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Title: Surveillance of Severe Chemical Corneal Injuries in the UK

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ABSTRACT

Aim

To estimate the incidence of severe chemical corneal injuries in the United Kingdom and describe presenting clinical features and initial management.

Methods

All patients with severe chemical corneal injury in the UK from December 2005 to November 2006 inclusive were prospectively identified using the British Ophthalmological Surveillance Unit. Reporting ophthalmologists provided information regarding presentation and follow up.

Results

Twelve cases were identified, giving a minimum estimated incidence in the UK of severe chemical corneal injury of 0.02 per 100 000. 66.7% of injuries were in males of working age, 50% occurred at work, alkali was causative in 66.7%. Only one patient was wearing eye protection at the time of injury, 75% received immediate irrigation. Six patients required 1 or more surgical procedures; most commonly amniotic membrane graft. At 6 months follow-up best corrected visual acuity was 6/12 or better in five patients, and worse than 6/60 in two.

Conclusion

The incidence of severe chemical corneal injury in the UK is low. The cases that occur can require extended hospital treatment, with substantial ocular

52 morbidity and visual sequelae. Current enforcement of eye protection in the
53 workplace in the UK has probabaly contributed to a reduced incidence of
54 severe ocular burns.

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56 **Abstract Word Count 200**

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INTRODUCTION

Chemical injuries to the eye represent an ophthalmic emergency that can result in extensive damage with significant ocular morbidity.¹ Most are mild and accidental and do not result in lasting ocular morbidity. Severe chemical eye injuries are rare, but can cause significant visual impairment.¹

The extent of ocular injury depends on many factors, including the strength of the chemical agent, duration of exposure, concentration, volume and penetration of the solution.^{2,3} Severe chemical injury to the cornea is usually secondary to strongly acidic and alkaline substances.⁴ Alkali injuries more commonly cause significant damage.⁴ Epidemiological data shows severe chemical eye injuries are more common in males, particularly those aged between 16 and 45 yrs.^{1,5,6,7} Most happen accidentally at work or at home, or deliberately from assault.⁴

Various classification scales exist to grade the severity of ocular chemical injuries. The Hughes classification, modified by Ballen and Roper-Hall, recognised the relationship between initial appearance and prognosis.¹ Subsequent classification schemes have been developed, but the Hughes-Roper-Hall classification remains simple and popular.^{8,9} In the acute stage it describes the clinical signs and severity in 4 grades. Grade 1 injuries show corneal epithelial damage, with no limbal ischaemia and a clear cornea. Grade 2 injuries show less than a third of limbal ischaemia and a hazy cornea through which iris details can be seen. Grade 3 involves total loss of corneal

epithelium, stromal haze obscuring iris details, and ischaemia between one third and one half of the limbus. Grade 4 injuries represent an opaque cornea and ischaemia of more than half of the limbus. Grades 3 and 4 are recognised as severe.¹

Acute chemical eye injury treated immediately with expedient irrigation and removal of trapped debris is associated with a significantly better visual outcome.⁴ Early management endeavors to preserve the globe integrity by healing of the ocular surface. Treatment is aimed at promoting ocular surface epithelial recovery, augmenting corneal repair, minimising ulceration and controlling the inflammatory response.¹ Surgery may be necessary in the acute setting if healing of the ocular surface is inadequate. In the chronic stages, features of limbal stem cell deficiency can manifest.¹⁰ Long-term management aims to restore the visual function by preserving tear production, managing limbal stem cell deficiency and addressing associated complications such as lid malposition, cataract and glaucoma.^{10,11,12}

The UK national incidence of severe chemical corneal injuries is unclear. Two previous studies in UK centers have reported eight severe chemical corneal injuries presenting to a large teaching hospital over a four year period and none to a district general hospital over a year.^{5,7} Based on this limited evidence we anticipated a maximum of 200-300 cases annually in the UK. This study aimed to estimate the true incidence of severe chemical corneal injuries with a UK wide prospective survey. In addition it aimed to outline the presentation and management of these cases.

METHODS

This was a prospective population-based study performed in association with the British Ophthalmological Surveillance Unit (BOSU) monthly reporting system as previously described.^{13,14} All ophthalmologists with clinical autonomy in the UK receive a monthly reporting card with definitions of the conditions currently under surveillance. They indicate how many new cases of each disorder they have seen or confirm they have seen no new cases. For the 12-month study period December 2005 to November 2006 inclusive, ophthalmologists were asked to report any case of severe chemical corneal injuries presenting to them. This was defined as any person sustaining an injury with all of the following:

1. Total loss of the corneal epithelium, and
2. Corneal haziness obscuring iris detail or worse, and
3. Over 120° of limbal ischaemia

This equated to Grade 3 or 4 on the Hughes-Roper-Hall classification scale.

