote the most beneficial care for patients with chemical ocular burn injuries by presenting the most precise and pertinent current information, and thus increasing communication and coordination between the various professionals involved in the prevention and treatment of such patients.

We are grateful to Oliver Mussate for translating this book from French to English.

Valmondois France François Burgher

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History of Chemical Burns and Relative Treatments

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Patrice Josset and Norbert Schrage

1.1 Burns for Doctors in Antiquity

The history of chemical burns and their relative treatments is still an unwritten chapter in the history of sciences. The present chapter aims to set up a framework of this history. We will first study the history of burns and their treatment from antiquity, before focusing on the treatment of chemical burns [1].

In Ancient Egypt, there were some recipes for the treatment of burns either in the critical phase or in the cicatricial phase and particularly a recipe to treat the ugly depigmentation of naturally tanned skins, daily exposed to a strong sun.

> Other remedy to prepare for a burnt zone, on first day: honey. Dress with it. Ebers 492 [2].
>
> "Other remedy for the conjuration of a burnt zone, on first day."
>
> (Dialog between a messenger and the goddess Isis)
>
> "Your son Heru is burnt in the desert. Is there any water there? There is no water. I have water in my mouth and the Nile between my thighs. I have come to extinguish the fire.
>
> Words to be spoken overt the breast milk of a woman who has borne a male child, gum, and ram's hair. This to be put on the burnt zone" Ebers 499
>
> "Other remedy (to eliminate white stains due to the burnt zone):
>
> Terebinth resin-Sntr 1 unit, honey 1 unit
>
> Anoint with this" Ebers 508

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Three thousand six hundred years ago, remedies such as honey and terebinth resin started to be used, and, since then, have been used all along history. The second recipe illustrates the mix of magic or religious practices and treatment.

As burns have always and very often occurred, most authors of Antiquity have written about them. Hippocrates has dealt with them in several writings and prescribed soothing substances and prevention from the cold. He has elaborated five formulae of medicines to prescribe for burns.

Much later, Guy de Chauliac (1298–1368) has written a few lines about burns in Chap. 6 of his surgery book (Fig. 1.1).

But the first author who has written about burns in a didactic way is Wilhelm Fabry von Hilden [3] (latine name: Fabricius Hildanus). In his essay, *de ambustionibus, quae oleo et aqua fervidis, ferro candente, pulvere tormentario, fulmine et quavis alia materia ignita fiunt*, written in Basel in 1607, the author classifies burns in three grades, and mentions the best treatment to apply for each case. He does not only prescribe a local treatment but also a general treatment, one of the goals of this latter being to prevent various complications. He gives indications on how to prevent the development of vicious scars. Wilhelm Fabry von Hilden seems to have been the first author to deal with burn treatment in a detailed and rational manner.

In the eighteenth century, Louis Laurent Heister (1683–1758) wrote a chapter about the study of burns in his "Institutions de chirurgie." He describes four grades of burns and prescribes the use of local treatments. He advises surgeons to look after the healing to prevent vicious scars.

In this century, various reflections about burns developed, particularly about the question of inner heat and nervous shock.

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Fig. 1.1 Guy de Chauliac

In the nineteenth century, this point of view completely changed, and Guillaume Dupuytren [4] (1777–1835) through his lectures, either self-published or published by his numerous disciples, brought remarkable changes about this point. At first, he classified burns into five grades, the first three of which have the ability to spontaneously heal. He noticed the importance of the burnt surface and that patients with superficial but wide burns may die when others with deep but local burns survive. Early death is accompanied by weak pulsation, anuria, and breathing weakness. The point of the difficulty to evaluate the burnt surface was already studied in a book written by Alexis Boyer [5] (1757–1833), published in 1814. The author thinks that wide burns irritate the central nervous system and thus cause fever, infection, and death. For all authors, pain is a major element, although in case of deep burns, pain disappears, which was noticed by Lelong and Dupuytren in an essay published in 1819 [6].

Dupruyten thought that a quick death could not be due to an inflammatory reaction but was caused by a violent pain exhausting the nervous system, which made this death similar to a death due to a loss of big quantity of blood. He was remarkably brilliant in the treatment of the retractile sequelae of burns, which he knew how to treat with enough detachment from the critical phase. Indirectly [7], we also know that Dupruyten considered that the fragments of preserved healthy skin among burnt areas played a key role in healing.

