The ROYAL COLLEGE *of*
OPHTHALMOLOGISTS

REVIEW ARTICLE

Chemical eye injury: pathophysiology, assessment and management

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Abstract

Chemical eye injury (CEI) is an acute emergency which can threaten sight and life. These commonly occur at home or the workplace with the former being generally mild and the latter more severe and bilateral. Major workplace accidents involve other parts of the body and can be associated with inhalation or ingestion of the chemical. Alkali injuries cause damage by saponification of tissue and deeper penetration as a consequence. Acid injuries cause rapid coagulation of tissue, which impedes penetration and limits damage. Irritants such as alcohols, cause superficial epithelial denudation. Severe chemical insult can affect all anterior segment structures causing iris, pupil and lens abnormalities. Eye pressure is variably affected and can be low or high or start as one and rapidly change to the other. Chorioretinal changes in the form of vasculopathy are seen and ascribed to be secondary to anterior segment inflammation rather than due to the direct effect of CEI. Final outcome related to structure and function is determined by the injurious agent, duration of exposure, nature of treatment and the rapidity with which it is instituted. Prevention of further damage by profuse and prolonged eye wash, after ascertaining pH of both eyes, together with exploration and removal of all particulate matter, is the key. Other management principles include a complete and thorough assessment, control of inflammation, facilitation of healing and prevention and management of sequelae and complications. Intraocular pressure is often forgotten and must be assessed and managed. Management often requires a multidisciplinary approach.

Introduction

A chemical injury is a non-mechanical injury-inducing chemical changes in the substance of contact. Most chemical injuries to the eye are mild but severe injuries, though rare, cause serious harm to one or both eyes with considerable morbidity and sight loss.

Ocular chemical injury represents 10–22% of all ocular trauma and is the second most common cause of work-based eye injuries at 12%, behind 'foreign body' injuries

which constitute the bulk at 43% [1]. Young males (16–25 years old) working in industry represent two-thirds of reported cases [1]. Domestic accidents also contribute. Household injuries with disinfectants and cleaning solutions are common amongst children. Hate crime especially acid attacks are on the rise compounded by the ease of availability and low cost of some acids such as sulphuric acid used in car batteries [2, 3].

Much of our knowledge of burns comes from the skin literature where the major cause is thermal rather than chemical insult. The severity and consequently the outcome and sequelae of skin burns depends on the depth of the burn. Skin burns are classified in six degrees or grades, defining involvement of structures from superficial to deep, starting with the epidermis composed mainly of keratino-cytes and their basement membrane (grade 1); epidermis and part of dermis, primarily made of collagen and extra-cellular matrix (grade 2); all of dermis and hypodermis, which is rich in adipose tissue (grade 3); affecting tissues deeper than hypodermis where the main blood vessels and nerves are located (grade 4); affecting the muscles (grade 5) and finally the bone, which lies at the core (grade 6) [4–6]. The arrangement of the orbital contents is somewhat in reverse to that of the skin (of a limb), with the bony socket

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being on the 'outside'. Analogous layers of the ocular surface (conjunctiva) are the epithelium, the substantia propria with its adenoid tissue, a fibrous layer, the Tenon's capsule, the episcleral and the sclera with its innermost surface lined by the lamina fusca, which encloses the suprachoroidal space. The extraocular muscles are in general more posteriorly located. The corneal structure is different with the epithelium being most superficial followed by the Bowman's layer, stroma with its population of keratocytes, the pre-Descemet's layer and the Descemet's membrane and endothelium. Internal ocular structures, namely the iris, ciliary body, choroid, lens, vitreous and retina can also be directly or indirectly affected. Another major difference with the eye is the intraocular pressure and its response to the chemical insult. The classification of ocular chemical burns however, unlike the skin, does not follow the same anatomical pattern but are based on the extent of involvement of the limbus, conjunctiva and cornea (see below) [7, 8].

The severity of ocular surface chemical injury is determined by the causative agent, the duration of contact, treatment given and the time from injury to initiation of treatment. These factors influence the depth of penetration of the chemical agent, consequent involvement of the extraocular and intraocular structures and the wound healing and repair and regeneration response. The latter can extend for 12–18 months with chronic inflammation, scarring and fibrosis perpetuating further damage to the structure and function of ocular surface, intraocular structures and alterations in intraocular pressure [9].

Pathophysiology

Causative agents

The main causative agents are alkalis, acids and irritants like alcohols. Common alkalis are ammonia and ammonium hydroxide found in cleaning solutions and fertilisers, sodium hydroxide in caustic soda and drain cleaners, calcium hydroxide in plaster and cement. Alkalis are hydrophilic and lipophilic causing dissolution of tissues by release hydroxyl ions which induce saponification of fatty acids in cell membranes (converting fat/oil to salts of fatty acids). Hydrolysis of interfibrillar glycosaminoglycans occurs rendering the tissue susceptible to enzymatic degradation with further disruption of extracellular matrix with thickening and shortening of collagen lamellae. These events lead to further and deeper penetration of the alkali. Magnesium hydroxide present in fireworks, can cause devastating injuries due to the thermal as well as the chemical effect. Lime, which is the most common form of alkali injury fortunately forms calcium salts as soon as it

penetrates the cell membrane. These precipitate and form deposits, which prevent further penetration and damage. However, retained lime particles in the fornices can act as a reservoir of the alkali and cause severe damage if not identified and removed promptly. Aqueous based solutions used for irrigation can dissolve the precipitates, releasing hydroxyl ions and cause further damage [10, 11].

Common acids associated with eye injury are sulphuric acid found in car batteries, hydrochloric acid in swimming pool disinfectants, nitric acid in dyes and acetic acid in vinegar. Sulphuric acid injuries are the most common. Acids in general interact with the water contents of the tear film and tissue to produce heat which causes additional charring of the corneal and conjunctival epithelium. Acids cause tissue coagulation and collagen shrinkage. Ocular surface proteins bind to the acids, thus acting as a buffer and prevent further penetration of the acid.

Trifluoroacetic acid used in several industrial settings and hydrofluoric acid found in rust removers and metal cleaners are exceptions. Because of their low molecular weight, dilute solutions of these acids penetrate deeply before dissociating. They form insoluble salts with calcium and magnesium, but soluble salts are also formed with other cations, which dissociate rapidly releasing more fluoride ions, which cause further tissue destruction and delayed symptoms and signs. These acids thus cause tissue damage by two mechanisms, corrosive burn by the free hydrogen ions and chemical burn by tissue penetration of the fluoride ions [12–14].

Irritants such as alcohols and household detergents cause de-epithelialisation of the ocular surface, which is the least severe of all chemical injuries and usually heals without visual consequences.

Ocular burns can be associated with surrounding facial burns or more generalised burns which can be serious if the agent has been ingested or inhaled with gastrointestinal and respiratory symptoms, including laryngeal oedema, that can be life threatening. Systemic toxicity can occur secondary to depletion of calcium and magnesium which are essential for cellular and enzymatic function. Cardiac arrhythmias precipitated by hypocalcaemia and consequent hyperkalemia can be fatal.

Duration of contact

Besides the nature of the agent, the duration of contact and surface area affected determine the depth of penetration and hence the severity of the damage. Depending on the degree of penetration, corneal epithelium, stroma, keratocytes and nerves can be affected with corresponding involvement of conjunctival epithelium, substantia propria, Tenon's capsule, episcleral and sclera. Further penetration can affect the iris, and lens. Damage to blood vessels at the limbus causes

'limbal ischaemia' with loss of limbal stem cells; scleral and uveal ischaemia contributes to serious damage. Damage to the ciliary body in the form of ischaemia or distortion of the trabecular meshwork, due to shortening and shrinkage of the collagen fibrils, can lead to hypotony or elevation of the intraocular pressure [15]. All chemicals cause marked reduction of glucose and ascorbate in aqueous humour from damage to the ciliary epithelium, leading to retarded collagen synthesis, which in turn can cause irreversible hypotony and phthisis specially with prolonged elevated aqueous pH levels of $\geq$ 11.5 [16, 17]. Ascorbic acid level in aqueous humour is about 15 times more than in plasma [18]. Oral and intravenous administration of ascorbic acid rapidly increase aqueous ascorbate levels, with the latter mode of administration being more effective [19].

Retinal damage is rarely due to the direct effect of the chemical agent. Anterior segment tissues i.e. the ocular surface, iris, ciliary body and lens act as buffers for intraocular penetration by reacting with the chemicals leading to their deactivation. pH, oxygen, and oxidation-reduction changes are restricted to the cornea and the anterior chamber, where they cause profound uveal inflammation and release of pro-inflammatory cytokines. These rapidly diffuse to the posterior segment, triggering retinal damage. Tumour necrosis factor-α was identified as a key pro-inflammatory mediator of retinal ganglion cell death [20]. Sudden hypotony or raised intraocular pressure can also contribute to retinal damage.

In severe chemical injuries, the entire limbus across 360 degrees is damaged and sloughs. However, in many instances, despite relatively severe injury, it has been shown that limbal stem cells initially survive and undergo gradual attrition over several weeks. Surviving stem cells contribute to the wound healing process as is evident by transient increase in cells bearing stem cell markers. Ongoing inflammation and infiltration of inflammatory cells in the limbal stroma leads to fibrosis and gradual loss of niche anatomy and physiology resulting in signs and symptoms of limbal stem cell deficiency [21, 22].

