# Epithelial Repair in the Rabbit Cornea following Exposure to Sulfur Mustard

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Sulfur mustard (SM; bis (2-chloroethyl) sulfide) is a potent vesicating agent that has been used in chemical warfare. Exposure of the eyes to SM can cause corneal erosions, epithelial defects, neovascularization, microblistering, and/or dry eye disease, all injuries that can lead to corneal epithelium sloughing and ultimately blindness. In the present studies, the effects of ocular exposure to SM vapor (0.420 mg/L for 8 min) on the corneas of male New Zealand white rabbits was characterized at 1, 3, 7, 14, 21 and 28 days post-exposure. During this time, corneal thickness increased from 400 microns to 900 microns (14d), then decreased to 600 microns (28d). Unexposed control corneas were clear throughout the time course. However, after SM exposure, increased corneal thickness was associated with increased corneal opacity and neovascularization. Histologically, SM exposure induced epithelial-stromal separation at 3 days, by which time 16% of the epithelia had separated from the stroma, and by 28 days detachment had decreased to 9%. Also observed was post-SM epithelial thinning, increased stromal disorganization, and edema. Sporadic keratocytes were also evident in the edematous stroma by day 14. At 28 days post-SM, an inflammatory cell infiltrate was observed in the stroma. In control corneas, keratin 17, a marker of wound repair, was constitutively expressed in the limbus and bulbar conjunctiva. By 14 days post-SM, keratin 17 was expressed in the peripheral corneal epithelium, and by 28 days it was expressed in the central cornea. PCNA, a proliferation marker, was constitutively expressed in the nuclei of control corneal epithelial cells. Three days post-SM, PCNA expression was decreased along the damaged basal layer. Twenty eight days post-SM, PCNA was upregulated in the nuclei of hyperplastic cells of the central cornea and cells of the limbus, indicating wound repair. These data suggest that limbal and /or conjunctival epithelial cells play a role in the repair of SM-induced corneal injury. A better understanding of the mechanisms of SM-induced corneal damage will lead to the development of new therapeutics for the treatment of these debilitating ocular injuries. *Supported by NIH grant AR055073.*