

## Severe Ocular Burns

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### Abstract

The worst ocular lesions are chemical burns caused by strong bases and acids. Associated with the destruction of limbal stem cells (LSCs), there are repeated epithelial ulcerations, chronic stromal ulcers, deep stromal neovascularisation, conjunctival invasion and even corneal perforations. The initial clinical examination is difficult because the symptomatology is severe, but nevertheless it helps to classify the lesions, to establish a prognosis and to guide the therapeutic care. The classification system used most is that implemented by Hughes and modified by Roper-Hall. It is now completed neatly by those proposed by Dua and Wagoner, which are based on the importance of the deficit of LSCs. Prognosis of severe forms has progressed significantly thanks to a better knowledge of the physiology of the cornea's epithelium. Surgical techniques to repair destroyed LSCs have changed the prognosis of severe corneal burns significantly. To limit the incidence of burns, prevention, especially in the industrialised world, is essential.

### Keywords

Ocular burns, chemical burns, ocular lavage, ocular irrigation, ocular surface, limbal transplant, amniotic membrane transplant

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Chemical or thermal ocular burns represent about 10 % of ocular traumas.<sup>1,2</sup> Generally, bilateral burns are found in young male subjects. Work-related, domestic or recreation accidents, as well as assaults, are the main sources of ocular burns.

### Epidemiology

Chemical burns are more common and caused by strong bases or acids. They are also responsible for the most severe and heavy psychological, social and legal consequences. The proportion of domestic accidents linked to 'do-it-yourself' or gardening is increasing constantly and exceeds one-third in some series.<sup>3</sup> A lesion's severity depends on the nature, concentration, quantity, length of exposure and pH of the chemical substance. Bases (ammonia [NH<sub>3</sub>], sodium hypochlorite [NaClO], sodium hydroxide [NaOH], potassium hydroxide [KOH], calcium hydroxide [Ca(OH)<sub>2</sub>], etc.) enter the ocular area easily. The anions saponify the fatty acid of the cells' membranes, which results in the instant death of epithelial cells.

Among the acids (hydrofluoric acid [HF], hydrochloric acid [HCl], chromic acid [Cr<sub>2</sub>O<sub>3</sub>], acetic acid [CH<sub>3</sub>COOH], etc.), sulphuric acid or vitriol (H<sub>2</sub>SO<sub>4</sub>) is the cause of the worst accidents. Acids infiltrate more slowly than bases because the protons (H<sup>+</sup>) accelerate and denature the proteins. The superficial coagulation then created limits deeper infiltration of the acid in the cornea. For contact thermal burns, solids that retain heat and those with a high fusion point lead to deep lesions that sometimes result in the loss of the ocular globe.

The course of an ocular burn depends on the nature of the responsible chemical component; nevertheless, all share several evolving elements.

Thus, an initial incineration phase is followed after a few minutes to a few hours by a detersion of necrosis lesions and then the scarring phase. Detersion is defined as a rush of inflammatory cells to produce several enzymes, such as the matrix metalloproteinases (collagenases, gelatinases and stromelysin). While taking part in the detersion, these enzymes increase the destruction of the ocular structures.<sup>4</sup> The scarring results from the regrowth of healthy tissues that surround the burn. This involves ischaemic lesions consequent to the destruction of the vascular network and to lesions of the corneal and conjunctival cells. Scarring of the cornea and the conjunctiva can happen through the differentiation of surviving cells into fibroblasts or by the division of stem cells.<sup>5</sup>

### Semiotics and Classification

An ocular burn is an emergency and the initial clinical examination must lead first to therapeutic measures, especially during the ocular lavage. Data from the initial examination should be considered baseline and distinguished from further lesions observed during the burn's evolution.