Epithelial injury

Epithelial damage with an intact limbus

Superficial mild chemical burns cause de-epithelialisation of the central corneal epithelium leaving a rim of 1–2 mm of peripheral corneal epithelium intact, adjacent to the limbus [23]. The peripheral and limbal epithelial cells have more complex hemidesmosome attachments than central epithelial cells. These epithelial defects heal rapidly from the remaining intact epithelium, which migrates centripetally as 3–6 convex sheets. Adjacent sheets meet, giving the remaining defect a geometric shape like a triangle,

quadrilateral, pentagon or hexagon (Fig. 1a–e). The epithelium continues to migrate centripetally till the sheets meet to form 'Y' shaped contact lines, along the final meeting points of the epithelial sheets. Two 'Y' shaped contact lines may be present lying end to end, and limb(s) of the lines may be missing to give the appearance of a pseudodendrite (Fig. 1c). The lines are best delineated with fluorescein staining. This pattern is very consistent in the healing of large corneal epithelial defects (rule 1 of corneal epithelial wound healing). As epithelial sheets expand to cover the denuded area, individual cells within the sheets break desmosome attachments to adjacent cells and migrate centripetally, each like an individual animal in a herd of cattle, that from afar would appear as a large sheet. Fluorescein (late) staining reveals this phenomenon in the form of a stippled pattern of the epithelium, resembling 'iron filings around a bar magnet' (Fig. 1d). When healing is complete, desmosomes and hemidesmosomes are re-established and the epithelium takes on a normal appearance

Epithelial damage with partial or sectorial involvement of the limbus

Relatively more severe yet superficial chemical injuries affect the corneal, limbal and conjunctival epithelium resulting in sectorial limbal involvement [24]. It is usually the inferior limbus and adjacent conjunctival epithelium that is affected together with the central corneal epithelium. This is most likely to be related to the gravitation of the chemical liquid to the lower fornix and also the reflex Bell's phenomenon causing the eye to roll up at the time of injury, covering the upper ocular surface relatively earlier than the lower half (Fig. 1f).

In such cases, the denuded limbus heals by the circumferential migration of tongue-shaped projections of epithelium from either end of the remaining intact epithelium. These follow the limbus until they meet each other to complete limbal healing (rule 2 of corneal epithelial wound healing). Thereafter the epithelial defect of the cornea becomes like that described above, with an intact limbus and subsequent healing follows rule 1. In areas where the limbus is substantially ischaemic, epithelial cover is slow to establish. While the limbus and cornea heal as described above, the denuded conjunctiva also heals by the centripetal migration of conjunctival epithelium from the fornix towards the limbus [24, 25] (Fig. 2).

Often the 'rule 2' pattern of healing is interrupted by the centripetally migrating conjunctival epithelium, which reaches the limbus before the circumferentially migrating tongue-shaped extensions from the remaining intact epithelium have met to complete limbal healing. Conjunctival epithelium migrates across the denuded limbus and covers varying areas of the cornea. This part of the limbus and
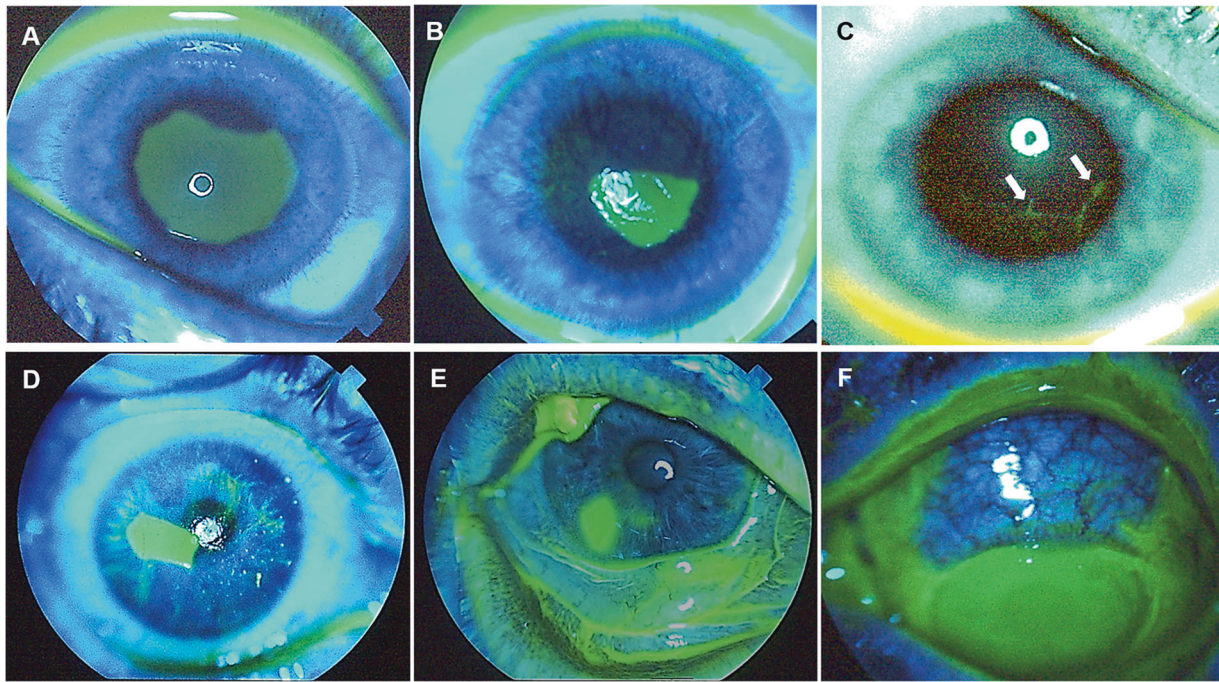
Fig. 1 Process of corneal epithelial wound healing with intact limbus. a Central epithelial defect with intact limbus is shown. **b** Healing is occurring with centripetal migration of epithelium. The defect assumes a trianglar shape. **c** Final closure of the defect with 'contact lines' resembling a pseudodendrite (*arrows*). **d** A pentagon-shaped defect with curvilinear lines of healing epithelium streaming towards it, like 'iron filings around a bar magnet' are seen. **e** A quadrilateral shaped healing defect with streaming of cells around it. **f** Chemical eye injury sparing the superior conjunctiva and limbus. The rest of the cornea and limbus (and majority of the rest of the conjunctiva, not shown in picture) were lost.

cornea become conjunctivalised, indicating limbal stem cell deficiency in that sector. Conjunctival epithelium on the cornea is thinner, irregular, shows late fluorescein staining, attracts blood vessels and is prone to erosions. Conjunctivalisation of the limbus and cornea is a hallmark of limbal stem cell deficiency [25, 26] (Fig. 3).

Total corneal and limbal epithelial cell loss

With more severe injuries a total loss of corneal and limbal epithelium occurs. This is associated with partial or 'total' loss of conjunctival epithelium. In cases with complete loss of corneal and limbal epithelium with some surviving conjunctival epithelium, the conjunctival epithelium migrates centripetally to reach the limbus, and covers the cornea [25, 26] (Fig. 4).

Often the conjunctival epithelium growing on the cornea, whether associated with sectorial or total limbal involvement, brings in its wake blood vessels, lymphatics and fibrous tissue, covering the cornea with a fibrovascular pannus of variable thickness. The extent of cover on the cornea too can be variable either covering the entire cornea or leaving a central or infero- central epithelial defect with heaped or rolled epithelium along the perimeter of the defect. The epithelial defect can be persistent, or recurrent

with repeated healing and break down of the epithelium. The epithelial cells are multilayered, of conjunctival phenotype with goblet cells and intraepithelial lymphocytes along the basal layer. All these elements, with presence of cystic spaces, are clearly visible on in vivo confocal microscopy (IVCM) and together constitute features of limbal stem cell deficiency [27] (Fig. 5).

Depending on the depth of corneal stromal involvement, there may be a plane of cleavage between the fibrovascular pannus and Bowman's layer (superficial burns) or the pannus may be integrated with the stroma with deep blood vessel invading the stroma. Corneal nerves are also damaged and can manifest as complete anaesthesia or hypoaesthesia of the cornea. In the later stages of wound healing, hyperaesthesia and photophobia may be a feature, probably related to aberrant nerve regeneration. Stroma not covered with epithelium is prone to melt, especially when associated with nerve damage, resulting in severe neurotrophic keratopathy [28].