Every ophthalmologist who notified a patient to the BOSU was sent an initial questionnaire requesting information regarding demographics, aetiology, protective eyewear worn, presenting features and initial management. A 6 month follow-up questionnaire was also sent to ascertain subsequent management and outcome. Ophthalmologists who did not return a questionnaire were sent a reminder letter.

Multi-Centre Research Ethics approval was obtained (REC reference number 05/SO801/111).

RESULTS

Reports to BOSU leading to estimates of the UK incidence of severe chemical corneal injury.

During the study period the BOSU used a reporting base of 1100 ophthalmologists. Each month a mean of 78% of these ophthalmologists provided surveillance information (range 75% - 81%). From December 2005 to November 2006 inclusive BOSU received 37 reports of patients with severe chemical corneal injury from 26 ophthalmology consultants. Initial questionnaires were received from 31/ 37 reports (83.8% response rate). Of these 19 were excluded (9 did not meet the inclusion criteria, 5 occurred outwith the study period, 2 were reporting errors and 3 were duplicate cases). Initial questionnaire data was therefore received in 12 true reported cases within the study period. Follow up questionnaires were returned in 10/ 12 (83.3%) cases.

The current UK population is estimated to be approximately 60 million¹⁵. The reported annual incidence of severe chemical corneal injury is therefore estimated by this study at 12 per 60 million or 0.02 per 100 000. Eight of the cases occurred in males of working age (16-65yrs), for whom the current UK population estimate is 20 million¹⁵. From this study the estimated incidence of severe chemical corneal injury in this group is therefore 8 per 20 million or 0.04 per 100 000.

Patient characteristics and presenting details

Initial details received on the 12 patients showed nine were male (75%). The mean age at time of injury was 33.8 yrs (median 38.5yrs, range 10-59 yrs). Eight were males of working age, 66.7%. The injury occurred during paid employment in six cases (50%), following assault in 4 (33.3%) and during another activity in two. One patient had a bilateral injury. The causative chemical was reported as alkaline in 8 (66.7%), acidic in 2 (16.7%), other in one and unknown in one. A liquid splash was the mechanism of injury in eight (66.7%), debris was causative in three (25%), there was one reported injury from a gas substance. One patient was wearing goggles at the time of injury, 11 (91.7%) were wearing no eye protection (including prescription spectacles).

The time from injury to first irrigation was less than 1hr in 9 (75%) cases. One case was irrigated at 1-3hrs and one at greater than 12 hrs after the injury (the time to irrigation remained unknown in one patient). Review by an ophthalmologist occurred in two (16.7%) patients within 1 hour of the injury, in five (41.7%) cases between 1-3 hrs and in two eyes at 3-12hrs. Initial review by an ophthalmologist was greater than 12 hrs after the injury in two cases and unknown in one patient. Nine (75%) had received immediate irrigation at the time of injury (including 5 of the 6 cases occurring in the workplace), seven were irrigated by the primary care department. In one case the initial irrigation was delayed until review by an ophthalmologist, unfortunately one of the cases taking greater than 12 hrs to present. Ten eyes were re-irrigated by ophthalmology. Six underwent eyelid eversion with removal of debris as

appropriate. Table 1 shows best corrected visual acuity (BCVA) in the affected eye at initial presentation. In a quarter this was worse than 6/60, although one third retained a BCVA of 6/12 or better.

Table 1. The Best Corrected Visual Acuity (BCVA) for Reported Patients with a Severe Chemical Corneal Injury at Presentation Compared to 6 months Following Injury

Patient	BCVA at Presentation	BCVA 6 mths Following Injury
1	6/9	6/12
2	CF	Not available
3	6/9	6/9
4	HM	Not available
5	6/18	6/18
6	6/60	6/60
7	6/18	6/5
8	6/12	6/6
9	6/9	6/36
10	POL	CF
11	6/18	6/12
12	6/24	POL

Details of the presenting clinical features in the 12 eyes is illustrated in Figure 1. For inclusion corneal epithelial loss was total in all patients, 58.3% had 240-360° of limbal ischaemia and two-thirds showed 50-100% of conjunctival epithelial loss. Four were referred from the presenting unit for a specialist corneal and external eye disease opinion.