At the acute phase, questioning of the patient provides more details about the circumstances of the appearance and time of the trauma, as well as the nature of the products responsible and the procedures already performed. Symptomatology can be very expressive (photophobia, weeping, etc.) and the pain significant. Instillation of an anaesthetic eye drop can help to lower eyelid spasms. The eye is usually red because of a hyperaemia of the conjunctiva, subconjunctival bleeding, a perikeratic circle and/or a chemosis. Besides destruction of the epithelium, severe corneal burns are associated with an oedema of a porcelain appearance. A more serious affect is characterised by the existence of ulcerations and/or ischaemia or necrotic areas of the limbal

region or of the bulbar conjunctiva (see *Figure 1*). Ischaemic areas are often predominant in the inferior part where the majority of the chemical product is found. These severe forms are associated with an inflammatory reaction in the anterior chamber, ocular hypertension and corneal anaesthesia. Eventually, palpebral lesions may occur, in particular of the free borders and of the lachrymal points.

The totality of clinical observations (corneal and conjunctival ulceration, ischaemic area, etc.) is outlined herein.

The goal of a classification system is, using the initial clinical data, to be able to establish a prognosis and to guide the therapeutic plan to adopt. The classification system most used is that of Hughes as modified by Roper-Hall (see *Table 1*).<sup>6</sup> This classification has four stages and relies on the importance of the stromal opacity and the spread of an eventual limbal ischaemia. Stages 1 and 2 burns have a good prognosis, whereas stages 3 and 4 burns have a poor prognosis. The Roper-Hall classification is not precise enough for stage 4 regarding the extent of limbal damage and is easily replaceable by Wagener or Dua's classifications (see *Table 2*) based on the importance of a deficiency in limbal stem cells (LSCs).<sup>7,8</sup> Indeed, a stage 4 burn under the Roper-Hall classification can evolve favourably when the extent of the limbal damage is less than 75 %, but with complete limbal destruction, the prognosis is very poor.<sup>9</sup> The more recent classification of Dua takes into account the extent of both limbal damage (not only ischaemic) and that of the conjunctiva. The extent of the damage in the limbal region is assessed using the number of clock hours involved and the extent on the bulbar conjunctiva in surface percentage. Grade IV, which comprises limbal damage from six to nine clock hours and 50–75 % conjunctival alteration, has a good prognosis. For a grade V burn the prognosis is poor and for grade VI it is very poor. Grades IV, V and VI correspond to stage 4 of the Roper-Hall classification, referred to as a poor prognosis.

Healing of the most severe corneal damage is determined by the deficiency in LSCs<sup>8</sup> at the origin of occurrence, chronic epithelial ulcerations, opacification, neovascularisation (see *Figure 2*) and even corneal perforation. Intraocular complications are frequent in cases of severe burns. These are usually cataracts, superinfections, intraocular inflammation, ocular hypertension and/or ocular hypotension.<sup>10</sup> Ocular dryness is often associated with complications. Complications with eyelid lesions involve distichiasis, entropion and/or ectropion.

## Treatment

There are two aspects to the goal of therapeutic care of severe ocular burns. First is to eliminate or to limit the aggressiveness as well as the penetration of the irritating or corrosive substance into the ocular field. Ocular lavage plays this role. Second is to control the inflammatory reaction and to encourage healing.

## Ocular Lavage

Ocular lavage is a crucial procedure. The course of the burn depends on the speed of application and quality of the lavage. It must be used as soon as possible at the accident scene.<sup>11</sup> Pain or the eyelid spasm mean that lavage used by the patient is not always efficient; therefore, lavage must always be applied when medical care is first provided. It is facilitated by the prior instillation of an anaesthetic eye drop and general anaesthesia may be necessary when treating children. The use of retractors is sometimes essential. The lavage must last for 15 minutes and about 0.5 litres of solution used.

**Table 1: Classification of Hughes Modified by Roper-Hall**

| Grade | Prognosis | Corneal Involvement                                        | Limbal Ischaemia (% of Limbal Circumference) |
|-------|-----------|------------------------------------------------------------|----------------------------------------------|
| 1     | Good      | Corneal epithelial damage                                  | 0                                            |
| 2     | Good      | Corneal haze, iris details visible                         | <33 %                                        |
| 3     | Guarded   | Total epithelial loss, stromal haze, iris details obscured | 33–50 %                                      |
| 4     | Poor      | Cornea opaque, iris and pupil obscured                     | >50 %                                        |