Conjunctival transdifferentiation

Conjunctival transdifferentiation is a term used to describe the transformation of conjunctival epithelial cells on the cornea to the corneal epithelial phenotype. Following
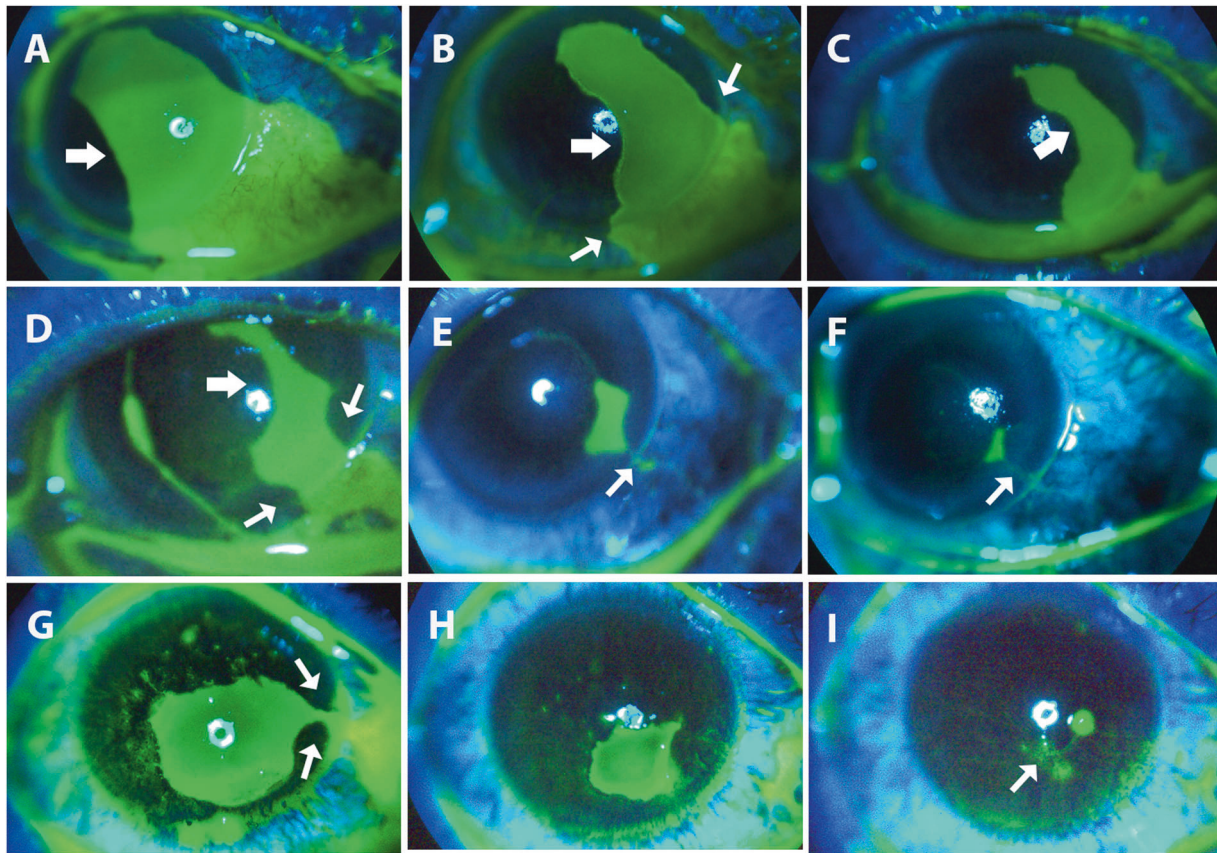
Fig. 2 Healing of corneal epithelial wound with partial limbal involvement following chemical eye injury. a Approximately 3 clock hours of the limbus, most of the central corneal epithelium and inferior bulbar conjunctiva of the right eye are affected. Centripetal migraton of cells from the temporal limbus is seen (*arrow*). **b** Circumferentially migrating sheets of epithelium are beginning to form at either end of the intact limbal epithelium (*small arrows*). The temporal sheet has advanced further, centrally (*thick arrow*). **c, d** The same pattern is seen with both the central corneal (*thick arrows*) and limbal epithelial defects becoming covered with epithelium. The circumferentiall migrating tongue-shaped sheets of limbal epithelium are clearly seen in **d** (*small arrows*). **e** The circumferentiall migrating tongue-shaped sheets of limbal epithelium have met to complete limbal epithelial wound healing. The meeting point of the two sheets is marked with an arrow. **f** As the corneal epithelial defect heals, a 'contact line' is clearly visible (*arrow*). **g, h** A similar pattern is demonstrated in another case. **g** The circumferentially migrating tongue-shaped sheets of limbal epithelium are clearly seen (*arrows*). **h** Centripetal migration of epithelium is seen from the recently healed limbus. **i** Complete healing is associated with the formation of contact lines (*arrow*).

chemical injury, surviving conjunctival epithelium initially covers the corneal defect as a single layer of cells, which later becomes 2–3 layers thick with goblet cells. The goblet cells disappear by 6 weeks and the epithelium appears to assume a corneal phenotype [29, 30]. However, biochemical studies related to enzymatic activity (lactate dehydrogenase) and glycogen levels suggest that true transdifferentiation of conjunctival epithelium to corneal phenotype does not occur [31].

By IVCM examination of conjunctival epithelium on cornea following chemical burns, we have shown that the central corneal epithelium has characteristic corneal epithelial phenotype appearing as dark polygonal spaces with a bright border while the limbus shows classical signs of stem cell deficiency in the form of hyper-reflective conjunctival cells, goblet cells, vessels and cystic spaces.

We have also noted ectopic palisade like structures in the bulbar conjunctiva, which could nest stem cells that regenerate corneal epithelium following conjunctivalisation (Fig. 6) (unpublished observations). A similar appearance has been demonstrated in eyes with total limbal stem cell deficiency with surviving central sheets of corneal epithelium, which can last for years, suggesting that the central basal epithelium can sustain a central cells mass and that the limbus may have a minor role in normal corneal epithelial homoeostasis but a major role following injury [32, 33].

It has also been postulated that clusters of cells expressing corneal epithelial stem cell markers such as ABCG2 are present in the conjunctiva, which could be responsible for regenerating the corneal surface with corneal phenotype of cells [34, 35]. Other theories supporting corneal epithelialisation in the absence of surviving limbus include the
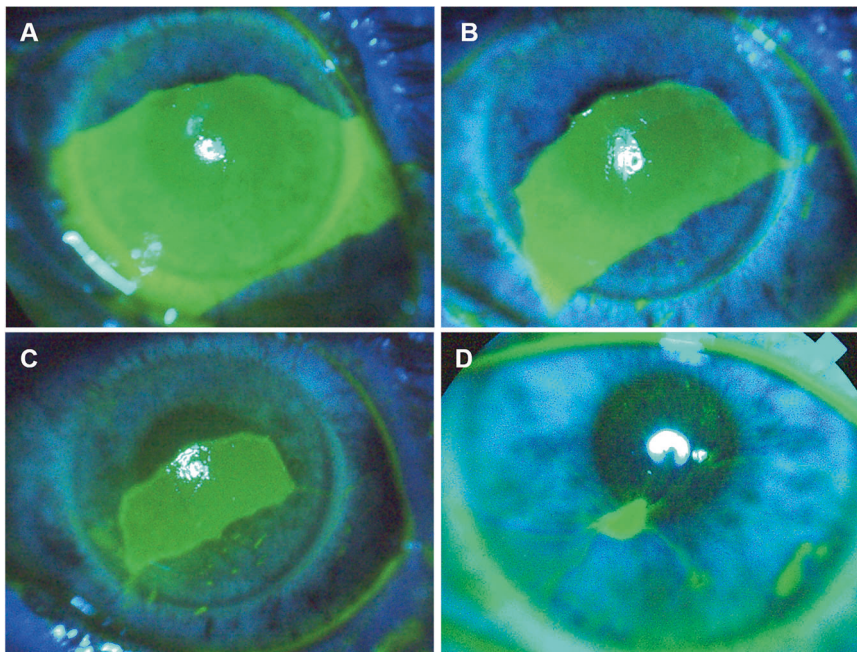
Fig. 3 Healing of corneal epithelial wound following chemical injury with subtotal limbal involvement. a Cells from the upper limbus show commencement of centripetal migration. A sheet of conjunctival epithelium has migrated close to the infero-nasal limbus. **b** Limbal healing is occurring by circumferential migration along the affected limbus but the conjunctival epithelial sheet has covered the infero-nasal limbus and cornea. **c** Progressing of limbus derived healing and conjunctival epithelial sheet migration on the cornea. **d** The cornea is covered by corneal (limbus derived) cells (upper 2/3) and conjunctival cells (lower 1/3). There is a persistent epithelial defect and late fluorescein staining cells in the area covered by conjunctival epithelium (signs of limbal stem cell deficiency).

Fig. 4 Total corneal and limbal epithelial defect after chemical eye injury. a The entire cornea, limbus and adjacent bulbar conjunctiva is showing fluorescein staining. **b** Total limbal stem cell deficiency with conjunctivalisation and 360 degrees of fibrovascular pannus. **c** Central persistent epithelial defect. Figures 4b, c are features of total limbal stem cell deficiency.

presence of conjunctival cells that express stem cell markers and can act as a source of regenerating epithelium which can migrate to cover the cornea [34, 35].

Corneal and conjunctival stromal injury

The corneal stroma is predominantly formed of regularly arranged collagen fibrils (I, III, V), of which type I is the major constituent. Other constituents include keratocytes and glycosaminoglycan ground substance. Following chemical injury, the keratocytes are mobilised to repopulate the cornea starting from the most posterior part of the stroma. In mild cases, type I collagen can be seen at the edge of the wound as early as the first day while in moderate injuries it can take 7–14 days. Collagen synthesis following chemical burn can take 7–56 days with a peak at 21 days. In severe cases keratocyte repopulation may not occur, however, monocytes transdifferentiating to fibroblasts have been described leading to corneal scarring. Ascorbic acid is essential for collagen synthesis, thus lower level of ascorbic acid following chemical burn can compromise collagen synthesis and lead to persistent corneal ulceration. Within 12–24 h of chemical burn, polymorphonuclear (PMN) leucocytes infiltrate the periphery of the cornea from damaged and necrotic conjunctival tissue and uveal vessels. These cells release PMN leucocytes type 1 collagenase and