Management by ophthalmology within the first 10 days

Table 2 summarises the non-surgical initial management of these cases.

Table 2. The Initial Non-Surgical Management Reported in Patients with a Severe Chemical Corneal Injury

Non- Surgical Treatment		Number of patients (n=12)
Topical	Steroid preserved	6
	Steroid unpreserved	6
	Antibiotic preserved	6
	Antibiotic unpreserved	6
	Citrate	3
	Ascorbate	6
	Anti- glaucoma	2
	Dilatation	8
Systemic	Vitamin C	9
	Tetracycline derivatives	4

All eyes received topical steroid and antibiotic either preserved or unpreserved. Topical ascorbate and/or systemic vitamin C was used in 83.3%, five received both. Five eyes received surgical treatment in the first 10 days. Two underwent division of symblepharon with a glass rod, two had an amniotic membrane graft (AMG). One eye was managed with debridement of the conjunctival tissue encroaching on the cornea.

Follow Up and Management by ophthalmology 10 days- 6mths.

Follow up data from the 6 mth questionnaire was received in 10 patients. The BCVA at final follow up is shown in Table 1. Half of patients had a BCVA of 6/12 or better 6 mths post injury. In 20% BCVA was worse than 6/60. Figure 2 shows the recorded complications during the six months follow injury. Central corneal pannus or scar was the most frequent problem in 70%. In two cases 6 mth BCVA was 6/5. In the remainder the reason for the reduction in vision was reported as being secondary to the associated corneal pathology. Table 3 summarises the non-surgical and surgical management modalities used between 10 days and final follow up. AMG was used in 50% of eyes between 10 days and 6 months. Limbal stem cell graft was performed in 20%. In total three (30%) eyes had required two surgical procedures at final follow up, three had required one.

Table 3. The Non-Surgical and Surgical Management Reported from 10 days Following Injury to Final Follow-Up at 6 months in Patients with a Severe Chemical Corneal Injury.

Management	Number of patients (n=12)
Artificial tears	6
Puncal occlusion	1
Therapeutic contact lens	5
Botulinum toxin ptosis	2
Tarsorrhaphy	0
AMG	5
Limbal Stem Cell Graft	2
Oral Mucosal Graft	1
Fornix Reconstruction	1

Clinical Details of the Patients Excluded who Met the Inclusion Criteria but Occurred Outwith the Study Period.

Five patients were excluded from analysis as the reported injury had occurred out with the study period. Their injury had occurred 1 mth- 2yrs prior to the study period. All were males of working age, 4 injuries occurred during paid employment, 1 following assault. None were wearing eye protection at the time of injury, 4 received immediate irrigation. The BCVA at presentation ranged from 6/12 to 6/60, 1 had 240° –360° limbal ischaemia, 2 had 50-100% conjunctival loss. All received initial treatment with topical steroid or antibiotic, 3 received topical ascorbate and/or systemic vitamin C. An AMG was used to treat 1 patient, 2 received a limbal stem cell graft. Six month BCVA was 6/6 or

6/9 in all patients except for one with a BCVA of hand-movements. Corneal pathology was the reported cause of reduced vision.

DISCUSSION

This study estimates the UK annual incidence rate of severe chemical corneal injury is 0.02 per 100 000. This incidence is low. A degree of under-ascertainment is a feature of studies of this nature, however, active surveillance as practiced by the BOSU has been shown to be more effective than other methods.^{16,17} Similar to previous surveillance studies the mean card return rate was high (78%) and questionnaire response rates were above 80%. Furthermore, the BOSU is generally well supported by reporting ophthalmologists, with previous estimated ascertainment rates of 75-95%.¹³ Based upon response rates it is safe to assume that ascertainment in this study is likely to be similar to previous surveillance studies using the BOSU reporting system. The incidence rate reported is a minimum rate and it is possible that the true incidence may be up to 25% greater than this. Under-reporting is usually attributed to random error (eg forgetting to report a case, misunderstanding the case definition), reluctance to participate, or management of cases by ophthalmologists who do not receive BOSU reporting cards^{13,14} rather than systematic error which would bias the representative nature of this population based co-hort. Even accounting for any potential under-ascertainment the reported incidence is lower than might

be anticipated from the limited previous data^{5,7} and probably reflects a true reduction in the UK incidence of severe chemical corneal injury