Oliguria or anuria was highlighted by Auguste Nélaton (1807–1873) in his surgical pathology essay [8], in which he has also mentioned the deep thirst appearing soon after the first instances of the burn. The renal lesions were highlighted by Frederick Edward Obenaus in his 1847 essay [9] in which he also mentioned that blood looked viscous, sometimes coagulated in big vessels, and, in doing so, was similar to the blood obtained by practicing a bloodletting on burn victims. Consequently, it seemed that the losses of fluid provoked very important troubles of the organic functions, and that the loss of fluid through skin and mostly through burnt areas should be reduced as much as possible, and that blood should be diluted.

In 1855, the notion of crush kidney was developed by Ludwig von Buhhl (1816–1880) [10]. In parallel, the damages made to lungs were described by Gustav Passavant (1815–1893) on the occasion of the fire of a powder mill in Frankfurt am Main [11]. He then noticed that lungs could be hurt by heat, smoke, and toxic gas. That was a really premonitory vision of what would be recognized more than a century later.

In 1860, the histological lesions of the kidneys were described by Samuel Wilks in London but he did not consider them as the cause of patients' death [12].

Despite the exaggerated attention paid to general considerations such as pain in the causes of death, it became more and more evident that the general treatment was more important that the local one, at the end of the nineteenth century.

With a few variations, these considerations have supported the treatment of burn victims until the second half of the twentieth century. Then, it became finally possible to secure the general treatment of burns, which we will study below after a brief study of chemical burn since Antiquity (Fig. 1.2).

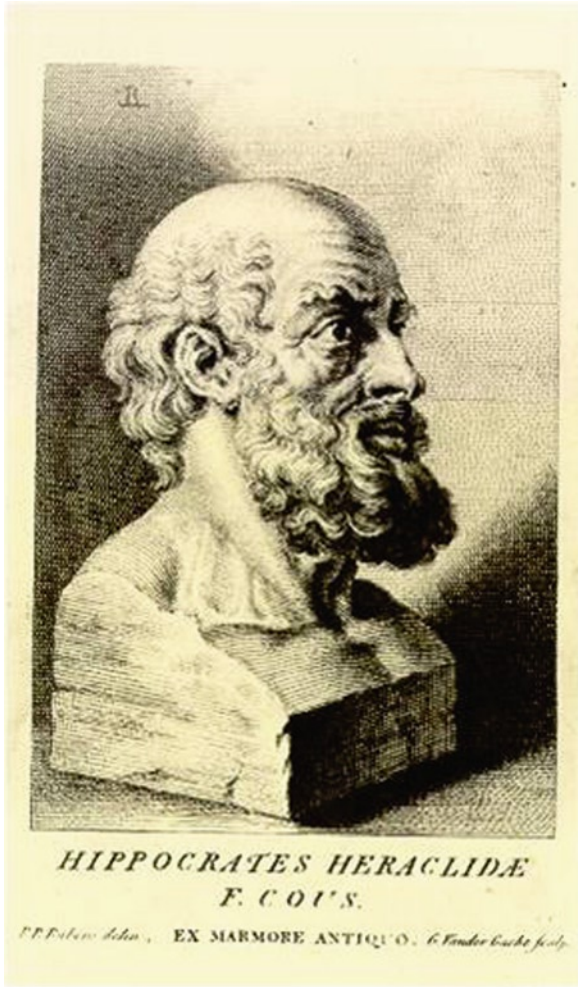

Fig. 1.2 Hippocrates Heraclidae

1.1.1 Chemical Burns Since Antiquity

It is not a surprise that there is no mention of chemical burn by antique authors such as Hippocrates, Galien, or Celse because the notion of chemical burn does not exist in their world; even cases of chemical burn might not have existed in their time.

Indeed, in Antiquity, substances or waters with acid or alkaline properties such as vinegar, lime, or alkaline products (soda, alkaline ashes) were well known but there was no mention of hurts specifically due to these substances. It is mentioned that some waters, particularly these from alkaline springs are not drinkable, but nothing more. Actually, it will take more than a thousand years so that concentrated acids and bases could be produced. Nevertheless, it is likely that accidents caused by lime have occurred.

The production of acids and bases is a direct consequence of the works of alchemists who did not start to work in the Middle Ages but in Hellenistic Alexandria [13]. So, from the twelfth to the sixteenth century, the following names appear: vitriol or sulfuric acid H_2SO_4, "eau forte" or nitric acid HNO_3, and "esprit de sel" or solution of hydrogen chloride (HCl) in water. The traditionally known bases such as potash, soda, or ammonia were called alkalis (from the Arabic word al-qâly designating the plants named soda).