Fig. 5 In vivo confocal microscopy (IVCM) of limbal stem cell deficiency. a 360 degrees of conjunctivalisation and vascularisation with a temporal fibrovascular pannus. **b** IVCM shows hyper-reflective conjunctival epithelium with cystic spaces. **c** Conjunctival epithelium on the cornea with rossettes of goblet cells (*arrows*). **d** IVCM of hyper-reflective conjunctival epithelum on the cornea showing a clear demarcation from the normal (dark spaces outlined by bright lines) central corneal epithelium.
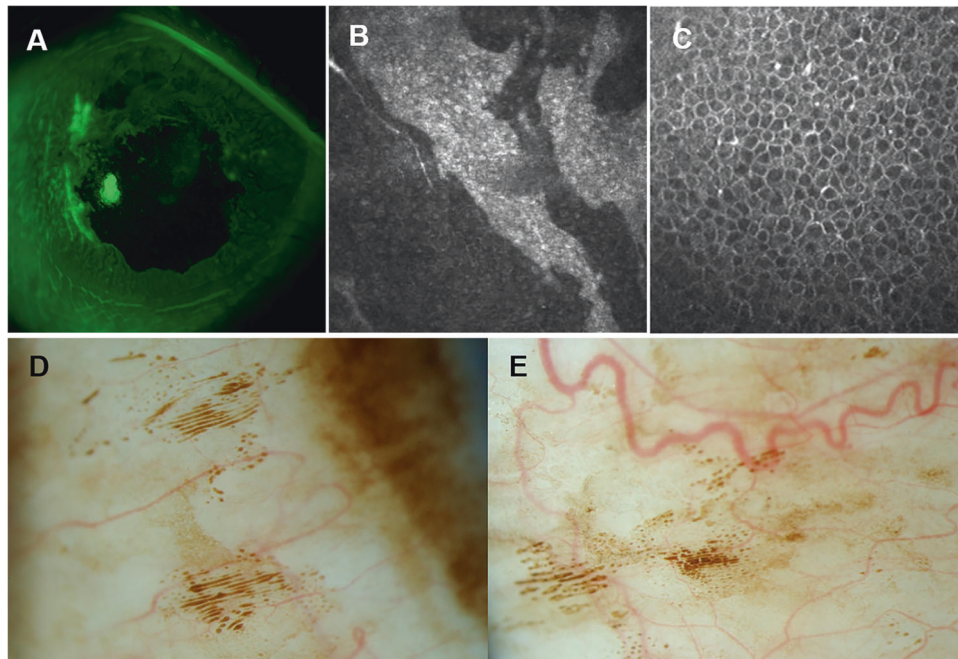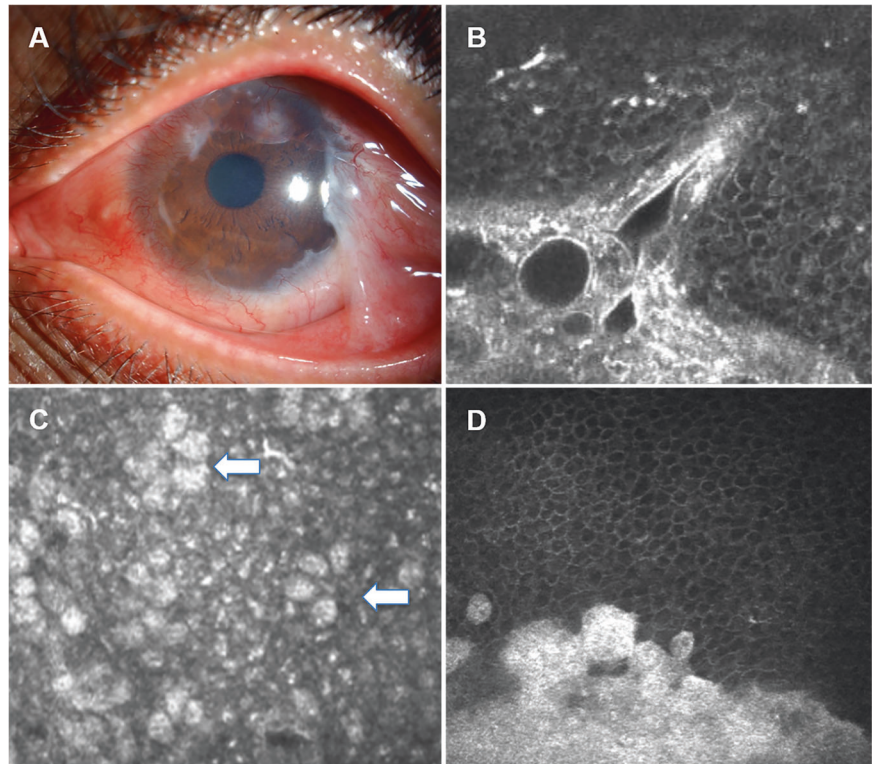

Fig. 6 Central islands of surviving corneal epithelium and conjunctival palisades. a A central island of corneal epithelial sheet is seen surrounded by fluoresceing staining conjunctival epithelial cells. **b** In vivo confocal microscopy (IVCM) of the limbal epithelium showing hyper-reflective conjunctivalised epithelium interdigitating with normal corneal epithelial cells. **c** The central corneal epithelium has IVCM morphology of normal corneal epithelum of dark spaces surrounded by bright lines. **d, e** Structures identical to pigmented palisades seen on the bulbar conjucctiva of both eyes of a dark-skinned lady. These ectopic palisades may allow regeneration of normal corneal epithelium after total limbal damage after chemical eye injury.

Fig. 7 Corneal stromal injury after chemical insult.
a, **b** Central stomal haze and melt with a large epithelial defect, staining with fluorescein dye. **c**, **d** Persistent inflammation, corneal vascularisation and a large area of corneal keratinisation (*arrows*) and conjunctival keratinisation with obliteration of the external canthus, indicating extreme dry eye.
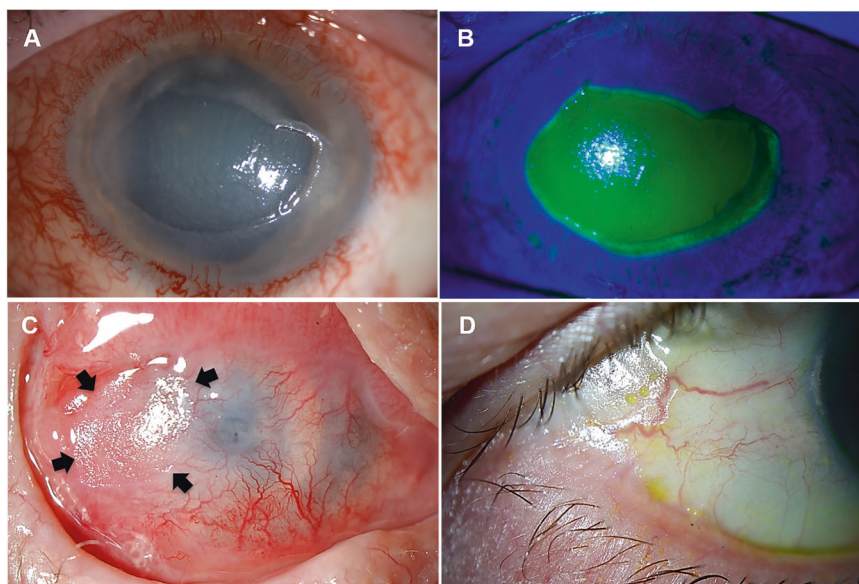
plasminogen activators which can cleave and scavenge damaged collagen fibrils. In severe chemical burns a second wave of influx of PMN leucocytes occurs at day 7, peaks between day 14–21 and persists as long as the epithelial defect remains [29]. Conversely, epithelial regeneration is retarded by enzymatic products from PMN leucocytes degranulation, and release of collagenases from activated keratocytes [36, 37]. All contribute to the stromal enzymatic digestion which occurs in the 2nd and 3rd week post chemical burn and can lead to persistent ulceration and perforation (Fig. 7a, b).

In severe chemical injury fibrovascular pannus can grow to cover the ocular surface with development of subepithelial fibrosis, superficial and deep scaring, tenons fibrosis and contracture, corneal vascularisation, nerve damage and progressive symblepharon with cicatrising lid deformities. Although this may temporarily maintain the globe integrity, the unstable ocular surface inevitably results in persistent or recurrent ulceration, continuous inflammation, repeated infection, stromal melting, and perforation. Severe dry eye disease is a serious sequel of chemical burns and can be associated with keratinisation of the ocular surface epithelium (Fig. 7c, d).

Assessment and management

According to the McCulley's classification [38], the clinical course of chemical eye injury (CEI) can be divided into three distinct stages; (1) immediate phase (<7 days) as a direct result of the injury-causing tissue necrosis and sloughing; (2) intermediate phase (1–3 weeks) characterised by the host healing and inflammatory responses (secondary to the release

of a milieu of chemotactic and inflammatory cytokines) leading to a range of clinical changes such as corneal ulceration, melt, vessel re-canalisation and haemorrhages, conjunctivalisation and pannus formation; and (3) late phase (>3 weeks) where changes secondary to host repair and regeneration or lack thereof are manifest, including fibrovascular pannus, deep corneal vascularisation, dry eye, neurotrophic keratopathy, persistent epithelial defect, and/or perforation. Guided by this natural course of disease, the management can be broadly divided into early or acute stage (<4–6 weeks) and late-stage (>6 weeks) management [39].

Acute stage management

It is always possible that the patient may have ingested or inhaled the noxious agent and may be at risk of asphyxiation from laryngeal oedema or damage to the oesophagus and stomach form ingestion. Checking the vital signs and obtaining a history from the patient or others who may accompany him and have witnessed the accident, is important to ascertain this. If vital signs are compromised immediate help should be sought [40].

Management of the eyes in the acute stage can be considered under the headings of removal of the injurious agent, assessment, control of inflammation and facilitation of the healing process, while the late stage involves management of sequelae and complications.

Removal of inciting agent and prevention of further damage

Timely irrigation of the eye to remove chemical irritants is recognised as the most important intervention in managing

CEI. It has been shown to reduce disease severity and improve visual outcome of CEI [41]. Therefore, initial history taking and irrigation should be performed simultaneously to avoid any unnecessary delay in treatment.

Before irrigation, pH should be measured in both eyes even when one eye is affected as the unaffected fellow eye may serve as a "normal" control for the affected eye [42]. The accuracy of the litmus paper strips has been questioned [43], but it has equally been argued that assessment of pH with the litmus paper is a crude but practical means of ascertaining whether the agent was an acid or alkali, but more so to know whether it is normal or not, and to serve as a baseline from which a change can be measured [40]. Copious irrigation of the open eye(s), preferably with a sterile neutral solution, is the essential immediate measure, regardless of the nature of the chemical. Administration of topical anaesthesia is important as it relieves pain, releases blepharospasm and allows the patient to open the eyes. Copious irrigation with water immediately for at least 30 min is recommended. Isotonic or physiologically equivalent irrigating solutions such as lactated Ringer's solution and balanced salt solution have been proposed as a more superior treatment than water as they cause less corneal oedema [44]. During the irrigation, the superior and inferior conjunctival fornices should be examined and any particulate matter removed with moistened cotton buds. At times, tissue impregnated with the particulate matter will need to be excised to remove the chemical. Amphoteric chelating agent such as ethylenediamine tetra acetic acid (EDTA), Diphoterine®, hexafluorine, and Cederroth Eye Wash are viable alternative options [45–48]. Diphoterine is amphoteric (can act as acid or alkali, i.e. neutralise both types of agents) and hypertonic. Such agents have been shown to rapidly neutralise pH and reduce tissue necrosis, with minimal exothermic reaction [45]. Once the pH returns to normal, irrigation should be stopped for ~5 min and the pH tested again. If the pH has changed, irrigation should be recommenced.