Source: Roper-Hall, 1965.<sup>6</sup>

**Table 2: Classification of Dua**

| Grade | Prognosis       | Clinical Findings                        | Conjunctival Involvement           | Analogue Scale*      |
|-------|-----------------|------------------------------------------|------------------------------------|----------------------|
| I     | Very good       | 0 clock hours of limbal involvement      | 0 %                                | 0/0 %                |
| II    | Good            | ≤3 clock hours of limbal involvement     | ≤30 %                              | 0.1–3/1–29.9 %       |
| III   | Good            | >3–6 clock hours of limbal involvement   | >30–50 %                           | 3.1–6/31–50 %        |
| IV    | Good to guarded | >6–9 clock hours of limbal involvement   | >50–75 %                           | 6.1–9/51–75 %        |
| V     | Guarded to poor | >9–<12 clock hours of limbal involvement | >75–<100 %                         | 9.1–11.9/75.1–99.9 % |
| IV    | Very poor       | Total limbus (12 clock hours) involved   | Total conjunctiva (100 %) involved | 12/100 %             |

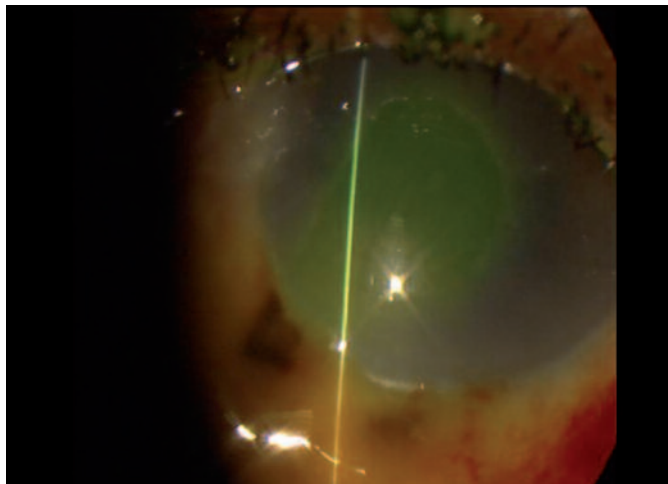
\*The analogue scale records accurately the limbal involvement in clock hours of affected limbus and percentage of conjunctival involvement. In calculating the percentage of conjunctival involvement, only the involvement of the bulbar conjunctiva up to and including the conjunctival fornices is considered.

Source: Dua et al., 2001.<sup>7</sup>

The two eyelids must be turned up and the conjunctival fornix washed off copiously. All foreign bodies must be removed using the operative microscope. Examination of the conjunctival fornix needs to be meticulous in the search for solid particles that adhere to the conjunctiva. Cleansing of a puncture with lavage of the anterior chamber is no longer advised. As it is usually available at the scene of the accident, water is the most used universal lavage fluid. However, compared to the intraocular surface, water is hypotonic and thus can be absorbed into the epithelium, worsen the oedema and carry acidic or basic molecules into the cornea. The use of isotonic or hypertonic solutions is preferred because they create a flux from the inside of the ocular surface to its outside. Running water and physiological serum do not have any absorption effect and only act by dilution and mechanical flow.<sup>12</sup>

Ringer's lactate and balanced saline solution (BSS) are better tolerated than physiological serum. Ringer's lactate has a small absorption capacity and BSS has an osmolarity close to that of aqueous humour, but does not have any absorption effect.<sup>13</sup> Currently, there is only one hypertonic ocular lavage solution with an osmolarity of 820 mOsm/l. Diphotérine® (Prevor Laboratory) is an amphoteric solution with a strong absorption capacity that has been used for several years in the chemical industry. Amphoteric chemicals, such as ethylenediaminetetraacetic acid, act by the capture of ions and their neutralisation through an amphophilic reaction. They can link with bases or acids without changing the pH of the environment and without an exothermic reaction. Burn lavages based on an amphoteric solution lead to a faster return to the normal extraocular pH.

**Figure 1: Alkali Burn Day Two**



Central corneal ulceration, major corneal oedema that prevents anterior segment visualisation, ischaemia of the superior limb at 75 % of the circumference and necrosis of the inferior bulbar conjunctiva.