In the twentieth century, the treatment of chemical burns becomes a bigger necessity during World War I. Combat gas burst into the battle provoking very severe lesions and a terrifying anxiety among fighters [14]. The town of Ypres (Ieper) in Belgium was one of the first towns contaminated by this combat gas on July 11, 1917, and thus has given the mustard gas its name as Yperite. This latter was then used in 1918 by the Germans in Verdun and "La Marne;" in 1919 by the British in Afghanistan; in 1925, on Winston Churchill's orders, by Britain on civil people in Kurdistan; in 1925 by France and Spain in Morocco; in 1934–1935 by Italy while it was occupying Ethiopia; in 1934–1944 by Japan against China; in 1963–1967 by Egypt in Yemen; and in 1983–1988, Saddam Hussein's regime used it against Kurd population in the north of Iraq. This mustard gas was also used during the war opposing Iraq and Iran.

As mentioned above, gas has been widely used and it is a powerful vesicant agent. In the form of vapor, it damages the respiratory tract. Eyes become temporarily blind and the skin in contact with the substance becomes inflammatory. The sweaty zones of skin are the most damaged as well as sensitive mucous membranes. If no treatment is applied, the cutaneous reaction provokes blisters full of liquid after 4–8 h. Spread in the form of particles, the gas penetrates the respiratory tract and destroys the mucous membranes with a respiration distress syndrome. Lungs suffer from emphysemae and edema due to the presence of fluids, which may cause a death similar to a drowning if the dose is too strong.

Finally, the patient suffers anemia, a drop of his immune resistance, and develops predispositions to cancers. Even when little concentrated, Yperite is indeed a mutagen agent.

It is easy to understand that, in this time, the treatment could only be purely symptomatic and only applied on skin and in absence of intense care, it could be qualified as "contemplative." When patients survived, their sequelae on skin were similar to those due to ordinary thermal or chemical burns. The ones suffering burns to the lungs often had a plus or minus serious definitive respiratory insufficiency.

Acid-base chemical accidents had already started earlier because of the industrial revolution but, as we know, the attention paid to the workers and risks on the workplace had been very deficient for a long time.

The only treatment, which is often revealed efficient enough, was the water washing of the chemical projections.

But, unfortunately, this was not always enough, particularly for eyes burns, because of the ocular epithelium being extremely fragile, or in case of wide burns or burns due to specific substances such as hydrofluoric acid.

Fig. 1.3 Marcel Legrain

1.1.2 Treatment of Thermal and Chemical Burns in the Second Half of Twentieth Century, the Revolution of Intensive Care

The very difficult situation of burnt patients lasted at least till the 1960s. It was deeply modified after the works and realizations of Prof. Marcel Legrain (1923–2003) (Fig. 1.3) who was the pioneer of renal physiology, and particularly of acute renal failure that he studied in the 1940s and 1950s. He went to Boston for two years and afterward he opened the first unit of renal dialysis, in Hotel Dieu Hospital in Paris. His disciples Aubert and Saisy opened the first center of Dialysis in Choisy Clinic and Saizy opened a Centre of Anaesthesia treating burnt patients in St Antoine Hospital in Paris. From Prehistory, the situation had evolved to accurate intensive cares that could compensate the huge losses of severe burned patients.

Scientists and doctors could thus discover hydroelectrolytic, caloric (up to 1,000 calories/day), endocrinous, and other losses.

Then the techniques by Saisy and his colleagues have widely spread in France, enabling a more and more efficient symptomatic treatment of burnt patients. Here, we won't study the points about surgery of burnt patients and skin transplantations.

Complicated by military secret, the issue of chemical war is still present today. For sure, the great powers have made big efforts to develop bacteriological and chemical weapons, among which are the neurotoxic agents. American soldiers suffering Gulf war syndrome may suffer consequences of this chemical pollution (because of the uranium and toxic substances released by bombing on Iraqi sites close to American soldiers). The secret about the production and nature of burns caused by chemical weapons confront doctors with strange burns and the collaboration between doctors (particularly between several countries) is in opposition with military actions. We shall remind that on February 6, 1918, [14] the Red Cross asked the belligerents not to use asphyxiating or deleterious gases, which with many other acts is to be credited to this institution and its founder, Henri Dunant.

A major progress toward the recognition of chemical burns was the recognition of pulmonary chemical burns, a discovery in which the Burns Surgery Department of St Antoine Hospital played an important part. Actually, the role of pulmonary burns due to chemicals had been unrecognized for a long time. Nevertheless, observers noticed that after 2 or 3 days victims of fire smokes might develop serious lung pathology, which was often lethal. The use of bronchial fibroscopies helped to authenticate the lesions of the mucous membrane and