Although irrigation can reduce the ocular surface pH effectively, it has limited effect in lowering the aqueous pH (by only ~1.5 units). In experimental animals, performing a paracentesis with removal of aqueous soon after the injury can reduce pH by a further 1.5 units. Injection of buffered phosphate solution to refill the anterior chamber can further neutralise the pH by another 1.5 units. This invasive procedure has the potential to rapidly reduce aqueous pH and in theory reduce damage to the intraocular structures but is not routinely practiced and human studies are lacking [11, 16, 49]. They also have potential for harm, like endophthalmitis, and in view of the current available evidence, this practice is not recommended [50, 51].

Complete and thorough assessment

Once the eyes are thoroughly irrigated and pH is neutralised, a systematic and comprehensive assessment needs to be performed to fully evaluate the severity of CEI. This could be achieved through systematic examination in an anatomical order (e.g. from the outside towards the inside and from the front towards the back of the eye), starting from the face, ocular adnexa, lid margin, conjunctiva, limbus, cornea, intraocular pressure, iris, pupil, lens and retina (Fig. 8) As stated at the outset, assessment of the patient for
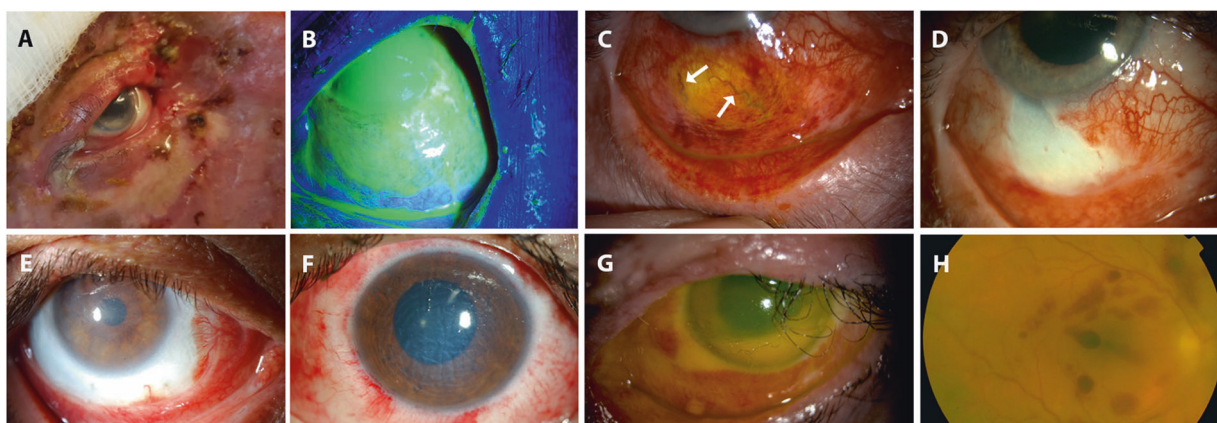

Fig. 8 Eye injuries after chemical trauma. a Extensive damages to lid margins, lids and face after acid injury. The lids are rigid and are causing exposure. **b** Subtotal corneal, limbal and inferior bulbar conjunctival epithelial and corneal epithelial defect after alkali injury. **c** An area of inferior bulbar hyperaemia and haemorrhages surrounding a pale area with dilated stagnant vessels (*arrows*). **d** The same area (shown in **c**) demonstrating marbleised appearance of total limbal and scleral ischaemia on which epithelium and vessels do not grow (alkali cement injury). **e** Nine clock hours of marbleised limbus and sclera indicating intense ischaemia (alkali, drain cleaner). **f** Stromal oedema and striae with surrounding limbal pallor and areas of haemorrhages (ischaemia, alkali injury). **g** Diffuse corneal stromal haze and inferior infiltrate (infection) with 8 clock hours of limbal pallor (ischaemia, acid injury). **h** Retinal haemorrhages after alkali injury.

signs of ingestion or inhalation must be considered immediately.

Eyelids lid and lid margin burns can affect lid blinks, lid movements and lid closure (lagophthalmos). Both chemosed and swollen lids and contracted and rigid lids can cause exposure. Distorted lid margins and inadequate lid movements affect tear distribution which contributes to ocular surface pathology (Fig. 8a).

Ocular surface epithelium Extent of involvement of conjunctival, limbal and corneal epithelia should be examined with fluorescein staining. Lower palpebral, inferior fornicial and bulbar conjunctival epithelium is easier to examine compared to upper palpebral and superior fornicial conjunctiva. Eversion of the upper lid is difficult when swollen or rigid. A Desmarre's retractor is useful in eversion and double eversion of the upper lid, which should be retracted to look for any chemical matter trapped beneath. Epithelial damage can change on a day to day basis in the immediate aftermath of CEI as continuing damage causes more areas to slough (Fig. 8b).

Stroma Limbal involvement, in the form of damage and loss of epithelial stem cells and limbal ischaemia are an important part of assessment and prognosis for corneal epithelial regeneration [7, 8]. Limbal ischaemia manifests as blanched or pale areas of the limbus, limbal oedema and necrotic tissue, haemorrhage and stagnant columns of blood in vessels that terminate abruptly or are unconnected at both ends of a dark column of blood. These latter changes can mask pallor and mislead one into thinking that there is a lesser degree of ischaemia than actually is. The greater the depth of CEI the paler the tissue appears, exposing ischaemic sclera as white marble (marbleised appearance of limbus and adjacent sclera (Fig. 8c–e).

Corneal stromal changes are clinically recorded as the degree of haze or transparency measured as the visibility of the iris and lens through the cornea. Corneal changes to be recorded include haze, opacification, oedema, striae and sensations, which should be assessed with a cotton wisp or a Cochet Bonnet aesthesiometer, ensuring that this is done when the effect of any instilled anaesthetic drops has worn off (Fig. 8f, g).

Intraocular anterior segment structures Iris changes in the form of colour, hyperaemia/engorged vessels, haemorrhage, atrophy or necrosis, and pigment dispersion should be noted. Posterior and anterior synechiae can develop rapidly when the iris is affected. The pupil may be dilated or constricted with limited or absent pupil response; show sector changes when partly affected in one sector, usually inferiorly.

The intraocular pressure can be raised, low or normal. The rise in IOP after CEI usually follows a bimodal pattern. The first rise is caused by the distortion of drainage angle consequent upon sudden corneal and scleral collagen shrinkage whereas the second spike is likely secondary to the clogging of trabecular meshwork with inflammatory debris and/or release of prostaglandin [52]. Alternatively, extensive scarring and fibrosis of the ciliary body may lead to persistent hypotony and phthisis bulbi. A swollen lens or intumescent cataract can cause phacomorphic glaucoma. Often the lens is not immediately affected but can swell rapidly, a few days after CEI. Occasionally low aqueous secretion due to ciliary body damage is compensated by defective drainage due to trabecular damage, giving a normal pressure. Measurement of eye pressure is not easy when the epithelium is lost as mires of the Goldmann's tonometer cannot be seen. Corneal oedema and/or collagen shrinkage can give aberrant readings with the iCare or Tonopen devices. Often finger palpation may be the only means of assessing pressure. Where visibility through the cornea and lens allows, an assessment of the vitreous and fundus should be made and any abnormalities, vascular stasis and retinal haemorrhages, recorded.
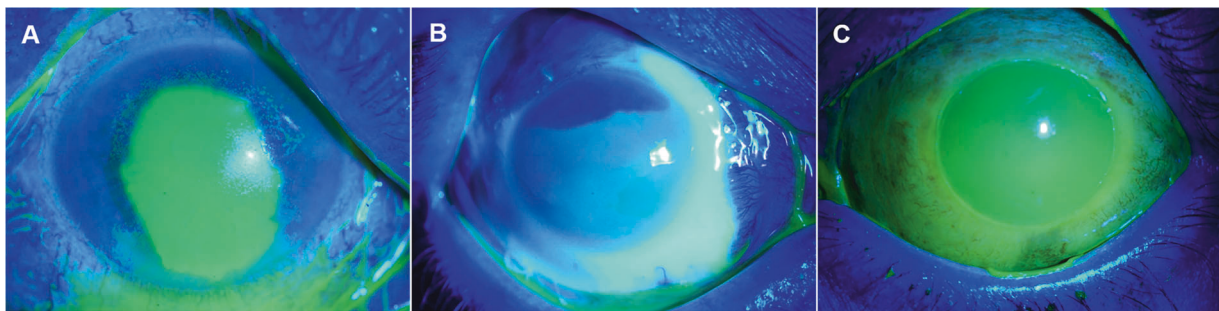
Classification of chemical burns of the eye Currently, there are two prognostic classifications used for grading CEI, namely Roper-Hall (modification of Balen) classification (Table 1) and Dua classification (Table 2). The Roper-Hall classification was introduced in 1965 to facilitate the grading and prognostication of CEI based on the extent of limbal ischaemia and corneal haze [8]. Though it is commonly used in clinical practice, this classification was introduced before the concept of limbal stem cells was established and did not account for conjunctival involvement or made any allowance for overlap between grades, particularly for the severe cases of CEI. In view of the limitations and recent advancement in stem cell therapy, Dua et al. [7] proposed a new classification in 2001 based on limbal and conjunctival involvement for grading the severity and predicting the prognosis of CEI. Limbal involvement in Dua classification, as determined by fluorescein staining and/or limbal ischaemia, is recorded as the number of clock hours of limbus affected, which serves as a more objective measurement. Surviving conjunctival epithelium provides vital cover to the cornea, based on the principle that any cover is better than no cover. Hence, recording the extent of conjunctival involvement is important in any classification system [7]. Studies have shown that Dua classification provides a better prognostic prediction than Roper-Hall classification, particularly in the Roper-Hall grade IV CEI cases [50, 53] (Fig. 9).