**Figure 2: Alkali Burn Day 15**



Total corneal ulceration, important corneal oedema that prevents visualisation of the iris, total limbal ischaemia and neovessels over 360°.

For alkali ocular burn, ascension of the intraocular pH curve is less important and the descent is faster.<sup>12,14</sup> With their mechanism of action and the results, both experimentally and clinically, amphoteric solutions seem more suited to the emergency rinsing of chemical burns.<sup>15</sup> In cases of severe burns, ocular lavages need to be continued throughout the patient's transportation to the hospital. The use of a catheter with perfusion maintained at about 20 cm of the ocular globe is preferred to the use of an automatic irrigation system. These devices, which include a polyethylene loop or a polymethyl methacrylate scleral lens (Morgan Lens), have some disadvantages, such as a difficult setting-up process as they are at the origin of the iatrogenic lesions and they do not guarantee a good rinsing of the complete ocular surface.<sup>16</sup> Lacrimal duct lavage is not advised, especially because of the fast appearance of an oedema of the lacrimal meatus, the aggravation risk of lesions and the risk of application to the wrong track.

## Medical Treatment

The use of local corticoids,<sup>17</sup> long-debated, can be justified by their ability to reduce the inflammatory reaction. They decrease

the stromal invasion by polynuclear neutrophils, stabilise cell and lysosomal membranes against polynuclear neutrophils and have an anticollagenase action. Corticoids limit the destruction of mucous cells of the conjunctiva.<sup>18</sup> Nevertheless, they reduce keratocyte migration, inhibit collagen synthesis and delay the healing process.<sup>19</sup> Local corticoids can be prescribed for over eight days with a positive outcome.<sup>20</sup> The incidence of infectious complications does not seem to increase with local corticotherapy. In association or as a replacement for the corticoids, anti-inflammatory non-steroidal treatments have also been proposed, but they should be advised against as they lengthen the epithelial scarring process and modify corneal sensitivity. In experimental burns, tetracycline reduced the collagenase activity and increased corneal ulcerations. This action is independent of the antimicrobial property and is caused by chelation of the zinc indispensable to the activity of the metalloproteinases.<sup>21</sup> Parenteral administration of tetracycline reduces the incidence of corneal ulceration and facilitates their healing.<sup>22</sup> The collagenase inhibitors, such as cysteine, acetylcysteine and synthetic thiols, proved to be efficient on experimental burns, but have not been studied in a clinical context. Cycloplegic eye drops reduce the pain and limit the formation of posterior synechia and are prescribed systematically.

Some drugs increase the chances of healing. Burns of the conjunctiva are associated with a reduction in the number of mucosal cells. The regular use of artificial tears with no preservatives is recommended. Ascorbate (ascorbic acid) is a co-factor of collagen synthesis, but in the case of burns its concentration in the aqueous humour is reduced. Pfister and Paterson<sup>23</sup> showed that a supplementation of ascorbic acid administered locally or parenterally prevented retinal thinning and the incidence of corneal ulcerations, both experimentally and clinically. Eye-drop administration at 10 % would be most efficient in the knowledge that ascorbic acid concentration must be limited because of potential lesions of the ciliary body in the anterior chamber.<sup>23</sup> Ascorbate by oral administration can be prescribed at a dosage of 2 or 3 g/day.<sup>9,15,17</sup> Growth factors (epidermal, fibroblast, etc.), such as fibronectin and retinoic acid, are not used in the usual clinical setting. Infections are prevented by the administration of an antibiotic eye drop with a large spectrum as well as parenteral tetracycline. Analgesics are easily prescribed by oral or parenteral administration because corneal nerve lesions can be associated with intense pains.

## Surgical Treatment

As with local corticotherapy, the aim of excision is to reduce the inflammatory reaction created by degradation products of the necrotic conjunctiva that participate in the detersion of the site. Excision consists of the ablation of necrotic tissues of the ocular globe surface.<sup>24</sup> In the case of severe ocular burns followed by a total loss of limbal vascularisation, besides the predictable impossibility of secondary re-epithelialisation, there is an immediate risk of necrosis of the anterior segment. To re-establish limbal circulation and to avoid the evolution towards necrosis or aseptic ulceration, a tenoplasty can be performed. This consists of the realisation of a Tenon advancement strip positioned along the limbus.<sup>25</sup> Prevention of symblepharons can be achieved using scleral glass or a polymethyl methacrylate ring.