Due to the small number of reported cases in this study it is difficult to come to firm conclusions regarding the current presentation and management of severe chemical corneal injury in the UK. In accordance with epidemiological data from other studies, this survey confirmed that severe chemical corneal injury is seen more commonly in men (75% of cases) mainly of working age (66.7%), with the injury most often occurring at work (50%) or following assault (33.3%) and an alkaline substance most commonly implicated. Previous studies have show severe chemical eye injuries are more common in males between 16 and 45 yrs, occurring accidentally at work or at home, or as the result of deliberate assault.^{1,4,5,6} A retrospective study of 221 chemical injuries by Morgan et al ⁵ in the UK showed alkali injuries were twice as common as acid injuries and men were affected 75.6% of the time. In his study, 63% of injuries occurred in the workplace and 33% at home, 10.6% were secondary to assault. None of their reported cases were classed as severe. Kucklehorn published a subsequent series of 236 eyes from Germany in which 70% of chemical injuries occurred in males between aged 16-45yrs.⁶ Industrial accidents accounted for 61% of injuries and household accidents 37%. A second series was limited to severe chemical injuries and showed these most often resulted from industrial accidents in males, aged 20-40 years.⁶

Only one patient was wearing any eye protection at the time of injury similar to previous reports of chemical eye injury which show the vast majority of patients are not wearing any protection at the time of injury.¹⁸ Lack of eye protection is a major risk for the development of a severe chemical injury should exposure occur. Legislation in the UK enforces appropriate use of eye protection in the workplace,¹⁴ Formal education, reinforcement, compulsory use and formal legislation have been shown to be effective in improving compliance.^{19,20} In addition safer working practices, hazard warnings and safety advice on chemical product packaging can help.^{19,20}

Immediate irrigation following chemical eye injury is probably the single most important intervention influencing outcome more than any other therapeutic approach.^{1,4,18} Three-quarter of our patients received immediate irrigation at the time of injury, including all but one of those that occurred in the workplace. It suggests occupational and public health measures in the UK highlighting the importance of this are partially effective.

Early management aims to reduce inflammatory cell infiltration and promote corneal re-epithelialisation, keratocyte proliferation and collagenase production.¹ Longer term management aims to restore the visual function by managing the effects of limbal stem cell deficiency, preserving tear production and addressing additional complicating factors.^{11,12,21} Initial treatment involves a combination of preservative-free topical antibiotic, steroids, cycloplegics and pressure lowering treatment as appropriate.⁴ Topical ascorbate, citrate, systemic vitamin C and tetracycline derivatives may promote collagen

remodeling, reduce the incidence of ulceration and prevent progression of established corneal ulceration.^{22,23,24} In this survey all patients received initial treatment with topical antibiotic and steroid, with preservative free varieties selected in half of cases. Topical citrate and systemic tetracycline derivatives were used in one quarter of the patients.

Surgical procedures reported in this survey included amniotic membrane graft (AMG), limbal stem cell graft, oral mucosa graft and fornix reconstruction. AMG was the most commonly reported surgical procedure. AMG is recognised to promote epithelisation, prevent conjunctival adhesions and aid conjunctival surface reconstruction.^{6,11,12,21} Limbal stem cell graft was used in only two patients, but may have been required later as inflammation of the ocular surface induced by chemical burns has a negative impact in the survival of limbal stem cells.²¹

Six months following injury BCVA was impaired to below 6/12 in half of patients, with two suffering very severe visual loss (worse than 6/60). Reduced vision was attributed in all cases to the corneal pathology indicating substantial ocular morbidity and visual sequelae may be the consequence of severe chemical corneal injury.

Initial questionnaire data was received in thirty one patients in total. Of these nineteen were excluded from analysis for a variety reasons. Five of these were non-duplicates cases, which met the inclusion criteria, but occurred out with the study period. Summary of their clinical information, supplements the

data from the included patients and shows they were broadly similar to those that occurred in the study period.

This study suggests that severe chemical injury is rare in the UK, occurring less often than previously. It seems that measures to enforce safe use of chemicals at work are generally enforced and effective, but when injury does occur it is evident that significant ocular morbidity and visual sequelae can result.

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DECLARATIONS

This work has been presented at the RCOphth Congress 2008

Competing Interests: None declared.