Table 1 Roper-Hall classification of chemical eye injury.

Grade	Cornea	Limbus	Prognosis
I	Corneal epithelial damage	No limbal ischaemia	Good
II	Corneal haze, iris details visible	<1/3 limbal ischaemia	Good
III	Stromal haze, iris details obscured	1/3–1/2 limbal ischaemia	Guarded
IV	Opaque cornea, iris and pupil obscured	>1/2 limbal ischaemia	Poor

Table 2 Dua classification of chemical eye injury.

Grade	Limbal involvement (clock hours)	Conjunctival involvement (%)	Analogue scale	Prognosis
I	0	0	0/0%	Very good
II	≤3	≤30	0.1–3/1–30%	Good
III	>3–6	>30–50	3.1–6/30.1–50%	Good
IV	>6–9	>50–75	6.1–9/51–75%	Good - Guarded
V	>9 to <12	>75 to <100	9.1–11.9/75.1–99.9%	Guarded - Poor
VI	12 (total limbus)	100 (total conjunctiva)	12/100%	Very poor

Fig. 9 Grading of chemical burns (Dua's classification). a Grade 0/0 burn, indicating that zero clock hours of limbus and 0% of conjunctiva are involved but there is considerable involvement of the central corneal epithelium. **b** Grade 7/60. 7 clock hours of limbal involvement and 60% of conjunctiva was involved (not shown in image.). **c** Grade 12/80. Complete limbal involvement (12 clock hours) and 80% of the conjunctiva was affected.

Control of acute inflammatory reaction

Topical corticosteroids are the mainstay of treatment for controlling the acute inflammatory reaction of CEI [54]. Potent corticosteroids such as dexamethasone 0.1% and prednisolone acetate 1% are the common choices. Any drops, particularly when administered frequently, should be preservative free, to reduce additional stress on the damaged ocular surface [55]. Studies have shown that topical corticosteroids were able to suppress the infiltration of neutrophils, reduce the release of pro-inflammatory cytokines (e.g. IL-1β and IL-6), modulate the production of matrix metalloproteinases (MMPs; reduced MMPs –1, –3, –9, and –13 and increased MMP-8), and reduce the risk of corneal opacity following CEI [56]. However, topical corticosteroids can inhibit corneal wound healing and collagen re-formation, usually occurring 1 week after the initial presentation. The general consensus is to taper the dose or frequency of topical steroids after 7–10 days, though longer duration of treatment can be used judiciously if daily monitoring is feasible or complete re-epithelialisation of the cornea has occurred [57].

Anti-proteases treatment such as tetracycline, sodium citrate, acetylcysteine, and EDTA play key roles in reducing and/or preventing corneal ulceration following CEI. Tetracyclines such as doxycycline, have been shown to suppress the production of pro-inflammatory cytokines and MMP–8 and –9, and reduce corneal ulceration [56, 58]. Common treatment regimens include oral doxycycline 100 mg twice a day (BD), minocycline 100 mg BD, or tetracycline 250 mg four times a day (QID), or topical tetracycline 1% suspension or 3% ointment QID. Citrate, commonly used at 10% concentration of the sodium salt, is another potent inhibitor of polymorphonuclear leucocytes (PMNLs) which suppresses the chemotactic effects of PMNLs and reduces inflammation and/or ulceration [54, 59, 60].

Amniotic membrane serves as another important adjuvant anti-inflammatory therapy for CEI. Studies have shown
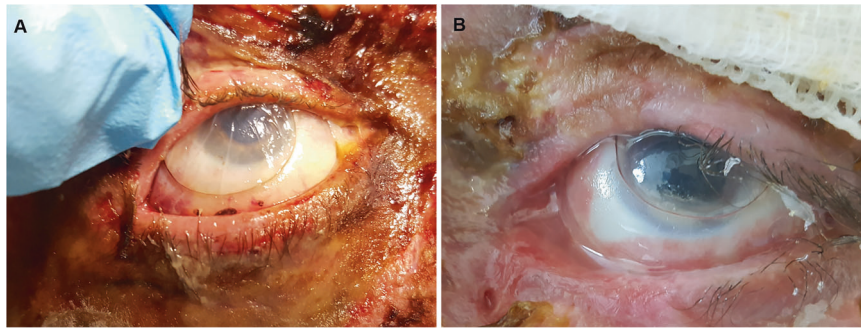
Fig. 10 Acute stage management of chemical eye injury. a, b Amniotic membrane (in this case Omnigen 2000) with a conformer ring in both eyes of a patient following acid injury. The membrane is first inserted in the palpebral aperture, then the conformer ring and the membrane is then wrapped around the conformer, thus making contact with the bulbar, fornicial and palpebral conjunctival surfaces.

that amniotic membrane transplant (AMT) was able to expedite the healing of damaged corneal epithelium, reduce pain, and/or improve visual outcome in moderate (grade II-III Dua) CEI [61–64], though a recent RCT did not demonstrate any additional benefit of AMT in severe (grade IV Roper-Hall or grade V-VI Dua) CEI [65]. Depending on the clinical circumstances and the preference of patients and surgeons, AMT can be performed using suture-assisted technique or sutureless technique with the aid of fibrin glue or by spreading a free large piece of amnion on the surface of the eye and tucking it into all 4 fornices (superior, inferior, medial and lateral) with an instrument like a squint hook and retaining it in place with a symblepharon ring, an eye shield or a conformer ring [66] (Fig. 10). Commercially available pre-mounted devices such as Prokera® and Omnilenz® (used with Omnigen 80®) achieve the same purpose [67, 68]. Amniotic membrane can be processed and stored under various conditions, including cryopreservation, lyophilisation (freeze-drying), and air-drying (or low-temperature vacuum dehydration) [69]. Lyophilised and air-dried amniotic membranes (e.g. Omnigen® 500 and 2000) have the advantages of easier application, storage and shipment, and long shelf life at room temperature with preserved biological properties [70]. Another advantage of air-dried amniotic membranes is that they can rehydrate better than freeze-dried amniotic membrane, enabling them to be used like normal amnion tissue and can be glued (fibrin glue) and/or sutured to the ocular surface.

Facilitation of healing process

Once the acute inflammation is controlled, the next step is to facilitate the healing process of the damaged ocular surface, which can be achieved through a wide array of medical treatments and surgical interventions. These include preservative-free artificial tears, ascorbic acid (vitamin C) [54, 71]. autologous serum [72], umbilical cord serum (UCS) [64, 73], platelet-rich plasma [74], fibronectin [75], chitosan [76], epidermal growth factors [77], heparin [78], regenerating agent (RCTA, CACICOL20) [79, 80], bandage contact lens [81], tenonplasty [82], free conjunctival autograft [83], amniotic membrane transplant [84], and sequential sector conjunctival epitheliectomy (SSCE) [85].

The level of ascorbic acid is usually 15 times higher in aqueous humour than in plasma, suggesting their potential ocular protective roles [18]. The aqueous level of ascorbic acid was found to reduce significantly in the event of CEI (based on in vivo rabbit studies) [86]. Commonly administered topically (at 5–10% concentration) and orally (1–2 grams/day), ascorbic acid has been shown to restore the aqueous level of ascorbic acid [19], and reduce collagen degradation, corneal ulceration, and perforation [19]. It also augments the therapeutic effect of citrate and reduces the risk of perforation when used in combination [87].

Autologous serum eye drops have been shown to be a useful adjuvant therapy for promoting corneal epithelial healing during the healing phase of CEI [72]. However, a recent double-masked randomised controlled trial suggested that UCS may be more effective than autologous serum eye drops for treating CEI in terms of speed of corneal healing, recovery rate from limbal ischaemia, and corneal transparency [64], though more clinical studies are required to validate these findings. Bandage contact lens can be used to protect the denuded stroma from collagenase-containing epithelium, tears, and PMNLs. Glued on contact lens, with cyanoacrylate glue applied along the circumference, has been suggested for the same purpose [88, 89].

Mydriatic and cycloplegic agents are needed to treat iridocyclitis and prevent or break synechiae. Adrenergic agents should be avoided as these cause vasoconstriction and can aggravate limbal ischaemia. Broad-spectrum antibiotics are used for prophylaxis, to reduce the load of commensal flora that may occur with necrotic tissue or to treat frank infection. Generally, fluoroquinolones are
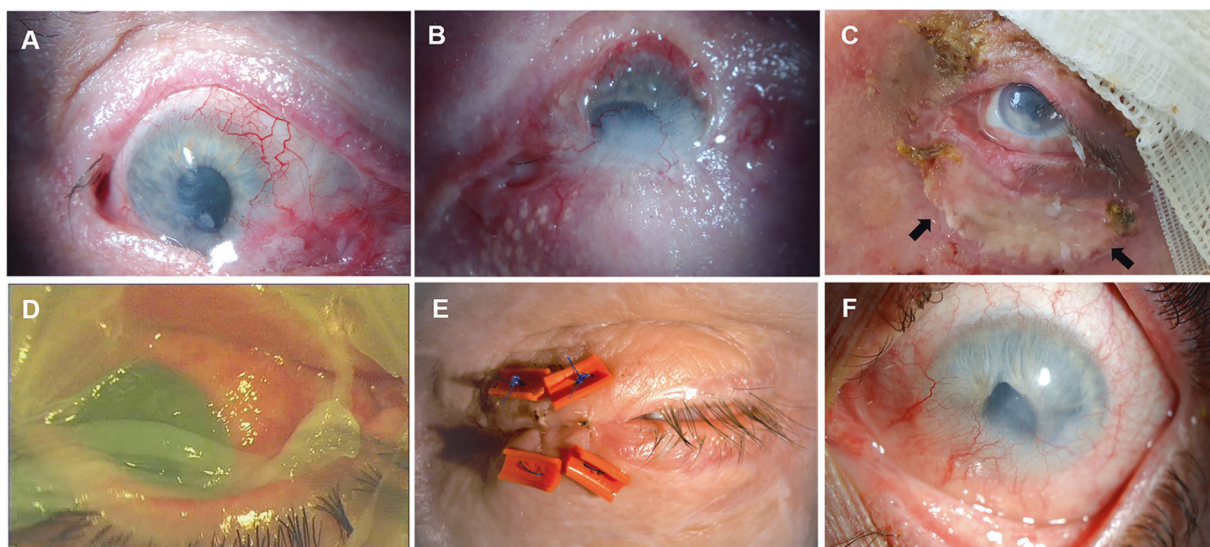
Fig. 11 Chemical eye injury and treatment options. a, b Right and left eyes of a patient following alkali injury. **a** Right eye: The photo illustrating that most of the damage is in the inferior half. The lower lid is distorted with symblepharon. The pupil is pulled down with damage to the lower part of the iris. **b** Left eye: The damage is more severe with obliteration of fornices and adhesion of the lower lid to the cornea. **c** A skin graft to the lower lid (*arrows point to the lower edge*) to allow lid closure. **d** Fresh frozen amnion is applied to the ocular surface to cover the entire denuded surface. After spreading the membrane as shown, an eye shield was inserted in the palpebral aperture. **e** Lateral tarsorrhaphy to facilitate healing of a recalcitrant corneal epithelial defect. **f** The image illustrates predominantly lower half extraocular and intraocular damage. Phacoemulsification with implant and a superior (optical) iridotomy was performed.