Proposed by Schermer and developed by Tseng, the LSC theory is the basis on which limbus transplant was developed.<sup>5,26</sup> Corneal epithelium renews rapidly, using undifferentiated LSCs located in the basal layers of the limbus. Limbal autotransplant is the technique of choice for

the treatment of corneal limbal destruction and its complications.<sup>27</sup> It addresses unilateral limbal insufficiencies when there is a contralateral healthy eye donor. The complete conjunctival pannus that covers the cornea is removed beyond the limbus by about 3 mm. The graft is removed through a cornea incision located 1 mm forward of the limbus. The dissection realises a tunnelling of about 2 mm behind the limbus. To avoid creating a limbal insufficiency in the eye donor, the graft cannot exceed a 180°. <sup>28</sup> Limbal autotransplant allows a corneal re-epithelialisation of good quality in 75–100 % of cases and constitutes a barrier to a neovascular cicatricial phenomenon of conjunctival origin.<sup>29</sup> The optimum period between the burn date and intervention is disputed. Most authors believe it is better to wait several months to allow diminution of inflammatory reaction. Nevertheless, some recommend to intervene early on, that is before the appearance of complications linked to the LSC deficit.<sup>8</sup> The aim of limbal allotransplant is identical to that of an autotransplant. Limbal allotransplant is recommended for widespread limbal lesions that are bilateral or unilateral on only one eye.

The amniotic membrane is a tissue located at the interface between the placenta and the amniotic liquid was first used for ocular burn by Sorsby and Simmonds in 1947.<sup>30</sup> It is composed of an unstratified epithelium, a basement membrane and an avascular mesenchyme. The amniotic membrane facilitates re-epithelialisation by decreasing the inflammatory and cicatricial reaction.<sup>31</sup> A piece of amniotic membrane, epithelial face up, is sutured to the cornea by separated points of nylon 10/0. The amniotic membrane is covered by the corneal epithelium, integrated with the stroma and then resorbed. The current practice is to realise the amniotic membrane transplant rapidly, during the early phase of the burn. Good results are also observed when it is performed later on.

Usually around 10 %, the rejection risk of transfixant keratoplasty (TK) is higher in cases of chemical burn, especially because of the frequency and the importance of stromal neovascularisation of the receptor cornea.<sup>32</sup> TK does not introduce LSCs and it is not

sufficient to treat widespread limbal ischaemia. It must be performed with a limbal transplantation. TK can be realised at the same time as a limbal allotransplant. Nevertheless, epithelial scarring and the corneal transparency are better when the TK is realised later on (between one and 13 months).<sup>27</sup>

Profound lamellar keratoplasty consists of stroma and graft epithelium transplants while respecting Descemet's membrane and the receiving endothelium. It is used for corneal burns that do not affect Descemet's membrane and the endothelium.

Keratoprosthesis remains the ultimate surgical resource for bilateral corneal blindness, when TK and LSC treatments are no longer realisable. Although harder to perform, the results of keratoprosthesis are sometimes very encouraging.<sup>33</sup>

Initially developed by Thoft, conjunctival transplants do not allow corneal epithelium healing.<sup>34</sup> In this area it has been replaced LSC transplants. Nevertheless, it remains indicated for conjunctival fornix reconstruction corrected by cicatricial fibrosis.

## Conclusion

Chemical burns can be responsible for severe, bilateral and irreversible alteration to the visual function. The initial clinical examination is sometimes hard to perform because of the severe symptomatology. Nevertheless, it allows classification of the lesions, establishes a prognosis and most importantly, guides the therapeutic care. Prognosis for the worst ocular burns has improved during the past decade thanks to a better knowledge of the corneal epithelium physiology. Surgical techniques to restore LSCs that were destroyed have changed the prognostics of severe corneal burns.

Above all, prevention is essential to decrease the incidence of burns, especially in the industrial world, since a large number of dramatic cases could have been avoided with a minimum of information, training and regulation. ■

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