All authors declare that the answer to the questions on your competing interest form are all No and therefore have nothing to declare

This research was run through The British Ophthalmological Surveillance Unit
The BOSU, run by the Royal College of Ophthalmologists, aims to provide a methodological framework for the systematic investigation of the incidence and clinical features of rare eye conditions with significant public health or scientific importance. Individual investigators submit proposals and the BOSU steering committee determines which conditions will be surveyed. The scheme involves all consultant or associate specialist ophthalmologists with clinical autonomy in the UK. Each month they receive a report card with case definitions of all conditions currently under surveillance. Respondents indicate how many cases of each disorder they have seen (including if they have not seen any). Individual investigators are notified of positive reports and contact the reporting ophthalmologist directly, using a questionnaire to collect information about the reported case. This establishes the patient's eligibility for inclusion and confirms the diagnosis. By collecting unique identifiers, duplicate reports of the same case can be excluded.

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451

452 The researchers remained independent from the funders

453

454 All authors, external and internal, had full access to all of the data in the study
455 and can take responsibility for the integrity of the data and the accuracy of the
456 data analysis.

457

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TITLES AND LEGENDS TO FIGURES

Table 1. The Best Corrected Visual Acuity (BCVA) for Reported Patients with a Severe Chemical Corneal Injury at Presentation Compared to 6 months Following Injury.

Table 2. The Initial Non-Surgical Management Reported in Patients with a Severe Chemical Corneal Injury.

Table 3. The Non-Surgical and Surgical Management Reported from 10 days Following Injury to Final Follow-Up at 6 months in Patients with a Severe Chemical Corneal Injury.

Figure 1. The Clinical Features of Reported Patients with a Severe Chemical Corneal Injury at Presentation

Figure 2. The Complications Reported During 6 months Follow-Up in Patients with a Severe Chemical Corneal Injury.

Figure 1

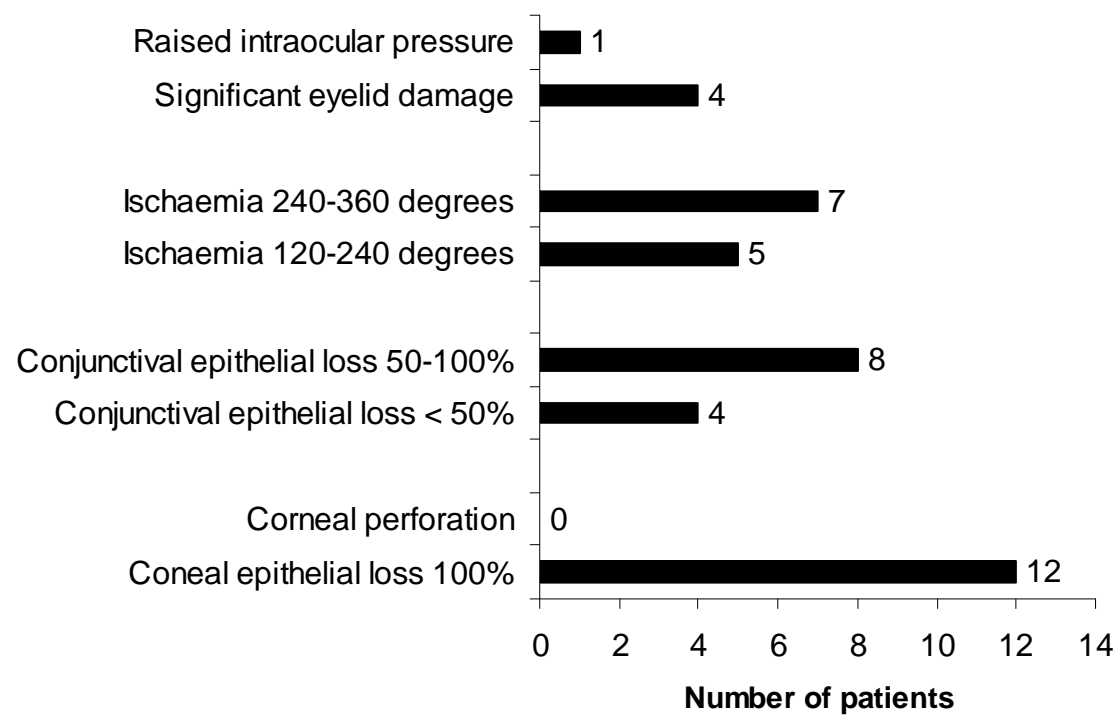


Figure 2