preferred as monotherapy but in the presence of infection the drugs should be tailored to microbes identified through culture and sensitivity. IOP- lowering medication is often required. Oral acetazolamide is preferred for two reasons, with the multitude of other drops required, one less would be welcome and with the damage and distortion of the trabecular meshwork and the uveoscleral pathway, the mechanism of action of some agents via topical instillation may not be effective for example prostaglandin analogues and alpha-2-agonists may not work as the uveoscleral out-flow pathway may be affected by the shrinkage of scleral collagen. With these, sometimes a 'try it and see' approach may be justified.

Tenonplasty is an early surgical intervention [82], wherein the fornix closest to the ischaemic area is explored to identify viable, perfused tissue (pink or red in colour and bleeds when manipulated) and mobilised and advanced to the cover the ischaemic area and affixed there with sutures. Free conjunctival autografts can be employed as an alternative to AMT or tenonplasty when corneal melting is not responding to other measures [83]. This option is only possible in unilateral burns where a sheet of healthy conjunctiva of appropriate size can be obtained from the unaffected eye. Occasionally in partial burns, it can be harvested from the unaffected part of the injured eye. The conjunctival sheet should be thin with minimal sub-conjunctival tissue and sutured to vascularised areas at the distal border of the ischaemic area. Blood vessels from the host bed establish connections with the transplanted conjunctiva allowing blood to flow in the donor tissue vessels and reach the ischaemic areas. As such it serves the same purpose as tenonplasty and is particularly useful when the viable Tenon's is deep in the fornix and cannot be mobilised sufficiently. The conjunctival transplant also acts as a readymade sheet of tissue with epithelial cover.

In cases with partial limbal involvement, the circumferentially migrating tongue-shaped sheets of epithelium may be inhibited from affording complete cover to the limbus by the migration of conjunctival epithelial cells across the limbus on to the central cornea. This can be prevented or treated by gently brushing or scraping the conjunctival epithelial cells and keeping them at bay by repeated brushing until the limbus has healed with limbal epithelium. The procedure is termed SSCE and can be done at the slit lamp under topical anaesthesia [85, 90].

Late-stage management

Treatment of sequelae and complications

Late-stage management involves a multidisciplinary approach to deal with the main areas that require reconstruction and restoration namely the lids and adnexa, the eye pressure, cataract, the ocular surface and the cornea (Fig. 11).

Lid repair and reconstruction should begin early especially when there is risk of exposure. Skin grafts and oral mucous membrane grafts are the mainstay when eyelid

tissue is lost due to necrosis. Tarsorrhaphy is often required to promote surface healing and prevent exposure. The risk of missing high eye pressure is significant especially when palpation is the only method of assessing pressure. Although medical therapy can provide some control, in severe cases a tube shunt is the preferred choice subject to conjunctival health. Cyclo-destructive procedures should be avoided as they can lead to increase inflammation, retro-lenticular or retro-corneal membranes and are associated with risk of inducing hypotony. Urgent removal of the lens may be necessary in phacomorphic glaucoma and the eye can be left aphakic, with the option of a secondary lens implant later. Planned cataract surgery is usually deferred until surface reconstruction provides a clear view.

A large variety of interventions are associated with ocular surface repair, restoration, regeneration and reconstruction. These include medical and surgical options, individually or usually in combination. One overarching dictum is that in severe dry eye situations, nothing provides sustained benefit and no living tissue transplant survives unless the dry eye disease is treated, at least partially. If this is not possible, then an osteo-odonto keratoprosthesis or a Boston type 2 keratoprosthesis are the only options. Regarding the ocular surface, five main sequelae are: 1. Dry eye disease. 2. Conjunctival adhesions/symblepharon. 3. Non-healing epithelial defects and/or neurotrophic keratopathy (NK), 4. Limbal stem cell deficiency and 5. Corneal scarring, decompensation, thinning, melting and perforation.

Dry eye disease The range of options include frequent instillation of artificial tear drops of which there are a multitude. Punctal occlusion if not already auto-occluded, correction of lid malposition, oral mucus membrane grafts, which may bring some moisture in the form of mucin from goblet cells, and salivary gland transplant.

Conjunctiva adhesions Release and repair of symblepharon and ankyloblepharon and fornix reconstruction with amniotic membrane graft or oral mucous membrane grafts can be reasonably successful. When scarring is excessive and requires excision, use of antimetabolites (5FU and MMC) may help.

Persistent epithelial defects (PED) A defect that does not heal or heals and breaks down repeatedly predisposes to infection and corneal stromal melting/perforation especially when associated with reduced or absent corneal sensations (NK) [28]. The advent of recombinant human nerve growth factor (Cenegermin) has been shown to specifically address this pathology and promote healing, which tends to stay healed even after cessation of the drug on completion of the recommended 2-month course [91, 92]. If conjunctival

sensation around the cornea is preserved, NGF drops can promote corneal nerve regeneration [93]. Eye drops of substrate regenerating agents (RTGA), and coenzyme Q10 promote substrate regeneration and epithelial healing respectively [28]. Tarsorrhaphy, amniotic membrane grafts and conjunctival flaps are useful interventions for recalcitrant cases. Corneal neurotisation may be an option when the entire corneal surface is anaesthetic [94, 95]. PED with total limbal stem cell deficiency require limbal stem cell transplantation (Fig. 11).

Limbal stem cell deficiency (LSCD) With mild CEI and partial LSCD where conjunctivalisation of the cornea without a fibrovascular pannus has occurred and the visual axis is involved, SSCE is all that is required (Fig. 12). Rapid visual recovery occurs when surviving limbus derived corneal epithelium covers the visual axis. When the ocular surface is completely covered by a fibrovascular pannus the options for ocular surface reconstruction depend on whether the CEI was unilateral or bilateral. In unilateral cases auto limbal stem cell transplant (LSCT) or an ex-vivo expanded sheet of limbal epithelial cells taken from the other eye (Holoclar) are options with a high success rate. In bilateral cases, limbal allografts from a living relative (HLA matched where possible), a living non-related individual or from a cadaver are options. These require aggressive long-term systemic immuno-suppression. Auto and living donor-derived grafts should be considered only when all inflammation is controlled or subsided. Inflammation can last up to 24 months post CEI [96]. Inflammation can destroy precious living donor-derived explants and especially with autografts, it is not a justified risk. For bilateral CEI, ex-vivo expanded sheets of autologous oral mucosal or conjunctival epithelial cells on fibrin, amnion or other substrates, are also options. These are also options for unilateral CEI where the patient is unwilling to have his only-seeing-eye operated on for donor graft retrieval. Amniotic membrane grafts as a patch (onlay) or graft (inlay) as in the amnion assisted conjunctival epithelial re-direction (ACER), can be combined with any of the procedures mentioned above [50, 97, 98]

Corneal scarring, decompensation, thinning, melting, perforation It is not uncommon to see a clear cornea with retained endothelial cell function upon removal of the fibrovascular pannus, despite some superficial and/or deep vessels. In these cases, LSCT should suffice (Fig. 13). When there is anterior stromal scarring, an anterior lamellar graft or a deep anterior lamellar keratoplasty are viable options. When there is corneal oedema related to loss of endothelial cell function or central necrotic stroma with thinning or frank perforation, a penetrating keratoplasty is

