

# Indications for the role of the immune system in the pathogenesis of corneal alkali burns

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**SUMMARY** We produced alkali burns (1.5 N NaOH) in the right eyes of 63 mice. Three weeks later the left eye of each mouse was similarly burned. All eyes were followed up weekly for 4 weeks after the burn and were graded according to the severity of the lesion. The lesions developed much faster and were more severe in the left eyes. These results suggest that the body's immune mechanism participates in the pathogenesis of alkali corneal burns and adversely affects the development of this condition.

The immunological aspects of chemical burns have received scant attention in ophthalmic research, and the subject is hardly mentioned in the literature. There are some indications that the immune system is intimately involved with the development of the delayed effects of burns. It is known that burns are not a local phenomenon only and that the burned area is a source of antigens.<sup>1,2</sup> These antigens are mostly autoantigens resulting from alterations in the body's own proteins and from unaltered antigens coming in contact with the immune system for the first time.<sup>3-6</sup> These antigens cause an immune response which participates in the healing of the burns.<sup>7-9</sup> The autoantibodies produced can cause severe systemic disease when they enter the circulation. Treatment with burns convalescence serum is reported to

improve considerably the survival of burned experimental animals.<sup>10</sup>

Evidence for the participation of the body's immune system in the pathogenesis of 'burn disease' of the eye is even more vague, circumstantial, and indirect. Ulceration, thinning, and melting of the cornea occur in severe cases 2 to 3 weeks after the injury.<sup>11,12</sup> This period coincides not only with the peak of collagenase activity<sup>13</sup> but also with possible humoral immune reaction, the 2 processes being possibly interrelated. The period of about 3 weeks after the injury is also associated with a tendency for inflammatory cells, including lymphocytes, to infiltrate the cornea and iris.<sup>14,15</sup> The occurrence of uveitis for a prolonged time after the burn<sup>16</sup> may also indicate that an immune mechanism is involved in the process. Another strong indicator of the involvement of the immune system in ocular burns is the presence of physiological and metabolic effects of unocular burns in the fellow eye.<sup>17</sup>

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Table 1 Number and percentage of eyes graded into each scale category at the weekly examination. Details of the gradation are given in the text

Days after burn	Mild				Moderate				Severe			
	First eye		Second eye		First eye		Second eye		First eye		Second eye	
	N	%	N	%	N	%	N	%	N	%	N	%
7	4	6.3	1	1.8	39	61.9	32	57.1	16	25.4	22	39.3
14	—	—	—	—	5	8.3	1	1.9	42	70.0	17	32.0
21	1	1.8	—	—	31	54.4	6	11.8	15	26.3	24	47.0
28	17	30.4	1	2.0	17	30.4	17	34.0	12	21.4	3	6.0

To determine whether the immune system has a role in the pathogenesis of alkali burns we investigated the rate of development of the effects of burns in the eyes of mice when one eye was burned 3 weeks after the fellow eye.

### Material and methods

An alkali burn was produced in the right eye of each of 63 ether anaesthetised black inbred (strain C-56) male mice. The burn was produced by prolapsing the eye and inserting it into a cup of 4 mm diameter filled with 1.5 N NaOH. After 10 seconds in the NaOH solution the eye was inserted into a larger cup filled with saline for 10 seconds. Each animal was bio-microscopically examined weekly for one month.

The state of the eye was graded according to the following scale: (1) mild—superficial corneal erosion, iris clearly visible; (2) moderately severe—deeper corneal erosion, iris not visible; (3) severe—deep corneal ulcer or descematocele; (4) perforation of the cornea; (5) healing (following erosion, ulcer, or perforation) with epithelisation and neovascularisation. The cases of phthisis bulbi were included in this category.

Three weeks after the production of the burn in the right eye an identical burn was made in the left eye of the surviving 56 mice. These eyes were examined and graded similarly to the right eyes.

### Results

The condition of the eyes burned first and the eyes burned 3 weeks later at the weekly examinations are given in Table 1. It is clear that the lesions of the eyes which were burned 3 weeks after their fellow eyes developed at a faster rate than the lesions in the first eyes. After 2 weeks 66% of the second eyes perforated while only 21.7% of the first eyes perforated. The respective numbers for the third week was 39.2% and 17.5%. The lesions in the second eyes tended to be more severe: less than half of the first eyes perforated, while almost all the second eyes reached that stage within a month.

The distribution of the eyes between the 4 grades of severity at each examination was statistically evaluated by the  $\chi^2$  test ( $2 \times 3$  contingency tables). It was found that the second eyes were significantly ( $p < 0.001$ ) more affected at all examinations except at the first week's examination.

### Discussion

Our results show that the rate of development and the final severity of the lesions were significantly more serious in eyes which were subjected to alkali burns 3 weeks after their fellow eyes were similarly burned. These results suggest that the body's immune mechanism is involved in the pathogenesis of the alkali burn lesion. A possible mechanism is the formation of new antigens by the action of the alkali in the cornea. The antigens, liberated into the circulation, may induce the appearance of humoral antibodies. These antibodies react with their specific antigens created in the eye burned subsequently and aggravate its condition. Alternatively or concurrently the chemical burn may cause the release into the circulation of antigens which are not normally present there. The antibodies which are consequently induced affect the second eye similarly burned. The suggestion that the immune system participates in the pathogenesis of alkali burns requires further proof.

We are now investigating the effect of immunosuppressants on the development of the lesions in second eyes. Negation of the accelerated development of the lesion in these eyes will prove participation of the immune system. The exact mechanisms will then have to be determined.

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Perforation				Healing				Total			
First eye		Second eye		First eye		Second eye		First eye		Second eye	
N	%	N	%	N	%	N	%	N	%	N	%
4	6.3	1	1.8	—	—	—	—	63	99.9	56	100
13	21.7	35	66.0	—	—	—	—	60	100	53	99.9
10	17.5	20	39.2	—	—	1	2.0	57	100	51	100
—	—	3	6.0	10	17.9	26	52.0	56	100	50	100

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