Fig. 12 Sequential sector conjunctival epitheliectomy (SSCE). a Conjunctivalised epithelium, showing late fluorescein staining, is seen covering the visual axis and the lower part of the cornea. The nasal and temporal limbal epithelium is preserved. **b** The abnormal epithelium was brushed off leaving the limbal and strip of corneal epithelium in situ. SSCE was carried out to allow complete healing to occur from limbal epithelium, showing no fluorescein staining (**c**) and a bright shiny lustre (**d**).
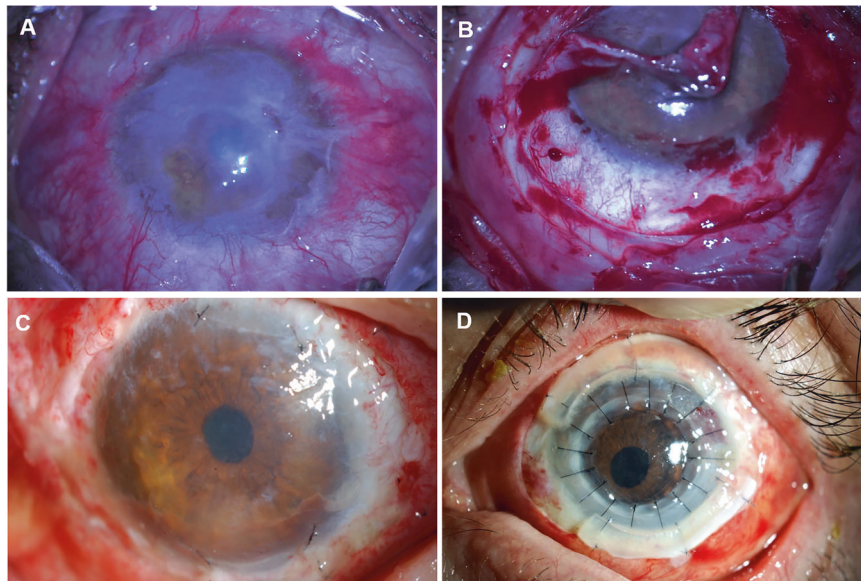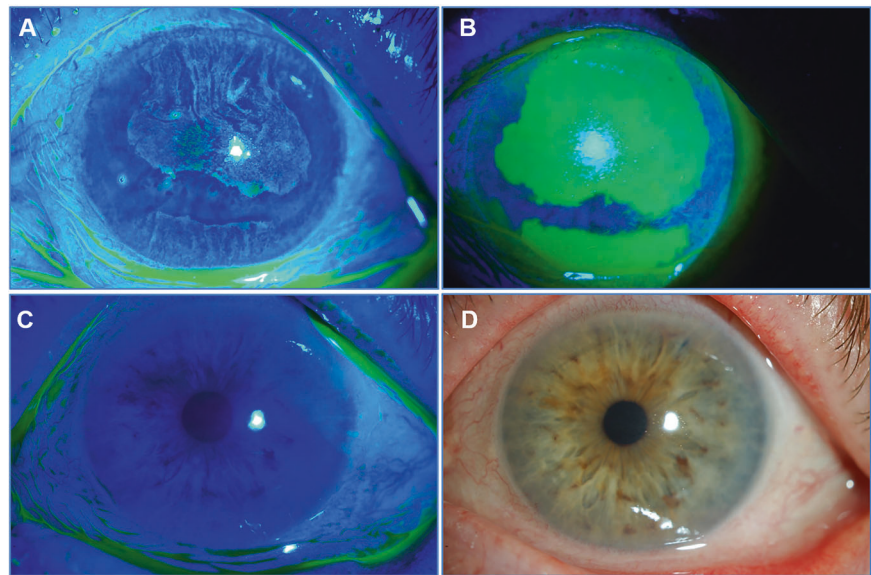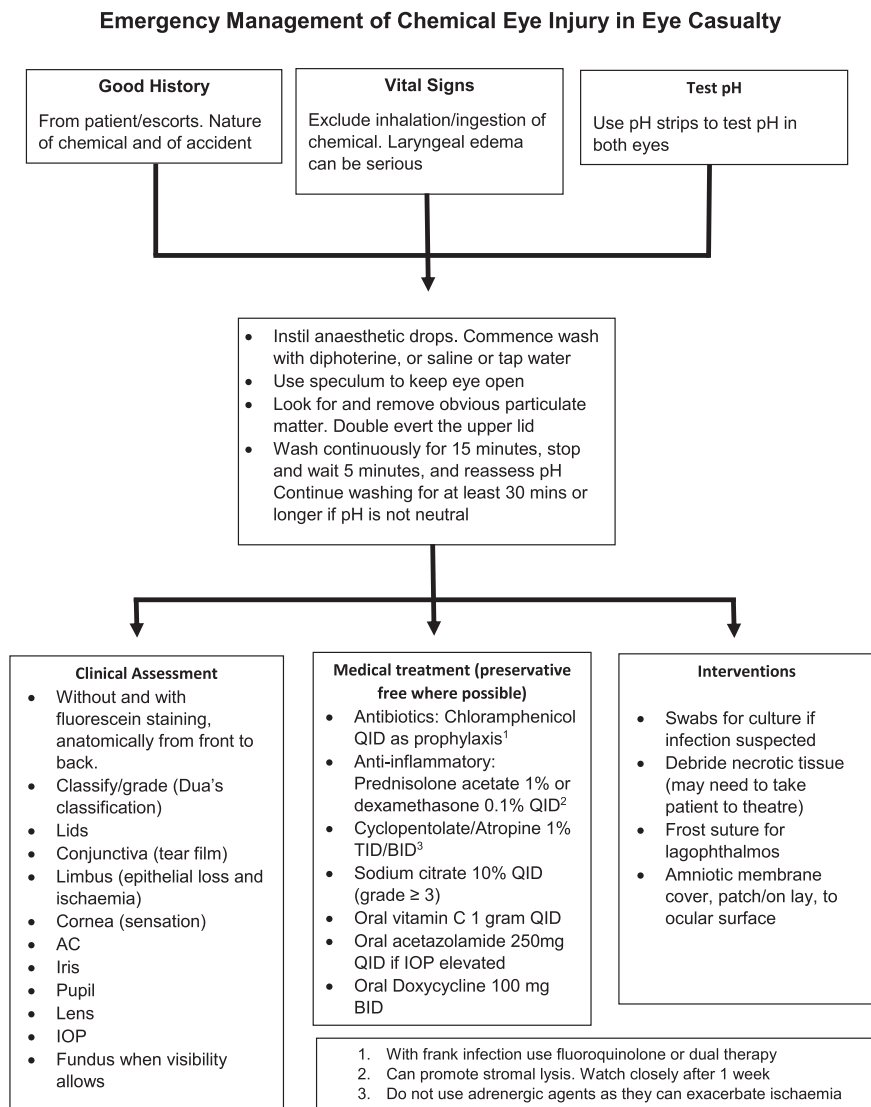

Fig. 13 Late-stage management of chemical eye injury. a Extensive cover of the corneal surface with a fibrovascular pannus and total limbal stem cell deficiency. **b** Same eye as in **a** illustrating that the fibrovascular pannus can often be peeled off to reveal a transparent and healthy stroma. **c** Autologous grafts of conjunctiva, limbus and a strip of peripheral cornea, were transplanted at 12 and 6 o'clock positions to restore normal epithelial cover and improve vision. This is the same eye illustrated in Fig. 8e with 7 clock hours of marbleised limbus. **d** The image illustrates simultaneous allo-limbal grafts and penetrating keratoplasty in a case of bilateral chemical injury. Such transplant procedure for visual rehabilitation are normally performed after all inflammation is controlled.

the procedure of choice. Generally speaking, the ocular surface reconstruction with LSCT should precede any form of keratoplasty. At times, as dictated by the state of the cornea, LSCT and keratoplasty have to be carried out at the same time (Fig. 13). Fine needle diathermy occlusion of deep vessels combined with subconjunctival injection of Avastin [99, 100] and cyanoacrylate gluing of perforations are useful adjuncts in preparation for the more definitive procedures of LSCT and keratoplasty.

Besides severity of the chemical insult, the key factor in determining outcome is the rapidity with which treatment was commenced and the treatment measures initiated. The crucial points where these opportunities arise are at the First Aid given and in the eye emergency department. A standard protocol must be available, especially in eye emergency departments, so that any healthcare professional can deal with the patient promptly and correctly. Such a protocol in the form of a flow diagram is provided (Fig. 14).

Fig. 14 A proposed protocol for acute stage management of chemical eye injury in the eye casualty.

Emergency Management of Chemical Eye Injury in Eye Casualty

Good History	**Vital Signs**	**Test pH**
From patient/escorts. Nature of chemical and of accident	Exclude inhalation/ingestion of chemical. Laryngeal edema can be serious	Use pH strips to test pH in both eyes

- Instil anaesthetic drops. Commence wash with diphoterine, or saline or tap water
- Use speculum to keep eye open
- Look for and remove obvious particulate matter. Double evert the upper lid
- Wash continuously for 15 minutes, stop and wait 5 minutes, and reassess pH Continue washing for at least 30 mins or longer if pH is not neutral

Clinical Assessment
- Without and with fluorescein staining, anatomically from front to back.
- Classify/grade (Dua's classification)
- Lids
- Conjunctiva (tear film)
- Limbus (epithelial loss and ischaemia)
- Cornea (sensation)
- AC
- Iris
- Pupil
- Lens
- IOP
- Fundus when visibility allows

Medical treatment (preservative free where possible)
- Antibiotics: Chloramphenicol QID as prophylaxis[1]
- Anti-inflammatory: Prednisolone acetate 1% or dexamethasone 0.1% QID[2]
- Cyclopentolate/Atropine 1% TID/BID[3]
- Sodium citrate 10% QID (grade ≥ 3)
- Oral vitamin C 1 gram QID
- Oral acetazolamide 250mg QID if IOP elevated
- Oral Doxycycline 100 mg BID

Interventions
- Swabs for culture if infection suspected
- Debride necrotic tissue (may need to take patient to theatre)
- Frost suture for lagophthalmos
- Amniotic membrane cover, patch/on lay, to ocular surface

1. With frank infection use fluoroquinolone or dual therapy
2. Can promote stromal lysis. Watch closely after 1 week
3. Do not use adrenergic agents as they can exacerbate ischaemia

Summary

What was known before

- Chemical eye injury is an acute ocular emergency.
- Most injuries are mild but severe injuries cause profound sight loss.
- Early and appropriate treatment fundamental to successful management.

What this paper adds

- This paper synthesises up to date evidence on pathophysiology of chemical eye injury.
- It explains the rationale for different treatment options and their timing.

- It presents a protocol that can be used for management of acute burns in most settings.

Compliance with ethical standards

Conflict of interest HSD received honoraria and travel expenses from Dompe, Croma, Santen, Allergan and Thea, and has shares in NuVision biotherapies and GlaxoSmithKline. NuVision Biotherapies is manufacturer of Omnigen, mentioned in the manuscript.

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